The Journal of Breast Health
meme sağlığı dergisi

The Journal of Breast Health 2010 Vol: 6 • No: 2
Meme Sağlığı Dergisi 2010 Cilt: 6 • Sayı: 2

EDITORIAL/EDİTÖRDEN

MEME HASTALIKLARI DERNEKLERİ ETKİNLİKLERİ

Prof. Dr. Vahit Özmen
Meme Hastalıkları Dernekleri Federasyonu Başkanı

Sevgili Meslektaşlarım,

Bildiğiniz gibi gerek dünyada gerek ise ülkemizde meme kanseri sıklığın giderek artmaktadır. Dünya Sağlık Örgütü'ne bağlı IARC'e göre (International Agency for Research on Cancer), 2002 yılında tüm dünyada yeni tanı konulan meme kanserli kadın sayısı 1.150.000 iken, bu sayı 2010 yılında 1.500.000'e ulaşacaktır. Önümüzdeki 10 yıl sonunda ise bu sayının yaklaşık %60 artacağı tahmin edilmektedir. Dünyadaki tüm meme kanserlerinin %55'i gelişmiş ülkelerde görülmekte, %45'i ise, gelişmekte olan ülkelerde görülmektedir. Ancak, mortalite oranlarında bunun tersi söz konusudur. Yani meme kanseri ile ilgili ölümlerin %55'i gelişmekte olan ülkelerde, %45'i ise gelişmiş ülkelerde olmaktadır. Gelişmiş ülkelerde, organize mamografik taramalarla, duktal karsinoma in situ (DKİS) oranı %25'e, non-palpabl meme kanserlerinin oranı ise, %50'nin üzerine çıkmakta, 50 yaş üzerindeki kadınlarda mamografi ile tarama, mortalite oranını %35'e yakın bir oranda azaltmaktadır. Gelişmekte olan ülkelerde, meme kanseri sıklığının artması, yaşam tarzının batıya benzemesi (Westernizing life) ve endokrin risk faktörlerinin artışı ile açıklanmaktadır. Bu ülkelerde mortalite oranının yüksekliği ise, meme kanseri farkındalığının olmaması, organize toplum tabanlı tarama yöntemlerinin uygulanamaması sonucu geç tanı ve yetersiz tedaviye bağlıdır.

Türkiye'mizde meme kanseri sıklığı da dünyadaki örneklerde olduğu gibi artmaktadır. Bu artış gerek yaşam tarzındaki (beslenme, çalışma koşulları, stres) gerek ise, endokrin fakrörlerdeki (erken menarş, geç menopoz, doğurmama, geç doğurma, uzun süreli hormon replasman tedavisi uygulanması, vs.) değişikliklerle ilişkilidir. 1992 yılında İzmir'de yapılan bir çalışmada, meme kanseri sıklığı 24/100.000 iken son yıllarda yapılan çalışmalarda bu oranın 50/100.000 ulaştığı tahmin edilmektedir. Yine bu çalışmalarda, doğu bölgelerimizde lokal ileri evre meme kanseri oranı %50'nin üzerinde iken, batı bölgelerimizde bu oran %20 civarında olup, oldukça yüksek oranlardadır. Ülkemizde meme kanserinin erken tanısı için, Sağlık Bakanlığı Kanserle Savaş Dairesi Başkanlığı ve Meme Hastalıkları Dernekleri Federasyonu (MHDF) oldukça önemli çalışmalara başlamış ve devam ettirmektedirler.

Sağlık Bakanlığı Kanserle Savaş Dairesi Başkanlığı (KSDB), Ulusal Kanser Danışma Kurulu'nu kurarak bu kurula bağlı erken tanı ve tarama kurullarını oluşturmuştur. Bu kurula bağlı Meme Kanseri Erken Tanı ve Tarama Kurulu, bu hastalıkla ilgili uzmanlardan oluşmuş ve düzenli aralıklarla toplantılar yaparak, meme kanserinin ülkemizde erken tanı ve taraması için standartları belirlemiş, bunların uygulanması için gerekli koşulları oluşturmaya başlamıştır. KSDB, tüm illerde bugün sayıları 100'ü aşan Kanser Erken Teşhis Tarama ve Eğitim Merkezleri (KETEM) kurmuştur. Bu merkezlerde, ücretsiz meme muayenesi ve mamografi çekilerek meme kanserinde erken tanı konulmaya çalışılmaktadır. Ayrıca, KSDB'nin öncülüğünde çıkarılan bir kanunla 50 yaş üstü kadınlarda ücretsiz mamografi çekilmektedir.

Değerli meslektaşlarım, devlet tarafından oluşturulan alt yapılar ve yapılan harcamalar, meme kanserinin erken tanı ve etkin tedavisi için yeterli olmamaktadır. Bunu sağlamak için, bu konu ile ilgili sağlık çalışanlarına (doktor, hemşire, sağlık teknisyeni vs.) çok önemli görevler düşmektedir. Özellikle KETEM'lerde çalışan doktorların ve Devlet Hastanelerinde meme kanseri ile ilgili olarak hizmet veren uzmanların (genel cerrah, radyolog, patolog, medikal onkoloji ve radyasyon onkolojisi uzmanı vs.) meme kanseri ile ilgili bilgilerini güncelleştirmeleri, özellikle kadınlarda olmak üzere tüm toplumda meme kanseri farkındalığı oluşturmaları ve birer gönüllü olarak çalışmaları şarttır.

Kuruluşunun dokuzuncu yılında olan Meme Hastalıkarı Dernekleri Federasyonu'nun kuruluş amaçlarından en önemlisi, meme kanseri ile ilgili olarak hedef kitlenin ve sağlık çalışanlarının sürekli eğitimini sağlayarak, meme kanseri farkındalığını ve sağlık çalışanlarının bu konudaki bilgi düzeyini arttırmaktır. Bunun sonucu olarak, ülkemizde de meme kanserinin erken tanısına ve ülke gerçekleri dikate alınarak etkin tedavinin oluşmasına katkıda bulunulacaktır. Bu amaçlara uygun olarak federasyonumuz, çok sayıda ulusal kongre, konsensus toplantıları, bölgesel toplantılar düzenlemekte, 5 yıldır yayım hayatında olan ve her ay binlerce kişiye ulaşan, TÜBİTAK, EBSCO ve Index Copernicus'ta yer alan Meme Sağlığı Dergisini çıkarmakta ve bugün sayısı 15.000'e ulaşan ulusal meme kanseri hasta kayıt programını uygulamaktadır.

Sağlık Bakanlığı Kanserle Savaş Dairesi Başkanlığı (KSDB) ile yaptığımız görüşmeler sonucunda, federasyonumuzun KSDB ile birlikte "Ulusal Meme Kanseri Eğitim Kursları" düzenlemesine karar verilmiştir. Bu kurslar, Türkiye'mizin tüm illerindeki KETEM'lerde çalışan doktorlarımızı ve Devlet Hastanelerinde meme kanseri ile ilgili olarak hizmet veren uzmanları (genel cerrah, radyolog, patolog, medikal onkoloji ve radyasyon onkolojisi uzmanı vs.) kapsayacaktır. KETEM çalışanları ve Uzmanlarımız için ayrı ayrı olarak düzenlenecek olan bu kurslarda, konularında deneyimli bilim adamlarımız, meme kanserinin epidemiyolojisi, risk faktörleri, erken tanısı, patolojisi, tedavisi ve takibi için konferanslar verecek, paneller dü-

zenleyecektir. Kurslarımız her iki ayda bir farklı illerimizde o illere yakın illeri de kapsayacak şekilde yapılacaktır. Böylece, ülkemizde bulunan tüm illerimizi kapsamış olacaktır.

Değerli meslektaşlarım, "Ulusal Meme Kanseri Eğitim Kursları'nın" ilki 21 Şubat 2010 tarihinde Bursa'da yapılmıştır. Bu kursa, Bursa ili ile birlikte Yalova, Balıkesir ve Bilecik illerindeki KETEM doktorları ve devlet hastaneleri uzmanları katılmıştır. Kurslar, KETEM doktorları ile Devlet Hastaneleri'nde çalışan uzmanlarımıza konularında deneyimli ve farklı disiplinlerdeki bilim adamlarımızca ayrı ayrı verilmiştir. Kursları tamamlayan meslektaşlarımız, başarı sertifikalarını almışlardır. Kurslarımızın ikincisi 15 mayıs 2010'da eskişehir'de yapılacaktır.

Bu kursun kadınlarımızda meme kanserinin erken tanısı ve etkin tedavisine katkı sağlamasını umuyor, hepinizi detek olmaya davet ediyorum. Kurs programları ile ilgili detaylı bilgiler, federasyonumuzun web sayfasından (www.mhdf.org) ve federasyonumuzun sekreterinden (rumisabirce@gmail.com) temin edilebilir

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EDITORIAL/EDİTÖRDEN

ACTIVITIES OF TURKISH FEDERATION OF BREAST DISEASE SOCIETIES

Vahit Özmen, MD, FACS

President
Turkish Federation of Breast Disease Societies

Dear Colleagues,

As you know, breast cancer incidence has been increasing in the world. According to the records of the IARC (International Agency for Research on Cancer), while the number of new diagnosed breast cancer patients was 1,150,000 in 2002, this number will reach 1,500,000 in 2010. And, it has been estimated that there will be a 60% increase in the next 10 years. If we look at all the breast cancers, 55% of them were diagnosed in developed and 45% was diagnosed in low-middle income countries (LMCs). But, there is a reverse relationship regarding mortality rates. 55% of breast cancer related deaths have been seen in LMCs. The reason of low mortality rate in developed countries is early diagnosis with organized population based screening and effective therapies. With the aid of screening mammography, the rates of ductal carcinoma in situ (DCIS), non-palpable breast cancer, and decrease in breast cancer mortality have reached to 25%, 75%, and 35% respectively. The increase in breast cancer incidence in LMCs is related with westernizing life and increased endocrine risk factors. High mortality rate for breast cancer in LMCs is related with lack of organized population based screening programs, late diagnosis, and inadequate treatments.

Breast cancer incidence has also increased in Turkey, especially in Western Turkey. This increase has related with changing life style (westernizing life- nutritional habits, working conditions, stress, less exercise, obesity) and endocrine related factors [early menarche, late menopause, nulliparity, age at first birth (>30), hormone replacement therapy, induced abortion, less breast feeding etc.]. In a study performed in 1992 in İzmir, breast cancer incidence was found 24/100,000. But it was estimated that this rate reached to 37/100,000 in 2006 (50/100,000 in western and 25/100,000 in eastern Turkey). Important studies and projects have been performed for early diagnosis and effective treatment of breast cancer by Cancer Control Department of The Ministry of Health of Turkey and Turkish Federation of National Breast Societies.

Breast Cancer Early Detection and Screening Sub-Committee has been funded by The National Cancer Advisory Board to establish early detection and screening standards of breast cancer in Turkey. This sub-committee has been performed regular meetings with experts on breast cancer epidemiology, diagnosis and treatment to evaluate breast cancer incidence, screening programs, and treatment modalities, and to promote studies on these subjects. Cancer Control Department also funded 84 Early Cancer Diagnosis, Screening and Education Centers (KETEM) for opportunistic and organized screening of breast cancer in 81 provinces in Turkey by 2008. The number of these centers has been increasing regularly.

However, the infrastructure and expenditures created by the government is not enough for early diagnosis and effective treatment of breast cancer. To achieve these aims, health workers dealing with this issue (doctors, nurses, medical technicians, etc.) have a very important role. Especially physicians in KETEM and specialists related with breast cancer in the State Hospitals (general surgeons, radiologists, pathologists, medical oncology and radiation oncology specialists, etc.) should update their breast cancer-related information and increase breast cancer awareness in the targeted population.

One of the most important purposes of Turkish Federation of Breast Diseases Societies which was funded in 2001 is to provide continuous education of health care workers (physicians, specialists, nurses, technicians etc.) and target population for early diagnosis and effective treatment of breast cancer. As a result, early detection, screening, and modern treatment of breast cancer will be realized in Turkey. Turkish Federation of Breast Diseases Societies organized numerous national breast congresses, consensus meetings, conferences, and regional postgraduate courses for family practitioners, specialists on breast cancer, nurses, and women. The Journal of Breast Health is one of its publications. It has been published for 5 years and included by TUBITAK, Index Copernicus, and EBSCO Publishing. The journal has been reached to thousands of readers and published every 3 months. In addition to these activities, our federation has a breast cancer registry since 2005 and registered 15,000 breast cancer patients from the every region of Turkey.

After several discussions with Cancer Control Department, we have decided to organize "National Breast Cancer Postgraduate Courses" every two months in different cities in Turkey. At the beginning, these courses will include physicians in KETEM and breast cancer related specialists in the State Hospitals (general surgeons, radiologists, pathologists, medical oncology and radiation oncology specialists, etc.). They will be educated on epidemiology, screening, diagnosis, and treatment of breast cancer

and later, other health workers (nurses, technicians, midwives etc.). The first course was performed in Bursa in February 21, 2010, by including physicians working in Bursa, Balıkesir, Yalova and Bilecik. The second one will be performed in Eskişehir in May 15, 2010.

I hope and expect that these courses will help to early diagnosis and effective treatment of breast cancer in women with your great support. The details of the course programs and other information can be reached at our web site (www.mhdf.org) or by emailing our secretary (rumisabirce@gmail.com).

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REVIEW/DERLEME

GENOMICS AND PROTEOMICS METHODS AND THEIR VALUE IN BREAST CANCER DIAGNOSIS

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ABSTRACT

Genomics and proteomics are newly developing fields and becoming widely used in cancer research especially in cancer diagnosis. The aim is to review the role of genomics and proteomics to discover new breast cancer biomarkers for diagnosis with higher sensitivity and specificity. Studies reporting on potential biomarkers in breast cancer were included in this review. In the future, platforms in genomics and proteomics will be used for the discovery of tumor specific genes and related proteins, which will lead to development of novel therapeutic targets leading to patient specific therapies.

Key words: cancer, diagnosis, genomics, proteomics

GENOMİK VE PROTEOMİK YÖNTEMLER VE MEME KANSERİ TANISINDAKI YERİ

ÖZET

Genomik ve proteomik yeni gelişen alanlardır ve kanser araştırmalarında, özellikle de kanser tanısında, sıklıkla kullanılır hale gelmektedir. Bu yazıda, meme kanseri tanısında daha yüksek özgünlük ve özgüllüğe sahip yeni belirteçlerin bulunmasında genomik ve proteomikin rolünün gözden geçirilmesi amaçlanmıştır. Meme kanserinde potansiyel önemi olan belirteçleri bildiren çalışmalar bu derlemede incelenmiştir. Gelecekte, genomik ve protemik alanlarında kullanılan yöntemler, hastaya özgün tedaviyi sağlayacak yeni hedeflerin geliştirilmesinde tümöre özgün gen ve proteinlerin bulunması için kullanılacaktır.

Anahtar sözcükler: kanser, tanı; genomik, proteomik

1. Introduction

The biology of cancer remains poorly understood and individual diagnostic factors provide limited information about the diagnosis of the disease. Genomics and proteomics are newly developing fields and becoming widely used in cancer research especially after the completion of human genome sequencing project. Genomic and proteomic technologies have evolved; rapidly accelerating the rate of clinical cancer research. The potential applications of genomics and proteomics in the field of oncology, especially in cancer diagnosis, are virtually unlimited. Systematic investigation of expression patterns of thousands of genes or proteins in tumors and their correlation to specific phenotypes might provide the basis for an improved description of cancer. Although there is a continuing progress in cancer therapy, early diagnosis of cancer undoubtedly remains the most important factor in improving long-term survival of cancer patients. The identification of tumor markers suitable for the early diagnosis of cancer holds great promise to improve the clinical outcome of patients. Emerging technologies in the fields of genomics and proteomics have enabled researchers to understand the biology of cancer and to discover new biomarkers for cancer diagnosis, treatment response, and clinical outcome with higher sensitivity and specificity. Reliable biomarkers will facilitate novel therapeutic discoveries and improve patient selection for clinical trials. Replacement of low throughput techniques such as Northern, Southern, and Western blotting, reverse-transcription polymerase chain reaction, in-situ hybridization, immunohistochemistry, and two-dimensional gel electrophoresis with high throughput techniques such as DNA, RNA, protein, and tissue microarrays, and mass spectrometry has been the mainstay of recent achievements in cancer diagnosis. The role of these new methods in the diagnosis of breast cancer are evaluated in this review.

2. Genomics

Genomics is related to comprehensive analysis of expressions of large number of genes in a single experiment. Recent developments in genomic technologies allow the evaluation of thousands of genes and the assessment of interactions between these genes at the same time. The basic premise of these emerging technologies is the simultaneous quantification of gene expressions and combination of these results into prediction scores that aid to establish clinical diagnosis more accurately than any single gene expression. Genomic technology has made a major impact in the understanding of cancer biology and is now widely used in clinical cancer research. Microarray technology has recently replaced low-throughput techniques such as Southern blot (hybridization of DNA-DNA) and Northern blot (hybridization of RNA-DNA).

Gönderilme Tarihi: 13 Temmuz 2009 • **Revizyon Tarihi:** 26 Ağustos 2009 • **Kabul Tarihi:** 28 Ağustos 2009

2.1 Platforms in genomics

Low-density and high-density arrays are the principally used methods in the field of genomics. In addition, real time quantitative reverse-transcription polymerase chain reaction (qRT-PCR) helps further defining gene sets described in microarray experiments. DNA microarrays are the primary tools used to perform gene profiling in cancer. Brown et al. have pioneered the development of high-density microarrays, which now have become the key technology in biomedical research (1). The process mainly consists of three steps: (1) array construction, (2) sample preparation and hybridization, and (3) image and data analysis. A microarray is a solid support (nylon or glass) containing thousands of different gene fragments called probes, which consist of either oligonucleotides or complementary DNA (cDNA). Study sample containing a mixture of unknown RNA or DNA is named as target and hybridizes with the probes if it contains the genes present on the microarray. The probe is immobilized on dot blots and microarrays, and, in contrast to this, target is immobilized on Southern and Northern blots. Probes labeled with fluorescence or radioactivity emits signals. These signals, present in each probe, are detected, quantified, and specialized hardware and software are utilized to give gene expression profiles. Data can be used to differentiate between normal and tumoral tissues, to gather information about the prognosis of the patients, and to discover the genes playing key roles in cancer biology for further manipulation in treatment.

The main difference between low-density and high-density arrays lies in the number of genes or samples studied in a single experiment. Dot blots are low-density arrays and are produced manually by spotting gene specific probes on a membrane. Labeled targets are added onto dot blots for hybridization and visualization via autoradiography. With the development of automated systems, spotting thousands of DNA fragments onto a single array became possible. Current technology enables the placement of over 50,000 elements on standard glass microscope slides. The most commonly used DNA microarrays can be categorized according to their method of manufacturing into two groups as robotically spotted microarrays and microarrays produced by synthesizing the DNA probe directly on the supporting material. Early microarrays deposited PCR amplified cDNA clones as probes, which resulted in variability in probe sequence between different clones. Recently developed microarrays utilize synthetic oligonucleotides as probes, but this requires information on gene sequence. In addition, cDNA quantity may change between various prints when spotted cDNA microarrays are used. These microarrays are analyzed by hybridizing two differently labeled targets and one of these targets is a reference RNA sample that is used as an internal control. In contrast, other group of microarrays works on a single sample instead of a mixture of two samples and the ratio of gene expression of two samples is compared. These microarrays contain short (25-mer) oligonucleotides directly synthesized on the substrate with photolithography method (2). Oligonucleotides comprise of probes, which contain a transition at the 13th base used to detect non-specific hybridization. This method of production decreases the possibility of variation due to the printing procedure allowing for one-color detection and comparisons to be made between arrays.

Low-density arrays and RT-PCR are utilized as validation techniques when a limited number of genes are determined to play a role in cancer with high throughput methods. Low-density arrays can be divided into two categories as custom-made spotted cDNA or oligonucleotide arrays with a limited number of genes and high throughput microfluidic cards based on real-time PCR assay. Custom-made low-density arrays resemble high-density arrays with more tailored gene content. On the other hand, high throughput microfluidic cards are composed of 384-well plates containing reagents and probes required for RT-PCR manufactured using automated systems. These arrays provide less experimental variations with higher standardization. However, for low-density arrays to be cost effective, hundreds of genes determined in high-density microarrays should be evaluated.

Another platform used in genomics studies is qRT-PCR, which is commonly utilized to validate a small number of genes in a small number of samples. This method requires 5-10 ng of RNA and detects the quantitative relationship between the amount of target sample and PCR product. This relationship can be determined "real-time" and the term "real-time" PCR denotes to the detection of PCR products as they accumulate. Available qRT-PCR systems utilize a set of primers and fluorogenic probes and the amount of fluorescence is measured at each amplification cycle, providing information on "real time" changes in the amplification product. Identification of the PCR cycle where exponential growth phase starts enables accurate quantization of gene expressions in study sample. However, there are risks of cross-contamination and experimental variations whenever this method is applied and this is reduced by optimization of each reaction with new primers. PCR-based low-density arrays can be widely used in laboratories at a reduced cost and time.

2.2 Genomics applications in breast cancer

In breast cancer, three genes were identified to express differentially between abnormal (atypical ductal hyperplasia, ductal carcinoma in situ, and invasive ductal carcinoma) and normal breast cells. Two of these genes are highly expressed in cancer cells and are coding for cytosine-rich intestinal protein 1 and hematological and neurological expressed sequence 1. The other gene is coding for the second epithelium restricted Ets transcription factor and is expressed at lower levels. Although previously mentioned studies suggested a few new biomarkers for breast cancer, the results reported in these studies should be cautiously evaluated due to the lack of standardization in most of them.

3. Proteomics

Proteomics can be defined as the detection, identification, and quantification of all proteins present in a particular tissue, organ, and organism to provide accurate and comprehensive data

about that system. Proteomics elucidates the properties of proteins, which cannot be understood by analyzing gene expressions such as post-translational modifications, compartmentalization of proteins, and formation of multi-protein complexes. Complete sequencing of human genome has led to the assembly of protein databases, which increased the speed of developments in proteomics research. Although there are about 20,000-30,000 genes in the human genome, due to alternative splicing and sequence deletions, human proteom consists of approximately a million different proteins which makes proteomic research even more difficult. However, methods used in proteomics allow the validation of multiple markers at once, greatly decreasing the study time.

3.1 Platforms in proteomics

There are various techniques utilized in the field of proteomics. Recent advances in technology have increased the resolution, accuracy, and speed of separation of peptide and protein mixtures to smaller number of proteins per fraction using chromatographic techniques, labeling and detection of proteins and antibodies using multi-color fluorophores, imaging equipment, computer software, and analyzing clinical samples without any extensive preparation with high throughput capacity (3). Enzyme-linked immunosorbent assay (ELISA) and immunohistochemistry (IHC) are standard methods in clinical laboratories whereas Western blot and immunoprecipitation are frequently used in basic science laboratories. Two-dimensional (polyacrylamide) gel electrophoresis was the most commonly used method to study differences in protein expression between two samples such as cancer and normal tissue. It sequentially separates proteins by their charge and molecular weight, but this technology cannot effectively separate and distinguish proteins below 10 kDa. In addition, it is a very labor-intensive method, and has limited resolution for the analysis of large numbers of proteins. Each protein has to be excised from the gel and the peptide fragments analyzed using mass spectrometry (MS). Although two-dimensional gel electrophoresis cannot separate complex mixture of proteins, subsequent protein identification can be accomplished. In addition, high-performance liquid chromatography, two-dimensional liquid chromatography, or capillary electrophoresis uses columns or multiple capillary loops to separate proteins on the basis of size and charge.

