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Hereditary angioedema type I in a female patient: a case report

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ABSTRACT

Hereditary angioedema (HAE) is rare autosomal dominant disease, characterised by spontaneous and recurrent swellings in various parts of the body. The main inflammatory factor in HAE is bradykinin (a key mediator of non-allergic angioedema) and it is responsible for capillary leak. C1 esterase inhibitor (C1-INH) is a protease inhibitor that blocks the activation of the classic complement pathway, but there are also many others biochemical pathways, including kinin. Type I HAE is defined by low plasma levels of a normal C1 inhibitor (C1-INH).

Case presentation. A 34-year-old female patient presented to the hospital complained of swollen and painful legs, flatulence, palpebral and labial edema, dyspnea, dysuria, frequent herpetic infections of mouth and nose, subfebrile body temperature and was hoarse. Over the last 20 years she suffered from occasional edemas of the extremities and abdomen. Laboratory testing showed a reduced level of C1-INH, and with other test results normal we diagnosed the patient with HAE type I. For emergency situations, we prescribed icatibant (B2 bradykinin receptor antagonist) subcutaneously.

Individuals with HAE report episodic attacks during childhood that become more severe during adolescence. There is non-pitting edema in 3 predisposed places : subcutaneous tissue, the abdomen and the larynx. Edemas amplify during 12-24 hours and disappear during 3-5 days, with migrations to other locations. Treatment can be prophylactic, for acute attacks (icatibant) and before medical treatments.

HAE is a potentially lethal disease and should be considered if repeating edema of various body parts, painful swelling and tightening of the skin are present.

Keywords: hereditary angioedema, bradykinin, B2 bradykinin receptor antagonist

Introduction

Hereditary angioedema (HAE) is an autosomal dominant inherited disease, characterised by spontaneous and recurrent swelling of various parts of the body. (1) The exact prevalence is unknown, approximately 1 in 10,000 people world-wide are affected. (2) There are 3 types of HAE. HAE type I has a decreased C1–INH level, and accounts for 85% of all HAE cases. HAE type II accounts for 15% of HAE cases and is caused by a normal or higher level of abnormal C1–INH. Type III is extremely rare and is not dependant on C1–INH levels.

Diagnosis of that type is is made through genetic testing. C1–INH is a protease inhibitor, which blocks the activation of the classic complement pathway, fibrinolysis, but also many other biochemical pathways, including some parts of the kinin pathway. It is produced mainly by hepatocytes and marginally by monocytes. Androgens stimulate C1–INH production. As already mentioned, bradykinin is considered to be the main inflammatory factor in HAE. It is formed by action of the plasma enzyme kallikrein on substrate – kininogen. We consider it responsible for capillary dilation and leak, smooth muscle relaxation, neutrophil chemotaxis. (3)

Case report

A 34-year-old female patient presented to the hospital complained of swollen and painful legs, flatulence, palpebral and labial edema, dyspnea, dysuria, frequent herpetic infections of mouth and nose, subfebrile body temperature and was hoarse. Over the last 20 years she suffered from occasional edemas of the extremities and abdomen, which significantly reduced her quality of her life. She

has polycystic ovary syndrome (since 2001) and Raynauld syndrome (since 2010). Since 2007, she has had problems with rectorrhagy, flatulence, was febrile up to 41 °C (axillary) and has had daily variations in body mass of up to 5 kg.

When admitted to hospital, her functions were stable. In clinical examination we found palpebral and labial edema, swollen legs and livedo reticularis on the lower extremities. We conducted laboratory tests for celiac disease, as well as tests for other immunological and endocrine diseases. These tests showed normal results, except for a lowered level of C1–INH (0.65, normal range 0.70-1.30). On the basis of these results, the patient was diagnosed with HAE type I. For emergency situations, we prescribed icatibant (B2 bradykinin receptor antagonist) subcutaneously.

Discussion

Although rare, HAE is a potentially lethal disease. (3) HAE should be considered when angioedema is not followed by a rash, or when an attack does not respond to usual therapy. (1,3) In HAE cases, most of the laboratory results are within the normal range, as it was in this case. HAE treatment consists of prophylactic treatment, treatment of acute attacks and prophylactic treatment prior to certain medical interventions (dental procedures). Patients who suffered from a more severe attack, or if the attack affected the larynx, the head or the gastrointestinal system, must have medications for acute attacks nearby (bradykinin B2 receptor antagonist for subcutaneous treatment). (4)

Long-term prophylaxis is provided in patients with frequent and/or severe attacks with weak androgens (danazol). With these patients, their liver function, full blood count, lipid profile and cardiovascular risk should be monitored.

Conclusion

HAE is under-diagnosed due to symptoms that are similar to other diseases and due to a lack of disease-awareness. Drugs for prevention and for treatment of attacks should be available. Emergency centres should either be equipped with drugs, or they should be informed on where and how to obtain them in cases of emergency.

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