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Hereditary Angioedema: The First Case Report from Afghanistan

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ABSTRACT

Introduction: Hereditary angioedema is an uncommon condition characterized by many symptoms, including skin edema, gastrointestinal mucosa, and larynx or throat. Even though there are three varieties, the most common is type I, which is caused by a lack of the complement C1 inhibitor. The purpose of this study is to document the first known cases of hereditary angioedema (HAE) reported in Afghanistan.

Case presentation: Herein, we describe the cases of Afghan patients diagnosed with HAE. The patients presented shortness of breath, swelling, and swelling in the face, hands, and feet. In all three cases, symptoms such as numbness in the face, hands, and feet, hoarseness, and alterations in the normal face form are observed.

Conclusion: HAE diagnosis is frequently a complex and time-consuming process. It necessitates a thorough physical examination, with a focus on the circumstances and frequency of clinical symptoms, as well as an in-depth review of the family history. Understanding the physical examination and the analysis of specified laboratory testing is critical to arriving at an accurate diagnosis.

Keywords: Hereditary angioedema, C1 protein (C1-INH), Afghanistan

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1. Introduction

Hereditary angioedema (HAE) is a rare and potentially life-threatening genetic disorder characterized by recurrent episodes of severe swelling (angioedema) in various parts of the body (1). The underlying cause is either a deficiency of functional C1 inhibitor (C1-INH) protein (type I HAE) or the presence of dysfunctional C1-INH protein (type II HAE). Type III HAE mainly affects women and involves normal levels of functional C1-INH, though some cases may be linked to mutations in the coagulation factor XII (Hageman factor) gene (HAE-FXII). Type III HAE is largely irrelevant in children and teenagers. Therefore, this consensus statement will focus solely on the more common types I and II of HAE (2).

HAE is characterized by recurrent spontaneous swellings of the skin and mucosal tissues, similar to allergic Quincke edema. These swellings are pale, hard, and doughy, sometimes causing tension-induced pain. They do not cause itching, which can aid in emergency diagnosis. Urticaria is atypical for C1-INH deficiency, and erythema marginatum-like erythema has been observed in individual patients. Abdominal colic caused by swelling attacks may require surgical intervention, and abdominal ultrasounds can help determine the underlying cause. Laryngeal swelling can be life-threatening, and deaths due to asphyxiation have been reported in many families (3, 4). While HAE has been well documented in many parts of the world, there has been a paucity of information regarding its prevalence and clinical presentation in Afghanistan. The first published case reports of HAE from Afghanistan provide important insights into this disease in a previously underreported region. The goal of this study is to document the first reported cases of HAE observed in Afghanistan. This represents the initial documentation of this rare genetic condition within the Afghan population.

Case Report

Case 1

The patient presented with a critical condition after experiencing a distressing event. Her primary concern was swelling, which initially appeared in her hands and feet and later spread to her face. She also reported persistent abdominal pain. Due to the severity of her symptoms, she was referred to the specialized Hemet Clinic department. The patient had a previous history of similar attacks when she was 10 years old, but the current episode was more intense and severe. The duration of symptom improvement had been prolonged temporarily. Upon examination, the patient exhibited facial redness and numbness in the face, hands, and feet. A vital sign assessment revealed normal blood pressure and arterial blood oxygen levels, but a regular tachycardia rhythm (rapid heart rate) was observed. The swelling was observed in the facial and lip regions, which later extended to the hands and feet. The patient also experienced persistent abdominal pain, which intensified upon palpation. Lung sounds were normal upon auscultation.

Based on the patient's clinical symptoms, family history, and a potential decrease in complement C4 levels (indicative of hereditary angioedema, or HAE), a

diagnosis of HAE was suspected. However, due to the unavailability of C1-esterase inhibitor (C1-INH) level testing in Afghanistan, the patient was referred to a healthcare facility outside the country for further evaluation. Following these diagnostic tests, HAE was confirmed. The patient was prescribed danazol, a medication used in the treatment of HAE. The prescribed dosage was 200 mg of danazol daily, and the treatment duration was 30 days. The use of danazol effectively reduced both the severity and frequency of HAE episodes experienced by the patient over one month. The patient's condition improved with the prescribed danazol treatment. Ongoing monitoring and management of HAE episodes will likely be required, as the condition is chronic and requires continuous care.

Case 2

The patient visited Hammet's specialized clinic due to throat congestion. Her medical history from when she was 25 years old revealed serological and C1-INH tests that indicated a deficiency in C1-INH. The patient reported that her attacks typically involved swelling in the face and hands, with less involvement in the legs and genital area. Interestingly, her sister and her sister's children also experienced similar attacks. The patient described these attacks as lasting from 3 days to a week and requiring hospital visits. Later on, new attacks were accompanied by abdominal pain.

During the physical examination, swelling was observed in the inner throat area, as well as in the face and hands up to the elbows. A palpation examination revealed abdominal pain in the hypogastric area. Hearing examinations indicated normal digestive system sounds. A vital sign assessment showed normal blood pressure, a blood oxygen level of 94%, and a heart rate of 108 beats per minute, indicating tachycardia. The patient has a medical history of being admitted to specialized throat hospitals and has previously been prescribed third-generation cephalosporin antibiotics (Ceftriaxone) and dexamethasone, as recommended by the doctor. After five days, there was a gradual improvement in the patient's condition, leading to discharge from the hospital. However, despite the improvement, the intensity and frequency of the attacks remained unchanged, and they continued to occur in the subsequent days.