Various ionization techniques such as matrix-assisted laser-desorption and ionization (MALDI), surface-enhanced laser-desorption and ionization (SELDI), and electrospray ionization have revolutionized the detection, identification, and structural characterization of proteins. Although these techniques enable the measurement of small protein molecules, it is possible to measure molecular weights above 200 kDa by first fragmenting the proteins. Rapid expansion of gene and protein databases has allowed the identification of proteins with greater ease. MS techniques analyze peptides, proteins, and polynucleotides as ions and distinguish them based on mass-to-charge ratio (m/z). Protein chips used in SELDI MS contain multiple spots with varied surfaces including hydrophobic, ion exchange, and metal affinity binding surfaces or normal chromatographic surfaces. MS output is shown as a chromatographic pattern with peaks at a given m/z. The resolution of MS unit directly correlates with its sensitivity. MS resolution capability varies between older and newer machines, proteomic chips containing different chromatographic surfaces, and different bioinformatics programs that reveal other discriminatory peaks.

Mass spectrometers are generally composed of three devices: (1) an ionization device which volatizes and ionizes the sample, (2) a mass analyzer which separates ions depending on their m/z ratios, and (3) a detector which detects ions after separation. After the separation of proteins or peptides, they must be ionized into a gas phase before MS analysis. Liquids can undergo electrospray ionization and MS analysis. On the other hand, solids can be ionized by MALDI or SELDI. MALDI technique utilizes a small volume of sample (<1µL) and digested proteins are mixed with an organic acid matrix. Molecular ratio of matrix to sample should be in the range of 5000-10000 for a better analysis. Upon drying, sample and matrix co-crystals form and change into an ionized form when irradiated by an ultraviolet laser. As a result, singly charged ion species are formed and ions accelerate through an electrical field in a time of flight MS which seperate them by their m/z. As the ions reach the detector at different times, a peptide mass profile is created reflecting the protein composition of the sample. MALDI analysis is well suited for resolution of proteins <20 kDa. One way of identification of proteins is by comparing the peptide mass profile to masses published in protein databases. However, there are certain limitations with MALDI technique such as signal background problems resulting from contaminants, which have hindered it from being used as a high-throughput screening tool for proteins in complex biological samples.

In order to overcome the limitations related to MALDI, SELDI method has recently been developed for protein analysis and it was first described by Hutchens and Yip (4). The SELDI method captures proteins from various body fluids on diverse biochip surfaces using modified chromatographic techniques. Biochip surfaces can vary due to their chemical properties as hydrophobic, ionic, and immobilized metal affinity capture and due to biochemical properties as antibody, DNA, enzyme, receptor, and drug covered surfaces (5). Proteins are combined with energy absorbing molecules at the surface of the biochip and pulsed with a laser into a time of flight MS. Proteins interact differently with different surfaces and this results in different mass spectra. A disadvantage of SELDI method is its inability to identify individual proteins from mass spectra and this is because SELDI method can only analyze small intact proteins. As a whole, advantages of MS technology are faster evaluation of small amount of protein samples, simple sample preparation, analysis of complex mixtures, and better data analysis.

On the other hand, electrospray ionization analyzes samples in solution instead of on platforms. Pushing the sample solution through a thin needle biased at positive voltage, which faces a grounded sampling skimmer electrode forms ions. Spraying proc-

ess forms very small droplets which progressively desolvate liberating ions. For proteomic analysis, sources are operated with flow rates between 0.5-1.5 µL/s and 0.02-0.5 µL/s. In electrospray ionization, m/z distribution for ions is below 4000 and around 800-1000. Ions produced by electrospraying carry multiple charges, which makes the analysis of complex mixtures difficult.

Another tool used to analyze proteins is protein-microarrays, which rely on the same principles as their DNA counterparts. This method principally depends on binding of antibodies and/or antigens to glass microarrays allowing the simultaneous assessment of thousands of proteins. Protein binding is measured by comparative fluorescence, providing a high throughput ELISA (6). However, there is a need for specific and high-quality antibodies against proteins of interest, and specificity of these antibodies must be validated by Western blotting before use. These protein arrays can utilize biologic samples such as serum or plasma, nipple aspiration fluid, cell lysates, or the surface membranes of microdissected cells. Protein microarrays are categorized as forward-phase and reverse-phase arrays. In forward-phase arrays, capture molecules such as antibodies, nucleic acids, or peptides are immobilized onto glass surfaces, membranes, or hydrogels similar to DNA microarrays. Biofluid containing the target protein is incubated with the prefixed antibodies and detected using labeled secondary antibodies. Forward-phase arrays have the advantage of detecting many different proteins in one experiment. In reverse-phase arrays, a target sample containing a mixture of proteins is immobilized onto a glass slide and specific antibodies against target proteins are incubated over the slide. This method allows the detection of target proteins in a large number of samples as a high throughput assay. Depending on the specificity of antibody binding and sensitivity of labeling methods, detection of target proteins in the concentration range equivalent to 10 cells is possible.

Tissue microarray is another method, which is modernized recently and utilized in proteomics research (7). Tissue microarray has a lower cost and can be developed using archival tumor tissues. In this method, a new block of tissue is formed containing different tissue cores with a diameter of 0.6-2 mm and sections from tens to hundreds of paraffin embedded tissue specimens can be combined on single glass slide. Tissue microarrays prepared by this technique can be used for histochemical and immunohistochemical staining or in situ hybridization. Tissue microarrays eliminate slide-to-slide experimental variation, reduce the amount and the cost of antibodies, and scoring time for pathologists. In contrast to gene microarrays, only protein products of one gene can be studied at a time using tissue microarrays. However, tissue microarrays can be used as an adjunct to cDNA microarrays to understand the correlations between gene and protein expressions. There are a few points to be taken into account when using tissue microarrays. During the construction of tissue microarrays, representative parts of paraffin blocks should be chosen and, in heterogeneous tumors, positive staining parts can be easily missed. In-situ and invasive lesions cannot be easily distinguished due to the lack of surrounding structures. In addition, candidate proteins with specific and high quality antibodies should be known. During the scoring process of tissue microarrays, automated tools can be used to decrease the variations between the pathologists (8). When formalin fixed tissues are used, recovery of intact or good quality genomic and proteomic material is difficult due to intense cross-linking between biomolecules induced by formalin. For this reason, tissue microarrays were constructed from frozen tissues recently and are called cryo-tissue microarrays.

3.2 Proteomics applications in breast cancer

Proteomics technology utilizes samples of serum, plasma, seminal plasma, saliva, urine, cerebrospinal fluid, nipple aspirate, ductal lavage fluids, and tumor tissue in the clinics in order to find novel biomarkers for cancer diagnosis with higher sensitivity and specificity. Protein profiling can be performed on complex mixtures from tissue extracts or biofluids. For cancer diagnosis, protein profiles are obtained from control and patient samples and compared to detect significant protein patterns unique to each group. Protein profiling has greater power to discriminate between cancer patients and healthy individuals than identifying specific disease-related proteins.

Breast cancer is another cancer type evaluated for new biomarkers. The diagnosis of proliferative or pre-invasive lesions such as atypical hyperplasia or in situ carcinoma in the breast places the patients in a high-risk group, although the progression to invasive cancer is expected to occur in a small proportion of these patients. Defining the patients with high risk in a better way with recently developed molecular techniques will decrease the screening costs alleviating the anxiety of the individuals. SELDI-TOF MS was widely used to analyze proteins secreted by epithelial cells of the ductal system in the breast. Previous studies have reported different protein profiles for patients with and without breast cancer (9-11). In those studies using serum samples, diagnostic protein profiles showed sensitivities and specificities ranging between 76-93% and 90-93%, respectively (11-13). Li et al. studied 169 serum samples from patients with breast cancer, benign breast diseases, and healthy controls and identified three protein peaks that separate breast cancer patient from non-cancer individuals with 93% sensitivity and 91% specificity (11). These biomarkers were validated in a different set of serum samples from patients with breast cancer, benign breast diseases, and healthy controls and two of these biomarkers were identified to be complement component $C3a_{desArg}$ and a C-terminal-truncated form of $C3a_{desArg}$ (14). Proteomic analysis of normal breast tissue and ductal carcinoma in situ revealed a difference in protein profiles between the two tissues suggesting that ductal carcinoma in situ is a pre-invasive lesion (15). Varnum et al. identified 15 proteins that had been reported as potential biomarkers for breast cancer, but had not been previously identified in nipple aspirate fluid (16). Paweletz et al., similarly studying nipple aspirate fluid, detected two proteins unique to breast cancer and two proteins unique to normal samples (10). Sauter et al. reported on five differentially expressed proteins in nipple aspirate fluid samples and these proteins were

present in 75-84% of breast cancer patients in contrast to 0-9% in healthy controls (9). In another study, nipple aspirate fluids from breast cancer patients were compared and no significant differences were identified in protein expressions between the breast with intact breast carcinoma and the contralateral non-cancerous breast (17). However, nipple aspirate fluid analysis revealed several peaks that differentiate between both breasts of the cancer patients and healthy individuals. Li et al., in another study, using nipple aspirate and ductal lavage fluids, identified three protein peaks, which differentiate breast cancer patients from high-risk women. These peaks were found to correspond to human neutrophil peptides 1 to 3 and persistent elevation of these peptides in high-risk women may imply early onset of breast cancer (18). Besides their functional activities in antimicrobial immunity, human neutrophil peptide expression has been shown in various tumor tissues and cell lines affecting tumor growth in a concentration dependent manner (18). Acetyl-LDL receptor is another biomarker related to early diagnosis of breast cancer. Its decreased concentration in nipple aspirate fluid compared to normal breasts indicates a strong likelihood of breast cancer or precancerous lesions. Similarly, a concentration difference of this protein between the two breasts of an individual may indicate the presence of breast cancer in the breast with lower concentration. Recently, protein profiling from serum samples was reported to differentiate highly suspicious lesions on mammography, which will result in a decrease in the number of unnecessary breast biopsies (19).

4. Conclusion

There are several obstacles to be addressed before genomics and proteomics reach an optimal yield and be beneficial for the patients. The requirement of fresh or frozen tissue samples to protect and obtain high quality genetic material to use in high-throughput techniques limits their wide spread use. The facilities for immediate freezing of tissue samples are not readily available in all hospitals. Establishment of high quality sample banks with databases containing information about all clinical and histopathological characteristics of the patients will help to collect uniform samples and data in clinical trials. Developing better techniques in order to utilize paraffin-embedded tumor tissue can be another way to circumvent this problem. Several groups are working on isolating RNA from paraffin-embedded tissue sections and studying gene expression by microarrays and RT-PCR (20,21). Recently developed LCM technique is used to obtain tissue samples from paraffin-embedded tissue sections and it increases the probability of getting more homogenous cell populations for genomic and proteomic studies (22). During this procedure, tumor cells can be isolated from other cells in the tissue and tumor cell specific gene expressions are shown by microarrays. However, with LCM, data from stromal and other surrounding cells should be analyzed separately, increasing the cost of the study. LCM also increases tissue processing time and manipulation. It is feasible to reach the appropriate results without employing LCM, if a molecular signature to use as a biomarker is investigated. However, if the goal of the study is to identify the biological differences between pre-malignant, pre-invasive, and invasive cells, LCM is necessary for precision on cell type (23). Although LCM method can overcome the heterogeneity of cancer tissue samples, an alternative way could be to compare expression profiles of macro dissection samples with those of cell lines representing the different cancer types, namely virtual micro dissection (24). In addition, the amount of material required for the experiments should be kept to a minimum due to limited sources and this could be achieved as improvements in nanotechnology provide better instruments. Besides from technical issues, careful experimental design, clearly defined outcomes, and a large enough sample size for independent validation of the data will help to overcome the problems encountered in genomic and proteomic research. In addition, there are several limitations specific to proteomics platforms. Tissue and protein microarrays can only be used if specific antibodies for the candidate proteins are available. Proteomics is an evolving field for which procedures and equipments lack the type of standardization, which was achieved in microarray gene expression studies.

Another issue is the processing of the large amount of data obtained from the use of high-throughput techniques in both genomics and proteomics. Statistical data analyses are tremendously challenging. The number of measured variables always outnumbers the number of samples evaluated. In order to minimize the problems in statistical analyses, acquired data must be filtered according to the goals of the researcher. Development of methods for statistical evaluation, normalization, and filtering of the data are all areas of active research. Although the development of specialized software is continuing, there is also a need for expert statisticians in this field. Collaborations should be established between researchers across disciplines for producing, storing, analyzing, and interpreting the data obtained from various experiments. Formation of centralized databases containing information on molecular characteristics of individual tumor types will help to reach already available data and may save time and resources during research.

Finally, cost of the high-throughput techniques is another prohibitive factor, which prevents them from gaining access to most of the laboratories. The accessibility to these tools is increasing rapidly and complexity and cost are likely to improve with the development of next generation of tools. Exquisite quality controls are required to optimize the results. Currently, advances in cancer diagnostic methods are integrated into clinical practice in a slow and uneven fashion.

Genomics and proteomics should be recognized as complementary fields of investigation in cancer diagnosis and strengths and weaknesses of each individual technology should be balanced to obtain maximum benefit. From all the work done until today, it is clear that genomics and proteomics have generated a considerable amount of data for breast cancer diagnosis. However, results obtained from previous studies must be validated, refined, and extended and the relevance of these data for clinical practice still has to be established. Integration of genomics and proteomics technology into clinical trials and practice could lead to individu-

alized patient care. Biomarkers used for early detection of breast cancer can be targets of new drugs individualizing treatment and increasing success.

Multi-center clinical trials are required to validate the available data and to set the standards in various methods utilized in genomics and proteomics for breast cancer. These trials will help to find the best ways to integrate genomics and proteomics in patient care. In this context, phase I studies will aim to define the predictive gene set, establish the prediction rules, and determine assay cutoffs in a well-defined patient population. In phase II studies, the predictors will be tested on independent cases, and the reproducibility and reliability of the assays will be determined and phase III studies will prove their efficacy in cancer diagnosis in prospective randomized trials (25). In the future, methods used in genomics and proteomics will be useful for the discovery of tumor specific marker genes and related proteins in breast cancer, but traditional methods will be applied in daily clinical practice.

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The Journal of Breast Health
meme sağlığı dergisi

The Journal of Breast Health 2010 Vol: 6 • No: 2
Meme Sağlığı Dergisi 2010 Cilt: 6 • Sayı: 2

RESEARCH ARTICLE/ARAŞTIRMA YAZISI

ISOLATED LOCOREGIONAL RECURRENCE IN PATIENTS WITH POSTMASTECTOMY ADJUVANT THERAPY FOR BREAST CANCER

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ABSTRACT

Objectives: To determine the predictive risk factors for isolated locoregional recurrence (LRR) in breast cancer patients with postmastectomy adjuvant therapy.

Patients and Methods: The impacts of patients' characteristics, tumor stage, and surgery on LRR were evaluated in patients with breast cancer having postmastectomy adjuvant therapy, according to their risk factors using univariate analysis. Factors influencing LRR-free survival were assessed by Cox regression analysis.

Results: Of 368 patients, 28 (7.6%) had isolated LRR. Patients' characteristics such as age, menopause, surgery, tumor size, stage and differentiation, and hormone receptor status were not attributable to LRR. Upper outer quadrant localization was significantly associated with lower LRR occurrence (p=0.048). Among 245 patients whose surgical margin could be assessed, LRR was detected in 6 (20%) of 30 patients with a close surgical margin, while of 215 patients with normal surgical margin, 13 (6%) developed LRR (p=0.007). Kaplan-Meier analysis revealed that larger tumor (p=0.04), presence of LRR (p=0.00001), closer surgical margin (p=0.0085), stage (p=0.0001), and presence of lymph node metastases (p=0.00001) have significantly negative impacts on patients' survival. Tumor size, lymph node status, and closer surgical margin were found to be the independent factors influencing LRR-free overall survival.

Conclusion: Postmastectomy LRR seemed to have a close relationship with the surgical margin status despite standard adjuvant treatments.

Keywords: breast cancer, locoregional recurrence, surgical margin, adjuvant therapy, tumor localization.

MASTEKTOMİDEN SONRA ADJUVAN TEDAVİ ALAN HASTALARDA İZOLE LOKOREJYONEL NÜKS

ÖZET

Giriş: Mastektomili hastalarda, adjuvan tedaviye rağmen lokorejyonel nüks (LRN) gelişiminde etkili prediktif risk faktörlerini belirlemek

Yöntem ve Gereçler: Meme kanseri nedeniyle mastektomi uygulanan ve adjuvan tedavi alan hastalarda, yaş, menopoz durumu, tümörün çapı, evresi, cerrahi şekli, pozitif lenf nodu sayısı, cerrahi sınır uzaklığı, histolojik grade gibi faktörlerin izole LRN'e etkileri tek değişkenli testle, lokal nükssüz sağkalıma etkili faktörler ise Cox regresyon analizi ile incelendi.

Bulgular:368 hastanın 28'inde (%7,6) izole LRN gelişti. Hastaların yaş ve menopoz gibi özellikleri, uygulanan mastektominin cinsi, hastalığın evresi, tümör çapı, aksiller lenf nodu durumu ile tümörün diferansiyasyonu, hormon reseptör durumu LRN üzerine etkili değildi. Tümörün üst dış kadranda yerleşiminde LRN daha az görülmekteydi (p=0,048). Cerrahi sınır uzaklığı kaydedilmiş 245 hastanın 30'unda cerrahi sınır yakındı ve bunların altısında (%20) LRN saptanırken, cerrahi sınırı normal olan 215 hastanın 13'ünde (%6) LRN gelişti (p=0,007). Kaplan-Meier analizinde, sağkalımı olumsuz etkileyen faktörler tümör çapının büyük olması (p=0,04), LRN gelişimi (p=0,00001), cerrahi sınır yakınlığı (p=0,0085), evre (p=0,0001) lenf nodu metastazı varlığıydı (p=0,00001). Tümör boyutu, lenf nodu durumu ile cerrahi sınır yakınlığı, lokal nükssüz sağkalımı etkileyen bağımsız faktörlerdendi.

Tartışma: Cerrahi sınır yakınlığı, mastektomi sonrası LRN gelişiminde, adjuvan tedavilerden etkilenmeyen tek faktördür.

Anahtar sözcükler: meme kanseri, lokorejyonel nüks, cerrahi sınır, adjuvan tedavi, tümör yerleşimi

Introduction

Breast cancer is the most common female cancer in our country as well as in other countries (1,2). Surgery is the essential therapy in stage I, II, and IIIA patients whereas later stages require a multidisciplinary approach. Recent randomized prospective studies on surgical treatment modalities showed that survival analyses of mastectomy vs. breast conserving surgery (BCS) plus radiotherapy were not statistically significant (3-10). Patients' age and choice, tumor localization, the tumor/ breast size ratio, pathological features such as the degree of nuclear atypia, and proliferation activity are major determinants for type of surgery (11-14). Hence mastectomy still continues to be the common surgery in surgical treatment of breast cancer.

External beam radiotherapy is considered for patients at high risk for local recurrence, as an adjunct to mastectomy. Four or more pos-

Gönderilme Tarihi: 13 Aralık 2009 • **Revizyon Tarihi:** 03 Ocak 2010 • **Kabul Tarihi:** 03 Ocak 2010

Table 1. Adjuvant therapies according to the patients' stage. (HT: Hormonotherapy, ChT: Chemotherapy. RT: Radiotherapy)

	HT	ChT	RT	HT+ChT	HT+RT	ChT+RT	ChT+RT+HT
Stage I	8	2	5	0	2	1	5
Stage IIA	3	5	29	4	19	31	32
Stage IIB	0	0	11	5	17	55	78
Stage IIIA	0	1	2	9	2	27	15

itive axillary lymph nodes, extracapsular invasion, greater primary tumor, and close or positive surgical margins are associated with the high risk of locoregional recurrence (LRR)(15-18). A meta-analysis of Whelan et al. revealed the advantage of postoperative radiotherapy on survival of these patients (19). Similarly, the National Surgical Breast and Bowel Project (NSABP) – 13 study showed the efficacy of adjuvant chemotherapy on patients' survival (20).

Although proven efficacy of postmastectomy adjuvant therapies, local recurrences are still seen. Almost detected just before or with the occurrence of distant metastases, LRR is appraised to be a precursor of metastatic disease. There are many studies for the effect of certain adjuvant or neoadjuvant therapies on LRR after mastectomy (21-24). This study aimed to identify the risk factors affecting the local or regional recurrence of the breast cancer in postmastectomy patients with isolated LRR having an appropriate and evidence-based adjuvant therapy.

Patients and Methods

In a 12 year period, 458 patients underwent surgical therapy for breast cancer in Gülhane Military Medical Academy, Department of General Surgery. All records were reviewed retrospectively. Patients suffering from early or locally advanced breast cancer with undetectable supraclavicular lymph nodes were included in the study provided that they had only a unilateral radical or modified radical mastectomy with removal of all breast tissue as surgical approach. Other inclusion criteria were the presence of at least 10 axillary lymph nodes in surgical specimen, no evidence of any systemic metastasis in physical and biochemical examination, chest radiogram, abdominal ultrasonography, whole body bone scintigraphy, and fitness for regular control.

Thus, 36 patients with initially metastatic disease, and 21 with insufficient number of lymph nodes were excluded. Subsequently, 17 additional patients having non-standardized chemotherapy or radiotherapy after an interval longer than 6 months following surgery for any reason and 16 other patients with poor compliance to follow-up schedule were out of the study. The remaining 368 were recruited for the study. Of these, 311 had invasive ductal carcinoma (84.5%), while invasive lobular carcinoma in 25 (6.8%), invasive ductal and lobular carcinoma in six (1.6%), invasive carcinoma arising from ductal carcinoma in situ (noninvasive ductal carcinoma?) in six (1.6%) were detected. Other 8 patients had medullary carcinoma while apocrine carcinoma in one, combined invasive ductal and mucinous cancer in one, comedo cancer in three, combined lobular and mucinous cancer in one, lobular and tubular cancer in one, mucinous cancer in three, and tubular cancer in two patients was detected. Histopathology revealed stage I breast cancer in 23, stage IIA breast cancer in 123, stage IIB breast cancer in 166, and stage IIIA breast cancer in 56 patients.

Solely hormonal therapy was given in 8 with stage I and 3 with stage IIA patients were given postoperatively. Other than these, all patients received adjuvant chemotherapy with the combination of cyclophosphamide, 5-fluorouracil, and either epirubicin (CAF) or metotrexate (CMF) if tumor diameter was greater than 2 cm and/or lymph node was involved. Medium or high-risk women with positive hormone receptor (according to their age, tumor size or grade) were managed with tamoxifen. Those with four or more lymph node metastases or tumor size greater than 5 cm, surgical margin closer than 1 cm or positive surgical margin were submitted to adjuvant radiotherapy to chest wall and axilla as well (Table 1).

Patients' characteristics such as age and menopause status were recorded. Then, tumor features such as size, closest surgical margin, histopathological grade (25) if available; numbers of overall and metastatic lymph nodes were assessed. If a re-excision was done due to close surgical margin, the latter was taken into account.

Follow-up was performed after staging procedures according to these features plus physical examination and standard therapies. Isolated locoregional recurrence (LRR) was defined as recurrences detected only at surgical wound, and surrounding breast skin, ipsilateral axillary, supraclavicular or infraclavicular fossa, ipsilateral internal mammarian lymph nodes, or ipsilateral chest wall during follow-up. Tumor recurrences outside these regions were considered as distant metastasis. Patients having synchronous metastases or metastases occurring within three months after the onset of LRR were classified as metastatic disease.

Relationship between patients' and tumor characteristics was analyzed with univariate analysis, and compared with surgical technique. Overall (from first diagnosis until last visit or death) and disease-free survival (from first diagnosis until first LRR or distant metastasis) times were assessed from outpatient charts and online digital hospital records.

