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AİLEVİ AKDENİZ ATEŞLİ BİR OLGUDA C1-İNHİBİTÖR EKSİKLİĞİ

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ÖZ:
C1 inhibitör (C1-INH) eksikliği ilk kez 1881 yılında tanımlanmıstır. Hastalığın prevalansının 1/50000 olduğu tahmin edilmektedir. C1-INH eksikliği nadir görülmesine rağmen, birçok hastalığın seyri sırasında da gelisebilmektedir. On yasında kız hasta hastanemize yüzünde ve ellerinde sislik ve karın ağrısı sikayetiyle basvurdu. Hasta beş yıl önce ailevi Akdeniz atesi (FMF) tanısı almıstı ve kolsisin tedavisi kullanmaktaydı. Ellerinde ve yüzündeki sislikler üç yıldır bir ya da iki ayda bir kere oluyor ve 2 gün içinde kendiliğinden düzeliyormus. Laboratuvar incelemelerinde kompleman C4 seviyesi 5mg/dl (normal sınır: 10-40mg/dl), C1-INH düzeyi 0,08 g/L (normal sınır: 0,15-0,35 g/L) idi. Hastaya C1-INH eksikliği tanısı konuldu. Traneksamik asit tedavisi baslandı. Hastanın altı aylık takibi süresince, sadece bir kez hafif bir anjioödem atağı görüldü. Bildiğimiz kadarı ile C1-INH eksikliği ve FMF birlikteliği daha önceden bildirilmemistir. Bu yazıda FMF seyri sırasında C1-INH eksikliği tespit edilen bir olgu sunulmustur.

Anahtar Kelimeler: C1 Inhibitör Eksikliği, Ailevi Akdeniz Atesi

A CASE OF C1-INHIBITOR DEFICIENCY WITH FAMILIAL MEDITERRANEAN FEVER

ABSTRACT
The clinical syndrome caused by C1-inhibitor (C1-INH) deficiency was first described in 1881. The prevalence of the disease has been estimated to be 1/50,000. Although it is a rare disorder, C1-INH deficiency may develop during the course of diverse diseases. A 10-year-old girl was referred to our hospital because of swelling on her face and hands and abdominal pain. She had been
diagnosed with familial Mediterranean fever (FMF) 5 years previously and treated with colchicine. The patient had had swelling on her face and hands monthly or bimonthly since 3 years old and the symptoms had been resolving without treatment within 1-2 days. Laboratory investigations revealed that her C4 complement level was 5 mg/dl (normal range: 10-40 mg/dl) and C1-INH level was 0.08 g/L (normal range: 0.15-0.35 g/L). C1-INH deficiency was diagnosed. Treatment with tranexamic acid was started. During the follow-up for 6 months she had only one mild attack of angioedema. To our knowledge, the coexistence of C1-INH deficiency and FMF has not been previously reported. We herein present a patient with C1-INH deficiency that developed during the clinical course of FMF.

Keywords: C1-İnhibitor Deficiency, Familial Mediterranean Fever

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INTRODUCTION

The clinical syndrome caused by C1-inhibitor (C1-INH) deficiency was first described in 1881[1]. There are two forms of C1-INH deficiency: hereditary and acquired. Clinical manifestations of both forms are similar and characterized by the occurrence of subcutaneous and submucosal swellings in any part of the skin, and in the respiratory and in gastrointestinal tracts. In the hereditary form, symptoms usually appear early in life and are normally accompanied by a family history[2]. Acquired C1-INH deficiency has been observed in association with lymphoproliferative disorders, malignancy, autoimmune diseases, and infections[3]. It primarily affects adults or elderly patients with no family history for the disease[4].

Familial Mediterranean fever (FMF) is an autosomal recessive disorder characterized by recurrent, self-limited episodes of fever and serosal inflammation accompanied with a marked acute-phase response[5]. To our knowledge, the coexistence of C1-INH deficiency and FMF has not been previously reported. We herein present a patient with C1-INH deficiency that developed during the clinical course of FMF.

CASE REPORT

A 10-year-old girl was referred to our hospital because of swelling on her face and hands and abdominal pain. She had been diagnosed with FMF 5 years before and treated with colchicine. She had recurrent fever and abdominal pain attacks, although the other findings (arthritis, arthralgia, myalgia, erysipelas-like erythema, and pleuritis attacks) associated with FMF were absent. The patient had had swelling on her face and hands monthly or bimonthly since 3 years old and the symptoms had been resolving without treatment within 1-2 days. Her physical examination was unremarkable except for swelling on her face (Fig. 1) and her right hand (Fig. 2). Laboratory investigations revealed that her C4 complement level was 5 mg/dl (normal range: 10-40 mg/dl), C1-INH level was 0.08 g/L (normal range: 0.15-0.35 g/L), and serum amyloid-A level was 15.3 mg/dl (normal range: 0-5.8 mg/dl). Complement C3 and IgD levels were within normal limits. Antinuclear antibodies (ANA) were negative. Serum BUN, creatinine, electrolytes, complete blood count, and urine analysis were unremarkable. Abdominal ultrasound and flow cytometry analysis of peripheral blood showed no abnormalities. An E148Q homozygous mutation was identified. C1-INH deficiency was diagnosed. Treatment with tranexamic acid 30 mg/kg/day was started. During the follow-up for 6 months she had only one mild attack of angioedema.

