Case Report

J Breast Health 2016; 12: 83-5
DOI: 10.5152/tjbh.2016.2844

A Rare Tumor that Mimicked Metastasis in a Patient with Breast Cancer: Epithelioid Hemangioendothelioma

Fatmagül Kuşku Çabuk[1], Fatma Aktepe[2], Ahmet Serkan İlgün[3], Dauren Sarsenov[3], Filiz Elbüken[4], Vahit Özmen[5]

[1]Department of Pathology, İstanbul Bilim University School of Medicine, İstanbul, Turkey
[2]Clinic of Pathology, Gayrettepe Florence Nightingale Hospital, İstanbul, Turkey
[3]Breasth Health Center, İstanbul Florence Nightingale Hospital, İstanbul, Turkey
[4]Clinic of Radiology, Gayrettepe Florence Nightingale Hospital, İstanbul, Turkey
[5]Department of General Surgery, İstanbul University İstanbul School of Medicine, İstanbul, Turkey

ABSTRACT

A woman aged 50 years was diagnosed as having an invasive ductal carcinoma in the right breast and ductal carcinoma in situ in the left breast and underwent bilateral mastectomy eight years ago. A mass was identified during follow-up in positron-emission tomography (PET) image in the left infraclavicular region, indicating metastasis. Histopathologic examination showed a mass of 1.9 x 1 x 0.7 cm in dimensions characterized by spindle or round nuclei cells that formed island or cords in hyaline and myxoid ground and intracytoplasmic vacuoles containing erythrocytes. In the immunohistochemical analysis, tumor cells were widespread with diffuse positivity with CD34 and vimentin. These findings redirected us from a diagnosis of metastatic carcinoma to epithelioid hemangioendothelioma, a rare tumor of intermediate vascular tumor groups. In this respect, confirmation through biopsy from considered cases of metastasis is important in making a definite pathologic differential diagnosis.

Keywords: Hemangioendothelioma, invasive ductal carcinoma, breast, breast carcinoma, metastasis, lymph nodes

Introduction

Epithelioid vascular tumors are challenging tumors for diagnosis in soft tissue pathology because of their nature. They may show confusing features resembling those of metastatic carcinoma or sarcoma. Epithelioid hemangioendothelioma (EHE) was first described as a vascular tumor of intermediate malignancy by Weiss and Enzinger in 1982 (1). EHE may develop as a solitary mass in middle-aged patients. They usually present in deep soft tissues, internal organs (the lungs and liver in particular), bones and skin (2-4). It accounts for less than 1% of all vascular tumors (3). It was reported in the latest World Health Organization (WHO 2013) classification that the fusion genes responsible for the development of EHE were WWTR1-CAMTA1 (WW domain-containing transcription regulator 1-calmodulin-binding transcription activator 1), and less often YAP1-TFE3 (yes-associated protein 1-transcription factor binding to IGHM enhancer 3) (5). It is indicated that in the presence of these fusion genes, EHE develops at a young age, multifocal, could have metastatic potential, and should be classified as a malignant tumor (6).

We detected a mass suspected to be metastasis in the infraclavicular region of a patient under follow-up who was diagnosed as having breast carcinoma. EHE was diagnosed in the microscopic examination following the mass excision. The association of HE and breast carcinoma has never been reported in the literature. The risk of a second primary tumor, especially in soft-tissue masses, should be kept in mind while following up patients diagnosed as having malignancy. EHE may easily be confused with epithelioid tumors in a microscopic examination. Therefore, keeping this in mind, a final differential diagnosis should be established using immunohistochemical methods.

Case Presentation

Osseous metastases developed after the 3rd year of follow-up in a woman aged 50 years who had undergone bilateral mastectomy and bilateral sentinel lymph node biopsy for the treatment of bilateral breast carcinoma and received adjuvant chemotherapy and Herceptin treatment eight years ago. For that reason, when the left ventricular ejection fraction (EF) dropped below 45% for the patient while she was on a continuous Herceptin treatment and in a stable condition, the Herceptin treatment was terminated in December 2014. Regression of the osseous metastases was discovered in a follow-up positron-emission tomography (PET) in May 2015, and a newly-developed

Address for Correspondence:
Fatmagül Kuşku Çabuk, e-mail: fatmagulkusku@hotmail.com