Table 2. Comparison of patients' characteristics according to locoregional recurrence *(LRR: Locoregional recurrence, MRM: Modified radical mastectomy, RM: Radical mastectomy)*

Patients	*LRR*	*p*	*Disease-free survival (mean±S.E.) (95% CI)*	*Mean follow-up (range)*	*5-year survival*	*Log rank p*
Age (368)						
< 49 (187)	16 / 187 (9.3%)	0.897	123±7(109;137)	83 (15-205)	64%	0.76
≥ 50 (181)	12 / 196 (7.1 %)	0.486	123±6(112;135)	77 (6-181)	70%	0.38
Menopause status						
Premenopause (202)	15 / 202 (7.4%)	0.884	123±7 (110;137)	82 (15-205)	63%	0.72
Menopause(166)	13 / 166 (7.8 %)		123±6 (111;135)	78 (6-181)	72%	0.39
Surgical technique						
MRM (318)	24 / 318 (7.5 %)	0.782	126±6 (114;138)	81 (10-205)	69%	0.91
RM (50)	4 / 50 (8%)		111±11 (91;132)	85 (6-181)	56%	0.34
Stage						
Early (146)	12 /146 (8.2 %)	0.720	138±6 (127;149)	89 (23-205)	78%	13.49
Locally advanced (222)	16 / 222 (7.2 %)		118±6 (106;130)	72 (6-199)	60%	**0.0002**

Data were given as mean ± standard deviation unless otherwise cited. Student's t test was performed for the comparison of independent variables, and chi-square test was used for significance of difference between groups by univariate analysis of group distributions. Disease-free and overall survival times were defined with Kaplan-Meier analysis, and were compared using log rank test. P value below 5 % was considered statistically significant. SPSS 10.0 for Windows was used for backward Cox regression analysis of significant parameters in prognosis of breast cancer such as greater tumor size, lymph node status, stage, and surgical margin status, and independent factors in recurrence-free survival were evaluated.

Results

Of 368 women recruited for the study, 28 (7.6%) developed LRR. Site of recurrences were at chest wall in 22 (78.5%), at axillary region in 5, at both sites in one patient. Between an interval of 6 months to 8.5 years (median: 18 months), metachronous systemic metastasis developed in 14 of these patients (50%).

Patients' characteristics

Age and menopause status were not related to the LRR occurrence in our study. LRR developed in 9.3 % of patients below 49 years old while this was 7.1 % in older patients. There was no statistical significance between two groups (X^2= 0.48; p=0.49). There was no significant difference in terms of disease free survival between age groups. LRR was not affected by menopause status, and also there was no statistical significance in disease free survival (DFS) between premenauposal and menopausal patients (Table 2). 318 (86.4%) of patients underwent modified radical mastectomy (MRM). Mostly before 1990s, 50 patients (13.6%) have had radical mastectomy (RM). LRR occurred in 24 of MRM patients (7.5%) and four of RM patients (8%) recurred on follow-up. Surgical approach did not seem to affect LRR occurrence and DFS (Fisher's exact test, p=0.782 and log rank: 0.91; p=0.34). In 12 of 146 early stage breast cancer patients (8.2%) developed LRR whereas 16 of 222 locally advanced breast cancer patients (7.2%) had LRR. Differences of LRR between two stages were not statistically significant (X^2=0.128; p=0.720). However, DFS of patients with early breast cancer was significantly higher than that of locally advanced breast cancer patients (5-year survival: 78 vs. 60 %, log rank: 13.49; p=0.0002) (Table 2).

Tumor characteristics

Half of the patients (184 patients – 50%) had their tumors in the right breast whereas the other half in left side. 17 of right sided breast cancers had LRR (9.2%) while 11 (5.9%) left sided breast cancer recurred locoregionally. Location was not a statistically significant factor for LRR (X^2=1.392 p=0.238). DFS had no significant difference between two groups (Table 3).

Considering the localization, LRR were lowest in tumors located in the upper outer quadrant (UOQ) and in tumors under the areola. While 12 (5.4%) of 219 UOQ cases were encountered with LRR, LRR occurred in 39 upper inner quadrant (UIQ), in 60 lower inner quadrant (LIQ), in 18 lower outer quadrant (LOQ) and in 32 periareolar tumors, the rate of LRR incidence were 10.3%, 11.6%, 16.6%, and 6.3% respectively (X^2= 11.2 p=0.048). By contrast, survival analyses showed that periareolar cancers had the longest DFS, but UOQ localization had the shortest DFS. This was probably due to unequal distribution of the groups. Consequently, this difference was not statistically significant (log rank: 6.87; p=0.230).

Assessing the tumor diameter of the recruited patients, 60 cases (16.3%) had tumors < 2 cm, in 278 cases (75.5%) tumors were ranging from 2 to 5 cm, and remaining 30 patients (8.2%) had tumors > 5 cm. Number of patients with LRR occurring in these groups were five (9%), 20 (7.2%), and three (10%) respectively. Mean tumor diameter was 3.4±2.0 cm in cases with LRR, while it was 3.1±1.7 cm in cases without LRR (t=0.734; p=0.469). Statistical

Table 3. Comparison of tumor characteristics for locoregional recurrence *(LRR: Locoregional recurrence)*

Tumor	*LRR (n=28)*	*p*	*Disease-free survival (mean±S.E) (95% CI)*	*Median follow-up (range)*	*5-year survival*	*Log rank p*
Localization						
Right	17 / 184 (9.2%)	0.238	133±6 (121;145)	82 (10-199)	66%	0.02
Left	11 / 184 (5.9%)		118±6 (107;129)	79 (6-205)	68%	0.900
Outer Upper Quadrant	12 / 219 (5.4%)	**0.048**	117±7 (104;130)	78 (6-205)	64%	6.,87
Inner Upper Quadrant	4 / 39 (10.3%)		132±10 (111;152)	101(42-175)	69%	0.230
Outer Lower Quadrant	7 / 60 (11.6%)		126±9 (108;144)	81 (21-165)	72%	
Inner Lower Quadrant	3 / 18 (16.6%)		111±15 (81;141)	85 (28-165)	72%	
Areola	2 / 32 (6.3%)		145±12 (122;168)	80 (23-181)	76%	
Tumor size						
< 2 cm	5 / 60 (9%)	0.837	144±8 (127;160)	81 (23-181)	78%	23.10
2-5 cm	20 / 278 (7.2%)		126±6 (113;138)	82 (6-205)	69%	**0.00001**
> 5 cm	3 / 30 (10%)		59±9 (42;76)	66 (21-128)	30%	
Axillary lymph node						
Negative	8 / 118 (6.7%)		145±8 (129;162)	86 (23-205)	78%	24.51
1-3 positive	8 / 114 (7.0%)	0.796	130±7 (116;143)	83 (21-181)	72%	**0.00001**
> 3 positive	12 / 136 (8.8%)		93±6 (81;105)	68 (6-170)	54%	
Surgical Margin (245)						
< 1 cm	6 / 30 (20%)	**0.007**	68±10 (49;88)	83 (6-205)	43%	12.22
> 1 cm	13 / 215 (6%)		126±5 (115;137)	65 (16-134)	72%	**0.0005**
Grade (177)						
I	1 / 17 (5.8%)	0.994	104±9 (87;121)	76 (54-120)	82%	2.92
II	6 / 109 (5.5%)		93±5 (82;103)	79 (21-150)	62%	0.2325
III	3 / 51 (5.8%)		83±6 (70;95)	78 (13-120)	61%	
Estrogen Receptor						
Negative	2 / 37 (5.4%)	1.0	62±7 (49;75)	79 (23-150)	51%	6.30
Positive	5 / 77 (6.5%)		101±5 (90;111)	81 (25-141)	72%	**0.0121**
Progesterone Receptor						
Negative	4 / 61 (6.5%)	1.0	84±7 (71;98)	79 (23-116)	57%	3.83
Positive	3 / 46 (6.5%)		103±6 (90;115)	79 (25-150)	76%	**0.0502**

analysis showed that mean tumor diameter was not significantly different among patients with or without LRR (X^2=0.357; p=0.837). However, in terms of DFS, especially in patients with tumors greater than 5 cm, DFS was significantly lower than that in other groups (log rank: 24.51; p=0.00001) (Table 3).

Whenever there was no enlarged lymph node in Level III group, standard axillary dissection including level I and II lymph node groups was done. Mean total removed lymph node was 18.2±7.1 in patients with LRR, and 19.1±7.6 in patients without LRR. Mean metastatic lymph node was 5.5±7.3 and 4.6± 6.5 respectively. When comparing, overall and metastatic lymph nodes were not statistically significant between patients with and without LRR (p=0.49 and p=0.50). When axillary LN status was assessed and it was found that LRR was encountered in eight cases (6.7%) of 118 node negative patients, another eight cases (7.0%) of 114 patients with one to three LN positivity, and in twelve (8.8%) of 136 patients with ≥ 4 LN. Statistical analysis revealed that axillary LN status had no effect on LRR occurrence (X^2=0.458; p=0.796).

In only 177 patients (48.1%), tumor grade could be assessed. Of those, ten (5.6%) have experienced LRR. One of 17 grade I patients (5.8%), six of 109 grade II patients (5.5%) and three of 51 grade III patients (5.8%) have had LRR. Grade differences also did not influence LRR (X^2=0.011; p=0.994).

As estrogen receptor (ER) and progesterone receptor (PR) could be studied later, we only have information of PR status in 107 patients (29.1%) and ER status in 114 patients (30.1%). While five of 77 ER positive patients (6.5%) have had LRR, 5.4% of ER negative patients have experienced LRR. Three of 46 PR-positive patients (6.5%) and four PR-negative patients (6.5%) have had LRN (Fisher' s exact chi-square test, p=1.0) (Table 3).

Kaplan-Meier analysis revealed that positive axillary lymph node, tumor differentiation, and positive estrogen receptor were significantly associated with disease-free survival, but positive PR had borderline significance (Table 3).

Surgical margin

Information on surgical margin could be defined in only 245 patients (66.5%) at histopathological diagnosis. In 19 (7.8%) patients of this group LRR developed. Closest margin from tumor to cut surface was below 1 cm in 30 patients whose 29 underwent MRM, and the last one RM (3.3%), while of 215 patients with close margin greater than 1 cm, 17 underwent RM (7.9%). Two surgical methods were not statistically significant in obtaining safe close margin (X^2=0.809 p=0.462).

Six of patients with surgical margin closer than 1 cm (20%) developed LRR while 13 of 215 patients with safe surgical margin (6%) have had LRR. Considering the surgical margin of 1 cm as critical cut-off value, LRR was statistically significantly higher in patients with closer margin (X^2=7.165; p=0.007) (Table 3).

Survival analysis

Mean follow-up of patients in the study was 81 months (range: 6-205 months). The two and 5-year overall survival rates were 96.4% and 72.3% in patients with isolated LRR while these were 97.3% and 85.1% respectively in patients without LRR (log rank: 10.79 p=0.001). The two and 5-year disease-free survival rates were 79.5% and 50.6% in patients with LRR, while 93.3% and 82.1% in patients without LRR (log rank: 18.09 p=0.00001).

When survivals were compared with patients' stage, the two and 5 – year overall survival rates of locally advanced breast cancer patients were 94.4% and 78.7% respectively, while those of Stage I and IIA patients 99.3% and 92.4% respectively (log rank: 15.65 p=0.0001).

Patients were also compared according to surgical margin status. The 5-year overall survival rate was 88.6% and DFS rate was 72.0% in patients with safe surgical margin. However, in patients with surgical margin closer than 1 cm, the 5-year overall and disease-free survival rates were 78.3% and 43.0% respectively (log rank: 9.53 P=0.0085 for overall survival rates, and log rank: 12.22 p=0.0005 for DFS) (Figure 1).

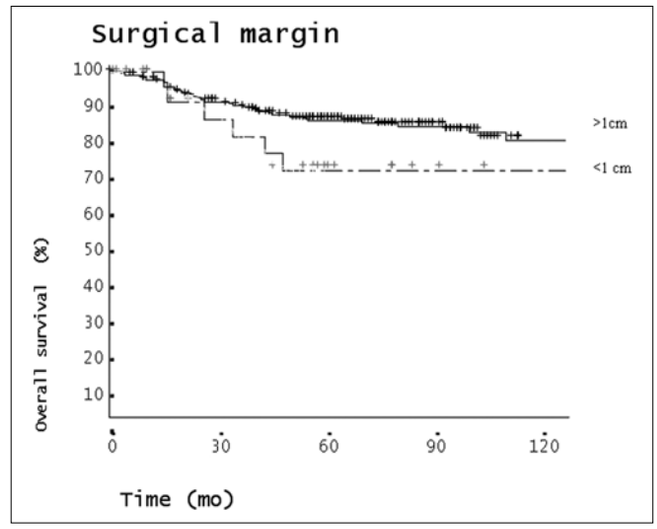

Figure 1. The effect of surgical margin on overall survival (log rank: 9.53 p=0.0085).

In the analysis of the effect of lymph node involvement on survival between patients with or without LRR, an overall survival rate for 340 patients without LRR was 81.8%. Of these, 110 have had negative ALN. 200 patients have had one to three positive ALN and the remaining 30 patients equal or more than four positive ALN. On the other hand, overall survival rates of the 28 patients with isolated LRR was 57.1% and among them, nine were node-negative, 14 had 1-3 positive ALN, and five had ≥ 4 ALN. There was statistically significant difference in overall survival between two groups (log rank: 27.4 p=0.00001) (Figure 2).

Although limited, the effect of tumor diameter on survival was statistically significant. In tumors < 2 cm, the two and 5-year survival rates was 98.3% and 91.5% respectively, while this was 97.5% and 83.9% in patients with 2-5 cm tumors. When the tumor diameter exceeded 5 cm, 2-year overall survival was not so much dif-

Table 4. Cox regression analysis; independent factors for locoregional recurrence-free survival.

Factor	*Beta*	*SE*	*Wald*	*p*	*Relative risk*	*CI (95%)*	
						Min	*Max*
Stage	-0.281	0.415	0.458	0.498	0.755	0.334	1.704
Tumor size	0.486	0.242	4.039	0.044	1.626	1.012	2.612
Lymph node positivity	0.596	0.160	13.977	0.0001	1.816	1.328	2.482
Surgical margin	-0.278	0.123	5.095	0.024	0.757	0.594	0.964

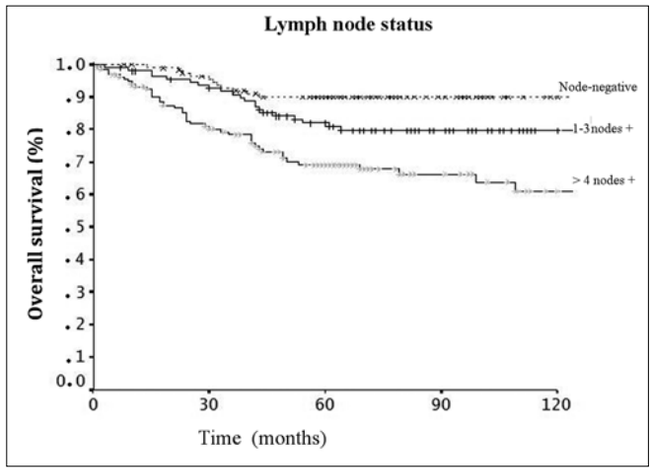

Figure 2. The effect of lymph node status on overall survival (log rank: 21.47 p=0.00001).

ferent (96.7%), however 5-year survival rates decreased to 71.8% (log rank: 6.56 p=0.0376).

In Cox regression analysis, tumor > 5cm, positive lymph node, close surgical margins were found to be independent prognostic factors for survival without locoregional failure (Table 4).

Discussion

The fact that postmastectomy LRR has no ideal definition, studies enquiring its frequencies run into some difficulties. In studies using different characteristics in staging, follow-up, and inclusion criteria, the occurrence of LRR has been reported to be from 6.2 to 29%(26-32). Especially seen earlier after surgery, LRR has a close relationship with distant metastasis (31,33-35). This association of LRR with systemic dissemination supports the hypothesis of being a precursor of metastasis, hence indicator of the poor prognosis, and increased risk.

For earlier stage cancer, more LRR is reported to be seen after BCS (10.8%) than that after mastectomy (5.9%)(36). It is shown that, in mastectomy patients, a direct correlation exists between tumor size and LRR occurrence (10.5% in pT1, and 15.6% in pT4)(33). On the other hand, in a study by Timothy et al. comparing mastectomy patients with those having a rather large tumor, and undergoing postmastectomy radiotherapy, LRR and 5-year survival rate were found to be similar (37). Subsequently, it is demonstrated that radiotherapy has no benefits on LRR in tumors > 5cm(38). In our study, tumor size, although significant with survival, was not directly associated with LRR occurrence. The importance of tumor size is obvious as it is a prognostic factor affecting the LRR-free survival. Possibly adjuvant radiotherapy for tumors > 5 cm in our study might affect the occurrence of LRR.

Beside uncontrollable tumor characteristics such as ALN involvement, and tumor grade (39), a controllable feature like surgical margin becomes prominent, especially in BCS (40,41). In the International Breast Cancer Study Group (IBCSG) study aiming the definition of risk factors for LRR in patients without postmastectomy irradiation, vascular invasion, and tumor size greater than 2 cm were found to be significant factors in node negative patients. Beside these features, the number of positive lymph nodes was also prominent in node positive women (21). Other studies revealed that the amount of positive lymph node (22,27,28,42), tumor size (27,28,42,43), ER status and the number of examined lymph nodes (27), close or positive surgical margin (28,42), multicentricity (28), and age (22,43) were predictors of LRR occurrence. In early breast cancer and ductal carcinoma in situ patients, while age, tumor diameter, and lymph node status are still significant factors, postoperative adjuvant therapy is becoming a new factor on LRR for BCS (44,45). The German Breast Cancer Study Group emphasized the importance of interval time from both mastectomy and BCS to isolated LRR and defined as significant prognostic factor (26).

It seems that the amount of removed lymph nodes is a prognostic factor for LRR. Suboptimal surgical technique leads to under-staging and poor performance of axillary treatment (27,29,30). LRR incidence increases with the number of lymph nodes involved (22,23). In our study, the number of involved lymph nodes was not statistically significant for LRR. However, it was the most prominent factor in LRR-free and disease free survival.

Nowadays, adjuvant radiotherapy strongly proven for patients with four or more positive lymph nodes is also investigated in patients with one to three positive lymph nodes. Van der Hage et al. showed that early breast cancer patients were the women who have had the most benefit from adjuvant radiotherapy (36). Studies mostly impressed the profits of radiotherapy on lowering LRR rates. However, Woodward et al. found these benefits for T1-T2 tumors and 1 to 3 involved lymph node patients and pretended that close or positive surgical margins, highly extracapsular invasion, and ALN dissection containing more than 10 lymph nodes are highly associated with LRR. Beside the number of dissected lymph nodes, a great number of positive lymph nodes, greater tumor size, negative ER are all good predictors of LRR in patients receiving radiotherapy (23). Feigenberg et al. revealed that T stage and the number of positive lymph nodes are highly related to the survival (32). It has been clearly showed that c-erb B-2 and p53 were investigated, and the negativity of bcl-2, a new biological marker, was a poor prognostic factor for predicting LRR (46).

According to the endocrine response of the tumor, more aggressive adjuvant therapies induce a decrease in LRR (47,48). Before the advent of systemic adjuvant therapies, more radical surgery was being applied to the chest wall, and subsequently radiotherapy was added in order to maintain local control. Radiotherapy lowered the death from breast cancer and achieved good locoregional control, however, beside two studies with limited mean dissected lymph nodes, its effect on overall survival has not been shown (18, 37, 49-54). In Danish Breast Cancer Study Group (DBCSG 82B) and British Columbia studies with their fewer mean lymph node number (7

and 11 respectively) and high LRR rates, it has been asserted that postmastectomy radiotherapy had a significant contribution to survival in high-risk premenauposal women (17,29,30). Due to the side effects such as lymphedema and radiation pneumonia as much as 21%, radiotherapy is advised only to the patients with high risk for LRR (18,32). In another study in which no patient received radiotherapy, timing for chemotherapy was investigated and LRR rates was found to be 27% in patients receiving neoadjuvant therapy and 15% in patients receiving adjuvant therapy (55). Thus, although surgical and systemic therapies were applied, risk factors associated with LRR should be determined.

In our study, tumor characteristics did not seem to be a significant factor for LRR occurrence beside lower inner quadrant localization. For example, patients' age seemed to be a significant factor for LRR and survival in some studies (22,36,56), however this was not so in our study. It is emphasized that surgical margin is named as "close" if it is closer than 1 mm (41,57,58). In another study, of patients re-excised for positive surgical margin 52.5% was found to have residual tumor (59). While the surgical margin was the most attractive and prominent factor for BCS (40,41), only one study including mastectomy patients stated that the surgical margin was an important factor for LRR (42). Comparing the LRR occurrence, although LRR in radical mastectomies were lesser than that in modified radical mastectomies, there was no statistically significant difference between two surgical modalities (22).

During the classical mastectomy incision, there are difficulties for tumors situated in inner lower quadrants, especially in neighborhoods of the skin or the fascia. It has been recently demonstrated that tumors localized in inner quadrants recurred more often than those situated in outer quadrants, and these localizations have shown poor prognostic features (60,61). By the way, the significance of upper outer quadrant localization for LRR occurrence can be the result of the fact that these tumors could be managed more conveniently preoperatively. At the other hand, lower inner quadrant localization can be a prominent factor in LRR as lymphatic drainage of these tumors is towards parasternal and internal mammarian lymph nodes (IMLN). So metastatic lymph nodes left in place during surgery could raise locally recurrent disease. Beside this, IMLN metastasis can only be detected with the techniques such as computerized tomography or dynamic breast MR rarely used for the diagnosis and management of the breast cancer, and these examinations clearly show the systemic spread.

As a conclusion, close surgical margins and tumor localization were found to be significant risk factors for LRR despite adjuvant therapies in this study. In tumors situated close to the skin flaps, mastectomy incision should specifically be modified for safer margins. For tumors in proximity of the pectoral muscles, modification of the surgical technique aiming the total or at least partial excision of the muscle can reduce the future LRR risk. Considering the high risk of LRR in tumors situated close to or excised with positive the surgical margin, or localized in inner quadrants of the breast, different oncological approaches during follow-up schedule and adjuvant therapies should be searched for local control.

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The Journal of Breast Health
meme sağlığı dergisi

The Journal of Breast Health 2010 Vol: 6 • No: 2
Meme Sağlığı Dergisi 2010 Cilt: 6 • Sayı: 2

RESEARCH ARTICLE/ARAŞTIRMA YAZISI

ANXIETY AND PAIN ASSOCIATED WITH PROCESS MAMMOGRAPHY: INFLUENCE OF PROCESS INFORMATION BEFORE

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ABSTRACT

Introduction: This study was carried out with the aim of determining the effect of information given in a leaflet to women who are about have a mammography on levels of anxiety before the procedure and pain levels after the procedure

Materials and Methods: This study consisted of 63 women. The data was "state anxiety scale" and "verbal category scale" before the experimental group went to the mammography unit, they were given information in a written leaflet, the control group was not. Before the procedures in the breast clinic and mammography unit anxiety was measured twice and pain levels were measured after the procedure in both group.

Results: There was no difference (p>0.05) between the anxiety levels of the experimental (46.19±11.88) and control (46.41±12.73) groups in the breast clinic before their mammography's (p>0.05), however in mammography unit the experimental group (35.35±10.30) was found (p= 0.00) to have lower anxiety levels than the control group (51.41±10.59). After the mammography in terms of pain, the difference between the groups was not found (p>0.05).

Discussion: It was determined that giving information using written leaflets to women who will have a mammography decreased anxiety levels, however, it did not affect pain levels.

