

Small bowel intussusception: An unusual presentation of angioedema

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ABSTRACT

This article presents a case report of a 13-year-old boy who presented to the Emergency Department with abdominal pain and vomiting. He had a known history of recurrent swelling but no previous abdominal episodes. A computed tomography scan revealed small bowel intussusception and he was scheduled for surgery. The patient had a history of multiple episodes of swelling of extremities, face, and genitalia. The Allergy Consult Service was consulted for perioperative management of his angioedema.

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Key words: Angioedema, bowel swelling, C1-INH, HAE, hereditary angioedema, intussusception, small bowel intussusception

CASE PRESENTATION

Chief Complaint

A bdominal pain and vomiting.

History of Present Illness

A 13-year-old African American boy presented with complaints of abdominal pain occurring off and on for 1 week. On the day of presentation he had noted exacerbation of the abdominal pain along with development of severe vomiting. He presented to a peripheral hospital where a computed tomography (CT) scan of his abdomen was obtained revealing small bowel intussusception involving the ileum. He was transferred to Pediatric Surgery at our hospital for possible surgical intervention. Given his medical history of recurrent swelling, the Allergy Service was consulted for perioperative management. He was passing flatus and had a bowel movement that morning.

Medical History

The patient had a reported history of multiple episodes of swelling of extremities, face, and genitalia. No previous abdominal or airway involvement was documented by history. He also had allergic rhinitis and asthma for which he was on allergen immunotherapy, mometasone nasal spray, and albuterol inhaler. He had bipolar disorder and was taking aripiprazole and bupropion mesylate. His review of systems was negative for fever, trauma, diarrhea, or illness in the family. The patient was living with foster parents.

Physical Examination

He was lying in bed and seemed in minimal distress. His vitals were stable with a temperature of 37.3°C, respiratory rate of 16/minute, heart rate of 76 bpm, and blood pressure of 127/59 mmHg. Some cervical lymph nodes were palpable but were <1 cm, discrete, and nontender. Abdominal exam revealed mild guarding and tenderness in the epigastric area, no rebound tenderness, and active bowel sounds. The remainder of the physical examination was within normal limits.

Laboratory and Radiological Findings

The initial and subsequent laboratory findings are presented in Table 1. Of note is the initial white blood cell count of 13.8 k/ μ L with 73% neutrophils and increase in absolute neutrophil count. His initial CT scan of abdomen is presented in Fig. 1.

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Table 1 Laboratory results

Results	Day 1	Day 2	Reference Range
WBC	13.8	10.1	4.8–12 k/ μ L
Hgb	14.3	11.6	14–18 g/dL
Hct	42	35.5	39–50%
Plts	378	343	140–340k/ μ L
Neutrophil (%)	73	61	35–71%
Lymphocyte (%)	19	27	25–45%
Monocyte (%)	7	9	0–10%
Basophil (%)	0	0	0–2%
Eosinophil (%)	1	3	0–6%
Neutrophil, absolute	10	6.1	1.7–8.5 k/ μ L
Lymphocyte, absolute	2.7	2.7	1.2–5.4 k/ μ L
Monocyte, absolute	1	1	0–1.2 k/ μ L
Basophil, absolute	0	0	0–0.2 k/ μ L
Eosinophil, absolute	0.1	0.3	0–0.7 k/ μ L

Hct = hematocrit; Hgb = hemoglobin; Plts = platelets; WBC = white blood cell count.



Figure 1. Computed tomography scan showing bowel wall edema.

QUESTIONS

What Is the Differential Diagnosis?

