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Case Report Open Access

Angiotensin Converting Enzyme (ACE) Inhibitor Associated Small Bowel Angioedema and Ascites Presenting as Recurrent Acute Abdomen: A Case Report

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Abstract

We describe a case of a patient who presented with recurrent abdominal pain due to small bowel angioedema believed to be caused by a recently started ACE inhibitor with classic imaging features. Very few cases of visceral angioedema due to ACE inhibitor use are described in the literature. This case demonstrates a unique direct causal association between the onset of drug administration and symptomatic bowel angioedema as well as ascites, spontaneous resolution on stopping ACE inhibitor, and recurrence of acute clinical symptoms and imaging features on resumption of the drug.

Keywords: Angiotensin converting enzyme inhibitor; Small bowel angioedema; Ascites

Introduction

Recent years have witnessed increasing use of angiotensin converting enzyme (ACE) inhibitors in hypertension and as drugs of choice in systolic dysfunction heart failure making it highly important to recognize all possible side effects and rectify them at the earliest time to reduce the morbidity. ACE inhibitors are known to cause acute GI symptoms due to various pathophysiological alterations including systemic hypotension leading to mesenteric hypoperfusion, pancreatitis, and angioedema. ACE inhibitor induced visceral angioedema is a rare and its incidence is not well documented [1,2].

Isolated involvement of the bowel presenting as acute abdomen is extremely uncommon and a direct temporal association between the drug intake and symptoms often gives the clue to the diagnosis. We present a rare case of recurrent ACE inhibitor related acute abdominal pain with classic imaging features of small bowel angioedema as well as ascites.

Case Report

A 37-year-old African-American woman presented to emergency department with acute onset of severe intermittent abdominal cramps, nausea and multiple episodes of vomiting of 12 h duration. She also had a few episodes of watery diarrhea. There was no history of fever, chills, stridor, facial swelling, dysuria or hematuria. She complained of no other constitutional symptoms. She gave no previous history of gastrointestinal illnesses or recent travel.

The patient also gave a history of long standing hypertension secondary to polycystic renal disease and associated renal failure. Her past history also revealed allergies to drugs such as acetaminophen and oxycodone. Vital signs were normal except for slightly raised blood pressure (130/86 mmHg) and physical examination revealed diffuse tenderness over the entire abdomen.

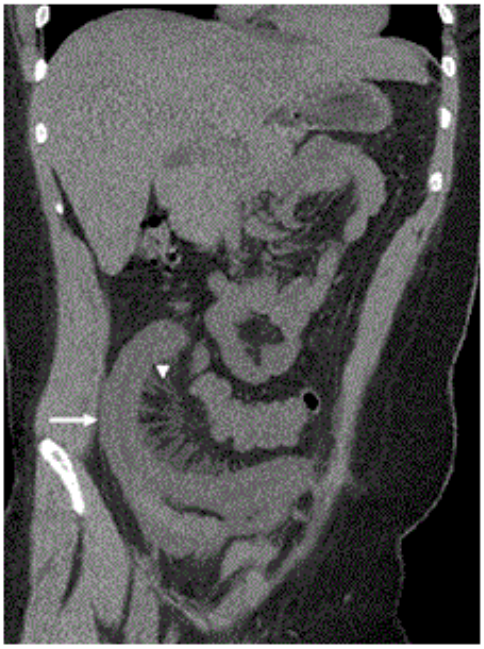

Figure 1: Non contrast enhanced computed tomography (NCET) coronal reformat image shows circumferential thickening of the small bowel wall (arrow) with inflammatory changes in form of mesenteric stranding and increased fat attenuation (arrowhead).

A non-enhanced CT (NECT) of the abdomen was first performed, which revealed severe localized ileal wall thickening in the right lower quadrant with surrounding inflammatory changes in the form of mesenteric stranding and increased fat attenuation without features of

intestinal obstruction, pneumatosis or intraperitoneal free air (Figure 1).

Mild free peritoneal fluid, moderate cardiomegaly with a small pericardial effusion and bilateral polycystic kidneys were the other positive findings. These NECT findings were confirmed with a contrast-enhanced CT (CECT) of the abdomen performed a few hours later using oral and 150 cc Omnipaque 300 (iohexol, GE Healthcare) intravenous contrast (Figure 2). Based on the imaging features a concern for ischemic bowel disease was raised at this point.

