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H. Haluk Akar[1], F. Tahan[1], T. Kurt[2], I. Solmaz[2]

A case of hereditary angioedema who presented with difficulty in urination and globe

[1]Erciyes University School of Medicine, Department of Pediatric Allergy and Immunology, Kayseri, Turkey
[2]Erciyes University School of Medicine, Department of Pediatrics, Kayseri, Turkey

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Hereditary angioedema; C1 inhibitor deficiency; difficulty in urination; globe

Corresponding author
Himmet Haluk Akar, MD
Erciyes University School of Medicine
Department of Pediatric Allergy
Kayseri, Turkey
Phone: + 90 352 2076666/25125
Fax: + 90 352 4375825
E-mail: himmetakar@gmail.com

Summary
Hereditary angioedema (HEA) is a disease characterized by decreased levels or function of C1 esterase inhibitor (C1-INH). The symptoms of HEA in pediatric age group generally consist of recurrent episodes of soft tissue swelling. These symptoms can be transient, subtle, and varied in severity. Genitourinary system is rarely affected in this disease. Here, a three-year-old girl who presented with angioedema on her hands, fingers, and face, and had difficulty in urination and globe is reported. The aim of this case is to focus on this rare disease, hereditary angioedema, which presented with difficulty in urination and urinary globe.

Introduction

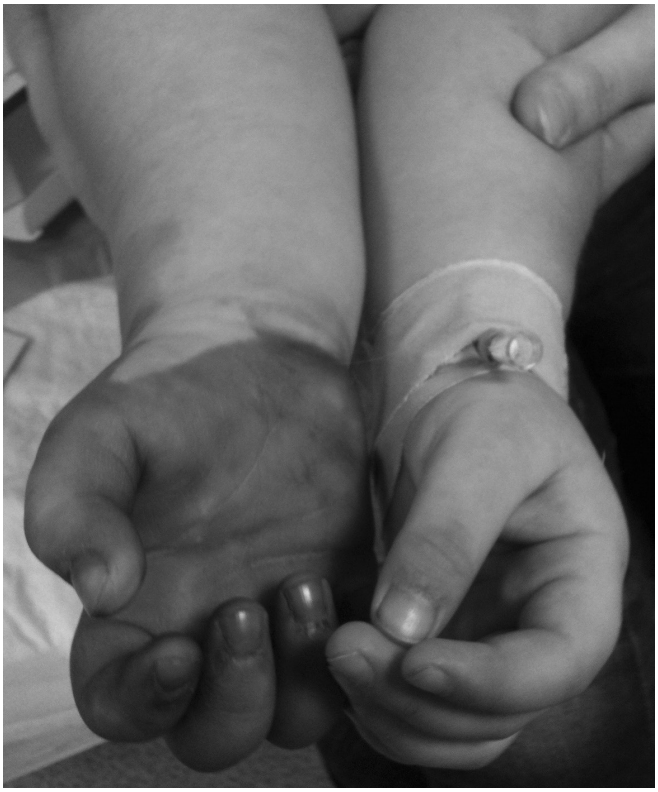
C1-INH deficiency can be genetic or acquired. HAE is a rare, life-threatening condition manifested by acute attacks of facial, laryngeal, peripheral or genital edema. The estimated prevalence of HAE is between 1 in 10,000 and 1 in 150,000 people (1,2). The genetic HEA deficiency is due to mutations in one of the two alleles of the C1-INH gene that result in reduced protein levels in plasma (type I HEA) or in normal protein levels but always in reduced function (type II HEA). A third type has also been reported, occurring exclusively in women who have normal C1-INH levels and function (Type III HEA). It is estimated that 20% to 25% of HAE cases are caused by spontaneous mutations in patients with no family history of the disease (3,5). The development of angioedema in C1-INH-deficient patients involves the inappropriate generation of kinins (particularly bradykinin) that stimulate vascular smooth-muscle relaxation and induce increased permeability. C1-INH is a serine protease inhibitor (serpin), also known as SERPING1, that blocks the activity of some complement components (e.g. C1r, C1s, Mannose binding lectin-associated serine protease; MASP-1 and MASP-2). C1-INH also controls contact-kinins, coagulation, and fibrinolytic cascades (6).
In this paper, we report a case with rarely manifested hereditary angioedema who presented with difficulty in urination and globe.