Received: 20.11.2015
Accepted: 08.12.2015

hypermetabolic focus of approximately 1.5 cm detected in the left infraclavicular area was evaluated as metastatic lymphadenopathy. Trucut biopsy was not preferred because of the mass's proximity to the vascular structures and the plexus brachialis. Left axillary incision was selected for the procedure owing to the uncomplicated access to the infraclavicular lesion from the previous incision area. The mass was excised from the patient under general anesthesia with intraoperative consultation. The irregularly-bordered, cream white mass sized 1.9 x 1 x 0.7 cm macroscopically was reported as a malignant tumor as a result of the intraoperative imprint cytology. In the low power magnification examination of the hematoxylin and eosin (H&E)-stained paraffin sections from the mass, islands and cords were created on the hyalinized and myxoid ground and fusiform and round nucleated cells were detected (Figure 1). Under high power magnification, intracytoplasmic vacuoles containing erythrocytes in cells were prominent (Figure 2). Some cells showed large nuclei, nuclear membrane irregularities, and nucleolus visibility. Mitosis was determined as 2/10 per high power field. In the immunohistochemical examination, the tumor cells were stained widely and diffusely positive for CD34 and vimentin (Figure 3), but were negative for pancytokeratin, smooth muscle actin, S100 and desmin. With these findings, the patient was diagnosed as having epithelioid hemangioendothelioma, a vascular tumor of intermediate malignancy.

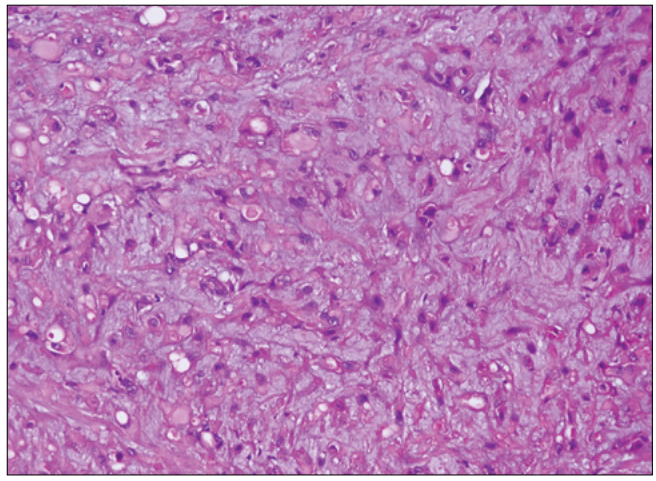

Figure 1. Cord structures consisting of fusiform and round nucleated and tumoral cells can be viewed in myxoid ground (H&Ex200)

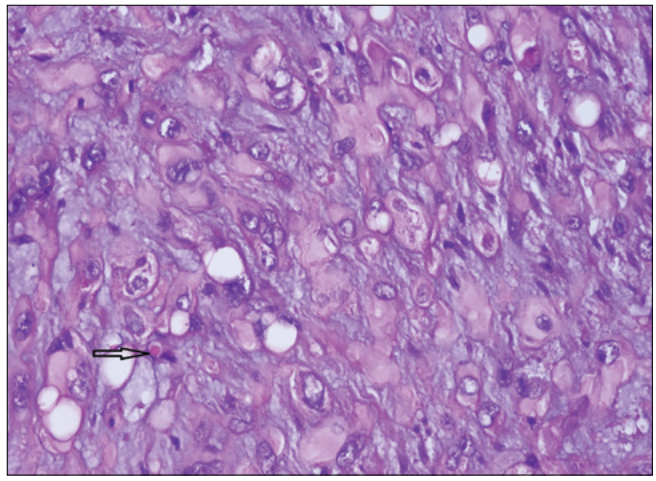

Figure 2. Atypical cells with characteristic intracellular lumen formation and erythrocytes (arrow) in some lumens can be viewed under high power magnification (H&Ex400)

