Acute pancreatitis secondary to treatment with isotretinoin☆

Pancreatitis aguda secundaria al tratamiento con isotretinoína

We present the case of a 14-year-old male who attended our hospital following hours of epigastric abdominal pain and vomiting. There was no associated choluria, jaundice or change in bowel habits. Prior history of interest included treatment with isotretinoin 30 mg/day for the last three months.

The physical examination found the patient to be afebrile and tachycardic, with a blood pressure of 100/66 mmHg. He experienced epigastric pain upon palpation of the abdomen, with no peritonism and no other findings of interest. No relevant abnormalities were observed in the abdominal X-ray. The blood tests revealed abnormal pancreatic clinical chemistry values (amylase 584 U/l and lipase 1392 U/l) with a normal lipid, phosphorus and calcium profile. An abdominal ultrasound found no significant biliary abnormalities, ruling out the presence of intra-abdominal collections or masses.

In light of these findings, mild acute pancreatitis (BISAP 0) of probable toxic-drug-induced aetiology secondary to treatment with isotretinoin was diagnosed. The patient's progression was satisfactory after withdrawal of the medicinal product, with no abnormal findings in the subsequent clinical examination, bloods and ultrasound.

Isotretinoin is a medicine used to treat severe and nodular cystic acne. Although its mechanism of action is unknown, it is believed to induce apoptosis in the sebaceous gland cells.

Acute pancreatitis induced by the ingestion of isotretinoin is an extremely rare and generally mild adverse effect.[1] Most cases are caused by an idiosyncratic reaction (as in our case), with a small percentage of cases attributable to secondary hypertriglyceridaemia.[2] It usually manifests between six weeks and six months after the start of treatment, with onset possible at any time.[3] It cannot be prevented, with the systemic monitoring of triglyceride levels during treatment having been shown to be an ineffective tool.

Despite being a rare side effect, acute pancreatitis should be taken into account when treating a patient with abdominal pain who is taking isotretinoin.

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Javier Tejedor Tejada*, Raúl Torres Yuste, Félix García Pajares

Servicio de Aparato Digestivo, Hospital Universitario Río Hortega, Valladolid, Spain

* Corresponding author.
E-mail address: jtejedor1991@gmail.com (J. Tejedor Tejada).
2444-3824/

Cytomegalovirus associated gastric ulcer: Case report and literature review☆

Citomegalovirus asociado a úlcera gástrica: caso clínico y revisión de la literatura

Cytomegalovirus (CMV) is a very common viral pathogen with significant morbidity and mortality in immunosuppressed patients.

We present the case of a 72-year-old woman, with a history of polymyalgia rheumatica undergoing chronic treatment with methotrexate (20 mg/week) and methylprednisolone 5 mg. She presented a one-month history of epigastric pain and postprandial fullness and a five-month history of constitutional symptoms. She reported no drug exposure. The gastroscopy revealed focal antral gastritis and a fibrin-coated ulcer in the lesser curvature, without identifying *Helicobacter pylori*. The gastroscopy revealed focal antral gastritis and a fibrin-coated ulcer in the lesser curvature measuring 10–12 mm, with regular and oedematous folds. The pathology study revealed an ulcer with chronic gastritis with an interstitial inflammatory component and adjacent foveolar hyperplasia, without identifying *Helicobacter pylori*.

Treatment was started with esomeprazole 40 mg/12 h for six weeks resulting in clinical improvement, with food intolerance due to vomiting, anorexia, polymyalgia

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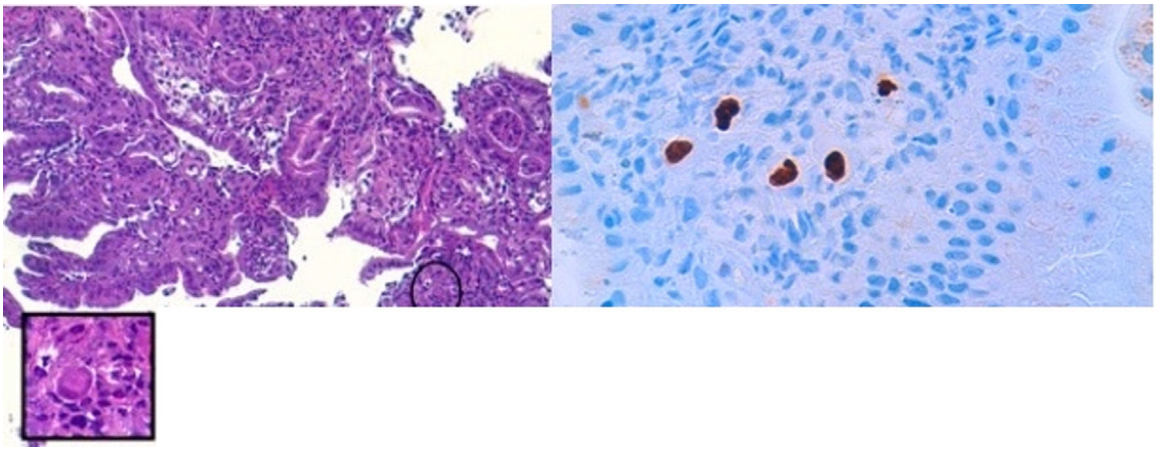

Figure 1 (A and B) Associated changes at the border of the ulcer, with marked foveolar hyperplasia, reactive epithelial abnormalities and chronic and acute non-specific inflammation. Focally, large stromal or endothelial cells with nuclear and cytoplasmic inclusions characteristic of CMV infection can be seen.

and severe asthenia. The blood tests identified hypoproteinaemia (4.8 g/dl), hypoalbuminaemia (2.53 g/dl) and macrocytic anaemia (haemoglobin 98 g/l). The second gastroscopy revealed three fibrin-coated ulcers measuring 1 cm in diameter, with geographic borders and with perilesional oedema. The pathology study showed CMV-associated gastritis with ulceration and the immunohistochemical study was positive (Figs. 1 and 2).