- Abdominal lymphadenopathy resulting in intussusception
- Acute appendicitis
- Hereditary angioedema (HAE) with abdominal exacerbation
- Viral gastroenteritis

Viral gastroenteritis is a common cause of abdominal pain and vomiting in children. However, our patient already had a CT scan of the abdomen suggesting another cause for his presentation. His white blood cell count was elevated on presentation with neutrophil predominance, which along with abdominal pain and

Table 2 Complement studies

Test	Results	Reference Range
Serum C4	<8	14–44mg/dL
C1-INH	3	11–26mg/dL

C1-INH = C1 esterase inhibitor.

vomiting puts acute appendicitis in the differential. However, white blood cell count elevation in this case was presumably caused by stress/dehydration because it reverted to normal the next day. Elevated white blood cell count can be seen in HAE abdominal exacerbations. The CT scan showed small bowel intussusception but failed to identify a cause for it.

What Additional Laboratory Data Would Be Helpful in Arriving at a Diagnosis for This Patient?

- Serum C1
- C3
- C4
- CH50

The single best screening test for diagnosis of HAE is serum C4. Because of the history of recurrent swelling, the Pediatric Surgery Service was concerned with the possibility of exacerbation of angioedema with surgery and wanted an allergy consult for perioperative management. After the Allergy Service was consulted, we considered that HAE can cause bowel wall edema. Theoretically, this edema can serve as a lead point for intussusception that would explain the patient's presentation. In light of this, we ordered serum C4, which confirmed the diagnosis (Table 2). In HAE C1 is not affected. C3 is often abnormal in systemic lupus erythematosus and other diseases with excessive immune complex formation but is usually normal in HAE. CH50 is also unlikely to be affected in HAE and is used as a screening for complement deficiency.

We reviewed the literature to see if small bowel or other types of intestinal intussusception had been previously reported in association with HAE. A literature search was conducted using PubMed search engine and keywords, HAE, hereditary angioedema, and intussusception. Three reports of colocolic intussusception and one report of colorectal intussusception are reported in patients with HAE. No previous report of small bowel intussusception was found in association with HAE. Because intussusceptions can result from a pathological lead point, a repeat CT scan was considered to rule out any other pathology for the current episode of intussusception.

TREATMENT AND CLINICAL COURSE

Surgery was deferred on the recommendations of the allergy consult team. The patient received ondansetron

intramuscular injection and his vomiting improved. He was put on bowel rest and given i.v. fluids. Two units of fresh frozen plasma were transfused. On the subsequent day, his symptoms resolved, his diet was advanced, and he was later discharged home. A follow-up outpatient CT scan of the abdomen was obtained, which was normal. On contacting his primary allergist it was found that he had been worked up for HAE and a low serum C4 level had been documented at some point in the past. At that point, no therapy was offered to him because due to his prepubertal age he was not a candidate for prophylactic androgen therapy. Unfortunately, this history was not forthcoming from his foster parents during his hospital stay. He remained asymptomatic at follow-up and was subsequently started on prophylactic therapy with danazol.

DISCUSSION

HAE is characterized by recurrent, unpredictable episodes of swelling affecting the extremities, face, abdomen, urogenital tract, or upper airway. It is mostly inherited in an autosomal dominant fashion but can also result from spontaneous mutations (20–25% of cases). The gene mutation is located on chromosome 11. Two main types are identified. Type 1 occurs in 80–85% and is caused by quantitative deficiency of C1 esterase inhibitor (C1-INH). Type 2 occurs in 15–20% and is caused by normal or elevated levels of C1-INH protein that is functionally abnormal. C1-INH plays an important role in inhibition of the complement, fibrinolytic, and contact systems. Deficiency of C1-INH leads to activation of these systems thereby leading to overproduction of bradykinin. This bradykinin leads to vasogenic edema resulting in the classic symptoms of the disease. Involvement of gastrointestinal mucosa/submucosa can result in symptoms such as abdominal pain, vomiting, and diarrhea. This presentation can mimic acute surgical conditions leading to unnecessary abdominal surgeries.¹

Diagnosis is based on thorough personal and family history as well as low serum levels of C4. As noted previously, up to 25% of patients may not have a family history and are due to spontaneous mutations resulting in HAE. Type 1 HAE will be expected to have low levels of C1-INH and low function, but type 2 has normal and at times high levels of the protein, but the protein functions poorly and thus the C1-INH functional level is low. The combination of low serum C4 and low C1-INH function is 98% specific for C1-INH deficiency; however, in the United States the functional assay is not sensitive or specific.² Genetic testing is also available at some research laboratories. Similar to cystic fibrosis, the failure to document a preexisting mutation does not eliminate the diagnosis of HAE.

