A Rare Cause of Abdominal Pain in Plain Sight

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Visceral angioedema, swelling of the soft tissues and organs of the abdominal cavity leading to significant gastrointestinal symptoms, is a rare adverse reaction associated with the use of an angiotensin converting enzyme inhibitor or angiotensin receptor blocker. While several cases of ACEI-induced visceral angioedema have been reported, only one case of ARB-induced visceral angioedema exists. We report a unique case of ARB-induced visceral angioedema from the use of irbesartan and discuss the management and clinical importance of visceral angioedema.

INTRODUCTION

Angioedema is the classic adverse drug reaction of an angiotensin converting enzyme inhibitor (ACEI) or angiotensin receptor blocker (ARB) that manifests as swelling of the face, tongue and lips and can be potentially life threatening. Even though universally recognized, this adverse reaction is rare with a defined incidence of 0.1% to 0.7% of patients taking an ACEI.¹ An even less frequent manifestation of angioedema is visceral angioedema which is characterized by swelling of the soft tissues and organs of the abdominal cavity leading to significant gastrointestinal symptoms. Visceral angioedema is classically associated with ACE inhibitors however it is also rarely observed with the use of ARBs. Only 28 cases of ACEI induced visceral angioedema have been reported in literature from 1980-2010 and the reported cases of ARB induced visceral angioedema are even less frequent.¹²

Case Presentation

A 59-year-old female presented to the emergency department at a community hospital with complaints of severe cramping periumbilical abdominal pain with radiation to the lower abdomen. Her history was significant for diverticulitis, gastroesophageal reflux disease and multiple abdominal surgeries including Nissen fundoplication, cholecystectomy, hysterectomy, appendectomy and sigmoid resection for suspected ischemic colitis. Her pain was associated with bloating and severe nausea without vomiting. Computed

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tomography (CT) of the abdomen and pelvis was suggestive of small bowel obstruction with surrounding edema. She was admitted to the hospital and ultimately underwent exploratory laparotomy. Intraoperative findings revealed a normal small bowel without evidence of ischemia or adhesions. Serial CT scans throughout her hospitalization displayed successive resolving free fluid, small bowel wall thickening and stranding in the surrounding mesentery with resolution of findings by hospital day three (Figure 1, 2, 3). Without a diagnosis and symptomatically improved, she was discharged and referred to the gastroenterology clinic at our tertiary medical care center. She again presented with symptoms of abdominal pain and nausea, similar to her initial presentation despite normal vital signs, abdominal exam and laboratory work up. Review of her recent hospital course revealed her home medications, including irbesartan, had been held while hospitalized. This coincided with her resolving CT findings. Her irbesartan was discontinued and, at one-month follow up, she was asymptomatic, confirming the diagnosis of ARB induced visceral angioedema.

Discussion

Visceral angioedema is a rare cause of abdominal pain. The presenting gastrointestinal symptoms of visceral angioedema can be broad (abdominal pain, cramping, colicky pain, nausea, vomiting, diarrhea) and are often mistaken for a surgical abdomen. In fact, it is not uncommon for the patient presenting to the emergency department with visceral angioedema to undergo surgical exploration due to the degree of symptoms and radiologic findings. CT images of visceral angioedema classically display thickening, dilation and straightening of the small bowel with preservation of luminal transit. Other potential etiologies of these radiographic findings include small-bowel ischemia, superior mesenteric and portal vein thrombosis, radiation, vasculitides, Crohn’s disease, hemorrhage, pneumatosis or ulceration, thus making the radiological diagnosis of visceral angioedema increasingly difficult. The pathogenesis of ACEI-induced angioedema is well described and felt to be due to the accumulation and potentiation of bradykinin, the molecule that evades degradation by angiotensin converting enzyme inhibition. This abnormal accumulation of bradykinin causes overwhelming vasodilation and increased permeability leading to the observed edema. The pathogenesis of
ARB-induced visceral angioedema, however, is not well understood. It is conceivable that ARBs also lead to bradykinin accumulation by the feedback-induced increase in angiotensin II levels in plasma, however further investigation is needed to help explain the phenomenon of ARB induced angioedema.\textsuperscript{2} A high degree of suspicion is needed to diagnose visceral angioedema. Once recognized, the symptoms of visceral angioedema often resolve in as little as 48 hours if the offending medication is removed.\textsuperscript{1} Unfortunately, many patients suffer from prolonged symptoms from unrecognized visceral angioedema. One study reported a median of 10 months elapsed between onset of visceral angioedema and withdrawal of the ACEI, and many cases are reported of patients with visceral angioedema who took an ACEI for years before the cause of their symptoms was diagnosed.\textsuperscript{1} In patients who have experienced any degree of angioedema, clinicians should be careful about switching a patient from an ACEI to an ARB. Recurrent angioedema has been reported to occur in 1.5\% to 10\% of patients after changing medication classes. Recurrent visceral angioedema has also been reported after switching from an ACEI to an ARB.\textsuperscript{2} It is recommended that clinicians wait a period of four weeks after discontinuing an ACEI and starting an ARB so that residual ACEI induced angioedema is not mistaken for new ARB induced angioedema.\textsuperscript{2}

This rare but important cause of abdominal pain can be easily overlooked without a careful review of the medication list however recognition of this process and discontinuation of the provoking medication will save the patient from unnecessary diagnostic evaluation and intervention and bring timely symptomatic relief.

References

Answers to this month’s crossword puzzle: