CASE REPORT

ACE inhibitor-induced intestinal angio-oedema: rare adverse effect of a common drug

Lokesh Shahani

Department of Internal Medicine, Southern Illinois University School of Medicine, Springfield, Illinois, USA

Correspondence to

Dr Lokesh Shahani, lokesh83@hotmail.com

SUMMARY

ACE inhibitors are the leading cause of drug-induced angio-oedema in the USA. ACE inhibitor-induced intestinal angio-oedema, a much rarer complication of this medication, has been reported. The author reports a patient presenting with a 1-day history of severe abdominal pain. The patient was started on lisinopril 2 days prior to this presentation. Computer axial tomography (CAT) scan of the abdomen demonstrated extensive and marked thickening, and oedema involving the duodenum and proximal jejunum associated with significant mesenteric oedema. Concerns for visceral angio-oedema and a possible association with lisinopril according to the Naranjo algorithm were raised. Lisinopril was discontinued and the patient was treated with antihistamines. The patient improved clinically in the next 24 h and discharged home with education and documentation of this serious allergy. ACE inhibitor-induced visceral angio-oedema is under-reported and most often missed resulting in waste of hospital resources towards working up this clinical diagnosis.

BACKGROUND

ACE inhibitors are a widely used pharmacotherapy to treat hypertension and other cardiovascular illnesses. ACE inhibitors block the effects of the enzyme ACE and impact the renin-angiotensin-aldosterone pathway as well as the degradation of bradykinin. High levels of bradykinin stimulate vasodilation and increased vascular permeability of the postcapillary venules and allows for plasma extravasation into the submucosal tissue leading to angio-oedema.

ACE inhibitors are the leading cause of drug-induced angio-oedema in the USA, accounting for 20–40% of all emergency room visits for angio-oedema each year. ACE inhibitors induce angio-oedema in 0.1–0.7% of recipients.^{1 2} ACE inhibitor-induced angio-oedema most commonly affects the lips, tongue, face and upper airway. The author reports a patient who presented with ACE inhibitor-induced intestinal angio-oedema, a much rarer complication of this medication.

CASE PRESENTATION

The author reports a 50-year-old white female patient with a history of long-standing, quiescent, Crohn's disease who presented to the emergency department with a 1-day history of severe abdominal pain, nausea and vomiting. The patient described her abdominal pain as severe dull pain located in her epigastric and right upper quadrant area without any radiation. She denied any aggravating or relieving

factors; however, the abdominal pain was associated with significant nausea and vomiting. She denied any change in her bowel habits. The patient had a history of Crohn's disease, which required segmental ileal resection 15 years ago; following which it was well controlled on mesalamine and azathioprine. The patient was recently diagnosed with hypertension and started on lisinopril 2 days ago for the same. She denied any recent travel or sick contacts, and denied any other symptoms associated with her presenting illness. On examination, the patient was haemodynamically stable and had a benign physical examination, except diffuse abdominal tenderness located in her epigastric and right upper quadrant area.

INVESTIGATIONS

Routine laboratory examination including a complete blood count, complete metabolic profile and pancreatic enzymes were within normal limits. There were concerns for an acute flare up of her Crohn's disease or an infectious gastroenteritis and the patient was worked up for the same. A computer axial tomography (CAT) scan of the abdomen with intravenous contrast was performed, which demonstrated extensive and marked thickening, and oedema involving the duodenum and proximal jejunum associated with significant mesenteric oedema (figure 1). Concerns for visceral angio-oedema were raised and the patient had a Naranjo algorithm score of 4 indicating possible association between lisinopril and visceral angio-oedema (figure 1).³

