CASE REPORT

Hereditary angioedema (HAE): a cause for recurrent abdominal pain

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Accepted 29 October 2016

SUMMARY

A 44-year-old Hispanic woman presented to the emergency room with a 2-day history of sudden onset of severe cramping left lower quadrant abdominal pain associated with ~20 episodes diarrhoea. Abdominal CT scan exhibited bowel wall oedema and acute extensive colitis. On the basis of the preliminary diagnosis of acute abdomen, the patient was admitted under the surgical team and treated for acute colitis. Since her family history was significant for hereditary angioedema (HAE), complement studies were performed which revealed low complement C4 levels and abnormally low values of C1q esterase inhibitor. Thus, the diagnosis of HAE type I was established. This case report summarises that the symptoms of HAE are often non-specific, hence making the underlying cause difficult to diagnose.

BACKGROUND

Hereditary angioedema (HAE) is a rare genetic disorder caused by deficiency or dysfunction of the C1 inhibitor. Its prevalence is estimated between 1:10 000 and 1:150 000 with no sexual or ethnic variations.^{1–3} HAE classically presents with recurrent episodes of angioedema and affects the skin, bowel or upper airway. The diagnosis of HAE (type I or II) is based on a suggestive clinical history and physical findings, combined with abnormally low levels of complement C4 on complement studies. Family history of angioedema strongly supports the diagnosis.⁴ The diagnosis of HAE is challenging due to its rarity and can be delayed further if the presentation is unusual mimicking other disorders. This case is reported due to its rare presentation with symptoms limited to gastrointestinal system without any pharyngeal or cutaneous manifestations.

CASE PRESENTATION

A 44-year-old Hispanic woman presented to the emergency room (ER) with a 2-day history of sudden onset of severe cramping left lower quadrant abdominal pain associated with ~20 episodes of non-bloody watery diarrhoea. She denied any fever, nausea, vomiting, anorexia or weight loss. She also denied any recent travel or sick contacts. Her medical history was significant for similar episodes of abdominal pain that resolved spontaneously. Her family history was significant for HAE in brother, sister and mother.

Her vital signs were stable on presentation. On physical examination, chest was clear to auscultation bilaterally, no wheezes. S1S2 were heard, no murmur, rubs or gallops. Abdomen was distended and tender with hyperactive bowel sounds. Labs

showed no leucocytosis, and normal erythrocyte sedimentation rate and C reactive protein. The workup for infectious diarrhoea including stool white cell counts, ova/parasites, stool culture and stool for occult blood was negative. Stool for *Clostridium difficile* toxin and antigen were also negative. Abdominal CT scan exhibited bowel wall oedema and acute extensive colitis involving the ascending and transverse colon without evidence of obstruction or perforation (figures 1 and 2).

The patient was admitted under the surgical team for preliminary diagnosis of acute abdomen. She was kept nil per oral, given intravenous fluids for hydration, morphine for pain control and intravenous antibiotics ceftriaxone and metronidazole were initiated empirically. In view of positive family history and bowel wall oedema, complement studies were performed which revealed low complement C4 levels and abnormally low values of C1q esterase inhibitor. Hence, the patient was diagnosed to have HAE type I.

TREATMENT

Management of HAE may include the treatment of acute attacks, short-term prophylaxis to prevent an attack and long-term prophylaxis to minimise the frequency and severity of recurrent attacks.⁵ Before 2009, fresh frozen plasma, anabolic androgens and antifibrinolytics were the major treatment options available for the management of HAE.⁶ Ecallantide (plasma kallikrein inhibitor) and icatibant (bradykinin B2 receptor antagonist) were approved by FDA in 2009 and 2011, respectively, for the management of acute attacks of HAE.^{7 8}

On the basis of the diagnosis, our patient was treated with ecallantide (kallikrein inhibitor) for her acute HAE attack. She was monitored for 48 hours in our hospital and was then discharged in a stable condition. She was also advised to avoid common triggers for HAE attacks like emotional stress or minor physical trauma.⁵

OUTCOME AND FOLLOW-UP

During the follow-up visits for a period of 8 months, the patient endorsed marked improvement in her symptoms with significantly decreased frequency of episodes of abdominal pain.

DISCUSSION

HAE is an autosomal dominant disorder due to deficiency (85% of patients) or dysfunction (15% of patients) of the C1 esterase inhibitor leading to dysregulation of complement and kallikrein-kinin systems.^{9–11} The classical presentation of HAE is

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To cite: Soni P, Kumar V, Alliu S, et al. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2016-217196

Figure 1 Axial CT image of the abdomen/pelvis showing bowel wall oedema involving the ascending and transverse colon.

recurrent episodes of severe swelling (angioedema) over limbs, face, intestinal tract and airway with its onset in childhood and early puberty. These attacks may be triggered by minor trauma or stress may trigger an attack, however swelling often develops in the absence of any known trigger. Symptoms of HAE may occur at any age, but most attacks start in the paediatric age group. According to the survey of 221 patients with HAE about half of first attacks of HAE occur before age 10 and nearly 90% of first attacks occur by age 20.¹

In the absence of the treatment, an individual can have attacks every week with most episodes lasting for ~3–4 days. The presentation of HAE mimics other cutaneous disorders such as cholinergic urticaria, solar urticaria, chronic urticaria

Figure 2 Coronal CT image of the abdomen/pelvis showing bowel wall oedema involving the ascending and transverse colon.

and drug eruptions. In our case, the patient presented with the gastrointestinal symptoms solely in the absence of any cutaneous manifestations and hence making the underlying cause difficult to diagnose.

This case demonstrates that gastrointestinal symptoms may be the only manifestation of HAE obscuring the diagnosis due to lack of cutaneous, oropharyngeal and respiratory involvement. The gastrointestinal symptoms are due to bowel wall oedema and may present as varying degrees of colicky pain, nausea, vomiting and/or diarrhoea. The absence of fever, peritoneal signs or neutrophilia may distinguish from peritonitis. However, during severe abdominal attacks, neutrophilia (without increased bands), hypovolaemia from fluid losses or haemoconcentration from plasma extravasation may mimic peritonitis.^{12–14} Treatment with C1 inhibitor concentrates, ecallantide (kallikrein inhibitor) and icatibant (bradykinin B2 receptor antagonist) may prevent further episodes.

Learning points

- It is important to recognise the various ways hereditary angioedema (HAE) can present, including isolated gastrointestinal symptoms. This will help us avoid unnecessary invasive procedures and provide timely administration of prophylactic therapy.
- Even though 90% of the first episode of HAE attack occurs by the age of 20 (according to a survey of 221 patients with HAE), HAE should still be ruled out in all the patients presenting with episodic abdominal pain irrespective of the patients age at first attack.
- Use of ecallantide (kallikrein inhibitor) as a treatment for acute HAE attack showed significant improvement in patient's condition with decreased frequency of abdominal pain attacks.

Contributors PS contributed to conception and design of the manuscript, drafting, critical revision and copy-editing of the manuscript. VK involved in the critical revision and copy-editing of the manuscript. SA contributed to drafting and critical revision of the manuscript. VS contributed to critical revision of the manuscript. The manuscript is an original work of all authors. All the authors have read and approved the final version of the manuscript.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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