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Small bowel angioedema from angiotensin-converting enzyme: Changes on computed tomography

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ABSTRACT

Intestinal angioedema is a rare side effect of angiotensin-converting enzyme inhibitors. We present a 41-year-old woman with sporadic right lower quadrant abdominal pain and diarrhea with multiple computed tomography scans demonstrating enteritis. Suspicion turned to angiotensin-converting enzyme inhibitor use as the cause for the patient's illness after an extensive negative evaluation including labs, stool studies, endoscopies, and capsule endoscopy. Weeks after stopping the medication, the patient's symptoms improved and repeat computed tomography showed a resolution of the previously seen findings of enteritis. This case illustrates the importance of a good medication review to make appropriate clinical decisions and diagnoses.

Case presentation

A 41-year-old woman with a past medical history of hypertension (on lisinopril-hydrochlorothiazide), hyperlipidemia (on simvastatin), and gastroesophageal reflux (on over-the-counter esomeprazole) presented to the digestive diseases clinic for consideration of capsule endoscopy for further evaluation of a 2-year history of sporadic, severe, right lower quadrant abdominal pain and nonbloody diarrhea. During these painful episodes, the patient made several visits to the emergency department (ED). Evaluation during these ED visits included routine labs, inflammatory markers, and computed tomography (CT) scans of the abdomen and the pelvis. Significant findings included white blood cell count elevations from 15,500 to 21,500/μL (normal 3500-11,000/μL) and elevated C-reactive protein level between 37.4 and 42 mg/L (normal <8 mg/L); however, the patient's hemoglobin and hematocrit levels, liver tests, and erythrocyte sedimentation rate were normal on each occasion. On several separate CT scans, focal small bowel wall

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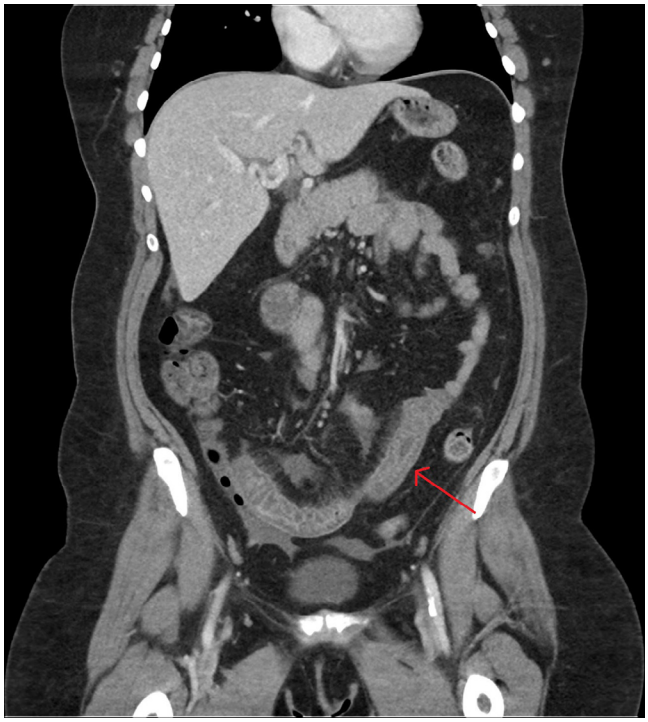

Fig. 1 – Long segment of submucosal edema, vasa recta engorgement, and a small amount of mesenteric-free fluid marked by the arrow on coronal computed tomography scan of the abdomen. Findings persisted in multiple studies over a 2-year period while taking angiotensin-converting enzyme inhibitors.

