

# Perforación intestinal relacionada con ipilimumab

Bowel perforation related with ipilimumab

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A 48-year-old man was admitted to hospital following four days of having suffered diarrhea and a febrile episode on the same day as he consulted. The diarrhea had increased to 6 episodes during the 12 hours before admission, regardless of the administration of loperamide or low doses of dexamethasone. He referred to no other symptoms upon admission.

The patient had a background of having had malignant melanoma stage IV due to the presence of cerebral, hepatic and peritoneal metastases. Such diagnosis was made at 43 years of age due to the presence of a malar lesion. A cerebral metastases appeared on the right frontal lobe four years after diagnosis (aged 47) which required surgical excision followed by stereotactic radiosurgery in the residual cavity. Local-regional recurrence led to it being managed with surgical excision plus brachytherapy. The appearance of a metastatic lesion required pulmonary wedge resection during the same year. He underwent an intestinal resection for the management of some other metastatic lesions five months prior to admission. Positron-emission tomography (PET/CT) developed one month before admission revealed the presence of 3 hepatic lesions, a right temporal one and visceral metastases due to the presence of various infracentimetric peritoneal nodules and a proximal small bowel lesion (around 3 cm diameter). The patient started treatment with ipilimumab after these findings, receiving the second dose 11 days before being admitted to hospital.

At emergency room the patient appeared ill and dehydrated on physical examination. His temperature was 37.8°C, heart rate 115 beats per minute, blood pressure 120/60 mm/Hg, respiratory rate 18 breaths per minute and 93% oxygen saturation while he was breathing ambient air. There were no other abnormal findings upon examination except from bowel sounds that revealed increased peristaltic movements; no abdominal tenderness was found, nor signs indicating peritoneal irritation. His white-cell count was 8,300 per cubic milliliter, with 59.3% neutrophils, 36.7% hematocrit and 238,000 per cubic millimeter platelet count. Serum chemical measurements were taken, revealing increased creatinine levels, while blood urea nitrogen, bilirubin and hepatic transaminase levels were normal. No alterations were found in electrolyte levels.

The patient was hospitalized and IV fluids were started along with high steroid doses. Coproscopic examination revealed *E. histolytica* cysts; treatment was thus begun with metronidazole and steroids started to become reduced. The patient had new episodes of diarrhea (up to 11 stools) on the third day of hospitalization; steroid doses were therefore increased and micofenolate was also considered. A colonoscopy was performed the next day, revealing abundant edema and erythema along with some areas of erosion being observed throughout the colonic mucosa and the visible part of the distal ileum. The patient complained of abdominal pain during day

#### DATOS DE CONTACTO

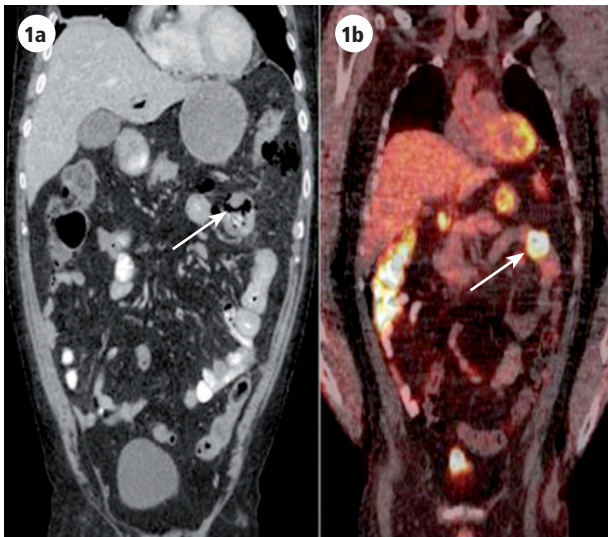
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**Conflict of interest:** the authors declare no conflicts of interest.

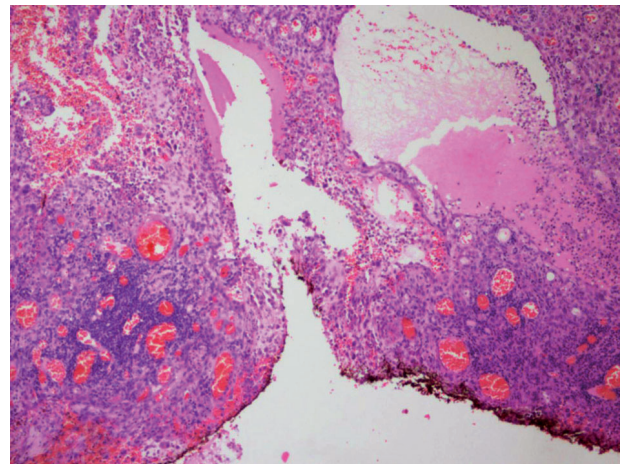
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five, mostly in the left upper quadrant; it was suspected that this could have been due to a perforated bowel. A CT (computed tomography) scan was performed with contrast; extravasation and pneumoperitoneum were observed in the left hypocondrium, along with the thickening of a proximal jejunal loop, probably being compatible with the level of the perforation (figure 1). The patient was thus taken to the operating room where serous liquid was found in the abdominal cavity along with infracentimetric metastatic lesions in the omentum and a 2 cm lesion located 20 cm from the ligament of Treitz with evidence of perforation in the anti-mesenteric border of the proximal jejunum.