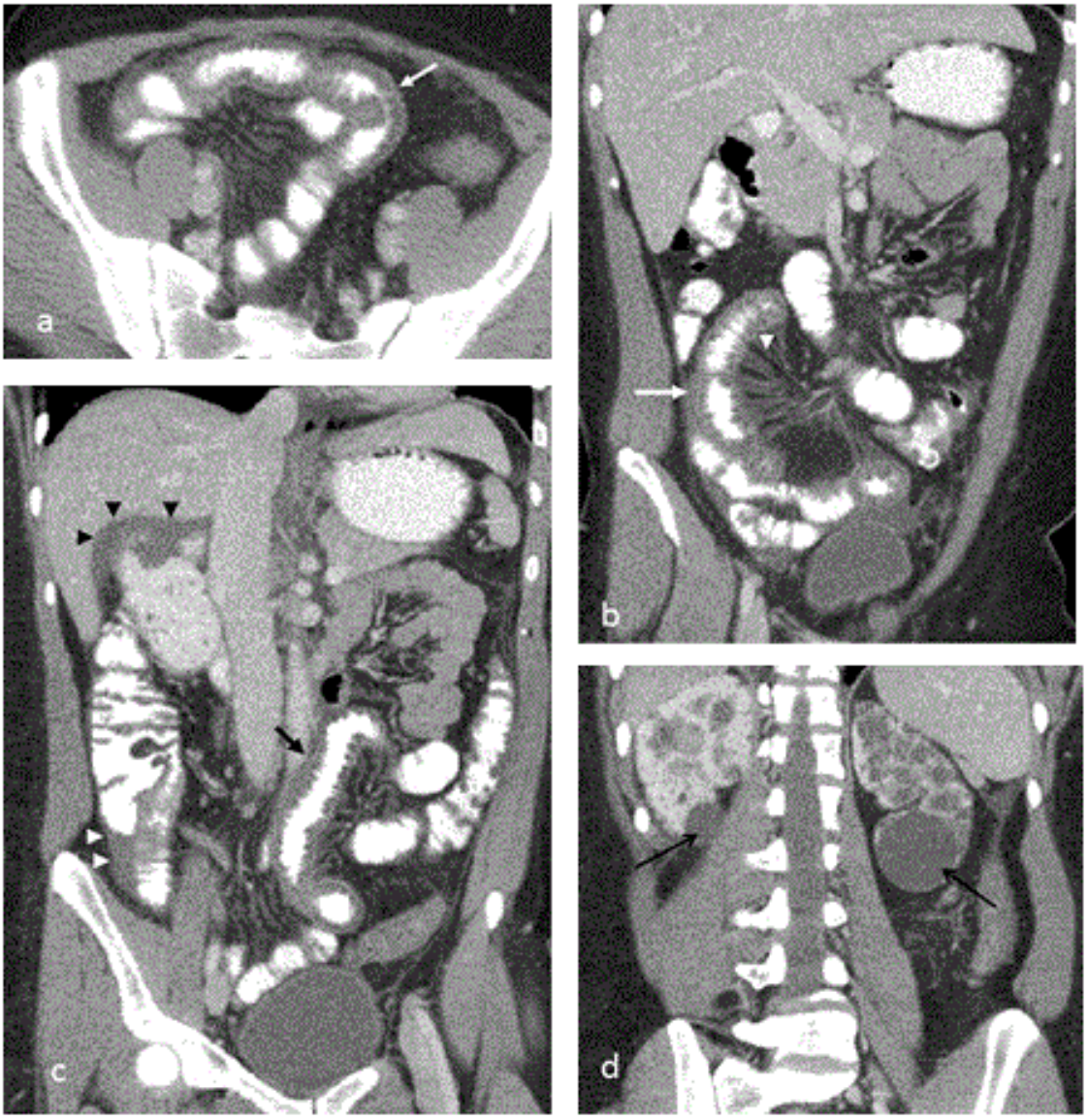

Figure 2: Axial (a) and coronal reformatted (b-d) images of contrast enhanced computed tomography (CECT) of the abdomen confirms the findings of the NECT study including circumferential small bowel edema involving all the three bowel wall layers (white arrows). Mild free peritoneal fluid is seen in the Morrison's pouch, the right paracolic gutter and pelvis (black and white arrowheads). Note bilateral multiple renal cysts (black arrows).

The patient was admitted, put on IV fluids and a NG tube inserted which showed 500 cc of bilious output throughout the night. Colonoscopy, performed the next morning, showed no signs of inflammation in the colon or terminal ileum. The patient improved symptomatically in the meantime and started having bowel movements. The NG tube was thus removed and a clear diet started. A CECT of the abdomen was repeated, which revealed near-complete interval resolution of the previously noted small bowel wall thickening, inflammatory changes in the right lower quadrant and the free peritoneal fluid (Figure 3). She was discharged to home in stable condition following complete resolution of her transient symptoms, but with no clear explanation of their etiology. She was advised to

report to the emergency department if her abdominal symptoms recurred.