Key words: mammography, giving information, pain, anxiety

MAMOGRAFİ İŞLEMİ İLE İLİŞKİLİ ANKSİYETE VE AĞRI: İŞLEM ÖNCESİ BİLGİLENDİRMENİN ETKİSİ

ÖZET

Giriş: Araştırma, mamografi çekilecek kadınlara yazılı kitapçıkla verilen bilginin işlem öncesi anksiyete ve işlem sonrası ağrı düzeyi üzerindeki etkisinin belirlenmesi amacı ile yapıldı.

Yöntem ve Gereçler: Deneysel olarak yapılan çalışmanın örneklemini 63 kadın oluşturdu. Veriler 'Kişisel Bilgi Formu', 'Durumluk Kaygı Envanteri' ve 'Sözel Kategori Ölçeği' kullanılarak toplandı. Deney grubuna mamografi ünitesine gitmeden önce yazılı broşür ile bilgi verildi, kontrol grubuna verilmedi. Her iki grubun meme polikliniğinde ve mamografi ünitesinde olmak üzere işlemden önce iki kez anksiyete, işlemden sonra ağrı düzeyleri ölçüldü.

Bulgular: Mamografi işleminden önce meme polikliniğinde deney (46.19±11.88) ve kontrol (46.41±12.73) grubunun anksiyete düzeyi arasında fark olmadığı (p>0.05), ancak mamografi ünitesinde deney grubunun (35.35±10.30) kontrol grubuna (51.41±10.59) göre anksiyete düzeyi düşük bulundu (p=0.00). Mamografi işlemi sonrası ağrı yönünden gruplar arasında farkın anlamlı olmadığı bulundu (p>0.05).

Tartışma: Mamografi işleminin yapılacağı kadınlara yazılı kitapçık kullanılarak bilgi vermenin anksiyete düzeyini azalttığı ancak ağrı düzeyini etkilemediği saptandı.

Anahtar sözcükler: mamografi, bilgi verme, ağrı, anksiyete

Introduction and purpose

Existing data in Turkey and as well in the world shows that among all cancer cases that seen in women breast cancer is number one and increasing each year. In Turkey, according to data of the Ministry of Health, cancer statistics while breast cancer in women was 33.93% in 2003, it has raised 35.47% in 2005 (1). However, breast cancer is a type of cancer whose early diagnosis can provide a cure for the disease.

Since breast cancer cannot be prevented, the most appropriate way to decrease mortality from breast cancer is to diagnose the disease early (2). The American Cancer Society (ACS) recommends breast self-examination (BSE), mammography, and clinical breast examination for early diagnosis of breast cancer (3). Researchers have noted that yearly mammography and clinical breast examination decrease mortality by 20-30% in women aged 50-65 years (4,5). It has been reported that yearly mammography or mammographic screening is the most appropriate and the most effective method for early diagnosis of breast cancer (3,6).

Studies from Turkey (7,8,9) have revealed that most of the women do not have a mammography which is congruent with the studies from other countries (10,11,12).

Gönderilme Tarihi: 11 Aralık 2009 • **Kabul Tarihi:** 28 Ocak 2010

The reason why women were not willing to undergo mammography is the belief that breast tissue is exposed to high doses of radiation (13), pain due to compression of breast tissue between the pressure plates of the mammography apparatus (14,15,16,17,18,19,20), destruction of privacy, and fear of cancer (19,21,22). All these factors cause anxiety in women (17,19,23) It has also been reported that the women who undergo mammography for the first time have higher anxiety levels (17,23).

Offering information to women may decrease the severity of their pain and anxiety due to mammography. It is one of the most important responsibilities and independent roles of nurses. It has been noted in the literature that when women are provided information about mammography by a nurse equipped with relevant knowledge, they feel less pain and less anxiety (21). However, there have been few studies on this issue in Turkey.

The patients presenting to the mammography unit in the hospital where this study was conducted are offered information about mammography. However, they are not given information about anxiety and pain concerning mammography. Therefore, the aim of this study was to investigate whether written information about mammography would decrease anxiety during the procedure and pain after the procedure.

Materials and Methods

This is an experimental study and was conducted in Breast Diseases Outpatient Clinic and Mammography Unit of Cumhuriyet University Hospital. The outpatient clinic and the unit are open between 8 am and 5 pm. There was one physician, one nurse, one secretary, and one auxiliary staff in the outpatient clinic and there were three professors, one radiologist, and one radiology technician in the mammography unit.

Women are examined consecutively as they present. After they are registered, they wear a robe appropriate for breast examination. The physician records patient history and performs breast examination. When the physician decides that mammography should be performed, the radiology technician performs mammography. The results of mammography are evaluated by the physicians specializing in mammography.

The study population included 879 women presenting to General Surgery and Breast Outpatient Clinics of Cumhuriyet University and underwent mammography after breast examination between 2005 and 2006. The study population included the women who were aged 35-60 years and literate, who had no mammography before and no problems with vision, hearing, or perception and who accepted to participate in the study. They were assigned into experimental and control groups.

A total of 63 women were enrolled in the study, of which 32 fulfilling the abovementioned criteria and getting prepared for mammography were assigned into the control group and 31 others fulfilling the above criteria and offered written information through pamphlets prepared by the investigator in the light of the literature. The first woman presenting to the breast outpatient clinic was assigned into the control group and the second woman presenting to the outpatient clinic was assigned into the experimental group and this procedure continued until an appropriate sample size was obtained. The following hypotheses were tested:

H_1: Information about mammography offered through visual-written material before the procedure will decrease anxiety experienced before the procedure.

H_2: Information about mammography offered through visual-written material before the procedure will decrease pain experienced during the procedure.

Data collection Tools and Procedures

Data was collected with Personal Characteristics Form, State-Trait Anxiety Scale, and Verbal Category Scale.

Personal Characteristics Form

The form was prepared by the investigator in the light of the literature and was composed of two parts. The first part included 13 questions about descriptive characteristics, the reason why women underwent mammography, and information the women had about mammography and the second part included 3 questions what the women remembered about mammography, whether they would have mammography for a second time, and why they did not want to have mammography.

State-Trait Anxiety Questionnaire

The questionnaire was developed by Spielberger et al. in 1970 to determine state anxiety levels of individuals and is based on Spielberger's anxiety theory. It is a self-reported scale composed of short statements and includes two scales and a total of 40 items. Each scale has 20 items on each page. The questionnaire requires that individuals should describe how they feel under certain conditions at a certain time and respond to the statements considering their feelings. Participants are requested to mark the most appropriate choice – almost never, sometimes, mostly, or almost always. Responses to items 3, 4, 6, 7, 9, 12, 13, 14, 17 and 18 are assigned positive scores (scores which increase the total anxiety score) and responses to the rest of the items are assigned negative scores (scores which decrease the total anxiety score). Responses to each item are scored between 1 (or -1) and 4 (or -4) and the total score is added 50. The highest total score is 80 and the lowest total score is 20. The higher the total score is, the higher the anxiety levels are. Scores above 35 indicates presence of anxiety and scores below 35 indicates absence of anxiety. The questionnaire was translated into Turkish by Öner and Lecompte and tested for its validity and reliability (24).

Verbal Category Scale (VRS)
The scale was developed by Melzack and Katz in 1992 and its validity and reliability for Turkish population were tested by Yazıcı, Eti- Aslan, and Olgun in 1998 (Figure 1). It is a simple, descriptive scale and requires that patients should select the most appropriate word to describe their pain severity. Pain severity ranges from mild to unbearable. The advantage of this scale is that it is easy to apply and simple. It is also more sensitive in description of moderate pain than Visual Analogue Scale. However, the scale has also disadvantages. In fact, patients have to keep the words used to describe pain severity in their minds and are dependent on the words available in the scale. In addition, it has been reported in the literature that patients tend to select the words in the middle rather than the ones towards the margins (25).

Preparation of the Pamphlet Including Written Information
It is thought that information transmitted orally can be affected by individual characteristics and that written information will be more effective.

The pamphlet was prepared in conjunction with the relevant literature. It was given to the women whose clinical examinations were made by the doctor and who would undergo mammography in the breast outpatient clinic 15 minutes before they went to the mammography unit. The pamphlet included information about what mammography is, how often it should be performed, patients' position during the procedure, pain likely to be felt by patients, radiation received, and the mammography apparatus. It is in Appendix 4.

Procedure
Data collection tools were completed at face to face interviews with both the control and experimental groups both before and after mammography between April 2007 and December 2007. The control group did not have any intervention, but the experimental group was asked to read the pamphlets prepared by the investigator.

The women who presented to the breast outpatient clinic, who would undergo mammography, and who fulfilled the inclusion criteria were included in the study. After all the women gave oral informed consent, the Personal Characteristics Form and State-Trait Anxiety Questionnaire were completed at face to face interviews lasting for 10 min.

The control group did not receive information about mammography. They completed State-Trait Anxiety Questionnaire at face to face interviews lasting for five minutes in the mammography unit before mammography. The experimental group completed Personal Characteristics Form and State-Trait Anxiety in a room in the outpatient clinic and then they were offered written information. Subsequently, the women went to the mammography unit and completed the State-Trait Anxiety Questionnaire at face to face interviews in five minutes for the second time.

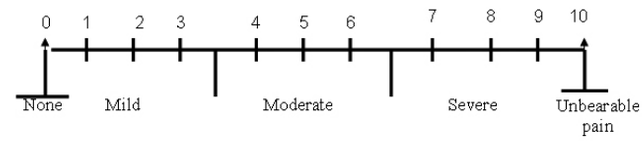
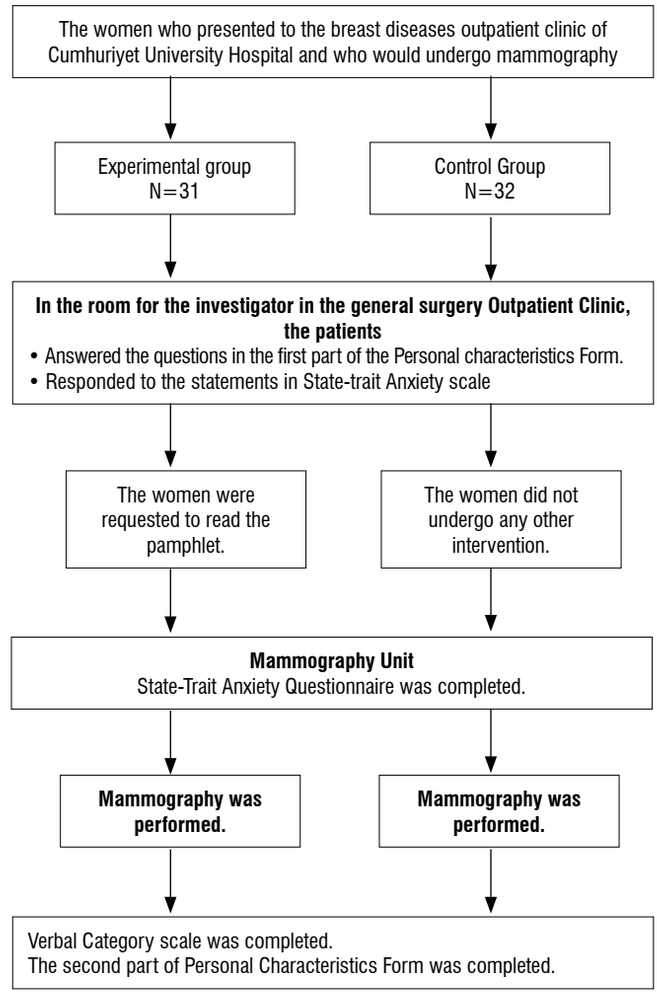


Figure 1. Verbal rating scale / verbal category scale (Melzack ve Katz 1992)

After mammography, both the control and experimental groups completed Verbal Category Scale in face to face interviews in 2-5 minutes and perceived pain severity during mammography was measured. Following completion of Verbal Category Scale, three questions in the second part of Personal Characteristics Form were asked: i.e. what they remembered about the procedure, whether they wanted to have mammography again, and why they did not have mammography again (Flow chart 1).

Flow chart 1. Practice Plan



Obtained data were evaluated with SPSS and analyzed with unpaired t-test, Chi-square test, Kruskal Wallis test and Mann Whitney U. data was expressed in means, standard deviations, numbers, and percentages and $p< 0.05$ was considered significant.

Limitations to the study

The number of patients enrolled in the study and the duration was limited since this study was planned as a master thesis and the thesis should be completed in certain time, also people who live in that place prefer to go to bigger cities where they can get service from bigger health centers. Although this limitations, we believe the data from the study will be helpful for the future studies.

Results

As shown in Table 1, most of the women included in the study were aged 35-39 years (67.7% of the control group and 65.6% of the experimental group), had low education levels (71% of the control group and 81.3% of the experimental group), were married (83.9% of the control group and 90.6% of the experimental group), and were unemployed (64.5% of the control group and 81.2% of the experimental group). Twelve point five percent of the women in the experimental group and 12.9% of the control group had a family member with breast cancer. Both groups were similar in their characteristics.

As presented in Table 2, 28.1% of the control group had nipple discharge, 25% had a palpable mass in breast self examination (BSE), 21.9% had pain in their breast, 21.9% presented for breast screening, and 3.1% presented for orange skin. Forty-one point nine percent of the experimental group had a palpable mass during BSE, 32.3% had breast pain, 16.1% had nipple discharge and 6.5% presented for breast screening, and 3.2% presented for orange skin. Eighty-seven point six percent and 12.4% of the control group had mammography for a mass and screening respectively. Ninety point three percent and 9.7% of the experimental group had mammography for a mass and screening respectively. Ninety-three point seven percent of the control group and 74.2% of the experimental group did not know why mammography is performed and 50% of the control group (n:1) and 62.5% of the experimental group learned why mammography is performed from health staff. Ninety-three point seven percent of the control group and 87.3% of the experimental group did not know how mammography is performed.

There was no significant difference in the mean anxiety scores in the outpatient clinic between the experimental (46.19±11.88)

Table 1. Characteristics of the Women

characteristics	*Control group*		*Experimental group*		*P*
	n	%	*n*	%	
Age					
40>	21	65.6	21	67.7	x^2=.032 p=.859
40≤	11	31.3	10	32.3	
Education*					
High education levels	26	81.3	22	71	x^2=.918 p=.338
Low education levels	6	18.7	9	29	
Martial status					
Married	29	90.6	26	83.9	x^2=.684 p=.421
Single	3	9.4	5	16.1	
Employment					
Employed	6	18.8	11	35.5	x^2=2.238 p=.135
Unemployed**	26	81.2	20	64.5	
Family history of breast cancer					
Yes	4	12.5	4	12.9	x^2=.02 p=.962
No	28	87.5	27	87.1	

*low education levels: literate and primary school graduates, high education levels: High school graduates and university graduates ** Housewife

Table 2. Reasons for Presentation to the Outpatient Clinic and Having Mammography and Information about Mammography

Characteristics	*Control group*		*Experimental group*		*P*
Reasons presentation to the outpatient clinic	**n**	**%**	**n**	**%**	
A palpable mass found during BSE	8	25.0	13	41.9	x^2=5.134 p=0.274
Nipple discharge	9	28.1	5	16.1	
Pain in the breast	7	21.9	10	32.3	
Orange skin	1	3.1	1	3.2	
Screening	7	21.9	2	6.5	
Reasons for having mammography					
A mass	28	87.6	28	90.3	x^2=0.127 p=0.722
Screening	4	12.4	3	9.7	
Knowing why mammography is performed					
Yes	2	6.3	8	25.8	x^2=4.510 p=0.034
No	30	93.7	23	74.2	
Sources of information about mammography					
Health staff	1	50.0	5	62.5	x^2=0.104 p=0.747
Women with prior experience with mammography	1	50.0	3	37.5	
Knowing how mammography is performed					
Yes	2	6.3	4	12.7	x^2=0.809 p=0.368
No	30	93.7	27	87.3	

Table 3. Mean Anxiety Scores in the Outpatient clinic and mammography unit before mammography

Anxiety levels							
Where anxiety was measured	***Control group***			***Experimental group***			
	Min	**Max**	**X±S**	**Min**	**Max**	**X±S**	**P**
Outpatient clinic	23.0	76.0	46,41±12.73	26.0	72.0	46,19 ±11,88	t: 0.06 p= 0.094
Mammography unit	32.0	77.0	51.41±10.59	24.0	62.0	35,35±10,30	t:6.09 p= 0.00
		t: 4.11	p=0.00				

Table 4. Comparison of Pain Severity between the Control and Experimental Groups

Pain severity during mammography	***Control group***		***Experimental group***		
	n	**%**	***n***	**%**	
Mild	13	40.5	16	51.6	p=0.561
Moderate	12	37.5	11	35.5	
Severe	7	22.0	4	12.9	

Table 5. Women's Decision to Have Mammography again and their reasons for not having Mammography

	Control group		***Experimental group***		
	n	**%**	***n***	**%**	
Having mammography again					
Yes	26	81.3	30	96.8	x^2=3.842 p=0.50
No	6	18.7	1	3.2	
Reasons for not having mammography again (n=6)					
Pain	5	83.3	1	100.0	x^2=5.64 p=0.53
Privacy	1	16.7		-	
What the procedure was like					
Painful	16	50.0	9	29.0	x^2=4.078 p=0.130
Created discomfort	14	43.8	16	51.6	
Comfortable	2	6.3	6	19.4	

and control (46.41±12.73) groups before mammography (p>0.05), but there was a significant difference in the mean anxiety scores in the mammography unit between the experimental (35.35±10.30) and the control (51.41±10.59) groups (p=0.00). In fact, anxiety levels measured in the mammography unit increased in the control group, but decreased in the experimental group (Table 3).

The women were found to experience mild pain during mammography and there was no significant difference in pain severity between the groups (p>0.05) (Table 4).

Eighteen point seven percent of the control group and 3.2% of the experimental group did not want to undergo mammography again and 83.3% of the control group (n:5) and one woman in the experimental group did not want to have mammography again due to pain. Fifty percent of the control group and 29% of the experimental group found mammography painful without a significant difference between the groups (p>0.05) (Table 5).

Discussion

The most effective way to decrease mortality from breast cancer is early diagnosis. Mammography is not the most successful imaging technique for early diagnosis of breast cancer but is cheap, easy to perform, and readily available. However, several studies from Turkey have revealed that rates of the women having mammography are low (7,8,9). In the present study, 87.6% of the control group had mammography for a mass and 12.4% for screening and 90.3% of the experimental group had mammography for a mass and 9.7% for screening. This finding shows that the women presented to health centers after breast cancer progressed. In a study in Turkey (26), the time from recognition of a breast problem to presentation to a health center was found to be 5.05 ± 9.3 months.

It has been reported in the literature that women feel anxiety about mammography due to fear of cancer and pain experienced during the procedure. It has been emphasized that a warm envi-

ronment with music, paintings, and magazines should be created and that women should be given information through pamphlets to decrease anxiety (17). Many authors (11,17,18,19,23) have claimed that anxiety prevented women from having mammography. In a study in Turkey (19) and many studies in other countries (17,23), anxiety felt before mammography was associated with the procedure itself and anxiety felt after mammography was associated with fear of cancer.

In this study, there was no significant difference in anxiety levels before the experimental group was offered information between the groups; however, the experimental group had lower anxiety levels after they were offered information. Lack of difference in anxiety levels between the groups before information was offered indicates that women are anxious about mammography and that offering information decreases anxiety (Table 3). This finding confirmed Hypothesis 1. However, another study in Turkey showed no effect of offering information on anxiety levels (19).

It has been reported in the literature that mammography was found to create discomfort and pain and that women did not want to undergo mammography (18,19,23). This study showed that most of the women had mild pain and that there was no difference in pain between the groups ($p>0.05$). This finding refuted Hypothesis 2.

Literature has reported that 0.2% - 90% of the women may feel pain during the procedure. In a study (12) 77% of the women found mammography painful, 31% had moderate pain, and 34% had severe pain. In a study by Alimoğlu et al. it was found that providing advance information to women about pain that can experience during mammography reduce severity of pain during the procedure and the cause of anxiety is not pain but is fear of being cancer.

In another study on this subject found similar results (20). Pain is the feeling causing discomfort and affected by cultural features. Pain is also an individual reaction and pain threshold varies from person to person. It has been noted in the literature that pain felt during mammography can be affected by cultural features and that some people may feel mild pain while others may feel severe pain (27). It has also been reported that pain felt during mammography was associated with breast thickness and that women with thick breasts felt more severe pain (17). It has been claimed that masses in the breast and fear of cancer may cause pain (20). In one study (28), women were allowed to control compression of their breast during mammography and felt less pain. It has been emphasized that self-control over a painful procedure helped women to adapt to pain more easily and felt less pain.

Women are not willing to undergo mammography again since they experience pain and anxiety in their first mammography (22). In the present study, most of the experimental and control groups noted that they would have mammography again and the rest did not want to have mammography due to pain.

Conclusions: It can be concluded that women feel anxiety and mild pain concerning mammography and that pamphlets including information about mammography can decrease anxiety but has no effect on pain. It can be recommended that the pamphlet used in this study could be used to give information about mammography in breast diseases outpatient clinics.

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The Journal of Breast Health
meme sağlığı dergisi

The Journal of Breast Health 2010 Vol: 6 • No: 2
Meme Sağlığı Dergisi 2010 Cilt: 6 • Sayı: 2

RESEARCH ARTICLE/ARAŞTIRMA YAZISI

ÜNİVERSİTE ÖĞRENCİSİ KIZLARIN MEME KANSERİ VE KENDİ KENDİNE MEME MUAYENESİ İLE İLGİLİ BİLGİ VE DAVRANIŞLARI

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Bu çalışma, Uluslararası Katılımlı VI Ulusal Hemşirelik Öğrencileri Kongresi'nde poster bildiri olarak sunulmuştur (26-29 Haziran, İstanbul).

ÖZET

Giriş: Araştırma üniversite öğrencisi kızların meme kanseri ve kendi kendine meme muayenesi (KKMM) ile ilgili bilgi ve davranışlarını belirlemek amacıyla yapılmıştır.

Yöntem ve Gereçler: Araştırma bir üniversitenin kız öğrenci yurdunda kalan 331 öğrenci ile yürütülmüştür. Veriler Kişisel Bilgi Formu ve Meme Kanseri / KKMM Bilgi Formu ile toplanmıştır. Araştırmacılar tarafından hazırlanan Meme Kanseri / KKMM Bilgi Formu 25 maddeden oluşmakta ve toplam 100 puan üzerinden değerlendirilmektedir. Veriler bilgisayarda değerlendirilmiş, istatistiksel analizde ki-kare, varyans analizi ve t testi kullanılmıştır.

Bulgular: Öğrencilerin %81'i KKMM'yi duymuştu, ancak %52.3'ü şimdiye kadar hiç KKMM yapmamıştı. Sağlıkla ilgili bölümlerde okuyan öğrenciler arasında KKMM yapma sıklığı (%79.7), sağlık dışı bölümlerde okuyan öğrencilerden (%40.8) anlamlı olarak daha yüksekti. Öğrencilerin Meme Kanseri / KKMM toplam bilgi puan ortalaması 37.86±17.59 olarak belirlendi. Sağlıkla ilgili bölümlerde okuyan öğrencilerin bilgi puan ortalaması (55.38±15.61), sağlık dışı bölümlerde okuyan öğrencilerden (34.05±15.60), KKMM'ni duymuş olan öğrencilerin bilgi puan ortalaması (40.25±17.52) duymadığını ifade eden öğrencilerden (27.68±13.97), KKMM yapmış olan öğrencilerin bilgi puan ortalaması (46.32), KKMM hiç yapmamış olan öğrencilerden (30.12±15.69) anlamlı düzeyde yüksekti.

