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CASE REPORT

Hereditary Angioedema Presenting as Isolated Jejunal Swelling

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Abstract

Hereditary Angioedema (HAE) is a rare disorder caused by C1 esterase inhibitor deficiency or dysfunction. Patients with HAE usually present without urticaria or pruritis affecting the skin, upper airway, or the gastrointestinal tract. They can also present with involvement of unusual sites making the diagnosis challenging and leading to unnecessary testing and complications. Prompt diagnosis and treatment is crucial to prevent mortality and morbidity associated with acute flare. Here we present, what is believed to be second case of isolated involvement of the jejunum from an attack of HAE.

Keywords: Hereditary angioedema, Acute abdominal pain

1. Introduction

Hereditary Angioedema (HAE) is a rare autosomal dominant condition caused by C1esterase inhibitor (C1INH) deficiency or dysfunctional C1INH resulting in increased bradykinin and nonpitting edema of subcutaneous and mucosal tissue in the upper respiratory and gastrointestinal tracts.[1,2] The prevalence of C1INH deficiency is between 1:50,000 to 1:100,000 and that of HAE with normal C1INH is unknown.[3] To date there is no reported disparity in HAE prevalence by gender or ethnic groups.[4] HAE can be life threatening if it involves the upper respiratory tract, and gastrointestinal manifestations are nonspecific, which might contribute to misdiagnoses and inappropriate surgeries.[5,6]

We present a case of a 33-year-old male with a known history of HAE who presented to the emergency department (ED) with nonspecific abdominal complaints and was found to have isolated jejunal swelling. Although, gastrointestinal presentations are common, based on our extensive literature review, we believe this is the second known case of HAE with isolated jejunal involvement [Appendix Table].

2. Case presentation

33-year-old African American male presented with abdominal pain, nausea and vomiting for one day. The pain was sudden in onset, initially diffuse and later localized to the epigastric region, severe in intensity, intermittent, crampy in nature and associated with nausea and vomiting. Patient reported having "lumps" on the left side of his abdomen and was concerned about the swelling. The review of systems was positive for poor oral intake and nausea; negative for facial or neck swelling, dysphagia, throat/tongue swelling, respiratory distress, or triggers for exacerbation (trauma, dental work, unusual foods, excessive excitement, or sleep deprivation). Past medical history was significant for HAE type I diagnosed in 1997 at age 10 and asthma since childhood. He reported having 5–6 attacks of HAE a year although previously attacks were as high as twice per month, and typically involved the face and neck. He had an endotracheal intubation in his 7th grade for laryngeal attacks. Patient reported allergy to eggs, and family history was significant for angioedema in maternal grandfather and paternal grandmother. It is unknown if there is any history of consanguineous marriage in the family.

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In the ED, patient was hemodynamically stable, afebrile and had oxygen saturation of 98% on room air. Clinical examination was positive for generalized abdominal tenderness to palpation, more pronounced at the left upper quadrant, but without any peritoneal signs. Laboratory results (from a year earlier) reported C1INH level 7 mg/dl (normal range 21–39 mg/dl), low C1 Esterase inhibitor function 13 (normal >67), Complement 4 serum levels of 8 mg/dl (normal range 14–44 mg/dl)]. White blood cell count at current presentation was 12,900 per m^3 (87% neutrophils without bandemia). Computerized tomography (CT) of abdomen and pelvis showed diffuse small bowel wall thickening throughout the jejunum, left sided abdomen, and moderate volume diffuse abdominopelvic free fluid (Figs. 1 and 2). The CT findings were thought to represent abdominal manifestations of hereditary angioedema. Patient was treated with C1INH concentrate IV, capsaicin topical cream, haloperidol, ketorolac, lorazepam, and ondansetron along with 1-L normal saline bolus. Following above-mentioned treatment, patient showed considerable clinical improvement and 12 h post treatment had complete resolution of all presenting symptoms including abdominal pain, nausea, vomiting and leukocytosis.

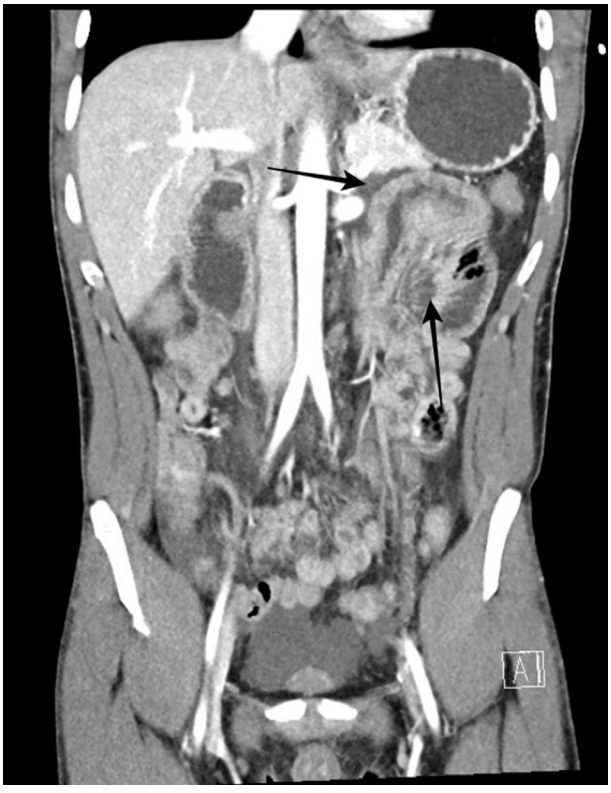

Fig. 1. Diffuse small bowel wall thickening throughout the jejunum.