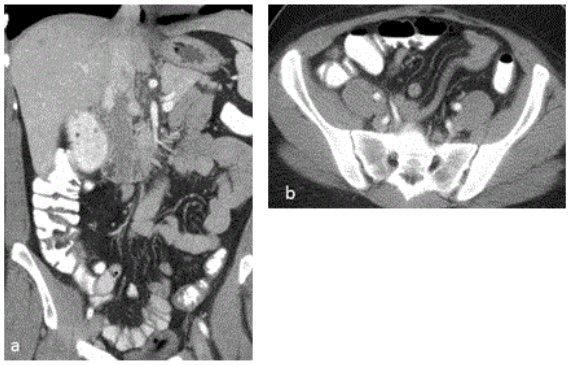

Figure 3: Coronal reformatted (a) and axial image (b) of the follow-up scan acquired a day later reveals near total resolution of the previously noted bowel thickening and inflammatory changes.

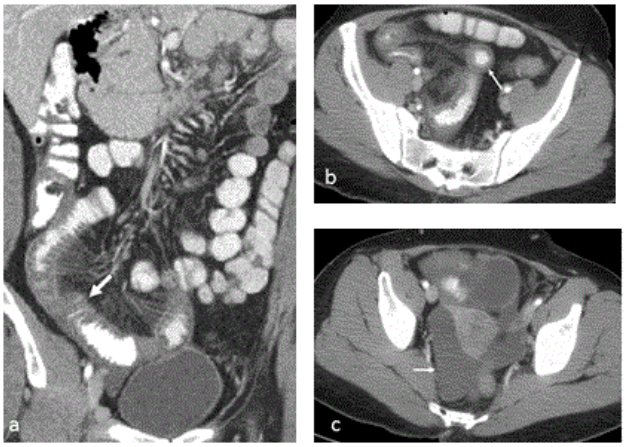

Figure 4: Coronal reformatted and axial CECT images performed during the readmission demonstrates similar small bowel wall thickening (arrow in a and b), mesenteric inflammation and ascites (arrow in c) as seen in the initial CT.

The patient was asymptomatic for a few days but returned to the emergency department five days later with similar complaints of severe abdominal pain, intractable nausea, vomiting, and diarrhea. She also complained of the development of new hives along her extremities and her trunk.

Abdominal CECT was performed which revealed interval development of bowel wall thickening and inflammation in the distal ileum similar to the findings on her initial study that had resolved in the interim (Figure 4).

Also, there was interval accumulation of significant pelvic free fluid. On detailed evaluation of her chart, an interesting association of patient's symptoms was observed with her oral use of a newly started angiotensin-converting-enzyme (ACE) inhibitor, Lisinopril. She started her Lisinopril on the day that she initially presented to the emergency room with abdominal pain, nausea, vomiting, and diarrhea.

Lisinopril was discontinued during the duration of stay at the hospital and not resumed until the day prior to this current admission when she again developed similar symptoms as well as imaging features. Thus, her clinical presentation was considered consistent with ACE inhibitor-induced angioedema of the intestine based on strong association with the medication intake and symptoms. Lisinopril was removed from her treatment regimen and she showed considerable improvement in her symptoms during the second term of hospital stay. The patient is symptom free on follow-up period of one year and she is off ACE inhibitors during the last one year.

Discussion

Angioedema is a non-inflammatory disease characterized by increased capillary permeability leading to extravasation of intravascular fluid and resultant edema of the mucosa [3-5]. Angioedema is a known, potentially life-threatening side effect of treatment with ACE inhibitors, occurring in 0.1-0.5% of patients treated with these drugs [2,6]. African Americans are known to have a substantially increased risk of ACE inhibitor-associated angioedema compared with Caucasian subjects and that this increased risk has not been attributed to an effect of dose, specific ACE inhibitor, or concurrent medications [7].

Angioedema caused by ACE inhibitors very often is localized on the lips, the tongue, pharynx and larynx, in many cases necessitating emergency measures. Other sites that could potentially be involved include hands and feet, arms, legs and scrotum. In general, angioedema occurs within hours to days after initiation of therapy; however, delayed occurrence of angioedema up to 10 years of therapy has been reported [8,9]. Gastrointestinal tract symptoms of angioedema can mimic acute abdomen. The more commonly reported symptoms include abdominal pain lasting from hours to days before initial presentation [1]. According to one study 35% of patients diagnosed with small bowel angioedema had undiagnosed abdominal pain before their diagnosis [10]. Nausea, vomiting and watery diarrhea are other frequently reported symptoms [11-13]. The underlying pathophysiology of bowel angioedema due to ACE inhibitors in not clear and various pathophysiologic mechanisms have been proposed. ACE inhibitors decrease the inactivation of bradykinin and thus increase the circulating levels of bradykinin. One of the proposed pathophysiological mechanisms of edema is the vasodilation and altered vascular permeability due to increased circulating bradykinin. Tissue specific and antinuclear antibodies induced by ACE might lead to immunologic reaction resulting in angioedema. Another hypothesis suggests that induction of C1 esterase deficiency by ACE inhibitors may also contribute to visceral edema [6,14,15].