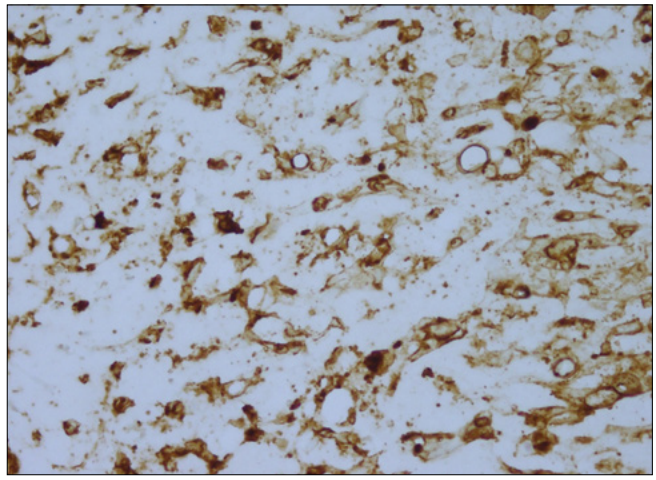

Figure 3. Widespread and strong positivity in tumor cells for CD34 can be viewed (x400)

Discussion and Conclusion

Epithelioid hemangioendothelioma is a rare vascular tumor with metastatic potential (4). Hemangioendothelioma (HE) is a group of vascular neoplasms that mostly involve skin and soft tissues divided into six categories, papillary intralymphatic angioendothelioma (Dabska tumor), retiform HE, kaposiform HE, epithelioid HE, pseudomyogenic HE (epithelioid sarcoma-like HE), and composite HE (7). Each of these neoplasms has histopathologic characteristics (8). A number of genes are reported to have a role in its etiology; however, there is no relationship between chemotherapy and the growth of EHE reported in the literature (5). It can occur in all age groups, but not in childhood, and affects both sexes equally (4). It can develop in the small veins of nearly 2/3 of patients, and the large arteries or veins of the rest as an intraluminal mass (4). Of these patients, more than 50-76% are asymptomatic (3). Similarly, a mass was found during a routine follow-up test when our patient had no symptoms. EHE can be confused with malignancies because of the PET and strong ^{18}F-fluorodeoxyglucose (FDG) involvement (8). Metastasis was the first consideration for our patient because of the infraclavicular mass, malignancy history, and strong FDG involvement. The mass was excised together with frozen sections in order to manage surgical margins.

In the histopathologic examination, EHE create islands and cords on hyalinized and myxoid ground substance, and consist of intracytoplasmic vacuoles that contain typical erythrocytes and are characterized by fusiform or round nucleated cells (2). Immunohistochemically, the tumor cells were stained diffusely positive for CD34 and vimentin but were negative for pancytokeratin, smooth muscle actin, S100, and desmin (2, 8). However, there have been cases that stained positive for cytokeratin and smooth muscle actin reported in the literature (9).

Adenocarcinomas take first place in the differential diagnosis of EHE because of epithelioid morphology and intracytoplasmic vacuoles (2). Therefore, it is crucial for EHE to be separated from metastasis particularly when treating patients with carcinoma. Our patient had also been diagnosed as having a malignant tumor as a result of the intraoperative imprint cytology, and EHE had not been considered. Intracytoplasmic vacuoles in EHE cells may resemble mucin-containing intracytoplasmic vacuoles in adenocarcinoma cells. When analyzed carefully, the presence of erythrocytes can be distinguished in intra-

cytoplasmic vacuoles. Furthermore, as with the case presented herein, immunohistochemically negative cytokeratin and a positive result for endothelial determinants such as CD34 are diagnostic findings. The presence of erythrocytes in vacuoles also strongly support the diagnosis of epithelioid hemangioendothelioma.

Epithelioid hemangioma, pseudomyogenic (epithelioid sarcoma-like) HE, epithelioid angiosarcoma, and epithelioid sarcoma are included in the differential diagnosis for the histologically epithelioid appearance of cells (2, 4). Epithelioid hemangioma is a benign vascular tumor and has the appearance of the so-called 'tombstone' pattern with epithelioid endothelial cells lining vessels (2, 4). It does not include intracytoplasmic vacuoles and has inflammatory cells rich in eosinophils present in the background and germinal centers formed by these cells (2, 4). Epithelioid sarcoma-like HE is a vascular tumor in the intermediary group and consists of sheets of myxoid fusiform tumor cells with a solid growth pattern. Immunohistochemically, CD34 is negative (2). Atypia and mitosis in malignant tumors such as epithelioid angiosarcoma and epithelioid sarcoma are much more distinctive than EHE cells in the intermediate group (2).