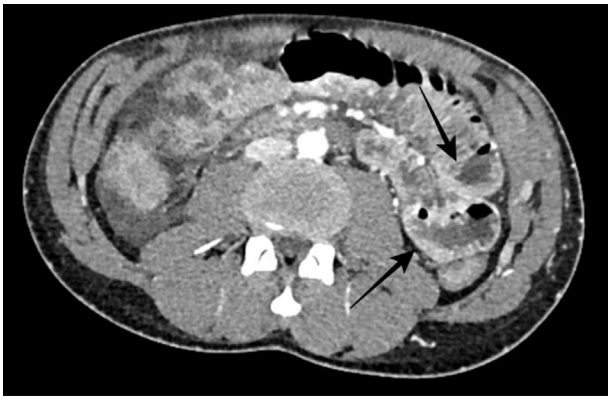

Fig. 2. Jejunum thickening and abdominopelvic free fluid.

3. Discussion

HAE is a rare autosomal dominant disorder which mostly is caused by a mutation in one of two alleles for C1INH gene, leading to reduced levels of C1INH or unfunctional C1INH. This results in complement activation and release of bradykinin, a potent vasodilator leading to angioedema flares.[7] HAE is distinct from angioedema-urticaria or histamine-mediated angioedema since it does not involve histamine and other mast cell-mediated pathway, which explains the lack of responses of HEA to antihistamines.[8]

Gastrointestinal manifestations of angioedema can include nonspecific complaints like abdominal pain, nausea, vomiting and diarrhea, which often lead to misdiagnoses. In a study conducted by Bork et al., 93.3% of patients had recurrent abdominal symptoms.[9] Diagnosis of HAE is challenging when the patients present only with abdominal symptoms.[10] CT scan as a part of investigation in such patients showed nonspecific bowel wall thickening. In the absence of skin findings, family history is the most important clue that guides diagnosis. C4 complement levels serve as a screening test due to high sensitivity and high negative predictive values.[11,12] If C4 complements levels are low, C1INH levels and function should be checked.[12] Our patient had low C4 complement/C1INH levels and low functional activity of C1INH. We found eight previously reported cases of HAE with gastrointestinal manifestations involving the small bowel. Among these, only one of them presented with isolated jejunum involvement, and our case is the second known case to present with an isolated jejunum involvement. All cases are illustrated in Appendix.

First line treatment of an acute attack includes plasma derived C1–INH concentrate, recombinant C1–INH, Icatibant, or Ecallantide. Fresh frozen

plasma (FFP) has been used for treatment of acute attacks, however, considered second line treatment. The most important intervention is patient education including identification and avoidance of triggers to prevent acute attacks. When attacks occur, patients should be advised to immediately go to the ED. Long term prophylaxis management with prophylaxis include use of C1–INH concentrate, lanadelumab (monoclonal antibody to plasma kallikrein), berotralstat (plasma kallikrein inhibitor), danazol or tranexamic acid. Mortality is 30–50% in untreated cases of HAE.[13]

4. Conclusion

HAE is a rare condition, which can present with recurrent nonspecific abdominal manifestations. Physicians should have high suspicion for HAE flares in patients with abdominal pain who either have a family history or personal history of HAE. Though gastrointestinal presentation is very common, there are not many documented cases of isolated jejunal involvement on imaging. Once a diagnosis is made, a treatment plan should include patient education regarding when, where, and how to seek medical care in an acute flare as C1–INH concentrate is not readily available at every ER. All newly diagnosed patient should be referred to allergy and immunology clinic for long-term care plan.

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Credit author statement

All authors have contributed to the preparation of the manuscript, Dr. Ishtiaq was the lead author and Dr. Khaliq was the senior author. Drs. Gnanaraj, Harris and Kotwal provided useful input and edited the manuscript. This case has not been reported at any professional meeting. Consent was obtained from the patient prior to preparing the case report.

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Appendix

Table. Cases of Hereditary Angioedema involving Small Intestine.

Author	Age in years	Gender	Race	Chief Complaint	Angioedema of the face at presentation	Prior history of Hereditary Angioedema	Past Medical History	Family History	Involved Segment	Intervention
Weinstock et al. [1]	40	Male		Recurrent episodes of abdominal pain	No	No		Positive	Jejunum	Danazol
Courtier et al. [2]	21	Male		Recurrent abdominal pain, nausea and vomiting	No	Yes		Positive	Duodenum and Jejunum	Danazol
LoCascio et al. [3]	34	Female	African American	Abdominal pain, nausea, vomiting and diarrhea	No	Yes			Proximal and middle small bowel	Danazol
Diaz et al. [4]	17	Female	Hispanic	Abdominal pain and loose stools	No	Yes		Positive	Jejunum and distal ileum edema, colo colonic intussusception in the splenic flexure	Supportive care with Ecallantide and fresh frozen plasma
Abuzakuok et al. [5]	27	Male	Emirati	Abdominal pain	No	No	Thalassemia carrier		Gastric Mucosa and Proximal Jejunum	C1 inhibitor concentrate Danazol at discharge
Benrajab et al. [6]	32	Male	Caucasian	Abdominal pain, nausea and vomiting	No	No	Irritable bowel syndrome		Fourth portion of the duodenum and the proximal jejunum	Danazol
Riguzzi et al. [7]	14	Female		Abdominal pain and nausea	No	Yes			Small bowel	IV fluids and FFP
Riguzzi et al. [8]	47	Female		Abdominal pain and nausea	No	Yes			Bowel wall appeared diffusely thickened	Icatibant, discharged on Danazol

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