Diagnosing ACE inhibitor induced angioedema as the cause of acute abdomen is not straightforward. ACE inhibitors can cause GI symptoms due to various other pathophysiological alterations that result in systemic hypotension leading to mesenteric hypoperfusion, pancreatitis and lastly, angioedema [16-18]. On the other hand, bowel angioedema produced by other etiologies can usually present with overlapping symptoms; however, a strong association with history of medication and associated symptoms is often the diagnostic clue to suggest ACE inhibitor associated angioedema. There is no definite diagnostic test for ACE inhibitor induced visceral angioedema [9]. Occasionally diagnosis is made after resumption of the ACE inhibitors and returning of the symptoms as described in our case [1].

In bowel angioedema, CT classically demonstrates segmental involvement of small bowel with circumferential edema and wall thickening [3]. Prominent mucosal enhancement is seen with prominence of the mesenteric vessels and mesenteric fat stranding. There is usually a striking contrast between the low-attenuation edematous submucosa, which separates the outer muscular layers and serosa from brightly enhanced thickened mucosa. It is less commonly seen to involve the large bowel and rarely the rectum [13]. Non-complicated ascites is a consistent associated finding. The CT findings invariably resolve on removal of the implicating agent, an ACE inhibitor in this case. This sort of reversible and segmental nature of the small bowel edema has a limited radiological differential diagnosis including ischemia, Henoch Schonlein purpura, and intramural bleeding from trauma, anticoagulation, or hemophilia [5].

As there are no specific diagnostic tests to confirm ACE inhibitor induced bowel angioedema, the diagnosis is based on the temporal relationship between the symptoms and the classic radiological findings with the drug administration, exclusion of other causes of angioedema. The resolution of the bowel edema after discontinuation of the ACE inhibitor is the key in diagnosis [5,13]. The fact that our patient started her Lisinopril the same morning that she had the episode, discontinued it during her stay in the hospital leading to spontaneous resolution of symptoms, and recurrence of symptoms after resuming Lisinopril strongly implicates ACE inhibitor as the cause for her small bowel edema and associated symptoms. Absence of similar symptoms during the period of follow-up since her ACE inhibitor was replaced with another class of anti-hypertensives also points to the ACE inhibitor as causative agent.

Although her complaints in the initial episode were purely gastrointestinal in nature, the second episode of acute abdomen was associated with development of hives along her extremities and trunk. GI manifestations may be the first and only presenting symptoms of this problem [19,20]. Angioedema has no pathognomonic feature that distinguishes it from a true surgical emergency, however, the absence of peritoneal signs, fever, or leukocytosis and the presence of bowel sounds may justify a more conservative management. The results of surgical exploration in these patients are not diagnostic, as the usual findings are ascites and bowel edema. A high index of suspicion is important because if not recognized early, patients with ACE inhibitor-induced visceral angioedema may be subjected to multiple radiologic and invasive procedures [21,22].

Isolated bowel angioedema can also be caused by acquired and hereditary C1 esterase deficiencies. Although hereditary and acquired angioedema have overlapping signs and symptoms, the age of the patient at onset differs [23,24]. Almost half of patients with the hereditary form are young and have episodes before they are ten years old [23]. Patients with the acquired form of angioedema generally are found to have episodes after the fourth decade of life and, similarly, diagnosis is difficult [23,24].

Conclusion

ACE inhibitor induced visceral angioedema is a rare but documented side effect of the medication. Isolated involvement of the bowel presenting as acute abdomen is extremely uncommon and a direct temporal association between the drug intake and symptoms often leads to the diagnosis. It is also important to rule out other causes of angioedema. This patient was unusual as her symptoms resolved when stopping the medication and recurred after restarting Lisinopril. CT findings, although not specific for this pathology, help to exclude more urgent surgical etiologies. ACE inhibitors are not only the antihypertensive of choice in many cases but also are drug of choice in systolic dysfunction heart failure making it highly important to recognize all possible side effects and rectify them at earliest to decrease the morbidity.

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