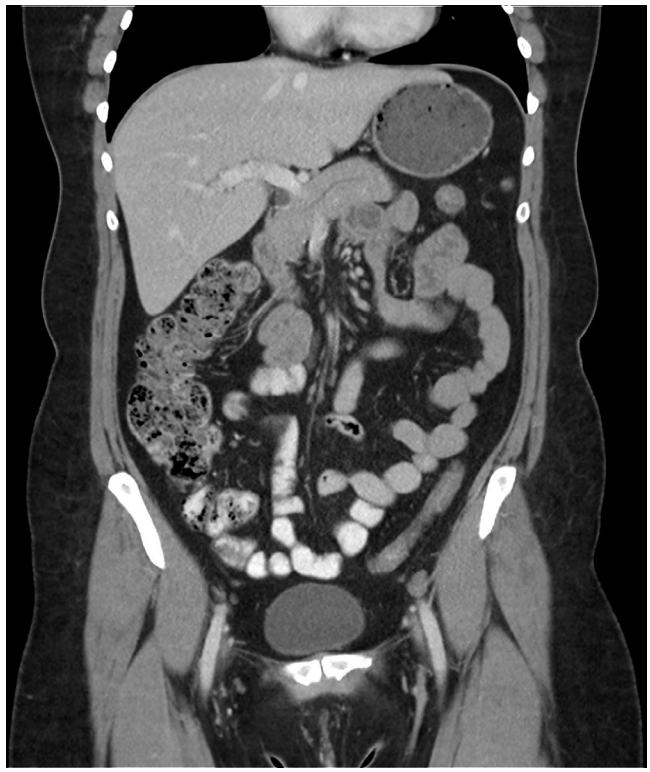

Fig. 2 – Coronal computed tomography scan of the abdomen showing a normal small bowel 3 years before starting the angiotensin-converting enzyme inhibitor.

thickening, mesenteric stranding, and prominent vasa recti, suggesting enteritis, were noted (Fig. 1). These findings prompted colonoscopy, which revealed a normal mucosa in the entire colon and terminal ileum; biopsies did not support the working diagnosis of inflammatory bowel disease.

Since the patient's symptoms persisted, further evaluation for infectious colitis, including routine stool culture, ova and parasites and testing for *Clostridium difficile* was performed and was negative. Push enteroscopy was then pursued, which was also unremarkable to the jejunum, and biopsies throughout the small bowel were furthermore unremarkable. After the initial clinic visit, a capsule endoscopy was performed with a normal evaluation of the small bowel. Fecal calprotectin, serology, genetics and inflammation (SGI) inflammatory bowel disease panel, *Mycobacterium tuberculosis* quantiferon, C1 esterase inhibitor and C4, antinuclear antibody, and urine porphobilinogen were unremarkable as well.

Oral prednisone at 60 mg daily was initiated by an emergency department (ED) physician after noting the small bowel findings on a subsequent CT scan. The patient partially responded to corticosteroids but still had residual discomfort. Several medications, including bile acid sequestrants, rifaximin, and anticholinergics, were trialed unsuccessfully with no improvement in the patient's symptoms. With the diagnostic evaluation up to this point otherwise stalled, we did a careful review of the patient's medical chart and noted that the lisinopril was started just weeks before the onset of the patient's symptoms. On further chart review, we also noted a separate CT scan of the abdomen and the pelvis, which patient had undergone 3 years before, even starting the lisinopril for the evaluation of acute right upper quadrant abdominal pain, which did not show any inflammation in the small bowel (Fig. 2). The decision was then made to discontinue the patient's lisinopril. Within just weeks of stopping the medication, the patient's right lower quadrant abdominal pain and diarrhea resolved. Repeat CT scan of the abdomen and pelvis just 2 weeks after stopping the angiotensin-converting enzyme inhibitor (ACEI) showed a resolution of the previously seen enteritis (Fig. 3). This finding confirmed the diagnosis of ACEI-induced angioedema. The patient was started on atenolol for her hypertension and remained asymptomatic at a 4-month follow-up at the clinic.

