Recurrent Abdominal Pain in 2 Years Old Girl due to Hereditary Angioedema

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ABSTRACT

There is considerable variation among children in their perception and tolerance for abdominal pain. This make the evaluation of chronic abdominal pain is difficult(1). Hereditary angioedema is a rare differential diagnosis to cause abdominal pain in 2 years old child. We report a 2 years old girl with recurrent abdominal pain that require recurrent visit to ER without accompanying skin swelling whose diagnosis as hereditary angioedema and it is the first case reported at this age.

Keywords: Recurrent abdominal pain, Hereditary angioedema

1. INTRODUCTION

Hereditary AngioEdema(HAE) affects about 1 in 10,000 to 1 in 50,000 people worldwide(2). HAE is a rare autosomal dominant inherited disease which is characterized by an episodic, self-limiting increase in vascular permeability. Symptoms commonly involve in nonpitting, nonpruritic skin swellings, abdominal pain, and airway swelling cause significant morbidity and potential mortality(2,3). abdominal angioedema attacks can lead to unnecessary surgery and delay in diagnosis, as well as to narcotic dependence due to severe pain; and cutaneous attacks can be disfiguring and disabling(4).

2. CASE REPORT

2 years old girl, complained of recurrent severe abdominal pain, generalized, not radiated, associated with vomiting and poor oral intake. three attacks happened within six months, Each attack proceeded by URTI. No history of diarrhea or constipation. Physical examination showed normal vital signs and normal growth parameters (on 50th centile), No edema or skin rash during the bouts of the abdominal pain, Abdomen was generalized tender but not rigid. Initial investigations where normal including CBC, CRP, ESR, electrolytes, lipase and LFT. IGD level and Familial Mediterranean fever genetic study came normal. Ultrasound of the abdomen done 3 times in ER which shows no abnormality apart from minimal free fluids in the abdomen. Every time she treated with IVF and pain killer for 3-5 days till pain subsided gradually and oral intake improved.
Six month later, she is still complaining of recurrent abdomen pain and stared to have non-pruritic swelling in the extremity after minor trauma, which persist for 24-48 hours then disappear spontaneously. It did not require ER visit or medications. And not associated with respiratory symptoms or swelling of the face. No family history of similar condition. Clinical diagnosis of hereditary angioedema was done after Investigations requested including: total complement activity (CH50) <10 U/mL (normal 32 - 58). C1-esterase inhibitor (activity) < 25% (normal 70 - 130). C1-esterase inhibitor (protein) < 0.05 g/L (normal 0.18 - 0.32). C4 < 0.056 g/L(normal 0.1 – 0.4 ). After diagnosis family was screened and show that father and her 5 years old sister had low c1-estrase inhibitor, but they had never have the symptoms. After diagnosis patient started on c1 esterase inhibitor upon complaining of abdominal pain. She showed marked improvement with disappearance of symptoms within 2 hours.

3. DISCUSSION

Although rare, hereditary angioedema (HAE) is associated with episodic attacks of edema formation that can have catastrophic consequences(4). There are three different subtypes(2) of HAE based on the underlying genetic defect in the control of the blood protein C1-esterase inhibitor:

- Type I HAE: This subtype is characterized by decreased levels of functional C1-INH protein. About 80-85% of patients suffer from this form of the disease.
- Type II HAE: This type is associated with normal or increased levels of a dysfunctional C1-INH protein resulting in reduced levels of C1-INH activity.
- Type III HAE: (estrogen-dependent hereditary angioedema or hereditary angioedema with normal C1 activity)(5). Recently a type III has been postulated: HAE type III arises independently of a C1-INH deficiency. It is relatively rare and primarily affects women. In some patients a mutation of factor XII was found(5,6,7,8).

C1 esterase inhibitor, a member of the serpin family of serine protease inhibitors, is the major inhibitor of several complement proteases (C1r, C1s, and mannose-binding lectin-associated serine protease [MASP] 1 and 2) and contact-system proteases (plasma kallikrein and coagulation factor XIIa) and a relatively minor inhibitor of the fibrinolytic protease plasmin and the coagulation protease factor Xia(9).

Characteristic locations for HAE attacks involve the skin, upper respiratory tract, and gastrointestinal system(10,11). Symptoms are self-limited, progressing over hours, and can persist from 1 to 4 days and the frequency of attacks can vary from weekly to a few attacks per year(10,12).

Fig. 1 Pathophysiology of HAE. Decreased C1-INH activity leads to increased production of bradykinin. Bradykinin binds to its receptor on endothelial cells, increasing vascular permeability and leading to the characteristic symptoms of HAE(21).

Premonitory symptoms associated with HAE can develop as little as hours or up to days before the start of an attack(13). Gastrointestinal tract involvement is an important feature and one of the most common in HAE. The difficulty in recognizing gastrointestinal symptoms as being related to HAE often leads to a delay in diagnosis and to unnecessary surgical procedures. The most common symptoms include varying degrees of nausea, vomiting, diarrhea, and abdominal pain, which are the result of intestinal edema. The abdominal pain can present acutely or as recurrent pain and is described by patients to be cramping and colicky in nature. The pain patients experience can be moderate to severe in intensity and is usually present in 43–93% of all HAE attacks. Many of these abdominal pain symptoms can occur for many years without any associated respiratory or cutaneous involvement. Not only does the transient edema of the bowel wall cause the aforementioned symptoms, but it may also lead to intestinal pseudo obstruction(14,15,16).
Table 1: The 3 types of HAE can be differentiated with complement testing and, in the case of type III, genetic testing

<table>
<thead>
<tr>
<th>laboratory markers that can be used to distinguish among hereditary angioedema (HAE) subtype</th>
<th>Type I HAE</th>
<th>Type II HAE</th>
<th>Type III HAE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antigenic C1-INH functional C1-INH</td>
<td>low</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>C1q level</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>C2 level</td>
<td>low</td>
<td>low</td>
<td>Normal</td>
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<tr>
<td>C4 level</td>
<td>low</td>
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<td>Normal</td>
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Currently, antifibrinolytics, attenuated androgens, and C1INH replacement therapy are used for the treatment of children with HAE. Antifibrinolytics are recommended for long-term prophylaxis because of their favorable safety profiles, but efficacy may be lacking. Attenuated androgens administered in the lowest effective dose are another option. C1INH replacement therapy is also effective and safe for children. Regular monitoring and follow-up of patients is highly recommended.²⁰

4. CONCLUSION

Gastrointestinal symptoms are a common feature of HAE attacks in children and can present in a wide array of clinical manifestations. Respiratory symptom is not the only presentation for HAE. Symptoms can be nonspecific and may overlap with other abdominal conditions leading to delay in diagnosis and treatment. Physicians should consider HAE as a differential diagnosis when presented with a cause of unexplained abdominal pain. A combination of an individualized action plan, pharmacologic therapy can help alleviate the pain and decrease patient distress and unnecessary surgeries and decrease mortality.

REFERENCES
