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LETTERS TO THE EDITOR

Drug-induced acute pancreatitis☆

Pancreatitis aguda farmacológica

To the Editor,

We read with great interest the case of drug-induced pancreatitis published in your journal by Cerezo-Ruiz et al.,[1] mainly due to the uncertainty expressed by the authors themselves regarding the aetiological role of amoxicillin-clavulanic acid. These echo our misgivings in routine clinical practice. Excluding the most common aetiologies (alcohol, calculi and the less frequent hypertriglyceridaemia, hypercalcaemia or trauma), finding the cause of acute pancreatitis is not always easy. Moreover, given the extensive use of prescription medication in Spain, it is always tempting to attribute its cause to previous drug intake.

In this respect, we would like to report a case of acute pancreatitis recently seen in our hospital, where the aetiology was initially attributed to drug intake (azithromycin).

A 47-year-old woman with no history of interest or toxic habits was admitted in December 2014 for epigastric pain radiating to the back that had commenced 3 h previously. On abdominal examination, the patient complained of epigastric pain on superficial palpation, with no masses detected, possible peritonism and presence of bowel sounds. No jaundice of mucous membranes was observed.

Laboratory tests revealed mild leukocytosis with neutrophilia, amylase 1854 U/L, lipase 2054 U/L, glutamic oxaloacetic transaminase [GOT] 24 U/L, glutamic pyruvate transaminase [GPT] 15 U/L, gamma glutamyl transferase [GGT] 15 U/L, alkaline phosphatase [ALP] 63 U/L, triglycerides 55 mg/dL and total calcium 8.5 mg/dL.

Abdominal ultrasound detected diffuse thickening and increased pancreatic echogenicity with a band of peripancreatic fluid, and a small amount of subhepatic and perisplenic free fluid. The gallbladder and bile duct were normal.

In the anamnesis, the patient reported having taken azithromycin a few days earlier for a common cold. As no cause could be found to explain her symptoms, it was thought that they might be related to the antibiotic.

The patient progressed well with analgesia and fluid therapy (discharge after 6 days). Although the diagnosis was mild idiopathic acute pancreatitis, the possible causal relationship was suggested to the patient and she was advised to avoid azithromycin and other macrolides in the future.

She remained asymptomatic at subsequent outpatient follow-up visits, but was readmitted 6 months later (June 2015) for similar symptoms, but with more intense pain, nausea, vomiting and few bowel sounds, with severe abdominal tenderness on examination. Blood tests found: amylase 1701 U/L and lipase 740 U/L. Computed tomography (CT) with intravenous contrast revealed pleural effusion, diffuse enlargement of the pancreas with signs of necrosis (<30%) associated with an abundant amount of peripancreatic fluid, between loops and in the perirenal space (Balthazar score C).

Magnetic cholangioresonance performed during admission showed no anatomical pancreatic alterations, and endoscopic ultrasound did not identify either calculi or biliary sludge. On this occasion the patient had not taken any medication.

IgG4 levels were normal, and antibodies to carbonic anhydrase and lactoferrin were negative. Molecular study of the CFTR, SPINK1 and PRSS1 genes found no variants. Oddi sphincter manometry was not performed.

Patient progress on this occasion was also satisfactory, but slower (discharge after 15 days). The patient was asymptomatic in subsequent outpatient follow-up visits, with normal imaging tests.

At least 100 drugs related with the development of acute pancreatitis have been described in the literature, but most are reports of isolated clinical cases[2,3] where the authors were unable to find any other cause. For ethical reasons, it is rare for clinicians to resume the same drug, with the same effect,[4] although this would effectively prove the pharmacological aetiology.

The classification of drugs related with the development of acute pancreatitis proposed by Badalov et al.[5] includes antibiotics of the macrolide group (erythromycin class II and clarithromycin class III). Although azithromycin is not included, the temporal relationship between drug intake and development of acute pancreatitis in our patient made

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us initially think of an association. However, her second admission ruled out this aetiology.

A recent article by Tenner,[6] which questions the existence of drug-induced pancreatitis, is extremely interesting. The author argues that there is sufficient evidence of causation for only 2 drugs (azathioprine and didanosine [DDI]), based on randomised and cohort studies, while for most of the other drugs implicated, only isolated cases with insufficient scientific basis and no drug rechallenge have been published. The diagnosis of drug-induced pancreatitis is not easy, as it is not associated with clinical findings such as a rash, or laboratory findings like eosinophilia. It is unwise to establish a diagnosis purely on the basis of abdominal pain and elevated amylase levels (both factors present in many other abdominal processes). If aetiology is attributed to a drug, confounding factors (such as the association between exenatide and acute pancreatitis described by Tenner) must always be borne in mind.

Nevertheless, the most reasonable approach when drug-induced pancreatitis is suspected is to withdraw the drug and avoid re-introduction (as described by Cerezo et al.). If the symptoms resolve and there is no other possible cause (we did not perform Oddi sphincter manometry as this was not available in our hospital), an aetiological relationship is possible, but not easy to prove. A firm diagnosis can only be made if the pancreatitis reoccurs on drug rechallenge.

Thus, according to Tenner,[6] establishing a causal relationship between a drug and the development of acute pancreatitis is not easy, both due to the complexity of collecting data which may contain bias and confounding factors, and to the ethical limitations of drug rechallenge. It is important to be extremely wary when associating a drug with the development of acute pancreatitis, and bear in mind the existence of acute idiopathic pancreatitis.[7]

Conflict of interests

The authors declare that they have no conflict of interests.

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Adult colocolonic intussusception due to adenomatous polyp: An exceptional cause of a rare entity☆

Invaginación colocolónica en adulto por pólipo adenomatoso: una causa excepcional de una entidad poco frecuente

To the Editor,

Colonic intussusception in adults is a rare process, normally caused by malignant lesions, which are treated surgically.[1–4] However, there are some cases in which the origin of this disease is benign, such as stromal tumours, lipomas, appendiceal mucocele[2,5–7] and polyps.[2,8,9] We present the case of a patient with intussusception of the sigmoid colon caused by a large adenomatous polyp, diagnosed by computed tomography (CT) and treated by endoscopic polypectomy.

The patient was a 55-year-old man, a heavy smoker, with no family history of interest and no previous surgical interventions. He had been diagnosed 1 year previously with lung cancer, stage T4N2M0; no pathological lesions in the colon or abdominal lymphadenopathies were observed on the tumour staging CT scan. He had a complete response to radio- and chemotherapy. A follow-up CT scan upon completion of treatment revealed an image at the level of the splenic flexure consistent with colocolonic intussusception, apparently caused by a 32 mm × 32 mm solid endoluminal lesion, located at the head of intussusception (Figs. 1–3). No retrograde dilation of the colon or signs of bowel loop involvement were observed, and the patient was asymptomatic.

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