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Single Case

Angiotensin-Converting Enzyme Inhibitor-Induced Gastrointestinal Angioedema: The First Danish Case Report

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Keywords
Angiotensin-converting enzyme inhibitors · Abdominal pain · Gastrointestinal angioedema · Bradykinin

Abstract
Angiotensin-converting enzyme inhibitors (ACEI) are widely used to treat hypertension and congestive heart failure. A rare side effect of ACEI therapy is angioedema, which in very rare cases may present as gastrointestinal angioedema (GA). A 45-year-old female presented with suddenly occurring diffuse abdominal pain. Imaging studies revealed small bowel wall edema. The patient had been on ACEI therapy for the last 6 months. The therapy was withdrawn, and the patient recovered quickly. There is no specific diagnostic test to confirm ACEI-induced GA, but symptoms usually regress completely after therapy discontinuation. An early diagnosis of ACEI-induced GA is important to avoid invasive diagnostic investigations and even laparotomy.

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Introduction

Angiotensin-converting enzyme inhibitors (ACEI) are widely used drugs in the treatment of hypertension and congestive heart failure. ACEI are known to induce angioedema, a side effect with an incidence of 0.1–0.7% that can affect the lips, tongue, face, upper airways, and

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very rarely the gastrointestinal system [1]. ACEI influence the renin-angiotensin-aldosterone pathway as well as degradation of bradykinin. High levels of bradykinin stimulate vasodilatation and vascular permeability in postcapillary venules, which leads to extravasation of plasma in the submucosal tissue and subsequently angioedema [2].

Case Report

Here, we present the case of a 45-year-old female with suddenly occurring diffuse abdominal pain of 24-h duration. She had nausea, heartburn, and vomited several times. Previously, the patient had undergone 2 cesarean sections. Her medical history included hypertension and asthma. On performing a physical examination, she had general abdominal tenderness and signs of peritoneal reaction. Her pulse was 89/min, body temperature 36.6°C, and blood pressure 160/119 mm Hg. Her leukocyte count was 16.8 × 10^9/L and C-reactive protein 20 mg/L; other values were normal. Urine dip test was positive for ketones and blood with traces of protein.

A computed tomography (CT) scan of the abdomen with contrast showed free fluid, especially in the pelvis. Thickening of the small bowel (SB) wall was visible in the middle and lower abdomen with an intestinal wall thickness of 9 mm (Fig. 1a). There were signs of mesenterial edema (Fig. 1b). No signs of ileus, free intraabdominal air, or enlarged regional lymph nodes were reported. The patient's medication and medication's side effects were meticulously analyzed. She had been on Enalapril therapy, an ACEI, for the last 6 months. Enalapril was withdrawn, and her symptoms abated during the next 24 h. Her antihypertensive treatment was changed to amlodipine, and at a follow-up examination a few weeks later, she was without abdominal complaints. Complete normalization of abdominal findings was reported on a follow-up CT of the abdomen after 1 month.

Discussion

ACEI-induced gastrointestinal angioedema (AIGA) usually develops within 4 weeks after initiation of therapy, but it has been reported up to 9 years after initiation [1]. AIGA may present with acute abdominal pain associated with nausea, vomiting, or diarrhea, therefore possibly mimicking an acute abdomen, which can lead to unnecessary invasive procedures [3].

Imaging findings in AIGA overlap with other causes of intestinal thickening, such as SB ischemia, intestinal intramural hemorrhage, vasculitis, infectious colitis, Crohn disease, trauma, previous radiation therapy as well as SB lymphoma, and, consequently, other causes have to be ruled out first. There are no routine laboratory investigations with specific findings indicating AIGA. It has been found that plasma bradykinin concentration is very high during acute ACEI-induced angioedema, but such investigation is difficult to perform routinely [4]. Prompt ACEI therapy discontinuation results in rapid resolution of AIGA, and a replacement therapy has to be introduced. Angiotensin II receptor antagonists are not recommended as an alternative therapy in patients with AIGA [5]. In conclusion, an early diagnosis of AIGA may spare the patient undergoing more invasive procedures, including laparotomy.

Statement of Ethics

The authors have no ethical conflicts to disclose.

Disclosure Statement

The authors have no funding or conflicts of interest to disclose.

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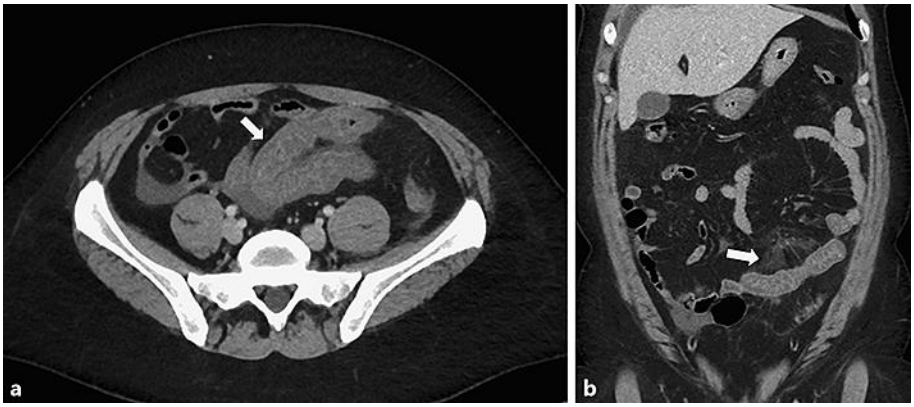

Fig. 1. **a** A computed tomography (CT) scan of the abdomen demonstrating segmental thickening of the small bowel wall. **b** A CT scan of the abdomen showing mesenterial edema.