Fig. 1. Angioedema on the face

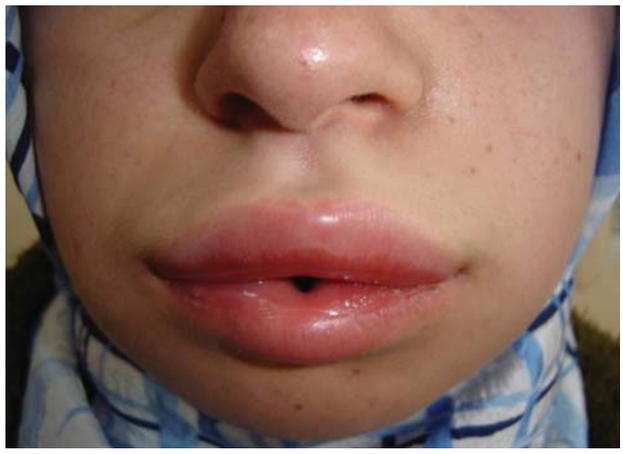
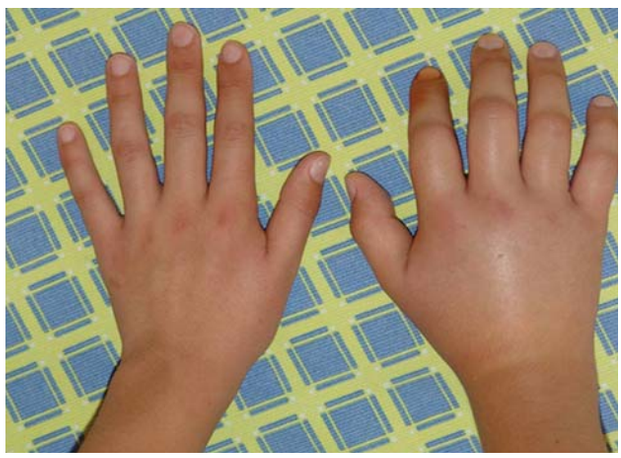


Fig. 2. Angioedema on the right hand



DISCUSSION

C1-INH is a serum α2-globulin molecule and a member of the serpin family of protease inhibitors. It primarily affects adult or elderly patients with no family history for the disease. The gastrointestinal involvement is thought to be segmental and transient with reversion to normal within several days of an attack. Abdominal pain, nausea, and vomiting are the dominant symptoms in approximately 25% of patients[6]. Acute attacks of abdominal pain can mimic surgical emergencies.

Cardinal signs and symptoms of FMF are peritonitis (93.7%), fever (92.5%), arthritis (47.4%), pleuritis (31.2%), myalgia (39.6%), and erysipelas-like erythema (20.9%).7 Abdominal FMF attacks resemble the clinical presentation of acute abdomen with severe abdominal pain and rigidity, and onset is sudden and acute, leading to rapid development of symptoms within 1-2 hours.

There are two forms of C1-INH deficiency: hereditary and acquired. In the hereditary form, symptoms usually appear early in life and are normally accompanied by a family history[3]. Acquired C1-INH deficiency has been observed in association with lymphoproliferative disorders, malignancy, autoimmune diseases and infections[2]. However, to our knowledge, no association between FMF and C1-INH deficiency has been previously reported. Our patient developed recurrent fever and self-limiting peritonitis attacks that were typical for FMF. Her symptoms resolved after colchicine started. She was homozygous for the E148Q mutation. The carrying of this mutation is reported to be high in healthy populations, and especially the Turkish population. Although E148Q mutation is speculated to be a polymorphism, we cannot rule out the possibility that E148Q has a disease-causing effect while many patients carrying this mutation have been reported in the literature[8]. However, during follow-up she developed clinical features of angioedema, and laboratory investigations revealed a low serum C1-INH level. Although recurrent abdominal attacks may complicate the clinical course of C1-INH deficiency, the good response to colchicine and positive MEFV gene mutation confirmed the diagnosis of FMF. Management of patients with C1-INH deficiency includes antifibrinolytics (tranexamic acid, epsilon aminocaproic acid), androgens (danazol), and C1-INH concentrates[3]. Treatment with tranexamic acid 30 mg/kg/day in our patient effectively reduced the attacks.

In summary, we herein reported the occurrence of C1-INH deficiency together with FMF for the first time in the literature.

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