Tartışma: Sonuç olarak üniversite öğrencisi kızların büyük çoğunluğu KKMM'yi duymuş olmasına karşın, KKMM yapma davranışları yeterli değildir. Ayrıca öğrencilerin Meme Kanseri / KKMM bilgileri düşük düzeydedir.

Anahtar sözcükler: meme kanseri, kendi kendine meme muayenesi, üniversite öğrencileri

THE KNOWLEDGE AND BEHAVIORS OF FEMALE UNIVERSITY STUDENTS ABOUT BREAST CANCER AND BREAST SELF EXAMINATION

ABSTRACT

Introduction: The research carried out in order to determine the knowledge and behaviors of female university students about breast cancer and breast self examination (BSE).

Materials and Methods: The research has been carried out 331 students staying at Girl Students Dormitory of a state university. The data has been collected through Personal Information Form and Breast Cancer / BSE Knowledge Form. Breast Cancer / BSE Knowledge Form consists of 25 items and it is evaluated out of 100 points. The data has been evaluated on the computer, in the statistical analysis, Khi-square, variance analysis and t test have been used.

Results: 81% of students have heard BSE, but 52.3% of them have never done BSE so far. Among the students studying in departments related to health, the frequency of doing BSE (79.7%) was significantly higher than the students studying in departments apart from health (40.8%). The students'totally Breast Cancer / BSE point average was determined as 37.86±17.59. The point average of the students studying in departments related to health (55.38±15.61) was significantly higher than the students studying in departments apart from health (34.05±15.60); the point average of students who have heard about BSE (40.25±17.52) was significantly higher than students who haven't heard (27.68±13.97); the point average of students who have done BSE (46.32±15.59) was significantly higher than the students who have never done BSE (30.12±15.69).

Discussion: Consequently, although the big majority of female university students have heard about BSE, their behaviors of doing BSE are not enough. Also the students'knowledge level about Breast Cancer / BSE are low.

Key words: breast cancer, breast self examination, university students

Giriş

Dünyanın hemen her bölgesinde önemli bir sağlık sorunu olan meme kanseri, kadınlar arasında en sık görülen kanser türü olup, bazı ülkelerde ölüm nedenleri arasında ilk sırada yer almaktadır. Yaşam boyunca yaklaşık her 10 kadından birinin bu hastalığa yakalanma riski ve yakalananların üçte birinin yaşamlarını bu hastalık nedeniyle kaybetme riski ile karşı karşıya olduğu belirtilmektedir (1,2). Türkiye'de son yıllarda meme kanseri insidansının arttığı ve 2012 yılında 51 binden fazla meme kanseri vakası olacağı tahmin edilmektedir (2).

Meme kanseri bu kadar yaygın olmasına karşın, genellikle yavaş bir gelişme hızı gösteren ve tanısı erken yapıldığında oldukça başarılı tedavi sonuçları elde edilebilen bir kanser türüdür. Meme kanserinin erken tanı ve tedavisi; yaşam süresinin uzamasında, mortali-

Gönderilme Tarihi: 30 Aralık 2009 • **Kabul Tarihi:** 28 Ocak 2010

tenin azalmasında, yaşam kalitesinin yükseltilmesinde, kadınlarda fiziksel acı ve psikososyal sorunların önlenmesinde etkili olabilmektedir (3). Klinik meme muayenesi, kendi kendine meme muayenesi (KKMM) ve mamografi gibi erken tanıyı kolaylaştıran meme kanseri taramaları sağlığı geliştirme aktiviteleri olarak tanımlanmakta ve bu uygulamalar meme kanserinin erken tanısında oldukça önemli rol oynamaktadır (4-8). Meme kanserinde mortaliteyi azaltmada etkili olan tek tanı yöntemi mamografi olmasına karşın, yöntemin pahalı olması, insan gücü ve teknik uzmanlık gerektirmesi nedeniyle özellikle az gelirli ülkeler için uygun olmadığı belirtilmektedir. Bu nedenle tüm kadınlarda meme sağlığı farkındalığı ve bilincinin geliştirilmesinin temel nokta olduğu vurgulanmaktadır (3,9,10).

Meme kanserinin erken tanı ve tedavisi için yapılan KKMM basit, herkes tarafından uygulanabilen, özel araç gereç gerektirmemesi ve maliyetinin olmaması nedeniyle tercih edilen bir erken tanı yöntemidir. Ayrıca KKMM kadının kendi sağlığının sorumluluğunu alarak sağlık bakımına katılması ve kendi bedeni üzerindeki farkındalığının artmasını sağlamaktadır. KKMM'nin 20 yaş üzerindeki tüm kadınlar tarafından aylık rutin bir şekilde yapılması önerilmektedir (3,11,12). Literatürde KKMM ile belirlenen meme kanserlerinin daha küçük ve meme dokusu ile sınırlı olma olasılığının daha yüksek olduğu belirtilmektedir (13). Ayrıca KKMM yapan kadınlarda, uygulamayanlara göre meme kanserinin daha erken dönemlerde saptanabildiği bulunmuştur. Yapılan bir çalışmada meme kanserli kadınların %90'ının memede belirledikleri ağrısız kitle yakınması ile kliniğe başvurduğu belirtilmektedir (3). Bu nedenle tüm kadınlar meme kanseri ve KKMM konusunda bilgilendirilmeli ve bu tarama yöntemini uygulamaları sağlanmalıdır. Geleceğin aydın ve eğitimli kadınlarını oluşturacak olan üniversite öğrencisi genç kızlar sağlık davranışları ile aynı zamanda toplumda rol modeli olacaklardır. Bu nedenle araştırma üniversite öğrencisi kızların meme kanseri / KKMM konusundaki bilgi ve davranışlarını belirlemek amacıyla yapılmıştır.

Yöntem

Bu araştırma üniversite öğrencisi kızların meme kanseri / KKMM ile ilgili bilgi ve davranışlarını belirlemek amacıyla tanımlayıcı olarak yağılmıştır. Araştırma bir devlet üniversitesinin Kredi ve Yurtlar Kurumu Kız Öğrenci Yurdunda Yürütülmüştür. Araştırmanın evrenini 2006-2007 öğretim yılında kız öğrenci yurdunda kalan 1882 öğrenci oluşturmuştur. Araştırmanın örneklemi ise evrenin belirli olduğu durumda olayın sıklığını incelemek amacıyla kullanılan formül yardımıyla hesaplanmış ve 331 öğrenci olarak bulunmuştur.

Veriler araştırmacılar tarafından hazırlanan Kişisel Bilgi Formu ve Meme Kanseri / KKMM Bilgi Formu olmak üzere iki ile form ile toplanmıştır. Kişisel Bilgi Formu'nda öğrencilerin yaş, okudukları bölüm, anne-baba eğitimleri, en uzun süre ile yaşadıkları yer gibi bazı tanıtıcı özellikleri ve ailesinde meme kanseri öyküsü olma, meme problemi yaşama, KKMM duyma ve yapma davranışları ile ilgili toplam 16 soru yer almıştır. Meme Kanseri / KKMM Bilgi formu ise, öğrencilerin meme kanseri ve KKMM ile ilgili bilgilerini ölçmek amacıyla hazırlanmış 25 maddeden oluşmuştur. Her bir maddenin karşısında bu ifade ilgili olarak "doğru", "yanlış" ve "bilmiyorum" seçenekleri yer almıştır. Formda doğru olarak bilinen her bir maddeye 1 puan verilmiştir. Yanlış bilinen ya da boş bırakılan maddelere ise 0 puan verilmiştir. Form toplam 25 puan üzerinden değerlendirilmiş, daha sonra alınan puan 100'e dönüştürülerek tablolaştırılmıştır.

Tablo 1. Öğrencilerin kendileri için algıladıkları meme kanseri risk kategorisine göre dağılımı

	Sayı	%
Risk Kategorisi		
Çok yüksek risk	8	2.7
Yüksek risk	11	3.3
Kararsız	166	50.2
Düşük risk	98	29.6
Çok Düşük risk	48	14.5
Toplam	331	100

Tablo 2. Öğrencilerin kendi kendine meme muayenesini duyma ve bilgi kaynaklarına göre dağılımı

	Sayı	%
KKMM duyma (n=331)		
Duyan	268	81.0
Duymayan	63	19.0
Bilgi kaynağı (n= 268)*		
Radyo / Televizyon	97	29.3
Arkadaş	89	26.9
Kitap / dergi	83	25.1
Sağlık personeli	78	23.6
Okul	48	14.5
Aile	42	12.7
İnternet	21	6.3

*Birden fazla yanıt vardır. Yüzdeler "n" üzerinden alınmıştır.

Hazırlanan formlar araştırma kapsamında yer almayan 20 öğrenciye uygulanarak ön denemeden geçirilmiş, ön deneme sonuçlarına göre gerekli düzenlemeler yapılarak formlara son şekli verilmiştir. Veri toplama formları basit rastgele örnekleme yöntemi ile seçilen ve araştırmaya katılmayı kabul eden belirlenen sayıda öğrenciye (331 öğrenci) uygulanmıştır. Araştırmacılar tarafında örnekleme seçilen öğrencilere formlar dağıtılmış, bireysel olarak doldurmaları sağlanmış ve daha sonra toplanmıştır. Formun doldurulması ortalama 15 dk. sürmüştür.

Elde edilen verilerin analizi bilgisayar ortamında SPSS programında yapılmıştır. İstatistik analizde ki-kare, varyans analizi ve t testi kullanılmıştır.

Bulgular

Araştırma kapsamında yer alan öğrencilerin %36.0'ı 18-20, %55.6'sı 21-23, %8.5'i 24 ve üzeri yaş grubundadır (Yaş ortalaması 21.14 ± 1.61). Öğrencilerin %17.8'i sağlıkla ilgili bölümlerde, %82.2'si sağlık dışı bölümlerde okumaktadır. Öğrencilerin en uzun süre ile yaşadıkları yer incelendiğinde %28.7'sinin büyük şehir, %31.7'sinin şehir, % 30.5'inin ilçe, %3.9'u kasaba ve %5.1'inin köyde yaşadığı bulunmuştur. Öğrencilerinin %56.5'inin anneleri ilkokul mezunu iken, babalarının ise %33.8'sinin lise mezunu olduğu saptanmıştır. Araştırma kapsamına alınan öğrencilerin %9.4'ünün yakın akrabalarında (anneanne, anne, kız kardeş/abla, teyze) meme kanseri olduğu ve %6.3'ünün şimdiye kadar herhangi bir meme problemi yaşadıkları saptanmıştır.

Tablo 1'de öğrencilerin kendileri için algıladıkları meme kanseri risk kategorisine göre dağılımı verilmiştir. Araştırma kapsamına alınan öğrencilerin %2.4'ü kendisini meme kanserine yakalanma açısından çok yüksek riskte, %3.3'ü yüksek riskte görürken, %50.2'si bu konuda kararsız olduğunu belirtmiştir. Diğer taraftan öğrencilerin %29.6'sı kendisini düşük riskte ve %14.5'i ise çok düşük riskte görmektedir.

Tablo 2'de öğrencilerin KKMM'yi duyma ve bilgi kaynaklarına göre dağılımı verilmiştir. Öğrencilerin %81'i kendi KKMM'yi duyduğunu, %19'u ise duymadığını ifade etmişlerdir. Öğrencilerinin KKMM ile ilgili bilgilerini aldıkları kaynaklar incelendiğinde %29.3'ünün bu bilgiyi radyo/televizyondan, %26.9'unun arkadaşlarından %25.1'inin kitap/dergilerden, %23.6'sının sağlık personelinden, %14.5'inin okuldan, %12.7'si aileden ve %6.3'ünün ise internetten edindiği saptanmıştır.

Tablo 3'te öğrencilerin KKMM yapma durumlarına göre dağılımı verilmiştir. Öğrencilerin %47.7'sinin en az bir kez KKMM yaptığı, %52.3' ünün hiç yapmadığı saptanmıştır. Öğrencilerin %6.0'ının KKMM'yi düzenli olarak yaptığı, %41.7' sinin düzenli olarak yapmadığı saptanmıştır.

Tablo 4'te öğrencilerin yaş ve bölümlerine göre KKMM yapma durumlarının dağılımı verilmiştir. Tabloya göre 21 ve üzeri yaş grubunda bulunan öğrencilerin en az bir kez KKMM yapma sıklıkları (%50.5) 18-20 yaş grubundan (%42.9) yüksek olmasına karşın gruplar arasındaki fark istatistiksel olarak anlamlı bulunmamıştır (p>0.05). Diğer taraftan öğrencilerin öğrenim gördükleri bölüme göre KKMM yapma davranışları arasında anlamlı bir fark olduğu (p<0.05), sağlıkla ilgili bölümlerde okuyan öğrencilerin KKMM yapma davranışlarının (%79.9) sağlık dışı bölümlerde okuyan öğrencilerden (%40.8) yüksek olduğu belirlenmiştir.

Tablo 5'te öğrencilerin bazı özelliklerine göre meme kanseri / KKMM bilgi puan ortalaması verilmiştir. Tabloya göre öğrencilerin meme kanseri /KKMM toplam bilgi puan ortalamasının 100 üzerinden 37.86 (SD=17.59) olduğu dikkati çekmektedir. Öğrencilerin bazı özelliklerine göre toplam bilgi puan ortalaması incelendiğinde; 21 ve üzeri yaş grubundaki öğrencilerin bilgi puan ortalamasının (39.69 ± 18.43), 18-20 yaş grubundaki öğrencilerden (34.38 ± 15.54) istatistiksel olarak anlamlı düzeyde yüksek olduğu belirlenmiştir (p<0.05). Öğrencilerin okudukları bölüme göre bilgi puan ortalaması arasında istatistiksel olarak anlamlı bir fark olduğu belirlenmiştir. Buna göre sağlıkla ilgili bölümlerde okuyan öğrencilerin bilgi puan ortalaması (55.38 ± 15.61), sağlık dışı bölümlerde okuyan öğrencilerden (34.05 ± 15.60) daha yüksektir (p<0.05). Ayrıca KKMM'yi duyan ve en az bir kez KKMM yapan öğrencilerin bilgi puan ortalamasının KKMM'yi duymayan ve hiç yapmamış olanlardan anlamlı düzeyde yüksek olduğu belirlenmiştir (p<0.001). Öğrencilerin meme kanseri risk algısına göre toplam bilgi puan ortalaması karşılaştırıldığında, gruplar arasında anlamlı bir fark olduğu (p<0.05) ve farkın kararsız olan gruptan kaynaklandığı belirlenmiştir. Kendini yüksek risk grubunda görenlerle (43.79±7.96) düşük risk grubunda görenlerin (41.01±19.16) toplam bilgi puan ortalaması arasında anlamlı bir fark bulunmazken, meme kanseri açısından risk grubu konusunda kararsız olan grubun bilgi puan ortalaması, kendini hem yüksek hem de düşük riskte gören gruptan anlamlı düzeyde düşük bulunmuştur.

Tablo 3. Öğrencilerin kendi kendine meme muayenesi yapma durumlarına göre dağılımı

KKMM yapma davranışları	*Sayı*	*%*
KKMM		
En az bir kez yapan	158	47.7
Hiç yapmayan	173	52.3
Düzenli olarak KKMM yapma durumu		
Düzenli olarak yapan	20	6.0
Düzenli olarak yapmayan	138	41.7
Hiç yapmayan	173	52.3

Tablo 4. Öğrencilerin yaş ve öğrenim gördükleri bölüme göre en az bir kez KKMM yapma durumlarının dağılımı

Özellik	*En Az Bir Kez KKMM*				*Test*
	Yapan		*Yapmayan*		
	Sayı	*%*	*Sayı*	*%*	
Yaş					
18-20	51	42.9	68	57.1	x^2=1.77
21 ve üzeri	107	50.5	105	49.5	p=0.183
Bölüm					
Sağlıkla ilgili bölümler	47	79.9	12	20.3	x^2=29.33
Sağlık dışı bölümler	111	40.8	161	59.2	p=0.001

Tartışma

Meme kanseri kadınlar arasında en sık görülen kanser türüdür. Yaşam boyu her 9 kadından birinde meme kanseri oluşacağı tahmin edilmektedir. Otuzlu yaşlardan menopoza kadar olan dönemde

Tablo 5. Öğrencilerin Bazı özelliklerine göre Meme kanseri / KKMM Bilgi puan ortalaması

Özellik	Meme Kanseri / KKMM Bilgi puan Ortalaması			Test
	X	±	SD	
Yaş				
18-20	34.38	±	15.54	t= -2.55, p= 0.011
21 ve üzeri	39.69	±	18.43	
Bölüm				
Sağlıkla ilgili bölümler	55.38	±	15.61	t= 9.51, p= 0.000
Sağlık dışı bölümler	34.05	±	15.60	
KKMM Duyma				
Duyan	40.25	±	17.52	t= 5.30, p= 0.000
Duymayan	27.68	±	13.97	
KKMM Yapma				
En az bir kez yapan	46.32	±	15.59	t= 9.41, p= 0.000
Hiç Yapmayan	30.12	±	15.69	
Meme kanseri risk algısı				
Yüksek Risk	43.79	±	17.96	F=6.84, p=0.001
Kararsız	34.40	±	15.38	
Düşük Risk	41.01	±	19.16	
Toplam	37.86	±	17.59	

göreceli bir artış gösteren meme kanseri, menopozdan sonraki dönemde oldukça sık görülmektedir (14). Üniversite öğrenimi sırasında genel olarak yirmili yaşlarda olan genç kızlar meme kanseri açısından nispeten düşük bir riskte olmalarına karşın, meme sağlığı ve meme kanserine yönelik farkındalığın bu yaşlardan itibaren geliştirilmesinin önemi vurgulanmaktadır (3,15). Bu çalışmada yer alan üniversite öğrencilerinin yarısının kendileri için var olan meme kanseri riskine ilişkin kararsız olduğu görülürken, yarıya yakınının kendini düşük risk grubunda gördüğü belirlenmiştir. Öğrencilerin risk durumuna ilişkin herhangi bir fikrinin olmaması ya da kendilerini düşük risk grubunda görmeleri öğrencilerin meme sağlığı ve hastalıkları konusunda bilgi edinmelerini ve erken tanıya yönelik davranışlarını olumsuz etkileyebilecek bir faktör olarak düşünülebilir. Nitekim bu çalışmada risk durumu konusunda kararsız olan öğrencilerin meme kanseri ve KKMM konusundaki bilgileri, kendini düşük ya da yüksek risk grubunda gören öğrencilerden daha düşük bulunmuştur (Tablo 1).

Çalışmada öğrencilerin çoğunluğunun (%81.0) KKMM'yi duyduğu belirlenmiştir. Öğrencilerin KKMM ile ilgili bilgi kaynakları arasında ise ilk sıralarda radyo televizyon, arkadaş, kitap/dergi ve sağlık personelinin yer aldığı saptanmıştır (Tablo 2). Benzer şekilde Salauden ve arkadaşlarının çalışmasında üniversite öğrencilerinin %81.9'unun (16), Chioma ve Asuzu'nun çalışmasında ise %82.5'inin (17) KKMM'den haberdar oldukları saptanmıştır. Her iki çalışmada da öğrencilerin KKMM bilgi kaynakları arasında yazılı / görsel medya ve sağlık personeli öncelikli olarak yer almaktadır. Bu sonuçlar çalışma bulgularımızla uyumludur.

Bu çalışmada üniversite öğrencilerin %47.7'sinin en az bir kez KKMM yaptığı belirlenmiştir (Tablo 3). Chouliara ve arkadaşlarının Yunanistan ve İngiltere'de üniversite öğrencilerinin KKMM yönelik tutum ve davranışlarını karşılaştırdıkları çalışmalarında en az bir kez KKMM yapan öğrenci oranı Yunanistan'da %52.9, İngiltere'de %50 olarak bulunmuştur (18) ve sonuçlar çalışma bulgularımızla benzerdir. Çalışmamızda öğrencilerin yalnızca %6.0'ının düzenli olarak bu muayeneyi yaptığı belirlenmiştir. Benzer şekilde Akkaş ve arkadaşları tarafından yapılan başka bir çalışmada üniversite öğrencilerinin yalnızca %5.6'sının düzenli meme muayenesi yaptığı saptanmıştır (15). Beydağ ve Karaoğlan'ın çalışma sonuçları da üniversite öğrencisi kızların %7.5'inin düzenli KKMM yaptığını vurgulamaktadır (19). Diğer taraftan Aydın Avcı'ın hemşirelik öğrencilerinde yaptığı bir çalışmada ise öğrencilerin %43.2'sinin KKMM yapmadığı, ancak meme muayenesi yapan öğrencilerin %22.7'sinin düzenli olarak KKMM yaptığı bulunmuştur (20). Hemşirelik öğrencilerinde yapılan başka bir çalışmada düzenli olarak KKMM yapanların oranı %41.3 olarak saptanmıştır (21). Aydın Avcı ve arkadaşlarının ebelik öğrencilerinde yaptıkları çalışmanın sonucunda da öğrencilerin %46.3'ünün her ay düzenli olarak KKMM yaptığı bulunmuştur (22). Çalışma sonucumuzdan yüksek olan bu bulgular öğrencilerin sağlıkla ilgili bir bölümde öğrenim görüyor olmalarından kaynaklanıyor olabilir ve beklenen bir durumdur. Nitekim çalışmamızda da sağlıkla ilgili bölümlerde öğrenim gören öğrencilerin en az bir kez KKMM yapma sıklığı sağlık dışı bölümlerde okuyan öğrencilerden anlamlı düzeyde yüksek bulunmuştur (Tablo 4).

Yukarıda belirtilen çalışma sonuçlarına göre düzenli olarak KKMM yapma davranışının üniversite eğitimi alan kızlar arasında oldukça düşük düzeyde olduğu söylenebilir. Bu durum öğrencilerin yaş grubu ile ilgili olabilir. Meme kanseri riski yaşla birlikte ve özellikle 50 yaşından sonra artmasına karşın, meme sağlığı ve korumaya yönelik davranışların erken yaşlarda başlaması, davranışın alışkanlık haline gelmesi açısından önemlidir. Aynı zamanda üniversite eğitimi alan genç kızlar toplumun aydın bireyleri olarak sergiledikleri sağlık davranışları ile topluma rol modeli olabilirler. Bunun için üniversite öğrencisi genç kızlara ve özellikle sağlıkla ilgili olmayan bölümlerde öğrenim görenlere yönelik eğitici ve farkındalığı geliştirici programlar düzenlenebilir. Yapılan çalışma sonuçları da çeşitli eğitim etkinliklerinin bireylerin meme kanseri ve KKMM bilgisini ve düzenli olarak meme muayenesi yapma davranışlarını geliştirdiğini göstermektedir (11,15,19,23,24).

Bu çalışmada yer alan üniversite öğrencisi kızların meme kanseri /KKMM toplam bilgi puan ortalamasının 37.86±17.59 olduğu belirlenmiştir. Bilgi formunu 100 puan üzerinden değerlendirildiği göz önüne alındığında, bu sonucun oldukça düşük olduğu görülmektedir. Ülkemizde diğer üniversitelerde yapılan bazı çalışmalarda da öğrencilerin meme kanseri ve KKMM ile ilgili bilgi düzeylerinin düşük olduğu belirtilmektedir (15,19,24,25). Öğrencilerin bazı özelliklerine göre bilgi puan ortalamaları karşılaştırıldığında

21 ve üzeri yaş grubunda olan, sağlıkla ilgili bölümlerde öğrenim gören, KKMM'yi duyan, en az bir kez KKMM yapan ve meme kanseri açısından kendini yüksek risk grubunda gören öğrencilerin bilgilerinin daha fazla olduğu belirlenmiştir. Sağlıkla ilgili bölümlerde okuyan öğrencilerin bilgi puanlarının diğerlerinden yüksek olması beklenen bir sonuçtur. KKMM'yi duyan ya da en az bir kez uygulayan öğrencilerin bilgilerinin diğerlerinden yüksek olması ise, gençleri meme kanseri ve KKMM'nin önemini konusunda bilgilendirme ve farkındalıklarını artırmaya yönelik müdahalelerin önemini göstermektedir.

