Letter to the Editor

Eur J Breast Health 2024; 20(1): 71-72
DOI: 10.4274/ejbh.galenos.2023.2023-12-9

Exploring the Relationship Between Tamoxifen and Hereditary Angioedema

Ana Raquel Pinto, Fabrícia Carolino
Department of Allergy and Clinical Immunology, Centro Hospitalar Universitário de Santo António, Porto, Portugal

Keywords: Breast cancer; hereditary angioedema; tamoxifen

Cite this article as: Pinto AR, Carolino F. Exploring the Relationship Between Tamoxifen and Hereditary Angioedema. Eur J Breast Health 2024; 20(1): 71-72

Dear Editor,

Hereditary angioedema (HAE) is a condition characterized by recurrent episodes of mucocutaneous edema, associated with abnormal levels or/and function of serum C1 inhibitor (C1-INH) (HAE type I or II, respectively) or with a normal complement study (1).

In at least two-thirds of women affected by this disorder, there is a distinct sensitivity to both endogenous and exogenous estrogens, and generally the frequency and severity of angioedema episodes increase in parallel with the rise in serum estrogen levels (1, 2). Some of the mechanisms involved in this process are the reduction in serum levels of C1-INH, coupled with the modulation of factor XII (FXII) gene transcription and of the kallikrein/bradykinin cascade, with induction of bradykinin receptors' expression and amplification of its action (2). Therefore, the general consensus between experts is the recommendation to avoid estrogen therapy in patients with HAE (2).

While the incidence of breast cancer in women with HAE mirrors that of the general population, caution is warranted when considering the use of estrogen modulators such as tamoxifen in these patients. This caution arises from the potential agonistic activity on estrogen receptors in specific tissues, which could exacerbate angioedema symptoms and, in severe cases, result in fatal outcomes. Physicians who frequently prescribe such medications should be mindful of these considerations in their decision-making processes (3).

We present a breast cancer patient whose angioedema episodes were exacerbated as a consequence of hormone therapy with tamoxifen.

A 54-year-old woman was referred to an allergy/immunology appointment due to recurrent episodes of facial and laryngeal angioedema exhibiting bradykininergic features. She reported previous history of angioedema, partially responsive to antihistamines/corticosteroids, whose initial manifestation occurred during adolescence, coinciding with the introduction of a combined contraceptive pill, subsequently controlled after replacement with a progestin pill. However, episodes currently recurred following initiation of hormone therapy with tamoxifen in the context of breast cancer diagnosis. She had no family history of angioedema.

In a prior assessment, C1-INH deficiency had already been excluded, and presently two consecutive quantitative and functional studies of this protein revealed no abnormalities-serum level of C1-INH = 24.6–37.5 mg/dL, with normal function. Given the clinical suspicion of HAE with normal complement, a genetic study was requested, identifying a mutation in the FXII gene - variant c.983C>A p. (Thr328Lys) in heterozygosity-and confirming the diagnosis.

In light of the symptomatic worsening observed after the initiation of tamoxifen, this agent was considered responsible. In collaboration with Oncology, this drug was replaced by anastrozole, an aromatase inhibitor, with subsequent complete symptomatic control, which reinforced our observations.

Tamoxifen, a selective estrogen receptor modulator, is widely used in breast cancer (3). To date, there are rare cases described in the literature, in which this drug was considered a factor in exacerbating HAE, namely due to its action as a partial agonist in certain estrogen receptors (2, 4, 5). Our observations not only reinforce these previous reports but also underscore the importance of increased awareness among physicians regarding this potential side effect of hormone therapy in women diagnosed with both HAE and breast cancer.

Corresponding Author:
Ana Raquel Pinto; araquel2@hotmail.com

Received: 12.12.2023
Accepted: 13.12.2023
Available Online Date: 27.12.2024

Peer-review: Internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: A.R.P., F.C.; Concept: A.R.P., F.C.; Literature Search: A.R.P.; Writing: A.R.P.

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

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

References

1. Gompel A. Angiœdèmes à bradykinines et hormones [Hereditary angioedema and hormones]. Presse Med 2015; 44: 65-69. (PMID: 25511652) [Crossref]
2. Rousset-Jablonski C, Thalabard JC, Gompel A. Tamoxifen contraindicated in women with hereditary angioedema? Ann Oncol 2009; 20: 1281-1282. (PMID: 19482875) [Crossref]
3. Yakaboski E, Motazedi T, Banerji A. Hereditary angioedema: Special considerations in women. Allergy Asthma Proc 2020; 41(Suppl 1): S47-S50. (PMID: 33109327) [Crossref]
4. Roldan Sevilla T GFM, Roldan Rincon A, Herrero Ambrosio A. The use of C1 esterase inhibitor in long term prophylaxis of recurrent acute hereditary angioedema exacerbated by tamoxifen. Eur J Clin Pharmacy 2013; 15: 124-127. [Crossref]
5. Bork K, Wulff K, Witzke G, Rietz S, Hardt J. Tamoxifen may cause life-threatening angioedema attacks in patients with hereditary angioedema. J Eur Acad Dermatol Venereol 2017; 31: e237-e239. (PMID: 27878882) [Crossref]