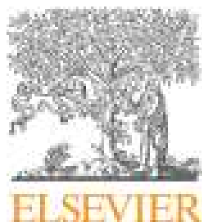
GE Port J Gastroenterol. 2016;23(3):130–131



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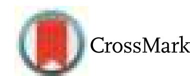

EDITORIAL

Acute or Recurrent Abdominal Pain: The Eyes Can Only See What the Mind Knows!

Dor Abdominal Aguda ou Recorrente: Só Vemos o que Conhecemos!

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Both angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin receptor blockers (ARBs) are largely used worldwide as effective treatment of blood hypertension and other cardiovascular diseases, including congestive heart failure and diabetic nephropathy. For instance, in 2011 there were 164 million prescriptions of ACEIs and 86 million prescriptions of ARBs in US.[1] Generally, these drugs are well tolerated and safe. However, angioedema has been reported to occur in 0.1–0.7% of ACEIs/ARBs users.[2–4] This drug-induced condition mainly involves the head and neck – i.e. the facial angioedema – with swelling of the face, tongue, and lips which occurs in about one of 2500 ACEIs users. An isolate gastrointestinal tract involvement – i.e. the visceral angioedema – occurs less frequently. Differently from the facial angioedema that suddenly manifests within few hours or days from the start of therapy, so that the diagnosis is easily suspected at clinical history, the visceral angioedema diagnosis may remain neglected for years. Indeed, visceral angioedema no rarely presents with no specific acute or recurrent abdominal symptoms, mimicking several other abdominal diseases. Therefore, these patients may undergo repeated investigations and, occasionally, worthless surgical interventions, with consequent waste of health resources and morbidity for the patient.

Since 'the eyes can only see what the mind knows', awareness of the ACEIs/ARBs-induced visceral angioedema is of paramount relevant for a prompt diagnosis in clinical practice. A systematic review described 27 cases (82% females) of ACEIs-induced visceral angioedema reported in literature until 2010.[5] Of note, it was found that diagnosis of visceral angioedema was performed within 72 h in only half of the cases, whilst in 46% of patients it was delayed between two weeks and nine years of ACEIs therapy. All these patients were hospitalized for further diagnostic workup, and some of them also underwent unnecessary abdominal surgery due to suspected cholecystitis or appendicitis. Clinical presentation always includes abdominal pain (acute or recurrent) with or without vomiting, ascites, and diarrhea. In addition, a relative reduction of both heart rate and blood pressure is frequently present. Elevated levels of bradykinin were detected in all cases when measured. On the contrary, mild leukocytosis appears in less than half of patients, whilst the C1 esterase inhibitor and complement levels are normal. At CT study, diffuse or localized thickening of small bowel is present, mainly involving the jejunum, ileum and duodenum, whilst gastric, oesophageal and colonic localizations are infrequent.[5,6] A typical CT finding is the so-called 'target sign' on the intestinal wall, with low-attenuation of the submucosa between an enhancing mucosal layer and an outer serosal layer.[7] Such a finding, together with ascites and absence of other radiological signs strongly suggests a visceral angioedema. Indeed, the absence of abdominal masses, lymphadenopathy, stenosis, fistulas, and abscesses allows to differentiate such diagnosis from other diseases, including inflammatory bowel diseases, lymphoproliferative diseases, mesenteric ischemia, radiation enteritis, Henoch-Schönlein purpura, and eosinophilic gastroentroenteritis.[7,8] A complete clinical recovery occurs within 24–48 h of drug withdrawal. Of note, the

DOIs of original articles:
http://dx.doi.org/10.1016/j.jpge.2015.09.008,
http://dx.doi.org/10.1016/j.jpge.2015.10.004

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http://dx.doi.org/10.1016/j.jpge.2016.01.007

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substitution of ACEI with an ARB is not always safe, given that angioedema can recur in up to one-third of patients, at least for the facial form.[7]

In the present Journal, visceral angioedema have been described in two Portuguese young women who presented at Emergency Department for acute (<24 h) abdominal pain that occurred two days and 15 days following ramipril and perindopril therapy, respectively.[9,10] Typical 'target sign' on intestinal wall and ascites were detected at CT. Both patients promptly recovered following ACEI therapy withdrawal. This further demonstrates that when the condition is suspected based on clinical history and CT findings, the diagnosis can be safely achieved without resorting in additional and useless examinations.

In conclusion, a patient on ACEI/ARB therapy presenting with acute or recurrent abdominal pain, particularly when female, should be suspected with visceral angioedema, and the clinician should alert the radiologist to look for 'target sign' at CT study.

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