

Hereditary angioedema: A rare presentation after anterior cervical discectomy and fusion

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ABSTRACT

Hereditary angioedema is an autosomal dominant disorder following a genetic defect of C1 inhibitor gene on chromosome 11. This rare condition presents itself as a recurrent attack of submucosal swelling mostly involving skin, gastrointestinal tract and upper respiratory airway and exacerbates with any physical and emotional stress. Prompt diagnosis and prevention of an acute attack with early recognition and effective treatment can protect the patient from potential laryngeal edema and fatality.

Key words: Angioedema, anterior cervical discectomy and fusion, cervical fixation

Introduction

Hereditary angioedema (HAE) is a nonallergic, autosomal dominant disease that is caused by either deficiency or impaired functioning of C1 esterase inhibitor (C1-INH). The condition was first described by Milton in 1876 and later Quincke in 1882 named it “angioneurotic edema” since it will worsen in stressful situations.^[1] William Osler was the first one to describe its hereditary nature in 1888.^[2] Although its prevalence in Western countries is reported to be 1/50,000-1,00,000 population, it is lower in Asian people.^[3,4] It presents itself as a brawny nonpitting, painless angioedema of the face, extremities or respiratory and intestinal mucosa, but the limbs are the most commonly affected region. The repetitive attacks are provoked by any physical or emotional stress. Three basic phenotypes have been described in the literature. In type I, there is absolute deficiency of C1-INH while in type II they are normal quantitatively but depleted functionally. Type III, occurring exclusively in females, has normal levels of C1-INH but presents because of gene mutation of coagulation factor XII.^[5,6] The incidence of type I is 5 times more than type II though the overall incidence varies from

1 in 1,50,000 to 1 in 10,000. The magnitude of illness varies and if untreated can be life threatening as 30% of patients succumb as a result of laryngeal edema during an attack.^[7] The acute presentation fails to respond to conventional treatment with glucocorticoid, antihistamine or transfusion of fresh frozen plasma (FFP). In such a state, the treatment of choice is a life-saving plasma-derived C1-INH, which is to be given intravenously. Nevertheless, close observation during an acute episode is warranted, for it may herald the emergence of an acute laryngeal edema requiring emergency tracheostomy. As for many other Asian countries, no data is available regarding the epidemiology of this disease in the Kingdom of Saudi Arabia. Our objective in presenting this particular case is to highlight this rare medical illness that can surprise any surgeon if the history and clinical features during an acute episode are misleading.

Case Report

Hereditary angioedema is a rare form of autosomal dominant inherited disease due to deficiency of C1-INH. We report a case of a 50-year-old male known to have diabetes mellitus, hypertension, ischemic heart disease, dyslipidemia, addiction to tobacco smoking and some unknown allergic reaction to face, mouth and legs, which according to him was mostly after taking milk or milk products. He presented to us with chronic cervical pain and intractable bilateral brachalgia with X-rays cervical spine showing C5/6 cervical spondylosis and magnetic resolution imaging revealing severe canal stenosis at the same level. He had angioplasty done 2 years back under general anesthesia for anterior wall myocardial infarction (ejection fraction of 35%). He gave a vague history of some allergic reaction to face and oral cavity a year back. No work up was done and without knowing the actual culprit, he was advised to restrain from milk and milk products. In view of his past

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DOI:

10.4103/1793-5482.161322

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medical history, cardiology and internal medicine consultations were taken for risk stratification. Internal medicine physician after evaluation advised to send serum levels of C3, C4 and C1 inhibitor levels and to transfuse about 2 L of FFP before surgery. Considering his cardiac status the anesthetist did not allow for the transfusion. So with the informed and written consent he underwent C5/6 anterior cervical discectomy with fusion that was uneventful. Eight hours after surgery he developed a progressively increasing swelling at both legs, lips, and tongue with difficulty in swallowing without any pruritus or urticaria that did not subside with glucocorticoid or antihistamine therapy [Figure 1]. His condition improved with the administration of intravenous plasma-derived C1-INH advised by the internal medicine physician, and the clinical features of the state started to disappear in the very next hour [Figure 2]. He thereafter recovered and was later discharged in good health.

