Intestinal Angioedema Induced by Angiotensin-Converting Enzyme Inhibitors: An Underrecognized Cause of Abdominal Pain?

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Intestinal angioedema caused by angiotensin-converting enzyme inhibitors such as lisinopril is rare but well documented in the literature. Patients with this condition typically present with common symptoms such as diffuse abdominal pain, cramping, nausea, and emesis. Imaging is needed to reveal segmental edema of the small intestine, often associated with free fluid in the abdomen. The authors report 2 cases of intestinal angioedema caused by angiotensin-converting enzyme inhibitors. Awareness of this allergic reaction and careful history taking—noting temporal relationship to occurrence of symptoms—are essential to diagnose this condition; laboratory and radiologic findings are needed to confirm the diagnosis. An accurate diagnosis helps the patient recover quickly and avoid complications from unnecessary tests and invasive procedures.

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Intestinal angioedema induced by angiotensin-converting enzyme (ACE) inhibitors is rare. As of 2010, according to Campbell et al,[1] 21 cases have been reported in the medical literature. Differential diagnoses include inflammatory bowel disease, enteritis, vasculitis, and ischemic bowel. Most often, patients are middle-aged women with complaints of acute, severe abdominal pain, nausea, or emesis. These symptoms can occur within days to weeks after the initiation of an ACE inhibitor. Other conditions frequently encountered are leukocytosis, ascites, and angioedema of the small intestine. Peripheral edema usually does not accompany visceral findings. Most patients are seen by multiple physicians and may undergo exploratory surgical procedures, including endoscopy, biopsy, and intestinal resection.[2] Treatment for patients with this condition is discontinuation of the ACE inhibitor. Patients have undergone repeated surgical procedures, however, because of recurrent symptoms when the medication was reintroduced postoperatively.[3] Awareness of this potential drug reaction is important because lisinopril is the most-prescribed antihypertensive and the fourth most-prescribed drug in the United States, having been prescribed more than 42.2 million times in 2011.[4]

We present 2 cases of ACE inhibitor–induced intestinal angioedema.

Report of Cases

Patient 1

A middle-aged woman presented to her primary care physician's office with severe abdominal pain, abdominal cramps, nausea, and emesis of 24 hours duration. Her past medical history was notable for hypercholesterolemia and hypertension. Medications included

atorvastatin calcium, ethinyl estradiol and norethindrone, and lisinopril. Lisinopril was initiated 48 hours before admission; the others were her regular medication. She had no prior surgical history and was otherwise healthy. On physical examination she had considerable periumbilical and right lower-quadrant tenderness. Her heart rate was 80 beats per minute, her blood pressure was 117/87 mm Hg, and her white blood cell count was 14,000/μL. An abdominal computed tomography (CT) scan obtained on admission revealed moderate ascites (6.6 Hounsfield units) and a segment of edematous small intestine (*Figure 1*). Radiologic interpretation suggested ischemia, vasculitis, or inflammatory bowel disease. After careful history taking, we conducted a literature search that assisted with the diagnosis of intestinal angioedema induced by ACE inhibitors. Lisinopril was discontinued. The symptoms resolved, and the patient was discharged to home within 48 hours. The patient was asymptomatic at follow-up.

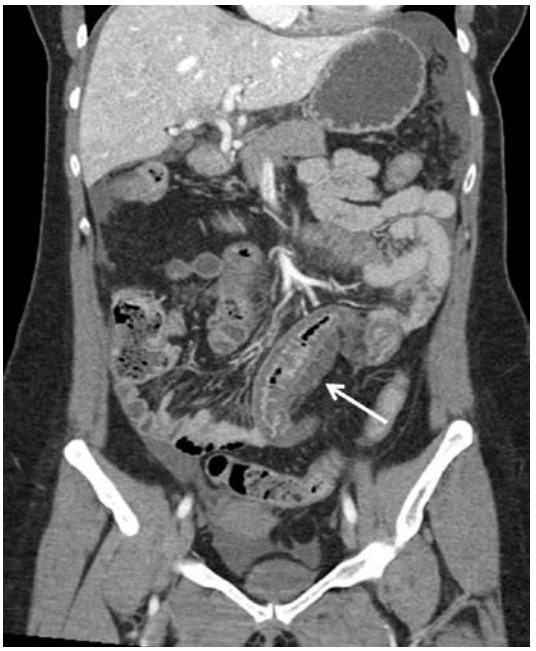

Figure 1.
Coronal computed tomography scan of the abdomen demonstrates segmental edematous small intestine (arrow) in a middle-aged woman.

