Case report: Hereditary angioedema treated with fresh frozen plasma

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Summary

Hereditary angioedema (HAE) is a rare autosomal dominant disease, characterized by recurrence swelling of the skin or mucosal tissue, and may cause airway obstruction. It is caused by C1-esterase inhibitor (C1-INH) deficiency, or dysfunction of C1-INH, therefore increased bradykinin and kallikrein production, which causes vasodilation, increases vascular permeability and localized fluid extravasation results in angioedema. The current recommendation for the treatment of an acute attack of HAE is with C1-INH, or synthetic bradykinin receptor antagonist. However, these drugs are not currently available in Vietnam, and the price is very expensive. Frozen fresh plasma is considered a safe alternative for patients because of its rapid and cheap effectiveness.

Keywords: Hereditary angioedema, frozen fresh plasma.

I. BACKGROUND

Hereditary angioedema is a dominant genetic disease, first described by William Osler in 1888. The disease includes 3 types: HAE type I due to deficiency of the quantity of C1-INH, HAE type II due to C1-INH dysfunction and HAE type III is caused by mutations in the gene encoding factor XII that increases bradikynin.

Actually, HAE is often misdiagnosed as IgE-mediated urticaria. The disease is characterized by acute, localized, recurrent edema of the skin and mucous membranes, without itching and urticaria. Some cases cause edema and airway obstruction, and the patient can die if not treated promptly, which is one of the medical emergencies.

Treatment for hereditary angioedema includes drugs providing C1-INH, bradykinin and kallikrein antagonists (Icatibant, Ecallantide), but the cost of these products is too expensive, and they are still not available in Vietnam. Since other therapies are not yet available, fresh frozen plasma is often used as a source of C1-INH to treat acute attacks, or it can be infused as a prophylactic measure before surgery to prevent an acute HAE exacerbation. We report a patient who was diagnosis of HAE and infused FFP to treat acute attack of HAE.

II. CASE PRESENTATION

A 56-year-old male patient with a healthy personal history and without a family history of factors suggesting a genetic disease. The disease started 1 year before admission to the hospital with isolated, localized swelling in scattered areas of the body (abdomen, legs, arms) with no pain, no itching, and no rash. The disease spontaneously subsided after a few days without any medication. Recurrences after the disease last longer than previous times.

2 days before entering the hospital, the patient suddenly developed swelling in the chin area. He took dexamethasone, cefotaxime, and alpha chymotrypsin, but the disease became worsened, leading to swelling of the entire face, best observed with 2 eyelids, lips and tongue, with difficulty in breathing. With the diagnosis of grade 3

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anaphylaxis, he was treated with adrenalin, solu medrol, dimedrol, intravenous fluids and transferred to the Allergy Department in a stable hemodynamic state, still swollen in the entire face, eyes, neck, tongue. The patient felt pain and tension throughout the head, could not speak, or swallow, and without urticaria.

Blood analysis showed: White blood cells increased: 16G/l, NEU: 93.4%, liver and kidney function was still normal.

The patient was given fluids, solu medrol, adrenaline, dimedrol.

After 2 days (total dose of medicine was 7 bottles of solu medrol 40mg, 5 tubes of dimedrol 10mg and 2 tubes of 1mg adrenaline), the local swelling decreased very little, the eyes opened a little, the patient only hardly drink milk, the swelling spread down his neck and still had difficult in talking.

The patient was considered with angioedema and received an infusion of 250ml of fresh frozen plasma of group B. After 60 minutes of infusion, the patient felt comfortable, his eyes opened wide, his throat was less sore, he could eat porridge and speak.

The patient was discharged after 5 days of treatment. Tests performed at the time the patient was discharged from the hospital: Quantification of C4: 12.4mg/dl, C1-INH: 28.3mg/dl, within normal limits. At that time, C1-INH function test was still unable in Viet Nam.

6 months later, the patient had another recurrence of angioedema, just after receiving a dental implant. The disease appeared with similar symptoms, the patient was prescribed FFP immediately. After infusing 2 units of FFP (500ml), the face, nose, and pharynx were no longer swollen, the patient could breathe more comfortably and speak. Tests at this time showed that C1-INH and C4 concentrations were both reduced, C1-INH: 14.9mg/dl (normal: 21-39mg/dl), C4: 4.04mg/dl (normal: 10-40mg/dl). The patient was diagnosed with hereditary angioedema type I and was prescribed attenuated androgen (danazole) for prophylaxis.

