Dermatology Practical & Conceptual

Hereditary Angioedema Exacerbated by Estrogen Supplementation Treatment for Uterine Fibroid: A Therapeutic Challenge

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Introduction

Hereditary angioedema (HAE) type 2 is a rare genetic disease caused by the decreased activity of C1-inhibitor (C1-INH), resulting in an increased bradykinin level in the blood [1]. There are several known triggers for exacerbations, including physical trauma, stress, or drugs, including angiotensin converting enzyme (ACE) inhibitors [1]. The clinical manifestations of HAE comprise recurrent episodes of subcutaneous and submucosal edema in any part of the body, although the face, neck, limbs, gastrointestinal tract, and genitalia are most commonly affected [2].

Case Presentation

A 30-year-old female in good general condition was admitted to the hospital with swollen joints and erythema marginatum on her wrists, palms, and around mammary papillae. The patient had neither a family history of similar symptoms nor had she previously experienced them. Initially, rheumatoid arthritis was suggested, though the diagnosis was not confirmed (European Alliance of Associations for Rheumatology guidelines; EULAR), and with symptoms receding, the patient was discharged from the hospital. Just before hospitalization, she had started taking ethinylestradiol and levonorgestrel combination contraceptive pills to reduce bleeding associated with uterine fibroid.

In the following months, the patient experienced recurrent abdominal pain and limb angioedema episodes. However, five months later, symptoms became more severe, and face angioedema was also accompanied by problems with swallowing (Figures 1 and 2). The patient had taken a high dose of antihistamines and systemic steroids at home, followed by epinephrine administration later in

Figure 1. Skin lesions accompanying angioedema; erythema marginatum.

Figure 2. Angioedema on the patient's hands.

the Emergency Department. She did not respond to the therapy but demonstrated gradual improvement over the course of time. With normal C1-INH serum concentration (0.17 G/L) and its low activity (28%), the final diagnosis was HAE type 2 [2]. The patient was instructed to avoid taking any medications containing estrogen and was given a plasma-derived C1-INH as a severe attack treatment and short-term prophylaxis. Nonetheless, due to the vaginal infection, the patient has used vaginal globules with estriol and Lactobacillus acidophilus, which triggered the symptoms of HAE type 2 again.

Overall, the withdrawal of estrogen hormone supplementation improved the symptoms significantly. However, management of uterine fibroid treatment was also required. As the uterine fibroid was difficult to operate, and a hysterectomy was not a reasonable option for such a young patient, progesterone-only contraceptive pills were administered, with positive outcomes.

Conclusions

The attacks of HAE type 2 may be fatal, especially because the treatment used in allergic histamine-dependent angioedema is not effective in bradykinin-dependent HAE type 2 [3]. Therefore, it is necessary to raise awareness of this rare disease.

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