Given the patient's history of attacks and the presence of C1-INH deficiency, a comprehensive management approach was implemented. During acute attacks, prompt intervention was necessary to alleviate symptoms and minimize complications. Second-generation antihistamines, such as cetirizine or fexofenadine, were prescribed to help relieve itching and reduce the inflammatory response associated with angioedema. Non-steroidal anti-inflammatory drugs (NSAIDs) or other analgesics were administered to manage pain during attacks. For long-term prophylactic treatment, the patient was prescribed danazol, an attenuated androgen, at a dose of 200–400 mg per day. This treatment helps increase C1-INH levels and reduce the frequency and severity of attacks. Regular monitoring of liver function, lipid profile, and hormonal levels was conducted due to potential side effects. The patient and their family were provided with comprehensive education regarding

HAE, including triggers to avoid, signs of impending attacks, and self-administration of rescue medications. They were also encouraged to join support groups and engage in counseling to improve coping strategies and quality of life. Regular follow-up visits were scheduled to assess treatment efficacy, monitor side effects, and adjust the treatment plan as needed.

Case 3

The patient sought urgent medical attention at Hammett Specialized Clinic due to recurring episodes of abdominal pain, accompanied by occasional swelling in the hands and face. The patient's medical records indicated that he was diagnosed with C1-INH deficiency when he was 15 years old. Additionally, his family history revealed that his sister and aunt also experienced similar attacks and were diagnosed with the same condition.

During the physical examination, diffuse abdominal pain localized around the umbilical region was observed, along with mild swelling in the lips and hands. The patient's vital signs, including blood pressure and respiratory rate, were within the normal range, indicating stable overall health. Despite previous attempts at treatment with antibiotics, ciprofloxacin, and dexamethasone, the severity of the attacks did not improve. Laboratory tests were conducted, confirming the presence of C1-INH deficiency in the patient. This result further supported the diagnosis and explained the recurrent episodes of abdominal pain and swelling. Based on the positive confirmation of C1-INH deficiency, the patient underwent successful treatment throughout five sessions, as mentioned in the second case. This case highlights the importance of prompt diagnosis and appropriate management of hereditary angioedema (HAE) in patients with a known history of the condition. The recurrent nature of the patient's abdominal pain and swelling, coupled with the family history of similar attacks, underscores the hereditary nature of this rare disorder. The successful treatment approach, as described in the second case, demonstrates the effectiveness of a comprehensive management strategy in addressing the unique challenges posed by C1-INH deficiency.

Dissscsion

Hereditary angioedema is a rare disease with low prevalence and no gender differences or predominance of race except hereditary angioedema type III, which appears among women and is X-linked. It manifests in a variety of clinical symptoms and is frequently misdiagnosed as an autoimmune illness or anaphylaxis. The development of glottis edema in 25 to 30% of cases and 13% of asphyxia fatalities explain the necessity for early identification and execution of preventive therapy to reduce severe symptoms that might jeopardize patients' lives (1). There are two classifications of HAE dysfunction. Type 1 HAE is attributed to a reduction in production or absence of a C1 esterase inhibitor (C1-INH). On the other hand, Type 2 HAE is characterized by functional impairment despite having normal levels of C1-INH. Additionally (2), Type 3 HAE exclusively affects females and is associated with normal C1-INH function levels (5).

In our case, all three patients had type 1 of this disease. Angioedema happens in HAE as a result of excessive bradykinin synthesis caused by low levels of functionally active C1 inhibitors (C1 INH). This activates the kallikrein-kinin system, resulting in the production of vasoactive peptides and, eventually, the development of angioedema. HAE episodes are prevalent in the skin, upper respiratory tract, and gastrointestinal system. Symptoms are self-limiting, progress over hours, and can last from 1 to 4 days, with attack frequency ranging from weekly to a few times per year. HAE-related premonitory symptoms might manifest hours or days before an attack (7).

In this study, the first and third patients experienced swelling that began in the hands and feet and progressed to swelling of the face and abdominal pain. The second patient's attacks were characterized by swelling in the face and hands and, less frequently, in the legs and genital area. The clinical signs of any variety of illness are nearly the same, regardless of its typology. These disorders involve repeated, self-limited bouts of face edema with highly variable symptoms that affect the viscera, subcutaneous tissue, and upper and lower respiratory mucosa. Other symptoms that can appear are edema of the glottis and/or pharynx, dyspnea, dysphagia, abdominal distention, vomiting, diarrhea, and constipation. So far, our patient has not had digestive symptoms. The intensity of the edema is determined by the location and degree of affectation (1).

The generic nature of HAE symptoms may necessitate a thorough work-up, and if there isn't a high level of clinical suspicion, a delayed diagnosis may result in unwarranted surgical procedures. One study of 235 patients indicated that 1/3 of patients with abdominal symptoms had appendectomies and exploratory laparotomies as a result of this delay, which frequently results in misdiagnosis (7). While conditions including physical trauma, surgery, emotional stress, menstruation, inflammation, and the use of certain medications (ACE inhibitors and contraceptive pills) can all trigger HAE episodes (8), management of HAE considering the recommendation of C1-INH: Preventive measures include weak administration of androgens such as danazol-stanozolol, fresh frozen plasma (FFP), and antifibrinolytic agents such as e-aminocaproic acid and tranexamic acid (9), avoiding activities known to trigger attacks in sick people, early intervention in medical surgeries (short-term prevention), and management of consecutive attacks of acute angioedema (acute phase) (8).

Conclusion

Even though hereditary angioedema is a rare condition, it can be fatal if not discovered early, since the clinical picture might lead us to misdiagnose individuals. Prevention and early detection of HAE attacks, especially laryngeal edema, may be life-saving for HAE patients.

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Conflict of Interests

The authors declare no conflicts of interest regarding the publication of this case report on hereditary angioedema in Afghanistan.

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