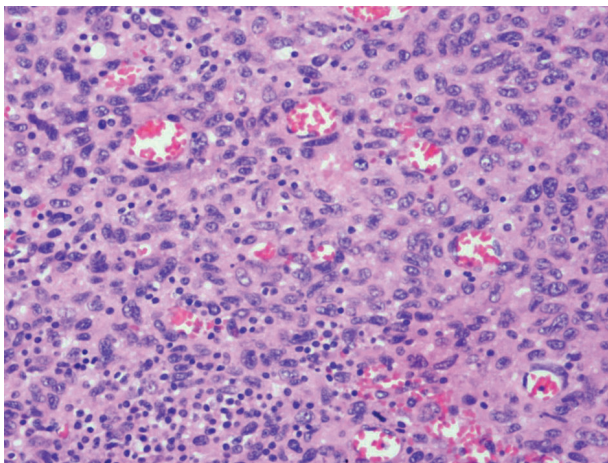
Pathology studies revealed a metastatic melanoma on the jejunum, with transmural involvement and a 0.3 cm perforation (figure 2). The tumor had epithelioid morphology with occasional melanic pigment. Only focal necrosis and lymphocytic infiltrate were found, although the latter was not prominent (figure 3). Immunohistochemistry revealed CD3-positive T-cell predominance over CD20-positive B-cells (figure 4). The CD4 to CD8 T-lymphocyte ratio favored CD8-positive cells. The non-tumor jejunal mucosa showed moderate villous blunting with a striking increase in intraepithelial lymphocytes (figure 5). Omental lesion pathology revealed a metastatic melanoma.



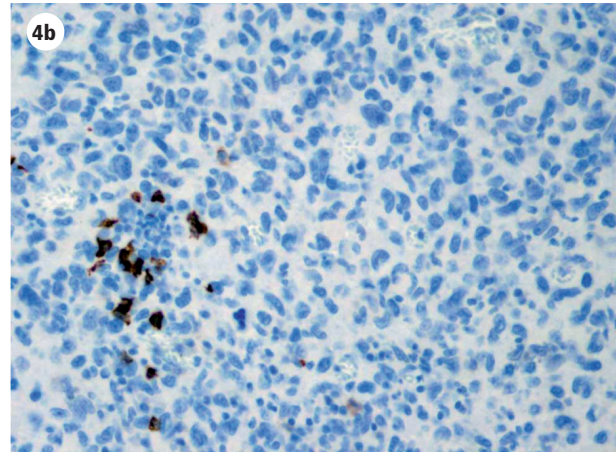
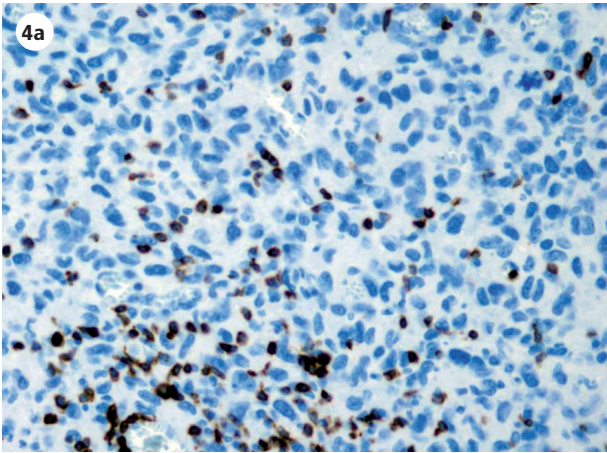
**Figure 1.** a) Thickening of a proximal jejunal loop, probably being compatible with the level of the perforation. b) Previous PET showing the tumor area on the jejunum with alteration in the metabolism of 18-FDG.



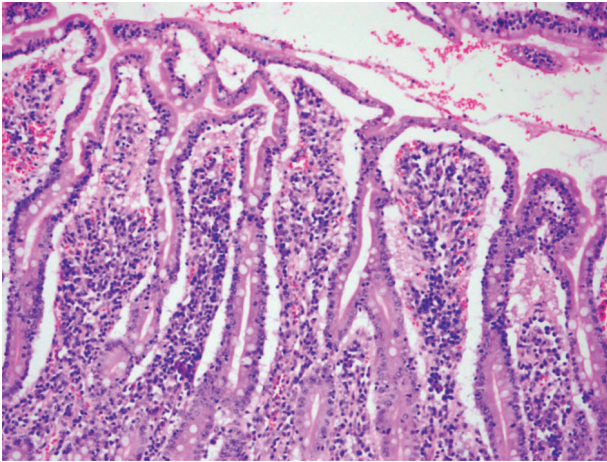
**Figure 2.** Metastatic melanoma to the jejunum: perforation. Note the minimal necrosis associated to the perforation. Serosal surface is inked.



**Figure 3.** Metastatic melanoma to jejunum, high power. The tumor has an epithelioid appearance with mild lymphocytic infiltrate.



**Figure 4.** a) CD3 and CD20 immunohistochemistry. IHC for CD3 shows a predominance of T lymphocytes. b) C20 shows few B lymphocytes in the same tumoral area.



**Figure 5.** Nontumoral jejunal mucosa with moderate to severe villous blunting, and a marked increase of intraepithelial lymphocytes.