Sonuç ve Öneriler

Bu araştırmadan elde edilen bulgulara göre; öğrencilerin büyük bir kısmının şimdiye kadar herhangi bir meme problemi yaşamadıkları, yarısının meme kanseri riski açısından kendini nerede gördüğü konusunda karasız olduğu, çoğunluğunun KKMM'yi duyduğu ancak yaklaşık yarısının şimdiye kadar hiç KKMM yapmadığı, KKMM yapan öğrenciler arasında düzenli olarak KKMM yapma davranışının oldukça düşük olduğu saptanmıştır. Öğrencilerin meme kanseri / KKMM bilgi puan ortalamasının düşük olduğu ve öğrencilerin bilgi puan ortalamasının yaş, okudukları bölüm, KKMM duyma ve yapma özelliklerine göre değiştiği saptanmıştır.

Bu sonuçlara göre üniversite eğitimi sırasında özellikle sağlıkla ilgili olmayan bölümlerde öğrenim gören kız öğrencilerin Meme kanseri / KKMM konusunda bilgilendirilmesi için çeşitli etkinliklerin düzenlenmesi önerilebilir.

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The Journal of Breast Health
meme sağlığı dergisi

The Journal of Breast Health 2010 Vol: 6 • No: 2
Meme Sağlığı Dergisi 2010 Cilt: 6 • Sayı: 2

RESEARCH ARTICLE/ARAŞTIRMA YAZISI

KIRSAL ALANDAKİ KADINLARIN MEME KANSERİ BİLGİSİ VE KENDİ KENDİNE MEME MUAYENESİ UYGULAMA DURUMLARININ BELİRLENMESİ

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ÖZET

Giriş: Bu çalışma Bolu İli Merkez Köylerinden Karaköy'de yaşayan 20 yaş ve üzeri kadınların meme kanseri bilgisi ve kendi kendine meme muayenesi uygulamalarını belirlemek amacıyla yapılmıştır.

Yöntem ve Gereçler: Kesitsel tipte, tanımlayıcı bir çalışmadır. Bu çalışma 150 kadının katılımıyla yapılmıştır.

Bulgular: Çalışmaya katılan kadınların sosyo-demografik özellikleri incelendiğinde; 20 yaş ve üzeri kadınların yaş ortalamasının 45 ± 18 (min:20, max:84), %72.7'sinin evli, %65.3'nün ilkokul mezunu, %88.7'sinin ev hanımı, oldukları belirlenmiştir (n: 150). Çalışmamıza katılan kadınlara meme kanserinin nasıl teşhis edildiği sorulduğunda, %30.0'unun bilmiyorum, Mammografi çektirmenin gerekli olup olmadığı sorusuna ise %31.9'unun gerekli bulmuyorum, %5.0'inin bilmiyorum cevabı verdikleri saptanmıştır. 20 yaş ve üzeri kadınların %71.3'nün KKMM yapmayı bilmediği, %72.0'nin ise KKMM yapmadıkları saptanmıştır. KKMM yapmayı gerekli bulanların (%56.0), yalnızca %47.6'nın KKMM uyguladıkları belirlenmiştir (X2: 36.690; P: 0.000).

Tartışma: Kadınların çoğunun KKMM'ni başta sağlık personeli olmak üzere yazılı ve görsel medya gibi çeşitli kaynaklardan duymuş olduklarını bildirmelerine karşın, KKMM yapma oranları çok düşük bulunmuştur. Bu nedenle; • Kırsal alanda yaşayan kadınlara meme kanseri, KKMM'si ve risk faktörleri hakkında eğitim verilerek farkındalıklarının artırılması, KKMM'ni nasıl yapacaklarını öğretmenin yanında sağlıklıyken KKMM yapmamın öneminin vurgulanması gerektiği düşünülmektedir.

Anahtar sözcükler: kadın, meme kanseri, kkmm, kırsal alan, hemşirelik

DETERMINE THE KNOWLEDGE OF THE WOMEN ABOUT BREAST CANCER AND THEIR PRACTICE ABOUT BREAST SELF EXAMINATION

ABSTRACT

Introduction: This study's aim was to determine the knowledge of the women about breast cancer and their practice about breast self examination who were 20 years old and above and live in Karaköy which is a country of Bolu.

Materials and Methods: This was a Cross-sectional and descriptive study. The research was carried on 150 woman.

Results: Socio-demographic features of the study group were; mean age of the women who were 20 years old and above was 45+/-18 (min:20, max:84), 72.7 % were maried, 65.3 % were graduated from primary school, 88.7 were housewives (n:150). In the applied questionare: 30.0 % of the study group didn't know how the breast cancer is diagnosed, 31.9 % of the women didn't believe the necessity of mammography, 5.0 % didn't know the necessity of mammography, 71.3 % of the women didn't know the breast self examination and 72.0 % didn't practice breast examination by herselves before. We found that only 47.6 % of the women do breast examination by herselves from 56.0 % who require to do breast self examination (X2:36.690; P: 0.000).

Discussion: Although most of the women learnt breast self examination firstly from health personnel than from press or mass media, practice of the examination was so low. That's why: • The women who live in the rural area must be educated about breast cancer, breast self examination and the risk factors. The necessity of the breast examination by herselves when they are healthy must be emphasised.

Keywords: woman, breast cancer, breast self examination, rural area, nursing

Giriş ve Amaç

Kanser, tüm dünyada olduğu gibi ülkemiz insanı için de önemli bir halk sağlığı sorunudur. Dünya Sağlık Örgütü (WHO), dünyada her yıl on milyon kişinin kansere yakalandığını, altı milyon kişinin ise kanserden öldüğünü bildirmektedir. Meme kanseri, kadınlarda en sık görülen kanser türüdür. Kadınlarda görülen kanserlerin %32'si ve kansere bağlı ölümlerin de %19'unu meme kanserleri oluşturmaktadır. Türkiye'de her yıl 30.000 kadın meme kanserine yakalanmaktadır (1,2,3,4,5). Meme kanserine yakalanmada rol oynayan pek çok faktör saptanmış ve bunların meme kanseri riskini artırdığı belirtilmiştir. Belirgin meme hastalığı, ailesel yatkınlık, genetik faktörler, geç yaşta gebelik, over aktivitesi, endokrin etkenler, erken başlayan menstrüel siklus, geç menapoz, geç yaşta doğum, hiç doğum yapmama ve laktasyonun kısa sürmesi, meme kanserine yakalanmada önemli faktörlerdir. Ayrıca alkol, sigara ve yağ oranı yüksek diyetle beslenmenin meme kanserinin gelişmesinde rol oynadığı da düşünülmektedir (6,7,8).

Gönderilme Tarihi: 04 Ocak 2010 • **Revizyon Tarihi:** 28 Ocak 2010 • **Kabul Tarihi:** 29 Ocak 2010

Günümüzde meme kanserini kesin olarak önleyen bir yöntem mevcut değildir. Fakat düzenli yapılan muayene ve taramalar yardımıyla meme kanserine erken tanı konulduğu takdirde beklenen yaşam süresi uzatılabilmekte ve tamamen iyileşme sağlanabilmektedir. Bu nedenle kadınların erken tanının önemini bilmeleri ve bu yönde bilgilendirilmeleri gerekmektedir. WHO raporunda (1998), meme kanserinden korunmaya yönelik olarak erken tanı ve tarama programlarını önermiştir. Amerikan Kanser Birliği ise ilk kez 1980 yılında erken tanı için gerekli yöntemleri belirlemiştir. Günümüzde bu yöntemler altın standartlar olarak belirlenmiş olup hala geçerliliğini korumaktadır. Meme kanserinde erken tanı için önerilen ve birbirini tamamlayan üç yöntem vardır. Bunlar "Kendi Kendine Meme Muayenesi" (KKMM), "sağlık personeli tarafından yapılan klinik muayene" ve "mamografidir". KKMM 20 yaşından itibaren her ayın adet bitimindeki 5.günde, post menapozal dönemdekiler için ise herhangi bir zamanda, ayda bir kez yapılması ve meme başı çöküklüğü, meme başı akıntısı, asimetri, portakal kabuğu görünümü vb. gibi şüpheli durumlarda sağlık personeline başvurması önerilir. Sağlık personeli tarafından klinik muayene, 20-40 yaş arası her üç yılda bir, 40 yaş üstündeki kadınlarda her yıl yapılmalıdır. Mammografi ise özellikle 40 yaş üstündeki kadınlara önerilmektedir (8,9,10).

Hemşireler Dünyanın birçok ülkesinde sağlıklı/hasta bireyin sağlık eğitiminde yer almaktadır. Meme kanseri ile ilgili olarak kadınların eğitiminde de hemşirelerin önemli rolleri bulunmaktadır. Ayrıca KKMM eğitimi, pek çok araştırmacı tarafından da önemli bir hemşirelik fonksiyonu olarak tanımlanmıştır. Hemşirenin bu eğitim işlevinde öncelikle kadınların meme kanseri ve KKMM ile ilgili olarak neleri bilip neleri bilmediğini ve risk grubunda yer alanları saptaması gereklidir. Bu nedenle 20 yaş üzeri kadınların meme kanseri ile KKMM hakkında bilgi ve uygulamalarının belirlenmesi önemlidir (6,8,9). Bu çalışma, Bolu İli Merkez Köylerinden Karaköy'de yaşayan 20 yaş ve üzeri kadınların meme kanseri bilgisi ve kendi kendine meme muayenesi uygulamalarını belirlemek amacıyla yapılmıştır.

Yöntem ve Gereçler

Bu çalışma kesitsel tipte, tanımlayıcı bir çalışmadır. Vehbi Koç Vakfı Hemşirelik Fonu tarafından finanse edilen "Toplum Merkezli Hemşirelik Bakımı: Eğitim-Uygulama Entegrasyonu" projesinin bir bölümünü oluşturmaktadır. Projenin amacı: öğretim elemanları ve öğrencilerin Toplum Merkezli Hemşirelik Bakım ve Uygulamalarını gerçekleştirebileceği bir uygulama alanı oluşturmak, hemşirelik bakım ve uygulamalarına rehber oluşturacak sağlıkla ilgili temel verileri toplayarak bazı sağlık sorunlarını (sağlık kuruluşuna başvuru durumu, aile işlevi, kronik hastalık, meme kanseri ve meme muayenesi, doğurganlık çağındaki kadınlar ve sorunları, ev kazaları, yaşlılık dönemi ve sorunları) saptamaktır. Bolu Sağlık Yüksekokulu öğretim elemanları ve öğrencilerinin Toplum Merkezli Hemşirelik Bakımının Eğitim-Uygulama Entegrasyonu için pilot bölge olarak Karaköy Şenol Sağlık Evi seçilmiştir. Araştırmanın evrenini, Bolu il merkezindeki Doğancı Sağlık Ocağı'na bağlı Karaköy Şenol Sağlık Evi ve buraya kayıtlı 102 hanedeki toplam 412 kişi oluşturmuştur. Karaköy'de ikamet edenlere Hane Halkı Anketi uygulanarak temel bir veri tabanı oluşturulmuş, araştırmalar için veri tabanından her bir alana özgü örneklem belirlenmiş, soru formları uygulanmış; eğitim ve bakım uygulamaları gerçekleştirilmiştir. Hane Halkı veri tabanından meme kanseri açısından risk grubuna giren 20 yaş ve üzeri kadınlar belirlenerek örneklem seçilmiştir. Buna göre Karaköy'de oturan 20 yaş ve üzeri 166 kadının çalışmanın evren ve örneklemini oluşturması planlanmıştır. Bu kadınlardan 150 tanesine ulaşılmış olup çalışma toplam 150 kadının katılımıyla yapılmıştır.

Veriler Mayıs-Haziran 2007 tarihleri arasında halk sağlığı uygulamasına çıkan öğrenciler ve araştırmacılar tarafından toplanmıştır. Soru formu literatüre dayalı olarak üç bölümden oluşmaktadır. Birinci bölümde sosyo-demografik özellikler, ikinci bölümde meme kanseri bilgisi, üçüncü bölümde ise Kadınların Kendi Kendine Meme Muayenesi bilgisi ve uygulama durumları yer almaktadır.

Bulgular

Tablo 1'e bakıldığında çalışmaya katılan kadınların sosyo-demografik özellikleri görülmektedir. Buna göre; Karaköy'de yaşayan 20 yaş ve üzeri kadınların yaş ortalaması 45 ± 18 (min:20, max:84) olup, %72.7'sinin evli, %81.3'nün çocuğu olduğu, %65.3'nün ilkokul mezunu, %88.7'sinin ev hanımı, %59.3'nün sosyal güvencesinin SSK olduğu ve %86'sının sosyal güvenceden yararlandığı belirlenmiştir (n: 150).

Kadınların sağlık algılarına bakıldığında genel olarak son 15 günde; %65'i kendilerini iyi algıladıklarını ifade etmişlerdir. Kadınların sağlık alışkanlıkları incelendiğinde, tamamının (%100) alkol kullanmadığı, %4.9'nun halen sigara kullandığı, %78'nin hiç egzersiz yapmadığı, görülmüştür.

Karaköy'deki kadınların yarıya yakınının (%46.1) beyaz et, sebze ve meyve ağırlıklı beslendikleri, %3.0'nün ağırlıklı olarak kırmızı et tükettiği, yalnızca %1.2 'sinin yağlı yiyecekleri ağırlıklı olarak tükettikleri saptanmıştır.

Çalışmaya katılan kadınların %4.7'sinin ailesinde meme kanseri olan biri olduğu tespit edilmiştir. Kadınların yalnızca bir tanesinin (%0.7) şu anda meme kanseri olduğu, %16.0'sının ise çevresinde meme kanseri olan bir tanıdığı olduğu belirlenmiştir. Karaköy'deki kadınların hiç birinin birinci derece akrabasında meme kanseri bulunmadığı görülmüştür. Kadınların %13.3'ü daha önce meme muayenesi yaptırdığını ifade etmiştir. Çalışmamızda kadınların ilk adet yaş ortalaması 13.1± 1.1 yıl (min:10, max:15, n:150), %56.7'nin adet düzensizliği olduğunu söyledikleri, %82.0'nin ise çocuk sahibi olduğunu (n:150) ve %2.5'nin ilk çocuğunu 30 yaş üzerinde doğurduğu saptanmıştır (n: 122). Çalışmamızdaki kadınların memeye ilişkin yakınmaları incelendiğinde, %13.8'inin daha önce meme muayenesi olduğu ve şuanda %1.3'ünün memesinde kitle, %2.6'sında memede buruşma, %8.6'sında memede sarkma, %2'sinde memede içe çökme, %2.7'sinde memede damarlaşma olduğunu söyledikleri belirlenmiştir (n: 150).

Çalışmamıza katılan kadınlara meme kanserinin nasıl teşhis edildiği sorulduğunda, kadınların %30'u bilmiyorum yanıtını vermiştir. Ancak kadınların menapoz (%16.7), kontrol (%41.7), ağrı (%41.7) nedeniyle daha önce mammografi çektirdiği (%3.1) belirlenmiştir. Mammografi

Tablo 1. 20 Yaş ve üzeri kadınların sosyo-demografik özellikleri

	n	*(%)*
Yaş Grubu		
20-39 yaş	63	42.0
40 ≥	87	58.0
Medeni durumu		
Bekar	21	14.0
Evli	109	72.7
Dul+Boşanmış	20	13.3
Eğitim düzeyi		
Okur-yazar değil	18	12.0
Okur-yazar/ilkokul	103	68.6
Ortaokul ve üstü	29	19.4
İşi		
Ev Hanımı	133	88.7
Emekli	2	1.3
Memur	5	3.3
İşçi	5	3.3
Öğrenci	5	3.3
Sosyal Güvence Tipi		
SSK	89	59.3
Emekli Sandığı	24	16.7
Bağ-Kur	23	15.3
Yok	13	8.7
Sağlık Algısı (n: 123)		
Çok İyi	8	6.5
İyi	80	65.0
Orta	26	21.1
Kötü	9	7.3
Sigara İçme Durumu (n:123)		
Evet	6	4.9
Hayır	114	92.7
Bırakmış	3	2.4
Egzersiz (n: 123)		
Hafta 4-5kez hafif	7	5.7
Ara sıra/Bazen	17	13.8
Hiç	96	78.0
Yalnızca Hafta Sonları	3	32.4

Tablo 2. Kadınların KKMM'ni ile ilgili bilgi kaynakları (n:93)

Bilgi Kaynağı	*n*	*%*
Sağlık personeli	43	(46.2)
Tv/Gazete/Dergi/Broşür	38	(40.9)
Arkadaş/Akraba/Komşu	12	(12.9)
Toplam	**93**	**100.0**

Tablo 3. Kadınların KKMM ile ilgili farkındalık durumları (n: 150)

	n	%
KKMM Daha Önce Duyma Durumları		
Evet	93	(62.0)
Hayır	57	(38.0)
KKMM Yapmayı Biliyor musunuz?		
Evet	43	(28.7)
Hayır	107	(71.3)
KKMM Yapıyor musunuz?		
Evet	42	(28.0)
Hayır	108	(72.0)
KKMM Yapmak Sizce Gerekli mi?		
Evet	84	(56.0)
Hayır	11	(7.3)
Bilmiyorum	55	(36.7)
Toplam	**150**	**100.0**

çektirmenin gerekli olup olmadığı sorusuna; %31.9'u gerekli bulmuyorum ve %5'i ise bilmiyorum şeklinde cevap vermiştir.

Karaköy'de yaşayan kadınların KKMM'yi duyma durumları incelendiğinde %62'si duyduğunu (n:93) (Tablo 3) ve %46.2'si sağlık personeli, %40.9'u televizyon/gazete/dergi/broşür, %12.9'unun ise arkadaş/komşu/akraba'dan duyduklarını söyledikleri saptanmıştır (n:93) (Tablo 2). Çalışmamızda kadınların %71.3'nün KKMM yapmayı bilmediği, %72.0'nin ise KKMM yapmadıkları saptanmıştır (n:150) (Tablo 3). KKMM yapmayı gerekli bulanların (%56), yalnızca %47.6'nın KKMM uyguladıkları belirlenmiştir (X^2: 36.690; P: 0.000). Bu sonuç istatistiksel açıdan ileri düzeyde anlamlı bulunmuştur (Tablo 4).

Yaş gruplarına göre bakıldığında KKMM yapan kadınların dağılımı benzer gibi görünmesine karşın çoğunlukla (%34.9) 20-39 yaş grubundaki kadınların KKMM yaptıklarını söyledikleri belirlenmiştir (X^2:2.581; P:0.078) (Tablo 4). Aynı zamanda bu kadınların ¾'ünden fazlasının (%79.4) sağlıklarını iyi algıladıkları tespit edilmiştir (X^2:4.703; P:0.195).

Yaş gruplarına göre KKMM yapma durumları incelendiğinde 20-39 yaş grubundakilerin %65.1'nin, 40 yaş ve üzeri grubun ise %77'sinin KKMM yapmadıkları saptanmıştır (X^2:2.581, P:0.078). Öğrenim düzeyi lise olanların %61.5'i, yüksekokul olanların ise %50'si KKMM yapıyorken, okuma-yazması olmayanların tamamının (%100), KKMM yapmadıkları tespit edilmiş ve bu bulgu istatistiksel olarak anlamlı bulunmuştur (X^2: 17.205; P: 0.004).

Tartışma

Çalışmaya katılan kadınlar çoğunlukla 40 yaş ve üzeri grupta olup, yaş ortalamaları 45 ± 18 (min: 20, max: 84) dir. Kadınların %72.7'sinin evli, %81.3'nün çocuğu olduğu, %65.3'nün ilkokul mezunu, %88.7'sinin ev hanımı, %59.3'nün SSK'lı olduğu ve %86'sının sosyal güvenceden yararlandığı belirlenmiştir (n: 150). Bu sonuçlardan çoğunlukla ilkokul mezunu, ev hanımı ve SSK'lı olma durumları Çadır ve arkadaşlarının (2004) aynı amaçla yaptıkları çalışma bulgularıyla benzer görünmektedir (10).

Sigara içmenin meme kanseri de dahil olmak üzere pek çok kanser türüne yakalanma riskini artırdığı bildirilmektedir (8). Bizim çalışmamız-

Tablo 4. Yaş grubu ve KKMM'ni gerekli bulma durumuna göre KKMM yapma durumları (n=150)

	KKMM Yapıyor n (%)	*KKMM Yapmıyor n (%)*	*Toplam*	*X^2 P Değeri*
Yaş Grupları				
20-39 yaş	22 (34.9)	41 (65.1)	63 (42.0)	X^2: 2.581
40 ≥	20 (23.0)	67 (77.0)	87 (58.0)	p= 0.078
KKMM 'ni Gerekli Bulma Durumu				
Evet	40 (47.6)	44 (52.4)	84 (56.0)	X^2: 36.690
Hayır	1 (9.1)	10 (90.9)	11 (7.3)	p= 0.000
Bilmiyorum	1 (1.8)	54 (98.2)	55 (36.7)	
Toplam	42 (28.8)	108 (72.0)	150 (100)	

da kadınların sağlık alışkanlıkları incelendiğinde (Tablo1), tamamının alkol kullanmadığı ve %5.6'sının halen sigara kullandığı, %1.2'sinin ise beslenirken ağırlıklı olarak yağlı yiyecekleri tükettiği ve %78.0'nin hiç egzersiz yapmadığı (n:123) görülmüştür. Alkol alımı ile meme kanseri arasındaki ilişki halen tartışmalı olmakla birlikte, vaka-kontrol ve prospektif çalışmalar alkol alımındaki artışa paralel olarak meme kanseri riskinin de arttığını göstermektedir (7). Çalışmamızda kadınların hiç biri alkol tüketmediği için meme kanserine yatkınlık açısından alkole ilişkin risklerinin bulunmadığı düşünülmüştür.

Dünya üzerinde meme kanseri görülme sıklığının ülkeden ülkeye değişmesi ve göç eden insanlarda meme kanseri sıklığının göç ettikleri ülkede ki meme kanseri sıklığına erişmesi nedeniyle dikkatler genetik faktörlerden çok çevresel etkenler ve beslenme üzerine toplanmıştır. Yağdan zengin beslenmenin ve kırmızı et tüketiminin fazla olmasının meme kanserini artırdığı, meyve sebzeden zengin ve yağdan fakir diyetle beslenmenin bu riski azalttığı bildirilmektedir (7). Karaköy'deki kadınların yarıya yakınının (%46.1) beyaz et, sebze ve meyve ağırlıklı beslendikleri, %3.0'nün ağırlıklı olarak kırmızı et tükettiği, yalnızca %1.2 'sinin yağlı yiyecekleri ağırlıklı olarak tükettikleri saptanmıştır. Bu nedenle beslenme alışkanlıkları açısından genel olarak risk düşük gibi görünmesine karşın 3/4'nün (%78.1) hiç egzersiz yapmıyor olması önemli bir risk faktörü gibi görünmektedir. Karaköy deki kadınların kırmızı et tüketimi ve yağlı yiyecek tüketimi fazla olması yanında egzersiz yapmıyor olmaları açısından bu grubun risk taşıyabileceği için bilgilendirilmeleri gerekmektedir.