Analyzed in terms of prognosis, approximately 10-15% of EHEs have localized lymph nodes and/or 20-30% may be lung metastasis (2); local recurrence is 12%, whereas mortality is nearly 17% (9). The best option reported in the literature is excision of the mass with clean surgical margins (1, 10). No difference has been found between the life spans of patients who undergo additional chemotherapy and/or radiotherapy (10).

However, in cases where the tumor diameter is larger than 3 cm and there are more than 3 mitoses in HPF, the 5-year life expectancy is 59% and it becomes a necessity that these patients are monitored. When these findings are not the case for the patient, the 5 year life expectancy has been found 100% (10). Our patient had a tumor diameter less than 3 cm; however, follow-up was recommended after 3 months because of local recurrence and metastasis when the mitosis was 2/10 cells per HPF.

Only one case of EHE with a supraclavicular location that was confused with metastasis has been reported in literature (8). However, no cases of EHE involvement and confusion with metastasis in patients with breast carcinoma have yet been reported.

We presented an association of EHE, a rare vascular-based soft-tissue tumor with malignancy potential, with invasive ductal carcinoma in our patient. Concordant with technological developments, there has been progress in follow-up and treatment of breast cancer as well as early detection of recurrence or metastatic disease. However, pathologic confirmation of diagnosis through biopsy is of vital importance in terms of the treatment and prognosis of patients in cases of suspected metastasis.

Informed Consent: Due to the usage of archive preparates that belong to pathology department, informed consent is not required in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - V.Ö., F.A.; Design - F.K.Ç.; Supervision - F.K.Ç., V.Ö.; Funding - S.E., F.E.; Materials - F.E.; Data Collection and/or Processing - D.S.; Analysis and/or Interpretation - F.K.Ç., S.İ., D.S.; Literature Review - D.S.; Writing - F.K.Ç., F.A.; Critical Review - V.Ö., F.A., F.E., S.İ.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study has received no financial support.

References

1. Weiss SW, Enzinger FM. Epithelioid hemangioendothelioma: a vascular tumor often mistaken for a carcinoma. Cancer 1982; 50:970-981. (PMID: 3303234) [CrossRef]
2. Ko JS, Billings SD. Diagnostically Challenging Epithelioid Vascular Tumors. Surg Pathol Clin 2015; 8:331-351 (PMID: 26297060) [CrossRef]
3. Sardaro A, Bardoscia L, Petruzzelli MF, Portaluri M. Epithelioid hemangioendothelioma: an overview and update on a rare vascular tumor. Oncol Rev 2014; 8:259. (PMID: 25992243) [CrossRef]
4. Mertens F, Unni K, Fletcher CDM. World Health Organization classification of tumors. Pathology and genetics. Tumors of soft tissue and bone. Lyon: IRAC Press; 2002.p.173-174.
5. Jo VY, Fletcher CD. WHO classification of soft tissue tumours: an update based on the 2013 (4th) edition. Pathology 2014; 46:95-104. (PMID: 24378391) [CrossRef]
6. Doyle LA. Sarcoma classification: an update based on the 2013 World Health Organization Classification of Tumors of Soft Tissue and Bone Cancer 2014; 120:1763-1774. (PMID: 24648013)
7. Requena L, Kutzner H. Hemangioendothelioma. Semin Diagn Pathol 2013: 30:29-44. (PMID: 23327728) [CrossRef]
8. Yun JS, Kang SK, Kim SH, Na KJ, Song SY. Epithelioid Hemangioendothelioma Arising from Internal Jugular Vein Mimicking Cervical Metastatic Lymphadenopathy. Korean J Thorac Cardiovasc Surg 2015; 48:294-297 (PMID: 26290844) [CrossRef]
9. Mentzel T, Beham A, Calonje E, Katenkamp D, Fletcher CD. Epithelioid hemangioendothelioma of skin and soft tissues: clinicopathologic and immunohistochemical study of 30 cases. Am J Surg Pathol 1997; 21:363-374. (PMID: 9130982) [CrossRef]
10. Deyrup AT, Tighiouart M, Montag AG, Weiss SW. Epithelioid hemangioendothelioma of soft tissue: a proposal for risk stratification based on 49 cases. Am J Surg Pathol 2008; 32: 924-927. (PMID: 18551749) [CrossRef]