Methotrexate was suspended and intravenous ganciclovir administered (5 mg/kg/day) for four weeks followed by oral valganciclovir. Follow-up gastroscopies were performed, revealing progressive improvement. However, the patient suffered a flare-up of her rheumatic disease and treatment was started with leflunomide and methylprednisolone 5 mg/day. At this time it was decided to maintain permanent secondary prophylaxis with oral valganciclovir (450 mg/day).

CMV is a highly seroprevalent herpes virus in the adult population. However, not all infected patients develop clinical symptoms. In immunosuppressed patients, its severity is directly related to the degree of immunosuppression. Its manifestations range from fever to organ involvement.[1] Very few cases of rheumatology patients receiving immunomodulators or biological medicinal products have been published in the literature. Infectious oesophagitis is probably the most common symptom, followed by colitis. A meta-analysis published in the *Revista Clínica de Reumatología* [Clinical Journal of Rheumatology] in 2013 found that stomach ulcers are extremely rare and are characterised by a wide variety of symptoms. In contrast, another review of case studies published in the same journal found ulcers of the upper gastrointestinal tract to be to most common symptom, with multiple ulcers found in 55% of patients, typically in the gastric antrum. Although a lack of mortality in this group of patients is a noteworthy finding, serious life-limiting manifestations secondary to the onset of hypovolaemic shock can occur. The risk of contracting the disease seems to be associated with significant weight loss and combinations with corticosteroids or immunosuppressants like cyclophosphamide and methotrexate. In these patients, the onset of CMV-associated disease may occur several months or even years after starting immunosuppressive therapy.[2]

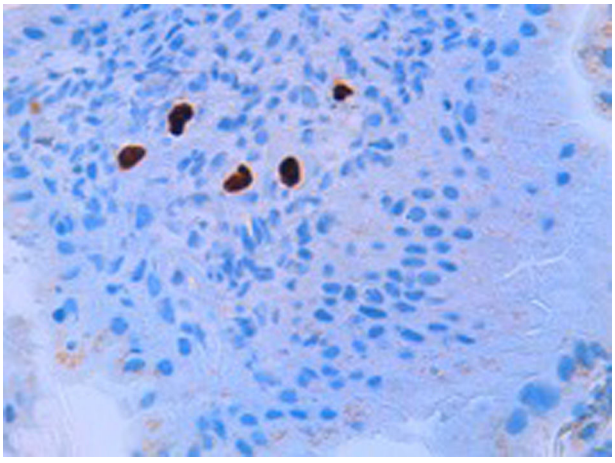

Figure 2 Immunohistochemical staining for CMV confirms the diagnosis and highlights a large number of cells with vital inclusions.

Macroscopically, CMV-induced gastric ulcers may look extremely similar to those caused by *Helicobacter pylori* or by NSAIDs. Deep biopsies must be taken as CMV can sometimes be found in the submucosal tissue. Diagnosis is confirmed by identifying intranuclear inclusion bodies in the haematoxylin and eosin stain. However, the sensitivity of this test is low, which is why immunohistochemistry is recommended if CMV is suspected.[3] It may be useful to administer a PPI to promote healing in immunocompetent hosts. However, immunosuppressed patients require the concomitant administration of an antiviral agent like ganciclovir. According to the literature, the most widely-used regimen is intravenous ganciclovir administered for three or four weeks, while foscarnet is an effective alternative. We only found one case of relapse in the form of a gastric ulcer in the published literature, which occurred 20 days after initiating the treatment. Some authors recommend a shorter intravenous therapy regimen followed by oral treatment with valganciclovir.[4]

There are no published data concerning primary prophylaxis in patients receiving immunomodulators or biological medicinal products. They should probably be considered low risk practically for life. Nevertheless, given the low estimated incidence, indefinite monitoring could be a questionable strategy. In the event of the onset of disease, it is recommended to adjust the immunosuppressive therapy if possible and maintain prophylaxis with oral valganciclovir over the long term, probably indefinitely, depending on the degree of immunosuppression, as disease relapse is common. It would be interesting to know the potential effects of changing immunosuppressive therapy to leflunomide in rheumatology patients given that this drug is active against CMV if administered orally and is inexpensive.[2] The successful use of leflunomide as an alternative in transplant patients (kidney and lung) resistant to ganciclovir and in secondary prophylaxis has been reported, primarily in cases of low viral load and without severe disease. However, cases of leflunomide failure in haematopoietic cell transplantation have also been published, meaning that the results found in the literature are open to debate.

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Claudia Martínez Huguet[a,*], Yolanda Arguedas Lázaro[b], Elena del Valle Sánchez[c], Teresa Omiste Sanvicente[a], Vanesa Bernal Monterde[b], Miguel Montoro Huguet[b]

[a] *Servicio de Medicina Interna, San Jorge, Huesca, Spain*
[b] *Servicio de Gastroenterología, Hospital San Jorge, Huesca, Spain*
[c] *Servicio de Anatomía Patológica, Hospital San Jorge, Huesca, Spain*

* Corresponding author.
E-mail address: cmhuguet@hotmail.com
(C. Martínez Huguet).
2444-3824/