A rare cause of recurrent abdominal pain: Three familial cases with hereditary angioedema

Sir,

Hereditary angioedema (HAE) is caused by a heterozygous deficiency of complement C 1 inhibitor and is characterized by recurrent angioedema in the face, trunk, larynx, and gastrointestinal system. C1 inhibitor regulates several inflammatory pathways, and patients with hereditary angioedema have intermittent cutaneous or mucosal swellings because of a failure to control local production of bradykinin.[1] Herewith reporting familial cases with recurrent abdominal pain.

A 33-year-old female patient presented several times at general surgery, obstetrics, gastroenterology and urology polyclinics and at the emergency service complaining of abdominal pain particularly occurring during the menstruation for 10 years and her two sisters (a 28-year-old and 16-year-old) had similar complaints for several years. In the last attack, the patient underwent a laparatomy to evaluate for ruptured cyst but did not show any rupture. Appendisectomy were planned for sisters for a few times, but the family refused the operations. Our patients' C4 levels were measured respectively to be 5.01 mg/dl, 4.71 mg/dl, and 6.72 mg/dl (normal value 16-38 mg/dl) and C1 inhibitor levels were measured respectively to be 0.03 mg/dl, 0.05 mg/dl, and 0.08 mg/dl (normal value 0.15-0.35 mg/dl).

Patient 1 and 2 were put on 200-400 mg/day danazole capsule treatment, and first patient was planning to become pregnant, so her treatment was not started. The patients were followed-up every month, and liver enzymes, lipid profile, complete blood cell count, alpha-feto protein, and urinalysis were performed. On month 4 of treatment, the doses were dropped by half in both cases. Neither patient developed any side effect associated with danazole, except for weight gain over the 4-month treatment period.

The patients' laboratory findings, positive family history, and response to danazole treatment confirmed HAE diagnosis.

Hereditary angioedema is also seen on the intestine wall and causes severe attacks of spasmodic abdominal pain. About 50% of the attacks are accompanied by abdominal attacks. Abdominal pain may be the most common symptom in some cases. Pain attacks may be co-present with nausea and vomiting and may cause unnecessary operations. These attacks never cause necrosis on the intestine wall, but the fluid leaking from intestinal loops may sometimes be too much and cause acid, hypotension, and obstruction in the intestine lumen. There are only a few patients who suffer from abdominal attacks only.[2] All of our patients did not have any swelling in their bodies, but they only had abdominal pain.

Although what triggers hereditary angioedema attacks is not clear, attacks may occur during menstruation and may increase in pregnancy.[3] Menstruation was the major triggering factor in all 3 of our patients.

Treatment of HAE involves short-term prophylaxis, long-term prophylaxis, and management of acute attacks. Protection is of utmost importance for HAE patients who should avoid trauma, cold, and stress as much as possible. Treatment of acute attacks should include respiratory support. Copious amounts of intravenous liquids, analgesics, and anti-emetics can be administered to ensure stability. Anti-fibrinolytic drugs, aminocaproic acid, and tranexamic acid can decrease acute attacks.[4] C1 inhibitor concentrations to be administered at a dose of 20 U/kg improve the acute attack in 30 to 60 minutes.[3]

The attenuated androgens, danazol, and stanozolol cure the symptoms and correct the biochemical defect of HAE by increasing C4 concentration and C1 inhibitör synthesis.[4] There are two different protocols in the use of the androgen steroid, danazol in HAE prophylaxis. The most common side effect in patients put on danazol is weight gain. Masculinization, headache, loss of or increase in libido, increased hirsutism, hair loss, shrinking of breasts, menstrual irregularity, impaired liver function tests, cholestatic jaundice, and hepatic adenomas may also be seen.[5]

Our patients reported a decrease in the frequency of attacks and severity of pain. On the fourth month of treatment, we dropped medication doses by half in both patients and planned the rest of the treatment in this way. We did not observe any critical side effect in our patients over the four-month treatment process.

The significance of this paper is that the family members were followed for long-recurring abdominal pain etiology, planned unnecessary operations for several times, and one patient even had an operation. Our patients did not display angioedema apart from recurrent colic pain which delayed the diagnosis. It is known from literature data that causes of recurrent abdominal pain include pancreatitis, cholecystitis, appendicitis, intestinal obstruction, porphyria, familial mediterranean fever, and there are only a few patients who suffer from abdominal attacks only. Thus, HAE should be among these differential diagnoses, and patients should be evaluated in this respect.

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REFERENCES

1. Longhurst H, Cicardi M. Hereditary angio-oedema. Lancet 2012;379:474-81.
2. Bork K, Staubach P, Eckardt AJ, Hardt J. Symptoms, course, and complications of abdominal attacks in hereditary angioedema due to C1 inhibitor deficiency. Am J Gastroenterol 2006;101:619-27.
3. Caballero T, Farkas H, Bouillet L, Bowen T, Gompel A, Fagerberg C, *et al*. International consensus and practical guidelines on the gynecologic and obstetric management of female patients with hereditary angioedema caused by C1 inhibitor deficiency. J Allergy Clin Immunol 2012;129:308-20.
4. Borum ML. Hereditary angioedema: an unusual case in an African-American woman. J Natl Med Assoc 1998;90:115-8.
5. Cicardi M, Bork K, Caballero T, Craig T, Li HH, Longhurst H, *et al*. Evidence-based recommendations for the therapeutic management of angioedema owing to hereditary C1 inhibitor deficiency: Consensus report of an International Working Group. Allergy 2012;67:147-57.

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