DIFFERENTIAL DIAGNOSIS

The classic radiological findings described for visceral angio-oedema include thickening, dilation and straightening of the small bowel with preservation of luminal transit. There is a long-segment involvement of small bowel, with a tendency to affect the jejunum. The majority of cases have involvement of continuous segments of small bowel.⁴ Differential for this radiographic presentation include vasculitis, intramural haemorrhage, ischaemia, Crohn's disease, infectious enteritis, radiation enteritis and lymphoproliferative disease.⁵ Crohn's disease may be associated with circumferential or eccentric bowel wall involvement and may result in either a striated or a homogeneous appearance of the bowel wall. In addition, mesenteric findings including fistulas, creeping fat and reactive adenopathy may be seen with Crohn's disease. Vasculitis may result in segmental bowel wall involvement identical to that seen with visceral angio-oedema. Helpful clinical clues may include cutaneous manifestations of

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Figure 1 Computer axial tomography scan of the abdomen showing thickening and oedema involving the duodenum and proximal jejunum associated with significant mesenteric oedema.

vasculitis or the presence of a previously known condition. Intramural haemorrhage may appear very similar to ACE inhibitor-induced visceral angio-oedema on contrast-enhanced CT, with the relatively low-density submucosa. Unenhanced CT will often show increased density in the bowel wall. Furthermore, patient would have a known bleeding tendency most often related to anticoagulant use. In patients with bowel ischaemia, arterial or venous occlusion may be seen and patients would have a history of mesenteric insufficiency. Lymphoma of the small bowel may result in segmental wall thickening, but the involved wall will have a homogeneous density rather than a striated appearance as would be seen with visceral angio-oedema. Lymphoma is also typically associated with lymphadenopathy and is often associated with involvement of other abdominal structures. Lastly, radiation enteritis may be differentiated from visceral angio-oedema by history of irradiation and mural thickening of bowel in a stratified manner in the area of previous irradiation.

TREATMENT

The patient did not have any evidence of angio-oedema of the oropharyngeal area and no associated respiratory symptoms. Lisinopril was discontinued and the patient was treated with antihistamines. The patient improved clinically in the next 24 h and discharged home with education and documentation of this serious ACE inhibitor allergy.

OUTCOME AND FOLLOW-UP

The patient was followed up few weeks later as an outpatient where she denied any family history of similar episodes of angio-oedema. She was screened for underlying defects in C1 inhibitor with functional C1-esterase inhibitor and serum C4 level which were within normal limit. The patient's hypertension was treated with amlodipine and she was educated on her allergy.

DISCUSSION

ACE inhibitor-induced visceral angio-oedema is under-reported and most often missed resulting in waste of hospital resources towards working up this clinical diagnosis. Appropriate recognition with prompt discontinuation of drug and appropriate treatment as indicated could prevent morbidity and mortality with this diagnosis. Previous reviews have reported an association of female sex and older patient (fifth to sixth decade of life) and development of ACE inhibitor-induced visceral angio-oedema.⁶ Although rare, physicians should be aware of visceral angio-oedema as a side effect of the medication. This could help physicians diagnose this condition appropriately and avoid use of resources towards further work-up of the patient's symptoms.

Learning points

- ▶ ACE inhibitors block the effects of the enzyme ACE and impact the renin–angiotensin–aldosterone pathway as well as the degradation of bradykinin. High levels of bradykinin stimulate vasodilation and increased vascular permeability of the postcapillary venules and allows for plasma extravasation into the submucosal tissue leading to angio-oedema.
- ▶ ACE inhibitors are the leading cause of drug-induced angio-oedema in the USA, accounting for 20–40% of all emergency room visits for angio-oedema each year.
- ▶ The classic radiological findings described for ACE inhibitor-induced visceral angio-oedema include thickening, dilation and straightening of the small bowel with preservation of luminal transit. There is a long-segment involvement of small bowel, with a tendency to affect the jejunum. The majority of cases have involvement of continuous segments of small bowel.
- ▶ ACE inhibitor-induced visceral angio-oedema is under reported and most often missed resulting in waste of hospital resources towards working up this clinical diagnosis. Appropriate recognition with prompt discontinuation of drug and appropriate treatment as indicated could prevent morbidity and mortality with this diagnosis.

Competing interests None.

Patient consent Obtained.

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