Discussion

The condition is autosomal dominant, and the genetic defect involves the C1-INH gene on chromosome 11, however X-linked mode of inheritance have been reported, and about 20% of patients do not have a family history.^[8] Faiyaz-Ul-Haque *et al.* for the 1st time defined the genetic causes of the disease in Middle Eastern Arab inhabitants.^[9] So far, more than 150 different C1 INH mutations have been recognized in these patients.

Eighty-five percent of patients have type 1 HAE.^[10] The age of onset of the disease is as variable as the frequency between episodes. It has been reported to appear as early as 3 years of age to individuals in their 70's, although the majority of cases are seen between 11 and 45 years of age.^[11] About 5% of patients with HAE remain asymptomatic. It presents itself as a sub-epithelial, nonpitting, nonpruritic, painless edema of the face, oropharynx, larynx, abdomen, and extremities.

Headache resembling migraine sometimes occurs because of the cerebral edema.^[12] Patients with gastrointestinal tract involvement complain of crampy abdominal pain and distention with nausea and vomiting. Hemodynamic shock can occur due to ascites from vasodilatation with severe abdominal pain, thus requiring aggressive fluid resuscitation and often indistinguishable from an acute abdomen.^[7] The disease is provoked by many inciting factors including physical or emotional stress, surgical or minor dental procedures, psychological stress as during menstruation, certain infections and medications including contraceptive drugs.^[12]

Life-threatening laryngeal edema is sometimes the only initial presentation and can become a nightmare for the primary treating physician requiring emergency tracheostomy as a last resort for survival. It can appear anywhere between 4 and 30 h following a minor dental procedure.^[13] The attack may last from a few hours to a week. About half of the patients with the disease have experienced at least one acute attack of laryngeal edema in their lifetime.^[14] Mortality is high since this would lead to asphyxiation if emergency medical measures are not taken promptly.

Delay in diagnosis is often due to lack of awareness with the clinical presentation of this disease and has ranged from 10 to 22 years.^[15] Although a number of inciting and precipitating factors are enlisted in the literature, much of the text available regarding the precipitation of acute attack and the potentially fatal laryngeal edema as a consequence of surgical intervention has been from oral and maxillofacial surgery.^[13,16-18] To the best of our knowledge, this is the first ever case reported regarding the acute episode of HAE presenting after routine single-level anterior cervical discectomy and fusion for cervical spondylosis.

The management of HAE is either prophylaxis that is, before any procedure and surgical intervention if the diagnosis



Figure 1: Photograph of the patient taken 8 h after surgery showing swelling of lips and tongue



Figure 2: Completely resolved angioedema after C1 esterase inhibitor administration

was made earlier or soon after the emergence of the clinical presentation of an acute episode. Plasma purified C1-INH provides the best medical solution not only during an acute attack but is also efficient in the short and long term prophylaxis. Since it is a nonallergic disease, therefore the acute presentation is unresponsive to administration of glucocorticoid and antihistamine. In situations where C1-INH is unavailable, FFP can be a substitute for short-term prophylaxis.^[19] FFP causes C4 excess that can exaggerate the existing laryngeal edema, therefore, its transfusion is not recommended in acute settings after a surgical procedure. Attenuated danazol, an androgen proven to reduce the incidence of cutaneous and visceral edema by increasing the endogenous C1-INH via hepatic stimulation, is the most frequently used alternative for the prophylaxis against HAE.^[12]

Scarce data are available regarding the epidemiology of the disease in the Kingdom. Even the masses are less educated regarding its pathophysiology. Lack of awareness of the disease process in the region can be a justifiable reason to overlook the timely diagnosis of the disease, especially in the face of an acute event.

Conclusion

Hereditary angioedema is an autosomal dominant disease with a high risk of mortality from laryngeal edema leading to asphyxiation. Since it is a rare but potentially life-threatening condition, all patients harboring the disease should be enrolled by the pertinent local health care council for timely availability of the life-saving intravenous C1-INH. The patients and their family members should be educated regarding the ailment, and it must be highlighted in their medical record as well so that necessary preparations can be made available for him before undergoing any surgical stress.

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How to cite this article: Umerani MS, Alzahrani K, Mostafa GA. Hereditary angioedema: A rare presentation after anterior cervical discectomy and fusion. *Asian J Neurosurg* 2015;10:253-5.

Source of Support: Nil, **Conflict of Interest:** None declared.