Patient 2

A middle-aged woman was admitted to the gastroenterology service with abdominal pain and diarrhea. Her past medical history was notable for hypertension, gastroesophageal reflux disease, and diverticulitis. Her medications included lisinopril, cyclobenzaprine, ferrous sulfate, hydrocodone and acetaminophen, levothroxine sodium, ethinyl estradriol and norethindrone, paroxetine, promethazine, and rabeprazole. She had been hospitalized twice during a 3-month period with the same complaints of abdominal pain. A CT scan of the abdomen obtained shortly after admission revealed a thickened small intestine. The patient was initially treated for enteritis—vs a differential diagnosis of acute inflammatory bowel disease—with a course of antibiotics (ciprofloxacin and metronidazole) for 7 days without complete resolution of her symptoms (*Figure 2*). During her hospital stays, lisinopril was stopped because her status was "not by mouth." After some improvement, she was discharged to home. Her symptoms worsened at home once she resumed lisinopril use, and she was re-admitted 2 months after the initial admission. A repeat CT scan obtained during the second hospitalization demonstrated increasing bowel angioedema. Surgical consultation was obtained for a possible bowel biopsy. Endoscopy had already been performed during the first and second admissions, with negative results. Capsule endoscopy during the second admission, however, revealed rare angioectasis in the proximal bowel. On the basis of our experience with patient 1, we deduced that the short duration of lisinopril use was responsible for the enlarged bowel angioedema. Lisinopril was discontinued, and the patient's symptoms resolved after 72 hours. She was discharged to home and remains asymptomatic.

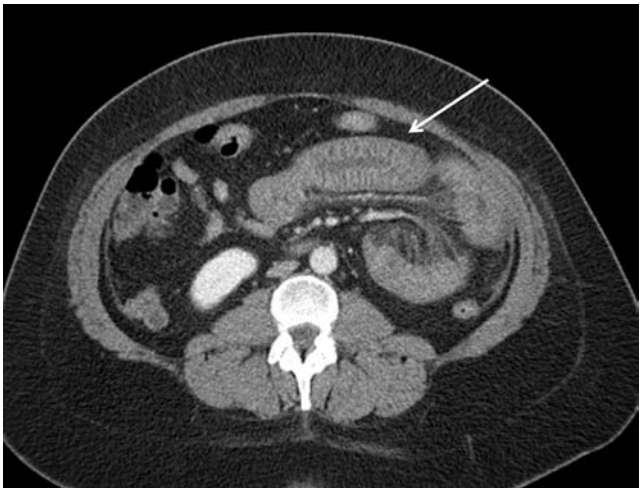

Figure 2.
Axial computed tomography scan of the abdomen demonstrates intestinal angioedema (arrow) in a middle-aged woman.

Comment

The use of ACE inhibitors in the general population is widespread, and awareness of potential intestinal angioedema is important. The angioedema is confined to part of the intestine, most commonly the small intestine. Patients typically present with tenderness, and after CT scanning, ascites is revealed. Early cessation of ACE inhibitors is curative and prevents unnecessary surgical intervention and morbidity associated with this syndrome.

Conclusion

The prevalence of ACE inhibitor–induced intestinal angioedema is underrecognized. Primary care physicians and surgeons must be aware of this presentation because the condition is often overlooked by those who care for patients at initial presentation. Discontinuation of ACE inhibitors should preclude exploratory surgical procedures, which may result in complications and will not help with diagnosis.

References

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