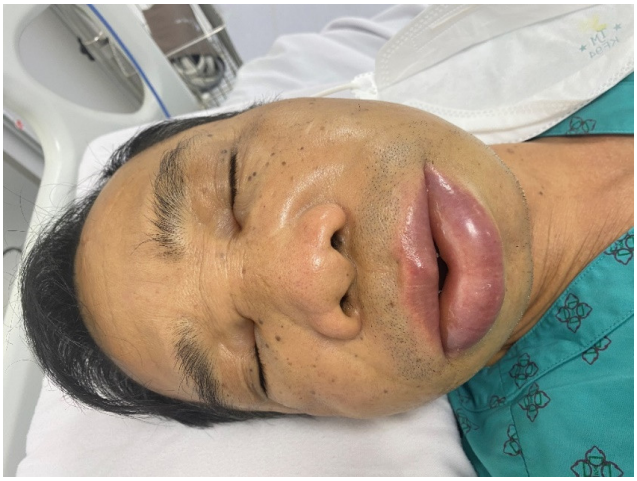

Figure 1. Before transfusion of fresh frozen plasma: Swollen eyes, lips and tongue, unable to speak, difficulty in swallowing, pain and tension throughout the head

Figure 2. After 60 minutes of fresh frozen plasma infusion: Eyes wide open, able to speak, much less headache (photo 2) and after 1 day (photo 3)

III. DISCUSSION

Angioedema is the physical manifestation of transient increases in vascular permeability. Bradykinin, generated by activation of the plasma contact system, has been conclusively identified as the mediator of swelling in hereditary angioedema with C1 inhibitor deficiency. The plasma contact system comprises coagulation factor XII, plasma prekallikrein, and high-molecular-weight kininogen. Despite the interactions between the activated plasma contact and fibrinolytic systems, patients with hereditary angioedema do not appear to be at an increased risk for bleeding or thrombosis.

In hereditary angioedema with C1 inhibitor deficiency or dysfunction, activation of the plasma contact system generates bradykinin, which is considered to be principally responsible for the active transfer of fluid into localized tissues, with resultant angioedema.

Hereditary angioedema is a rare disease, with an incidence of 1/50,000 people, including 3 types, of which types I and II are caused by SERPING 1 gene dysfunction[1]:

Type I: due to C1-INH deficiency, accounting for 85%.

Type II: due to C1-INH dysfunction, accounting for 15%.

Type III: rare, common in women, related to estrogen use, due to mutations in the gene encoding factor XII, increasing kallikrein[2].

Hereditary angioedema is usually not accompanied by urticaria or itching. Because it is not involved in mast cell reactions, it does not respond to corticosteroids, antihistamines, or adrenaline. Angioedema in the gastrointestinal tract causes abdominal pain, angioedema in the upper respiratory tract can cause edema of the pharynx, uvula, and airway obstruction, which is a medical emergency. Some factors that trigger angioedema include: stress, surgery, medical interventions, trauma, infection and fatigue[2].

Diagnostic tests for hereditary angioedema: Decreased C1-INH quantification (less than 50% of the normal value on 2 different times), decreased C4 (because C1-INH participates in the complement activation pathway), or if only C4 is reduced, do an additional test to evaluate C1-INH function (lower than 50% of the normal value on 2 different times).

The first choice for treating hereditary angioedema is human plasma derived C1-INH or subcutaneous injection of icatibant (bradikynin B2 receptor inhibitor) and ecallantide (kallikrein inhibitor). However, even in the US, these preparations are very expensive, and not all patients have the opportunity to use them.

Fresh frozen plasma (FFP) is one of the treatments for angioedema because it provides C1-INH. Common dosage: 1 to 2 units/1 infusion (10ml/kg). However, using FFP may be associated with risks when transfusion of blood products such as infection with infectious diseases, fluid overload or hypersensitivity reactions. However, the related risks must be weighed carefully against the danger of a life-threatening airway compromise. FFP is used effectively in patients with angioedema if C1 INH is not available (usually due to its high cost), or when epinephrine, steroids, or antihistamines are ineffective. FFP helps emergency treatment of upper respiratory tract edema, preventing many patients from having to be intubated[3].

Our patient was first diagnosed with IgE mediated allergy. Since the earlier treatment of corticosteroid, adrenalin and H1 antihistamine did not improve his symptoms, the diagnosis of HAE was considered. Blood analyses showed a low complement 4 (C4) and a low C1-INH concentration, the diagnosis of type 1 HAE was thereby confirmed. And all the symptoms were improved impressively right after he was infused FFP 60 minutes.

According to Michael Prematta's research, using FFP for emergency treatment of 23 cases of AE, 22 patients (96%) all improved within 45 minutes, the longest being 90 minutes. No patients had side effects[4]. Rui Tang used FFP for 13 HAE patients with an average dose of 586ml, only 1 case had allergic rashes. Quantification of C1-INH concentrations in 2 patients after 400ml FFP infusion showed a statistically significant increase[1].

FFP dosing for HAE has not been studied and generally is administered as in coagulation disorders, infusing 2 units of 200 mL each (10mL/kg). If volume overload is an issue, then 10–15mL per kg body weight is recommended instead, with careful monitoring of volume status and cardiopulmonary function[5].

FFP is also used in AE prophylaxis in patients who prepare for surgeries, and side effects are rare. Patients are usually given fresh frozen plasma infusions 5 days before surgery and 3 days afterward[6].

IV. CONCLUSION

Hereditary angioedema is a rare skin disease, but can be dangerous because of edema and airway obstruction. Emergency treatment requires drugs that work quickly, safely, and effectively. Fresh frozen plasma is the optimal choice for doctors in clinical practice in Vietnam and is the consensus choice around the world in the emergency situation of hereditary angioedema.

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