

A Case of Pregnancy Complicated with Type 1 Hereditary Angioedema (HAE 1)

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Abstract

Hereditary angioedema (HAE) is an inherited autosomal dominant trait and symptoms of HAE include sudden onset of edema in various organs, such as subcutaneous edema, laryngeal edema and gastrointestinal tracts mucosa. We have experienced a case of a pregnant woman diagnosed with HAE and successfully managed her pregnancy. The patient was 37 years old, gravida 1, primiparous. She had experienced two attacks of angioedema during pregnancy but her delivery course was not affected by her HAE. The frequency of attacks during pregnancy had decreased compared with before and after pregnancy. Treatment using human C1-inactivator concentrate was as effective for attack suppression during pregnancy as it had been in her non-pregnant state.

Keywords: Pregnancy; Hereditary angioedema; Complement 1 inhibitor

Introduction

Hereditary angioedema (HAE) is a rare disease and its incidence has been estimated to be 1 in 10,000 to 50,000 [1]. HAE is caused by either the amount or the activity of complement 1 inhibitor (C1-INH). HAE is an expression of an inherited autosomal dominant trait and symptoms of HAE include sudden onset of edema in various organs, such as subcutaneous edema, laryngeal edema and gastrointestinal (GI) tract mucosa. The episodes of an attack have been reported as transient and usually resolve within several days. However, upper airway edema may be a life-threatening event. We have experienced a case of a pregnancy complicated with HAE and successfully managed the pregnancy course.

Case Report

The patient was a 37-year-old, gravida 1, primiparous woman. Her medical history showed sudden onsets of facial swelling, vomiting, abdominal pain and dyspnea several times a year since infancy. And her previous pregnancy ended at 20 weeks of gestation due to intrauterine fetal demise of an undetermined cause. In another medical facility, her laboratory tests showed low levels of serum C3 (72 mg/dL) and C4 (2 mg/dL) and less than 25% C1-INH. Her immune complex C1q was less than 1.5 mg/dL; however, her family had no medical history of these problems. Thus, she was diagnosed as having a sporadic case of HAE 1.

When the patient was 31 years old, she was referred to our dermatology outpatient ward for treatment of HAE (Figure 1). At 32 years old she came to our emergency ward due to choking. Her symptom was resolved by the infusion of two 500 unit vials of lyophilized human C1-inactivator concentrate (hC1-INH) (Berinert® P I.V injection 500; CSL Behring, King of Prussia, PA, USA). She has since visited our emergency ward every one to two months due to attacks of HAE and been effectively treated with an injection of hC1-INH.

She was referred to our obstetric outpatient ward for the care of pregnancy. At 18 weeks of pregnancy, she had an episode of abdominal pain and GI tract edema was suspected. Following an injection of hC1-INH, her symptoms were resolved. At 24 weeks of gestation, she visited our dermatology outpatient ward with the complaint of skin redness (erythema) on the inner side of both thighs and left forearm (Figure 2). No medication was given but she remained under observation. At 29 weeks of gestation, she was admitted to our emergency ward mainly complaining of nausea and vomiting; she received an injection of hC1-

INH and her symptoms were resolved. At 39 weeks of gestation, she was admitted to our obstetrics ward for the planned induction of labor in response to the risk of having an attack of HAE. Laboratory data for her at admission were as follows: C3, 155 mg/dL; C4, 4 mg/dL; C1-INH, 25%; PT-INR, 0.97; and APTT-sec, 23.7 sec (control, 34.0 sec). We had prepared hC1-INH for the treatment of her HAE during labor if needed but no prophylactic injection was given. Before starting induction of labor, her uterine cervix had ripened and, from an infusion of oxytocin, labor was successfully started. She delivered a 2492 g female infant



Figure 1: Hand swelling (left hand).

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Figure 2: Erythema of both thighs and left forearm.

by vacuum extraction at station +3 due to the indication of repetitive severe variable decelerations. The neonate's Apgar scores were 8 and 8 at 1 and 5 minutes, respectively, and the umbilical arterial cord blood pH was 7.26. Her post-partum course was uneventful and she was discharged with her infant without significant complications. Following the delivery, the frequency of HAE attacks increased to almost once a month, the same as before her pregnancy, and treatment with hC1-INH injections with/without tranexamic acid has been effective.

Discussion

HAE is an autosomal dominant disease caused by quantitative

(type I) or functional (type II) deficiency in C1-INH (C1-INH-HAE) or normal C1 inhibitor associated with mutations of the *F12* gene (FXII-HAE) [2]. Martinez-Saguer et al. reported 22 cases of type I HAE and recommended the use of prophylactic administration of hC1-INH before labor [3]. However, according to a report on the international consensus and practical guidelines on the gynecologic and obstetric management of female patients with hereditary angioedema caused by C1 inhibitor deficiency [4], it is recommended that patients with HAE deliver in a hospital that provides quick access to consultants in obstetrics, anesthesiology, perinatology, and hC1-INH. In addition, a routine administration of prophylactic hC1-INH before spontaneous normal delivery is not recommended. However, they also mentioned that the number of case reports is limited. In our case, the patient had type I HAE and had been treated for two attacks during her recent pregnancy. No prophylactic administration was given during delivery or the postpartum period. There is no evidence to suggest that the risk of an attack during forceps or vacuum-assisted vaginal deliveries is greater than during spontaneous deliveries. However, the international consensus and practical guidelines according to Caballero et al. recommend administration of hC1-INH as soon as possible [3,5]. In our case, there were no problems during our vacuum extraction delivery. Thus, there is a need for further investigation into the routine prophylactic administration of hC1-INH when performing an operative vaginal delivery.

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