Aile öyküsü ve meme kanseri ilişkisi de oldukça araştırılan bir noktadır. Ailesinde meme kanseri olanlarda meme kanseri olma riskinin yüksek olacağı belirtilmektedir. Özellikle annesi, kız kardeşi gibi birinci dereceden akrabalarının herhangi birinde meme kanseri olanlarda risk 2 kat artmaktadır (7,8). Çalışmaya katılan kadınların %4.7'sinin ailesinde meme kanseri olan biri olduğu tespit edilmiştir. Kadınların yalnızca bir tanesinin (%0.7) şu anda meme kanseri olduğu, %16.0'sının ise çevresinde meme kanseri olan biri olduğu saptanmıştır. Karaköy'deki kadınların hiç birinin birinci derece akrabasında meme kanseri bulunmadığı görülmüştür. Çalışmamızda kadınların menarş yaş ortalaması 13.1± 1.1 yıl (min:10, max:15, n:150) olarak belirlenmişti. Kadınların %56.7'sinin adet düzensizliği olduğunu söyledikleri, %82'sinin ise çocuk sahibi olduğunu (n:150) ve %2.5'inin ilk çocuğunu 30 yaş üzerinde doğurduğu saptanmıştı (n: 122). Özaydın ve arkadaşlarının çalışmasına göre (2009) kadınların ilk adet yaşı ortalaması 13.1 ± 1.3 yıl (min 9, max 21) olduğu ve katılımcıların %7.8'inin ilk adet yaşının 12'den erken olduğu, kadınların %6.6'sının hiç doğum yapmamış oldukları saptanmıştır (9). Kadınların ilk adet yaşı (menarş) ve yaş ortalamasına ilişkin bulgu bizim çalışmamızın bulguları ile benzerdir. Aynı çalışmaya göre araştırma grubundaki kadınların %6.6'sının hiç doğum yapmadığı, %11'inin ise 30 yaşından sonra ilk doğumlarını yaptıkları belirlenmiştir. Bizim çalışmamızda 30 yaş üstünde doğum yapan kadın sayısının (%2.5) daha az bulunmuştur. Bunun nedeninin bizim çalışmamızın kırsal alandaki kadınlarda yapılmış olmasıyla ve kırsal alanda evlenme ve çocuk sahibi olma yaşının büyükşehirde yaşayan kadınlara göre daha erken oluşuyla bağlantılı olabileceği düşünülmüştür. Çalışmamızdaki kadınlardan memeye ilişkin yakınmaları incelendiğinde, %13.8'inin daha önce meme muayenesi olduğu ve şuanda %1.3'ünün memesinde kitle, %2.6'sında memede buruşma, %8.6'sında memede sarkma, %2'sinde memede içe çökme, %0.7'sinde meme başında akıntı ve kan, %2'sinde memede damarlaşma olduğunu söyledikleri belirlenmiştir (n: 150).

Meme kanserinden korunmanın ve mortaliteyi azaltmanın en güvenilir yolu farkındalık yoluyla erken tanı ve tedavidir. Erken tanının sağlanması ise kadınların bu konuda bilgilendirilmesi ve tarama programlarının uygulanması ile olacaktır. Bu tarama programlarının amacı hiçbir şikayeti olmayan kadınlarda memesinde herhangi bir anormallik olanlarla olmayanları ayırt etmektir. Kendi Kendine Meme Muayenesi (KKMM), mamografi ve klinik meme muayenesi kanserin erken tanısı için önerilen başlıca erken tanı yöntemleridir (6,10). Çalışmamıza katılan kadınlara meme kanserinin nasıl teşhis edildiği sorulduğunda, kadınların %30.0'u bilmi-

yorum yanıtını vermiştir. Kadınların menapoz (%16.7), check-up (%41.7), ağrı (%41.7) nedeniyle daha önce mammografi çektirdiği (%3.1) belirlenmiştir. Mammografi çektirmek gerekli mi? sorusuna; %31.9'u gerekli bulmadığını ve %5'i ise bilemediğini söylemiştir.

Günümüzde kadınların meme kanseri ve erken tanı konusunda duyarlılıklarını artırmak için sağlık eğitimcileri, televizyon, gazete, dergi, broşür ve internet gibi çeşitli kitle iletişim araçlarını yaygın olarak kullanmaktadır (6,10). Çalışmamızda kadınların KKMM'yi duyma durumları incelendiğinde %62'si duyduğunu ve %46.2'si sağlık personeli, %40.9'u televizyon/gazete/dergi, %12.9'u arkadaş/komşu/akraba'dan duyduklarını söylemişlerdir. Fındık ve Turan'ın çalışmasında da kadınların KKMM'yi duyma durumu %49.9, bu bilgiyi televizyon, gazete, dergi, broşür ve arkadaştan duyma durumu %56.9 olarak bulunmuştur. Güner ve arkadaşları (2007), KKMM duyma durumunu %49.8 olarak tespit etmişlerdir. Aynı çalışmada KKMM'yi %17.4'ünün TV, %38.8 sağlık personeli, %33.8'nin de komşu/akrabadan duyduklarını saptamışlardır. Çadır ve arkadaşlarının çalışmasında ise, %24.1'i sağlık personeli, %42.4'ü TV/gazete/dergi/broşür, %13.5'i ise arkadaş/komşu/akraba olarak bulunmuştur (11,12).

KKMM meme kanserini kesin olarak tanılayan bir yöntem olmamasına karşın, kadınların kendi bedenleri üzerindeki farkındalıklarının artması ve meme kanseri konusunda daha duyarlı olmalarını sağlaması açısından önemlidir. Diğer taraftan meme kanseri vakalarında kitlenin, çoğunlukla kadının kendisi tarafından saptandığı da vurgulanmaktadır (10). Bu nedenle kadınların KKMM yapma durumlarının belirlenmesi önemli görünmektedir. Çalışmamızda kadınların %28.7'nin KKMM bildiği, %28'nin KKMM yaptığı, %56'sının KKMM'yi gerekli bulduğu saptanmıştır (n:150). KKMM yapmayı gerekli bulanların (%56), yalnızca %39.3'nün KKMM uyguladıkları belirlenmiştir (X^2: 30.949, P: 0.000). Bu sonuç istatistiksel açıdan ileri düzeyde anlamlı bulunmuştur. Kadınların KKMM yapmaları ile ilgili literatür incelendiğinde, Akyolcu'nun çalışmasında %32.5, Çadır'ın çalışmasında %45, Güner ve arkadaşlarının çalışmasında %47.9 olarak belirlenmiştir. Bizim çalışmamızda kadınların KKMM yapma durumlarının düşük olması kadınların kırsal alanda yaşaması, meme kanserine ilişkin yeterli bilgilerinin olmaması ve farkındalık düzeylerinin düşük olmasıyla ilişkili olabileceği söylenebilir.

Yurt dışında yapılmış çalışmalara bakıldığında, Çinli kadınlar arasında yapılan bir çalışmada kadınların % 16'sının son bir yıldır her ay KKMM yaptığı bulunmuştur. Klug tarafından 25-75 yaş grubundaki Alman kadınlar üzerinde yapılan çalışmada ise kadınların %43.1'inin aylık KKMM yaptığı bulunmuştur. Harris ve arkadaşları tarafından Amerika'da yapılan bir çalışmada da kadınların %40.8'inin son bir yıl içinde en az 9 kez KKMM yaptığı belirlenmiştir. Kore'de 35-65 yaş grubundaki kadınlar arasında yapılan bir çalışmada kadınların düzenli olarak meme muayenesi yapma sıklığının %25.3 olduğu belirlenmiştir (10). Literatürde bu oranlardaki değişikliğin nedenleri incelendiğinde, Nahçivan ve Seçginli'nin makalesine göre, kadınlarda erken tanıya ilişkin tutum ve davranışları etkileyen birçok neden olabilir. Bu nedenler arasında; bireyin kültürel inançları, sağlık/hastalık algısı, aile ve çevre desteği, hastalığa yönelik bilgisi ve risk algısı, hastalığın erken dönemde tanılanmasında önemli olan uygulamalara olan inancı vb. faktörler yer almaktadır şeklinde ifade edilmiştir (13,14).

Bizim çalışmamızda kadınların aile ve çevre desteği alma durumu, kültürel inançları incelenmemiş olup yalnızca sağlık algılarına bakılmıştır. Buna göre, kadınların yarıdan fazlası kendilerini iyi algıladıklarını ifade etmiştir. KKMM yapanların ¾'ünden fazlasının (%79.4) sağlık algısının iyi olduğu belirlenmiştir (X^2:4.703, P:0.195). Bu nedenle bizim çalışmamızda kadınların KKMM yapmamalarının bu konu hakkında yeterli bilgiye sahip olmamaları yanında sağlık algılarının iyi olması yani kendilerini sağlıklı hissetmeleri ile de ilişkili olabileceğini düşündürmüştür.

Yaş gruplarına göre KKMM yapma durumları incelendiğinde 20-39 yaş grubundakilerin %74.6'sının, 40 yaş ve üzeri grubun ise %79.5'inin KKMM yapmadıkları saptanmıştır (X^2: 0.514, P: 0.300). Öğrenim düzeyi lise olanların %50'si, yüksekokul olanların ise %30'u KKMM yapıyorken, okuma-yazması olmayanların tamamının (%100), KKMM yapmadıkları tespit edilmiş ve bu bulgu istatistiksel olarak anlamlı bulunmuştur (X^2: 13.426, P: 0.020). Okuma-yazması olmayanların KKMM yapmama nedenlerinin gazete/dergi/broşür gibi yayınlardan yararlanamamaları, KKMM'ni nasıl yapacağını bilememeleri, meme kanseri ve KKMM'ne ilişkin farkındalıklarının olmayışıyla ilişkili olabileceği söylenebilir.

Sonuç ve Öneriler

Kadınların çoğunluğunun 40 yaş üzerinde, ilkokul mezunu ve ev hanımı oldukları saptanmıştır. Çalışmamızda yer alan kadınlarda meme kanserine ilişkin önemli bir bulguya rastlanmamış olup meme başında çökme, sarkma, damarlaşma gibi bulgular olduğunu ifade eden kadınlar Aile Sağlığı Hekimine yönlendirilmiştir. Kadınların çoğunun KKMM'yi başta sağlık personeli olmak üzere yazılı ve görsel medya gibi çeşitli kaynaklardan duymuş olduklarını bildirmelerine karşın, KKMM yapma oranları çok düşük bulunmuştur. Okuma-yazması olmayan kadınların ise tamamının KKMM yapmadıkları saptanmıştır. Bu nedenle;

- Kırsal alanda yaşayan kadınlara meme kanseri, KKMM ve risk faktörleri hakkında eğitim verilerek farkındalıklarının artırılması, KKMM'yi nasıl yapacaklarını öğretmenin yanında sağlıklıyken KKMM yapmamın öneminin vurgulanması,
- Sağlık personelinin kadınlara KKMM'yi anlattıktan sonra birkaç kez uygulama yaptırması, belli aralıklar eğitimlerin tekrarlanması,
- KKMM uygulama noktasında kadınların kültürel inançları, aile ve çevre desteği, hastalığa yönelik bilgisi ve risk algısı gibi hastalığın erken dönemde tanılanmasına ilişkin çalışmaların yapılması gerektiği düşünülmektedir.

Teşekkür

Vehbi Koç Vakfı Hemşirelik Fonu tarafından finanse edilen bu çalışmanın yapılmasına imkan sağlayan "Toplum Merkezli Hemşirelik Bakımı: Eğitim-Uygulama Entegrasyonu" projesinin yürütücüsü Prof.Dr.Feray GÖKDOĞAN'a ve proje veri toplama aşamasında katkı sağlayan 4.sınıf Halk Sağlığı Hemşireliği Dersi alan öğrencilerimize teşekkür ederiz.

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The Journal of Breast Health
meme sağlığı dergisi

The Journal of Breast Health 2010 Vol: 6 • No: 2
Meme Sağlığı Dergisi 2010 Cilt: 6 • Sayı: 2

CASE REPORT/OLGU SUNUMU

OSTEORADIONECROSIS ON THE CHESTWALL DUE TO RADIOTHERAPY

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ABSTRACT

Osteoradionecrosis is a rare, but severe complication of radiation therapy in patients with breast cancer. Radionecrosis developed in a 40-year-old patient 10 months after radiation therapy for breast cancer. The patient was hospitalized and operated on for chest wall necrosis. The results of the treatment were evaluated and discussed under the light of the literature.

Key words: osteoradionecrosis, chest wall, breast cancer

GÖĞÜS DUVARINDA RADYOTERAPİYE BAĞLI OSTEORADYONEKROZ

ÖZET

Osteoradyonekroz (ORN), meme kanserinin radyoterapi ile tedavisinden sonra nadir görülen, ancak ciddi bir komplikasyondur. Bu yazıda, meme kanseri tanısı ile radyoterapi uygulanan, bu tedaviden 10 ay sonra ORN gelişen ve kliniğimize yatırılarak tedavi edilen 40 yaşındaki bir hasta sunulmakta ve bu komplikasyon ile ilgili bilgiler gözden geçirilerek tarışılmaktadır.

Anahtar sözcükler: osteoradyonekroz, göğüs duvarı, meme kanseri.

Introduction

Osteoradionecrosis (ORN) is a severe complication of radiation therapy in patients with breast and lung cancers. While more frequent in the era when radiotherapy (RT) was carried out through conventional techniques and ortho-voltage devices, ORN is now less commonly witnessed due to the use of modern devices in radiation therapy and better planned treatment regimens (1-4). The treatment of ORN is difficult and includes the control of infections via antibiotics, surgical debridement, hyperbaric oxygen treatment, resection of chest-wall, and reconstruction (5).

In this report, the findings of a patient dying of osteoradionecrosis and the treatment developing as a result of adjuvant radiotherapy performed with the diagnosis of breast cancer have been evaluated and discussed.

The case

In the mammographic, ultrasound, and magnetic resonance imaging (MRI) of the 40-year-old coming into the clinic with a complaint of a mass in her right breast, solid lesions in the sizes of 20x29mm, 16x10 mm, and 7x4 mm in the right breast and lymph nodes in the axillary region were determined. Invasive ductal carcinoma was removed as a result of through-cut biopsy. The patient was clinically diagnosed with stage-IIIB (cT2multicentric N2 M0) breast cancer. She was discussed at The Council of Breast Cancer, Medical School of Istanbul University. The Council recommended that neo-adjuvant chemotherapy, surgery, chemotherapy, radiotherapy, and treatment of tamoxifen. After the administration of 3 courses of 5- Florourasil, Epirubisin, Cyclophosphamite neoadjuvant treatment (FEC), and the surgical treatment was decided to be carried out with the determination of partial remission (the size of the biggest tumor decreased to 15 mm and all the lymph ganglions in the axillary region could not palpably be felt: cT1N0M0). Because of clinical non-palpation of the axilla, sentinel biopsy of lymph nodule was performed with blue dye and radioisotope due to previously prepared protocol. Although 2 noted sections of sentinel lymph nodules were found to be negative during frozen section investigation, as a result of protocol, axillary dissection and mastectomy were performed, as the cancer was multicentric prior to treatment. In the pathological evaluation of the removed specimen, only one tumor of 15 mm in the breast (the other two disappeared as a result of chemotherapy) and all of 12 lymph nodules in the axilla were found to be negative. In the histopathological evaluation; nuclear grade was reported to be 3, lymphovascular invasion to be present, estrogen receptor (ER) positive at the rate of 10%, progesterone receptor (PR) to be positive at the rate of 20%, and HER-2 to be negative. Adjuvant radiotherapy (RT) given for peripheric lymphatic radiation and thorax wall of the patient administered postoperative 3 cures of FEC was given radiation therapy as 5000 cGy at 25 fractions using linear accelerator, and then tamoxifen treatment of 20 mg/day/5 years started to be administered. As a result of the development of deep vein thrombosis one month after the tamoxifen,

Gönderilme Tarihi: 06 Temmuz 2009 • **Revizyon Tarihi:** 13 Temmuz 2009 • **Kabul Tarihi**: 24 Temmuz 2009

Figure 1. Osteoradionecrosis in the field of radiotherapy.

this treatment was discontinued, and the patient was given medical ovarian ablation (goserelin) was routinely followed up. In the patient, a wound not recovering in the radiation area 10 months after the radiotherapy occurred. The finding of the biopsy performed in this area was reported as "chronic infection with necrosis." According to the results obtained from wound debridement, irrigation with physiological saline, and culture from the wound, a treatment regime with antibiotics was started (Picture 1). Due to the slow improvement, the wound was re-debrided and Vacuum Assisted Closure (VAC) was applied. Since the strain of "pseudomonas aeruginosa" was produced in the culture samples taken from the wound, the antibiotics were altered. In the tomography of thorax wall, MRI, and bone scintigraphy; a diffusal increase was determined during vascularization in the lower part of the right hemithorax, and there was no increase in the osteo-blastic activity. These results and histopathologic examination suggested necrosis of radiation. As a consequence of the result that no desired improvement of the wound could be obtained through conservative and minimally invasive treatments given over nearly 3 months, surgical treatment was decided to be performed on the patient with the consultation of the clinics of thorax surgery and plastic reconstructive surgery. The resections of right frontal chest wall and fibrotic lung, the flap of rectus abdominis muscle (TRAM), and free skin grafts, as well as repair operations, were performed in the patient. Histopathology of the removed material revealed common necrosis, chronic infection, and fibrosis in the bone and striated muscle tissue, fibrosis, and pneumonic infiltration in the lung tissue. Eight days after the surgery, the patient had sepsis and died from multiple organ failure.

Discussion

An important treatment providing local control in the multidisciplinary treatment of breast cancer is radiation therapy (RT). While radiotherapy decreases the rate of local recurrence after conservative surgical treatment of the breast is more than 50%, it is emphasized in various studies that it also provides the patients with a high rate of survival (6, 7, 8). The existence of adjuvant radiotherapy performed after mastectomy is also controversial. Thorax wall and regional lymphatic radiation therapy is almost routinely performed in the patients with tumors of a size of more than 4 cm and in those with the involvement of four or more lymph nodes the axilla (9-13). In the patients with lymph nodes between 1 and 3 involved in the axilla, there are also centers recommending radiotherapy by evaluating other prognostic factors (14-16).

Unless radiotherapy is performed with modern systems and techniques, thorax wall necrosis, ulceration on skin, brachial plexopathy, cardiac morbidity/mortality, secondary cancer, pneumonitis, edema of the arms, and costa fracture are encountered (17-19).

As the dose of radiation increases, the changes in the target tissue become correspondingly higher and irreversible depending on the increase. In doses over 4000 cGv, permanent changes take place in the bones; however, ORN produced in the doses over 6000 cGv becomes generally more resistant to conservative surgery. Contrary to the ortho-voltage devices leading to an increase of the absorption of radiation in the bone tissue, new megavoltage devices reduce the damage to the tissues in the areas where RT is applied (2,3). The use of fractioned RT techniques hyperfractioned and accelerated was reported to decrease the incidence of ORN (1). With the introduction of intensity adjusted RT (IMRT), the condition is expected to get more decreased. Still, despite all the developments in RT, ORN, even if rare, may also be seen (20).

Predisposing factors for ORN include the following: trauma, infection, inflammation, overdose RT application, involvement of the tumor with bone tissue or its occurrence around the bone tissue, and individual sensitivity and endurance characteristics of the patient (21). Application of radiotherapy after mastectomy may cause more damages in thorax walls and inner thorax organs (lungs, heart etc.), if the radiation technique, the device to be used, treatment planning, and dose of radiation are ignored. In our patient, radiotherapy applied after mastectomy increased this risk. The sensitivity of the patient to radiation is an important risk factor in the occurrence of this complication.

Pathogenesis of ORN is development of vascular necrosis stemming from radiation. Cytotoxic effects of radiation on the osteogenic layer cause soft tissue fibrosis, the blockage of endosseous arteries, hypoxic, hypocellular and hypo-vascular bones, and soft tissue. This decreases the recovery capacity of tissues with a decline in the development of matrices and deformation in the bone mineralization (22). In our patient, the development of deep vein thrombosis as a result of tamoxifen shows that the patient tends to be coagulopative and chemotherapy, and radiation slows down the circulation in the region and causes malnutrition with effects, such as vasculitis, thus it can be responsible from radio-necrosis.

The time in the formation of ORN after the completion of RT is variable and it may take a few months or many years. In a study of 33 cases including head and neck malignancy, the formation period of ORN after RT was between 4 and 228 months (23). It was 10 months in our patient.

The most frequent finding in ORN is pain, infection, or pathologic fractures. ORN can be diagnosed through joint evaluation of clinical findings, pathology, and radiology (20).

Although RT was applied at lower doses with modern devices in our case, the development of ORN may be related to infection seen in the wound after surgery. The infection is accepted as a predisposing factor for ORN (21). Moreover, it is reported that significant acute and chronic complications were formed in those with collagen vascular diseases after RT (24). Therefore, breast conservative treatment (local excision and breast irradiation) in those known to have collagen vascular diseases are accepted as contraindication (25).

ORN is a late and obstinate complication rarely seen after radiotherapy. Thus, even if modern RT devices and techniques are used, patients administered RT should be closely followed for early and late complications and effective treatment options should be implemented, if necessary.

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The Journal of Breast Health
meme sağlığı dergisi

The Journal of Breast Health 2010 Vol: 6 • No: 2
Meme Sağlığı Dergisi 2010 Cilt: 6 • Sayı: 2

CASE REPORT/OLGU SUNUMU

A RARE CASE: INVASIVE PAPILLARY CARCINOMA OF BREAST. DIAGNOSTIC CLUES IN FINE NEEDLE ASPIRATION CYTOLOGY

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Bu çalışma, IV.Ulusal Sitopatoloji Kongresinde sunulmuştur.

ABSTRACT

Fine needle aspiration cytology (FNAC) is an easy and rapid method in the differential diagnosis of breast masses. Papillary carcinoma, a rare malignant tumor of the breast, accounts for only 1-2% of the breast tumors. Benign and malignant papillary lesions of the breast can be difficult to distinguish in both cytological and histological preparations. Here we presented a case of suspicious lesion in FNAC, which was diagnosed as invasive papillary carcinoma in tissue.

Keywords: papillary carcinoma, breast, fine needle, aspiration cytology.

NADİR BİR OLGU: MEMENİN İNVAZİV PAPİLLER KARSİNOMU. İNCE İĞNE ASPİRASYON SİTOLOJİSİNDE TANI KOYDURUCU İPUÇLARI

ÖZET

İnce iğne aspirasyon sitolojisi (İİAS) meme kitlelerinin ayırıcı tanısında kolay ve hızlı bir yöntemdir. Papiller karsinom meme tümörlerinin sadece %1-2'ini oluşturan nadir malign tümörlerdendir. Memenin benign ve malign papiller lezyonlarını sitolojik ve histolojik preparatlarda ayırt etmek güç olabilir. Burada İİAS'nde şüpheli lezyon, dokuda invaziv papiller karsinom tanısı alan olgu sunulmaktadır.

Anahtar sözcükler: papiller karsinom, meme, ince iğne aspirasyon sitolojisi

Introduction

Papillary lesions of the breast have been evaluated in a wide spectrum ranging from benign intraductal papilloma (with or without atypia) to papillary carcinoma in situ and invasive papillary carcinoma (1). It could be difficult to distinguish benign and malignant papillary lesions of breast in cytological and histological preparations (2). In this paper, because of the difficulties that could be experienced in differential diagnosis of benign and malignant papillary lesions, we present FNAC findings of a special type of breast cancer, invasive papillary carcinoma, which was rarely encountered.

Case report

A centrally localized, 3 cm solitary mass with irregular contours was seen in the ultrasound evaluation of a 79 year-old female patient who presented to the general surgery outpatient clinic with a mass and bloody nipple discharge in the right breast. FNAC was planned to patient due to prior diagnosis of fibroadenoma and breast carcinoma. US-guided fine needle aspiration cytology was performed and then excisional biopsy was carried out because the mass was diagnosed as suspicious lesion.