Acute management includes supportive care including pain management and fluid replacement. There is

no Food and Drug Administration–approved drug for acute treatment in the United States. Fresh frozen plasma replaces C1-INH and has been used with good results and without significant adverse events despite previous concerns regarding possible worsening of acute exacerbations.³ C1-INH human concentrate (Cinryze; ViroPharma, Exton, PA) has recently been approved for prophylactic treatment. It is available for treatment of acute exacerbations *via* research protocols at sites involved in clinical trials and can be used off label for acute exacerbations if available. Ecallantide (Dyax, Cambridge, MA) is undergoing review by the Food and Drug Administration for the treatment of acute attacks of HAE. Danazol, an attenuated androgen, has been the conventional agent for prophylaxis and has been used at high doses for acute exacerbations, but the activity is dependent on up-regulation of proteins and thus the benefit is delayed making it unlikely to benefit acute exacerbations.⁴ Other drugs under investigation for therapy of acute exacerbations include icatibant (Shire, Wayne, PA), and C1-INH (Viropharma, Exton, PA; CSL Behring, King of Prussia, PA; and Pharming, Leiden, The Netherlands).⁵

Our literature search identified four previous reports of large bowel intussusception in association with HAE. A case report in the French literature describes a 15-year-old girl with HAE and colocolic intussusception.⁶ One adult patient with HAE had colocolic intussusception affecting the transverse colon and required surgery, during which he received C1-INH infusion.⁷ Another 13-year-old girl with HAE had recurrent colocolic intussusception and was treated with air reduction enemas with each of her four episodes of colocolic intussusception.⁸ Lastly, a 21-year-old man with HAE had protracted abdominal pain that failed to respond to C1-INH infusion. A CT scan was subsequently done, which revealed extensive colorectal intussusception. He ultimately required surgical intervention. The intraoperative examination suggested initiation of intussusception by local mucosal edema in the transverse colon.⁹

Intussusception of the colon has been described as a rare complication of HAE.¹⁰ However, small bowel intussusception has not been previously described in association with HAE. Small bowel intussusception is seen mainly in young children, usually <6 years of age. The majority of the cases in young children are idiopathic or related to enteric viral infections. Pathological lead points, which can be identified in approximately one-fourth of cases, include Meckel diverticulum, polyps, small bowel lymphoma, duplication cysts, vascular malformations, inverted appendiceal stumps, parasites (*e.g.*, *ascaris lumbricoides*), Henoch-Schönlein purpura, cystic fibrosis, and hemolytic-uremic syndrome. Rare causes include inflammatory fibroid polyps of ileum, gastrointestinal stromal tumors, intestinal lipoma, eosinophilic enteritis, and blunt abdominal

trauma. Treatment modalities include pneumatic reduction and surgical intervention.

Final Diagnosis

Small bowel intussusception caused by HAE.

CONCLUSIONS

This case illustrates the varied presentation and difficult nature of diagnosing HAE. To the best of our knowledge, this is the first report of a case of small bowel intussusception caused by HAE. In previous case reports of patients with colocolic intussusception, most have been treated with pneumatic reduction or surgical intervention without a trial of HAE therapy. We found only one case where treatment with C1-INH was tried, and we suspect that it was not successful because of the extensive area of involvement. Our patient responded very well to fresh frozen plasma. Now that C1-INH is available in the United States, it appears to be the intervention of choice in patients with HAE and intestinal intussusception before more invasive procedures.

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