Case report

One day, a three-year-old girl with HEA was admitted to our emergency pediatric department with swelling of right forearm and urinary globe, and difficulty in urination (**figure 1**). She didn't have dysuria, fever or pelvic pain. Urinary globe, mild external genital swelling and right forearm angioedema were examined in her physical examination. Her urine analyses,

complete blood counts, biochemical tests, C reactive protein were normal. The patient was treated with C1 esterase inhibitor concentrate. Within a few hours, her difficulty in urination decreased, and urinary globe as well as right forearm angioedema resolved. She was being followed in pediatric allergy department. In her past life, the patient has experienced a lot of angioedema on her hands, fingers and face. When she was 1.5 year old she had experienced her first angioedema attack, which had been treated with intravenous corticosteroids and antihistamines without effect in a private hospital. At first, the symptoms usually subsided spontaneously within a few days. On the day of her first pediatric allergy clinic visit (she was 20 months old), on her physical examination blood tests [eosinophil counts (3.1%, 370/mm^3), nephelometric IgE 70 (0-90 iU/mL)] and skin prick test were normal. C1 inhibitor [41.7 and 63 (210-345 mg/dL)] and C4 [2.9 and 2.7 (16-38 mg/dL)] levels were low for two times. There was no similar history in her family. Father's and mother's C4 and C1 inhibitor levels were normal. These laboratory data and clinical features were compatible with a diagnosis of type I HAE.

Figure 1 *- Angioedema on forearm*



Discussion

Hereditary angioedema accounts for approximately 2% of all cases of angioedema. Three types of HAE have been described in the literature: type I HAE (approximately 85% of cases), type II HAE (approximately 15% of cases) and type III HEA (less than 1% of cases) without abnormalities of complement or C1 inhibitor characterized by a coagulation factor XII gene mutation and seen primarily in females. In 50% of patients with HAE, the initial symptoms appear during the first decade of life, in 35% symptoms appear during the second decade, and in the remaining 15% symptoms appear after 20 years of age. Almost 20-25% of patients lack a family history, which can make difficulty in diagnosis (4,5).

The C1NH gene maps onto chromosome 11q12-q13.1 and it is organized into 8 exons and 7 non introns, particularly rich in repetitive *Alu* sequences (7). Although the de novo mutation also made diagnosis difficult because of the lack of family history, this type of mutation seems not so rare. In the literature, more than 300 deficiency-causing mutations have been identified, and approximately 25% of them occur de novo. De novo mutations can belong to all types of deleterious changes (single nucleotide changes, microdeletions-insertions, and gross deletions) and their distribution according to these types is similar to that found for hereditary angioedema in general (8). In our patient's family, there was no similar history for HEA. Anamnesis and laboratory finding suggested that our patient most likely had de novo mutation.

In the literature, episodes affecting the urinary bladder were very rare (3:1000) (9). Hematuria association with HEA was rarely published in the literature (10,11). Our patient was admitted with forearm swelling, difficulty in urination and globe, without hematuria and dysuria, and her symptoms were decreased with the administration of C1 esterase inhibitor concentrate. Her laboratory tests (urine, blood) were normal for the other etiologies of urinary globe and difficulty in urination.

In summary, we have described a case of type I HEA with most likely de novo mutation. The patient had recurrent episodes of angioedema, urinary globe and difficulty in urination, which resembled manifestations of urinary infections and other etiologies of urinary globe. HAE should be taken into consideration for the differential diagnosis of urinary globe etiology.

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