There were abundant cells; cell groups which shows pleomorphism, columnar cells which were occasionally formed papillary structures, and scattered as single cells in some situations in the FNAC of firm mass with irregular contours which was fixed to surrounding tissue (Figures 1, 2, 3). Case was diagnosed as suspicious lesion after cytological examination so an excisional biopsy was suggested to distinguish between intraductal papilloma and papillary carcinoma. In the excisional biopsy specimen, a 3 cm mass was seen with irregular borders and central necrosis. Microscopically, it was seen that there were papillary, adenoid, and cribriform structures with increased arrangement around the fibrovascular core that fill the cystic spaces and these structures were lined by columnar epithelium. No myoepithelial layer was observed on the basal (Figures 4,5). Case was diagnosed as invasive papillary carcinoma by histopathological findings. In immunohistochemical staining, 3+ nuclear staining was obtained by estrogen and progesterone, whereas a negative result was obtained by cerB2.

Discussion

Papillary lesions of the breast account for less than 10% of benign breast lesions; while they were accounted from 0.5-2% of all malignant breast tumors (3, 4). Typically, it was seen more commonly in elderly women. Similar to our case, it was mostly seen in postmenopausal women (1, 4). Patients presented with mass and 30% of patients presented with bloody nipple discharge (3). Our patient also presented with bloody nipple discharge and a mass. Fifty percent of papillary neoplasms were located in the central

Gönderilme Tarihi: 05 Mayıs 2009 • **Revizyon Tarihi:** 02 Eylül 2009 • **Kabul Tarihi**: 02 Eylül 2009

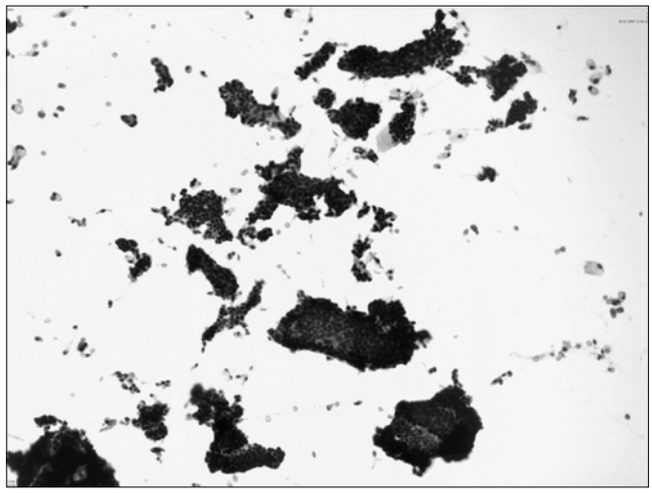

Figure 1. Hemosiderin-loaded histiocytes on cellular background, MGGx10

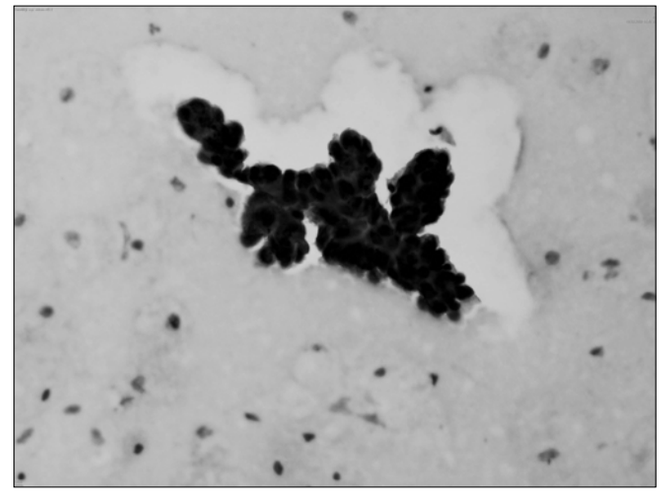

Figure 2. Papillary cell groups with nuclear hyperchromasia PAPx10

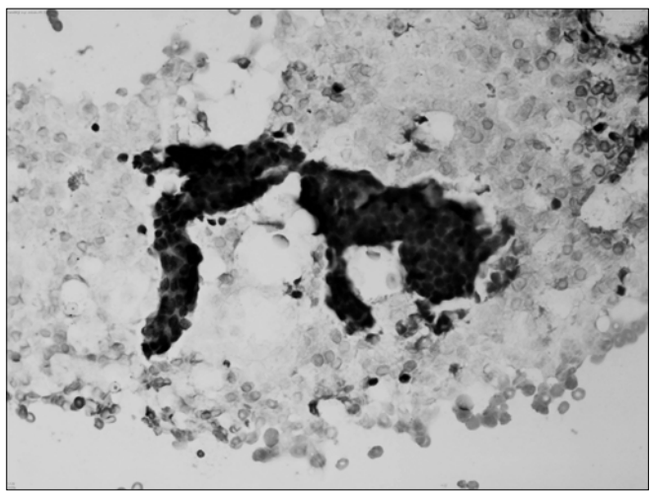

Figure 3. Papillary cell groups on hemorrhagic background PAPx10

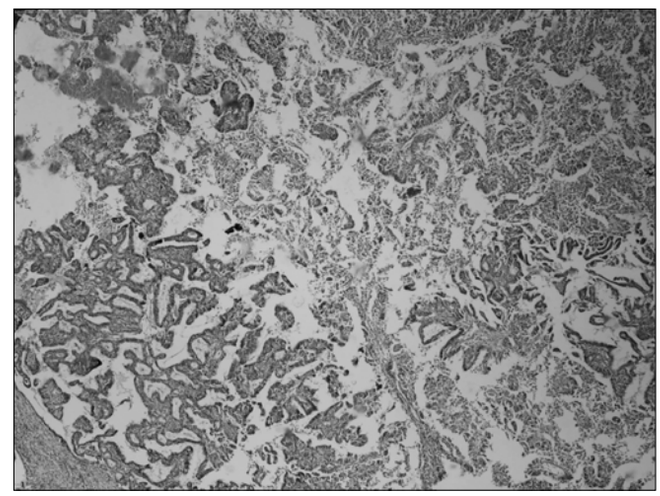

Figure 4. Invasive papillary carcinoma HEx20

region, as it was in our case (Table 1). Prognosis of papillary carcinoma was better when compared to invasive ductal carcinoma.

Papillary lesions of the breast have been evaluated in a wide spectrum ranging from benign papillomas to invasive papillary carcinomas (1, 2). Most papillary carcinomas are in situ lesions. The invasive component of papillary carcinomas could be not only papillary structures extending thorough fibrovascular core but it could also carry the features of invasive ductal carcinoma.

Cytological and histological differential diagnosis between benign and malignant papillary lesions of breast is difficult to establish. Cytological findings including hypercellularity, 3 dimensional cell groups which no longer display papillary structure, hemorrhagic background, hedge-like array of high columnar cells, scattered single cells, mild-moderate cellular atypia, regular or irregular contours, mixed cell type, single cell type, hemosiderin-loaded macrophages with foamy cytoplasm, apocrine metaplasia, mitosis, and calcification were used in the differential diagnosis of papillary lesions of breast (1, 2, 5, 6) (Table 2). Interestingly, in a study by Kumar et. al. (6), presence of eosinophilic bipolar cytoplasmic granules was reported in papillary carcinoma.

Table 1. Clinical findings in papillary lesions of breast

	Papilloma	***Tumor***
Incidence	Frequent	Rare
Age	Young, mean age 40 years	Elder, mean age 50-60 years
Nipple	Serous	Bloody
Size	<3cm	>3cm

In another study, Dawson et. al. (2) reviewed cytological criteria that should be used for discriminating papilloma and papillary carcinoma by comparing 29 fine needle aspiration cytology.

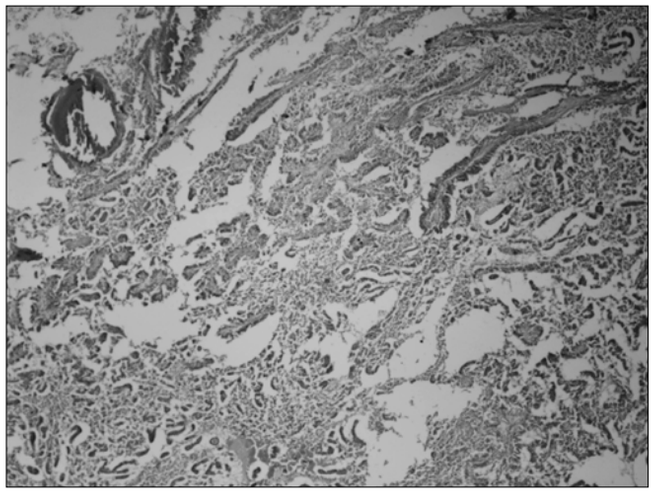

Figure 5. Papillary structures aligned around fibrovascular core HEx20

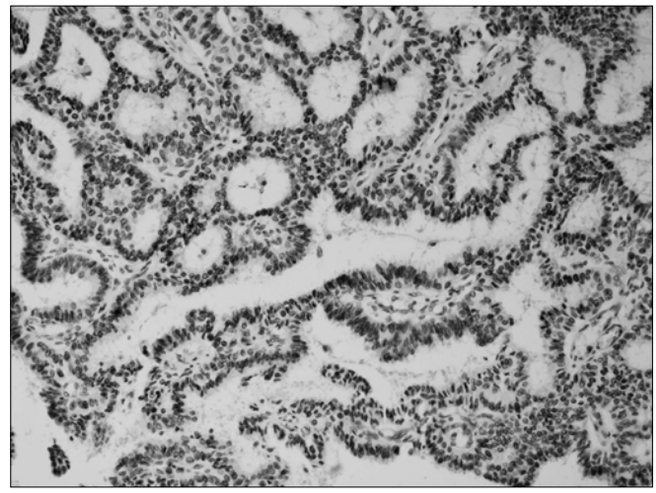

Figure 6. Immunohistochemical estrogen staininx40

Table 2. Cytological criteria those used in papillary lesions of breast

	In Favor of Papilloma	*In Favor of Tumor*	*In Our Case*
Hypercellularity		+	+
3 dimensional cells which no longer display papillary structure		+	+
Hemorrhagic background, necrosis		+	+
High columnar cells		+	
Scattered single cells		+	+
Mixed cell type	+		+
Single cell type		+	
Apocrine metaplasia	+		
Mild-moderate cellular atypia		+	+
Regular contour	+		
Irregular contour		+	+
Macrophages in background	+		
Mitosis		+	
Calcification		+	

Among of these, there was 7 intracystic papillary carcinoma, 6 invasive papillary carcinoma, and 17 intraductal papilloma. All cases underwent evaluation regarding cellularity, single epithelial cell, atypia, and papillary structures. Severely increased cellularity was found in 10 of 12 carcinomas and in 4 of 17 papilloma. Scattered single cell was found in 5 of 12 carcinomas and in 2 of 17 papilloma. There was mild-moderate atypia in most of the cases. Apocrine metaplasia, cells with foamy cytoplasm, and bipolar cells were observed in the background of 9 papilloma. No apocrine metaplasia was seen in any papillary carcinoma in this study. In the discrimination of papillary carcinoma from papilloma, absence of benign cells such as nuclear hyperchromasia, increase in arrangement, and apocrine metaplasia in the background was stated as diagnostic clues (2). In our case, there were nuclear hyperchromasia, single columnar cells, papillary structures, and increased cellullarity, but not apocrine metaplasia (Table 2).

In a study (5) by Simsir et. al., evaluated 70 cases which were consisted of 46 benign (23 intraductal papilloma, 6 intraductal papillomatosis, 11 fibrocystic changes, 6 fibroadenoma) and 24 malignant cases (1 low-grade phyllodes tumor, 23 ductal carcinoma in situ and invasive carcinoma). In this study, it was found that the criteria which show statistical significance between papilloma and carcinoma were cellularity, cellular atypia, and presence of single columnar cells. In the present case, a FNAC showed abundant cells, cell groups with pleomorphism, and columnar cells which were occasionally forms papillary structures and scattered as single cells in some situations. Due to diagnostic difficulties which could be faced in a FNAC, those criteria should be used in differential diagnosis in conjunction with what is presented in literature.

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The Journal of Breast Health
meme sağlığı dergisi

The Journal of Breast Health 2010 Vol: 6 • No: 2
Meme Sağlığı Dergisi 2010 Cilt: 6 • Sayı: 2

CASE REPORT/OLGU SUNUMU

PLEOMORPHIC LIPOSARCOMA OF THE BREAST MISDIAGNOSED AS CARCINOMA IN A TRU-CUT BIOPSY

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Bu çalışma, 9. Ulusal Meme Hastalıkları Kongresi'nde (2007) sunulmuştur.

ABSTRACT

Although liposarcomas are one of the more common sarcomas found in other tissues, they are among the rarest tumors in the breast. The purpose of presenting this case is to highlight one of rarest and interesting variant of breast sarcoma and the importance of misdiagnosis of liposarcoma in a tru-cut biopsy.

Keywords: breast sarcoma, liposarcoma, pleomorphic

TRU-CUT BİYOPSİ İLE YANLIŞ OLARAK KARSİNOM TANISI ALAN MEMENİN PLEOMORFİK LİPOSARKOMU

ÖZET

Liposarkomlar diğer dokularda en sık görülen sarkomlar içinde bulunmasına rağmen, meme tümörleri için en nadir görülenler arasındadır. Bu liposarkom olgusunu sunmadaki amaç, en nadir ve ilgi çekici meme sarkomlardan biri olması ve tru-cut biyopsi ile yanlış tanı verilmesinin önemini vurgulamaktır.

Anahtar sözcükler: meme sarkomu, liposarkom, plemorfik

Introduction

A primary breast liposarcoma is a tumor, representing 3-24% of all breast sarcomas. Breast sarcomas comprise approximately <1% of all malignant breast tumors (1). Preoperative diagnosis is important in planning the most appropriate type of treatment. Here, we report a case of primary pleomorphic liposarcoma of the breast, first initially diagnosed as carcinoma in a tru-cut biopsy.

Case report

A 55-year-old Albanian woman was admitted to a hospital in Albania with a mass in her right breast. She had no significant previous medical history. A tru-cut biopsy was performed and the diagnosis was breast carcinoma. The treatment administered consisted f four courses of chemotherapy. No surgery was performed. She came to us due to an increase in the growth of the mass in her right breast after chemotherapy. The physical examination revealed redness, tenderness, induration, and a palpable ill-defined mass in her right breast. There was no nipple discharge. There were no palpable axillary lymph nodes. There were no other masses in her other organs or tissues according to either the physical or radiological examination. Mastectomy and intraoperatively frozen examination of the sentinel lymph node biopsy were planned.

The mastectomy and sentinel lymph nodes were thoroughly examined and accurately sampled. The surgical specimens were fixed in 10% buffered formaldehyde and embedded in paraffin, and routine histological sections of 4-5 µm were prepared and stained with hematoxylin and eosin. Immunohistochemical detection with vimentin (NeoMarkers), cytokeratin (NeoMarkers), and epithelial membrane antigen (EMA, NeoMarkers) was performed on paraffin tissue sections.

Sentinel lymph nodes (two pieces 7 and 4 mm in diameter) were dissected intraoperatively for frozen examination. The sentinel lymph nodes were reported as tumor negative and no axillary dissection was performed.

The resected specimen of the right breast, measured 36 cm by 27 cm by 18 cm Almost all of the breast tissue had been replaced by the tumor, which measured 33 cm by 25 cm by 16 cm. It was covered by skin that had erosive foci in some areas. The areola and the nipple were normal in appearance (Figure 1).

The cut section of the breast showed a solid nodular growth pattern with cystic and hemorrhagic areas in some foci. The tumor had a gelatinous appearance and was white to yellow with pushing margins (Figure 2). The skin had no tumoral infiltration. The sentinel axillary lymph nodes were homogeneous on the cut surface. The microscopic examination of the tumor revealed scattered spindle cells and giant cells containing pleomorphic,

Gönderilme Tarihi: 09 Temmuz 2009 • **Revizyon Tarihi:** 04 Eylül 2009 • **Kabul Tarihi:** 04 Eylül 2009

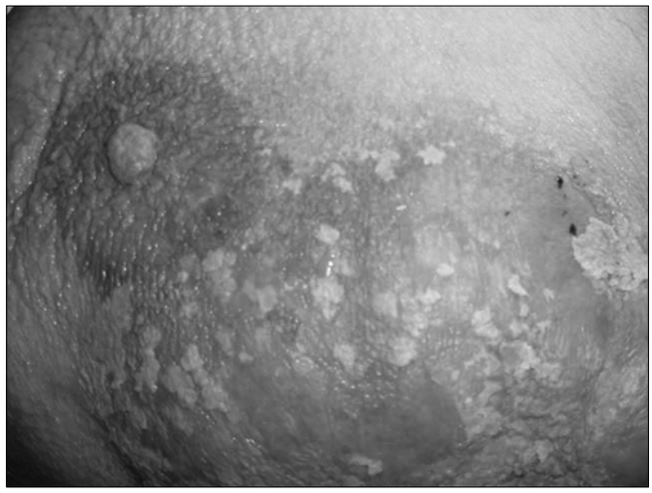

Figure 1. Macroscopic appearance of the breast demonstrating erosive areas in the skin without tumoral infiltration of the areola and the nipple.

Figure 2. The cut section of the breast showed a solid nodular growth pattern with cystic and hemorrhagic foci in some areas. The tumor had a gelatinous appearance and was white to yellow with pushing margins.

multilobated, and hyperchromatic nuclei (Figure 3). Occasional atypical cells with vacuolated cytoplasm and scalloped nuclear margins were observed. Increased mitoses and geographic necrosis were seen. The immunohistochemical examination revealed vimentin positivity and cytokeratin and EMA negativity in tumor cells. The skin, nipple, and fascia were intact. There were no features of a phyllodes tumor. The final diagnosis was pleomorphic liposarcoma. No other subtypes of liposarcoma or cystosarcoma phyllodes were observed. Chemotherapy was recommended; however, she returned to Albania and was lost to follow up post-operatively.

Discussion

Sarcoma of the breast represents less than 1% of all primary breast malignancies (2,3,4). The most common sarcomas are fibrosarcoma and osteosarcoma in the breast (5). Although over 90 cases of breast liposarcoma are documented in the literature, a critical review of the literature showed only 39 cases with sufficient data to be classified as pure liposarcoma of the breast (6).

Primary breast liposarcoma arises directly from mammary interlobular stromal tissue (7). Most patients are women; only three men have been reported to our knowledge (8). The age ranges from 19 to 76, with the median age at occurrence of 47 years. They are generally unilateral at presentation, but bilateral involvement is also reported. They manifest as slowly growing, painful breast masses of variable duration; rapid growth is seen in the setting of malignant phyllodes tumor (7). Typical gross appearance shows a median size of 8 cm in greatest diameter, ranging from 2 to 40 cm in diameter. These masses are well circumscribed in some tumors; some are multinodular or infiltrative. Necrosis and cavitation are rarely described. There is no consistent relationship between tumor histologic subtype, size, and age at diagnosis (9).

Liposarcomas are classified as well differentiated, myxoid, round cell, pleomorphic, and de-differentiated according to the World Health Organization classification. Their behavior and pattern of recurrence depend on their histological subtype (10). Pleomorphic liposarcomas are highly cellular tumors with spindle shaped and polygonal tumor cells. They have prominent nuclear atypia. Multinucleated lipoblasts are often numerous (11).

Cystosarcoma phyllodes are regarded as a distinct entity, since the diagnosis depends on the demonstration of scattered epithelial elements in a predominantly cellular stroma. The sarcomatous elements of malignant cystosarcoma phyllodes, described in descending order of frequency are fibrosarcoma, liposarcoma, fibrosarcoma with liposarcoma, chondrosarcoma, rhabdomyosarcoma, and osteogenic sarcoma (12). Pleomorphic liposarcoma arising within a phyllodes tumor is an extremely rare event (13). However, many reports of liposarcomas of the breast actually are malignant phyllodes tumors with liposarcomatous stroma (14).

Cangiarella reported a very interesting case of pleomorphic liposarcoma in the breast that most likely represented metastasis from liposarcoma of the thigh rather than a primary neoplasm (15). Pleomorphic liposarcoma tends to occur on the extremities; the trunk and retroperitoneum are less frequently affected (10) and thus the remote possibility of a metastasis should be suspected in such cases.

The differential diagnosis of breast liposarcoma includes silicon granuloma, fat necrosis, malignant fibrous histiocytoma, and signet ring cell carcinoma. The recognition of typical lipoblasts that have scalloped, irregular, hyperchromatic nuclei with sharply defined intracytoplasmic vacuoles and that stain with S100 is the key feature in differentiating liposarcoma from others (7). However, silicone can be seen within vacuoles closely resembling multi-

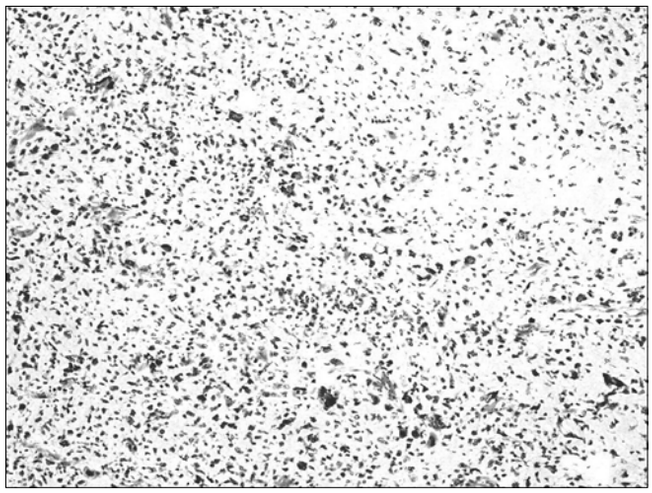

Figure 3. Microscopic examination revealed scattered spindle cells and giant cells containing pleomorphic, multilobated, and hyperchromatic nuclei (Hematoxylin and eosin x100)

vacuolated lipoblasts, but it does not stain with Oil Red-O unless it is contaminated by organic oils (6). In addition, there are inflammation with lipid-laden macrophages and multinucleated foreign body-type giant cells in both silicon granuloma and fat necrosis (9). In cases of signet ring cell carcinoma and high grade primary breast carcinomas, an immunohistochemical study demonstrating cytokeratin and EMA positivity is very helpful.

The distinction of pleomorphic liposarcoma from high grade malignant fibrous histiocytoma is probably of little importance since both are high grade sarcomas with a poor prognosis (16,17). Pleomorphic lipoma, another entity in the differential diagnosis, contains characteristic floret cells and no lipoblasts (6).

Mastectomy is the standard treatment for breast sarcomas. Limited surgery carries an increased risk of local recurrence. Distant metastates are also relatively frequent except for malignant cystosarcoma phyllodes and liposarcoma (3). Tumors that are large and high grade with uncertain surgical margins require adjuvant radiotherapy and chemotherapy (18).

There is no established protocol for the treatment of liposarcomas of the breast. Histological grade and the degree of microscopic invasion influence the prognosis (19). Complete excision is essential even in low grade liposarcomas, because of the possibility of dedifferentiation to more malignant forms (20). Most of the liposarcomas that recurred were of the pleomorphic subtype (9). It metastasizes hematogenously to the lungs, liver, and bones, and rarely metastasizes to axillary lymph nodes (19).

Austin and Dupree suggested that primary liposarcomas arising from cystosarcoma phyllodes behave similarly to primary breast liposarcoma, and so the distinction between the two entities may be of little clinical importance (9).

In conclusion, although breast sarcomas are very rare when compared to carcinomas of the breast, they must still be taken into account in the differential diagnosis. An immunohistochemical study should be considered in order to avoid misdiagnosis, especially in more pleomorphic tumors when an epithelial differentiation is not apparent and when the biopsy material is limited.

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