Discussion

ACEIs are commonly used drugs to treat hypertension and other cardiovascular diseases. ACEIs have their effects on the renin-angiotensin-aldosterone pathway and inhibit the breakdown of bradykinin. Angioedema is a result of high levels of bradykinin, which causes vasodilation and increased permeability of postcapillary venules, allowing plasma extravasation into the surrounding tissues [1]. ACEI-related angioedema occurs in about 0.1%-0.7% of patients and typically affects the oropharyngeal region, most commonly, the lips, the tongue, the face, and the upper airway [2]. Angioedema of the small bowel is much less common but has been well reported. Scheirey et al. reported on imaging findings of 20 patients with ACEI

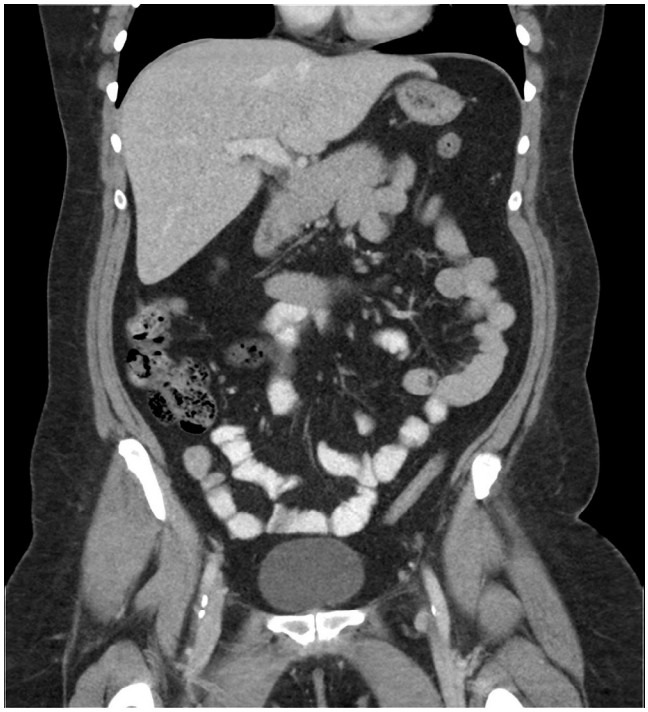

Fig. 3 – Coronal computed tomography scan of the abdomen demonstrating a resolution of enteritis 2 weeks after stopping the angiotensin-converting enzyme inhibitor.

intestinal angioedema between 1996 and 2010. The majority of patients were female in this review, as in our case, and the review also showed that the initial episode of symptoms prompting CT evaluation ranged from 2 days to 10 years after the start of the ACEI [3].

Factors leading to the delay in diagnosis include the intermittent nature of the abdominal pain. Clinically, ACEI-induced intestinal angioedema may mimic Crohn disease, and this alone can subject patients to additional testing and procedures [4]. Furthermore, radiographic findings related to ACEI-induced intestinal angioedema are largely nonspecific. These findings can include bowel wall thickening and dilation concerning for enteritis as in this patient.

Radiographically, ACEI-induced bowel edema can appear similar to many other disease states. In addition to medication use, detailed patient history and clinical findings are needed to exclude other causes of bowel edema. Imaging differential considerations include ischemic bowel, vasculitis, intramural hemorrhage, Crohn disease, lymphoma, C1 esterase deficiency, radiation enteritis, infectious enteritis, and nephrotic syndrome with hypoproteinemia [3,5]. Vascular occlusion may be identified with ischemic bowel, and patients may have a history of mesenteric insufficiency [6]. Cutaneous symptoms and a history of systemic lupus erythematosus or Henoch-Schonlein purpura would suggest vasculitis [6]. Intramural hemorrhage may be indistinguishable from ACEI-induced edema on contrast-enhanced CT as both would display a low-attenuating submucosa, but intramural hemorrhage can be differentiated on noncontrasted CT where there is hyperattenuation of the bowel wall [6]. Lymphadenopathy, creeping fat, and fistulas help to distinguish Crohn disease [6]. Lymphadenopathy can also be seen with infectious enteritis and lymphoma; however, other organs may be involved with lymphoma and the bowel wall will be homogenous rather than the striated appearance typically seen with ACEI-induced bowel edema [6].

In conclusion, careful review of a patient's medication list and considering the diagnosis of ACEI-induced angioedema may facilitate a more timely diagnosis, thus reducing the risks and avoiding the costs and delays in diagnosis associated with procedures, imaging, and medications.

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