

Anorexia, vomiting and weight loss in a 22-year-old woman

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Anorexia, vomiting and weight loss in a 22-year-old woman

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Abbreviations:

ALP- alkaline phosphatase

CT- computed tomography

CTLA-4- cytotoxic T-lymphocyte-associated protein 4

irAE- immune-related adverse event

MRI- magnetic resonance imaging

NR- normal range

NSC- non-small cell

PD-1- programmed cell death protein 1

Introduction

A 22-year-old woman presented in December 2017 with a two-month history of post-prandial abdominal pain, nausea, vomiting, early satiety and 4kg weight loss. She had entirely normal bowel habit. She did not use non-steroidal anti-inflammatory drugs and omeprazole had not helped her symptoms. Her past medical history included resection of 1.8mm Spitz melanoma in June 2010 and left axillary dissection November 2012 (3/22 nodes positive). She received first line ipilimumab and nivolumab starting November 2016. Cycle 2 was complicated by grade 2 hepatotoxicity that resolved spontaneously; cycle 4 by grade 3 hepatotoxicity requiring steroids and mycophenolate mofetil (discontinued August 2017). She had stereotactic radiosurgery for a right temporal lobe metastasis June 2017 and restarted maintenance nivolumab monotherapy in July 2017. In December 2017 her blood tests showed: normal haemoglobin; normal U&Es except potassium 3.4mmol/L (NR 3.5-5.0mmol/L); and bilirubin 6 µmol/L, ALT 13 IU/L, ALP 50 IU/L and albumin 31 g/L (NR 32-50). Recent CT and MRI staging demonstrated maintained response after 14 cycles of nivolumab. She had an oesophagogastroduodenoscopy, and the antrum is shown (Figure 1). Figure 2 shows the antral histopathology. The duodenum was normal macroscopically and histologically. What is the diagnosis and how is this treated?

Answer:

This patient has immunotherapy-related gastritis which presented one year after the start of treatment. Checkpoint inhibitor immunotherapy has revolutionised the management of metastatic melanoma, and is approved for renal cell and NSC lung cancer (1,2). Ipilimumab is an anti-CTLA-4 antibody and nivolumab inhibits PD-1. The resultant immune activation is non-specific, leading to several well-described gastrointestinal immune-related adverse events (irAEs) including colitis, hepatitis and pancreatitis (3). Gastroenterologists should be aware that immunotherapy can also cause an isolated gastritis in the absence of duodenitis, and without concomitant diarrhoea or steatorrhoea. The treatment of irAE-gastritis is corticosteroids, which runs counter to conventional treatment of gastritis (of which one of the causes is oral steroids). Her symptoms responded completely within 24 hours of starting oral prednisolone 40mg. At her next clinic visit, she had gained weight and was eating normally without pain or vomiting. This is the first description in the literature of isolated immunotherapy-related gastritis. The key learning points are: to recognise that gastritis can occur on immunotherapy; that the presentation can be delayed; and that, unlike other forms of gastritis encountered by gastroenterologists, irAE-gastritis is steroid-responsive. As per the management of irAE-colitis, we suggest that steroids are weaned over a two-month period.

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Figure 1. Endoscopic appearance of antrum/pylorus. The stomach mucosa is generally erythematous and appears oedematous with excess overlying mucus, but without frank ulceration. This appearance was seen throughout the whole stomach.

32x24mm (300 x 300 DPI)

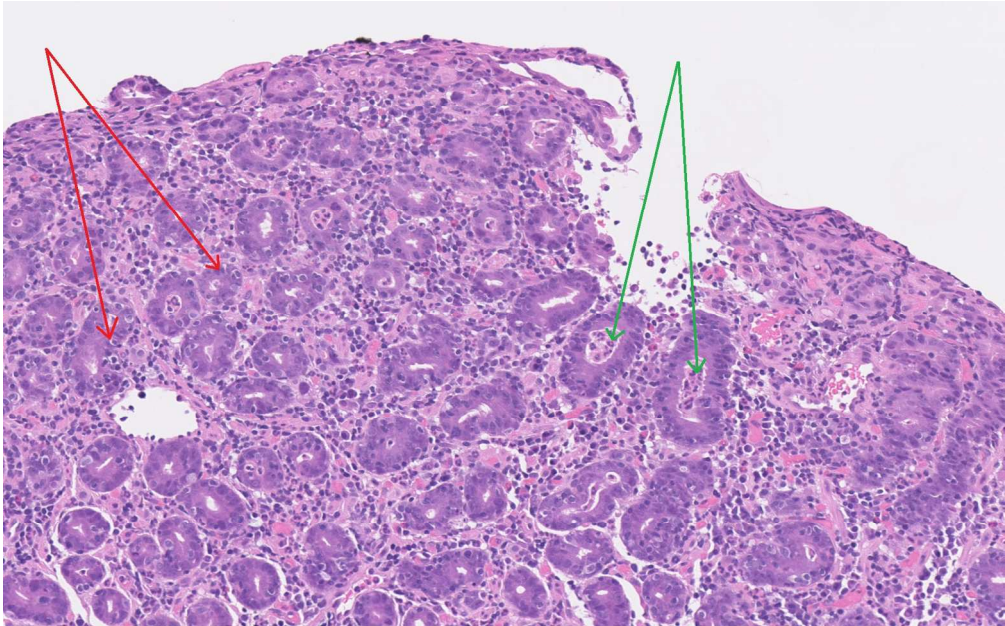


Figure 2. Histopathology slide showing the antrum (x200). The stomach specimens comprised gastric mucosa showing a dense, mixed inflammatory infiltrate. There are neutrophilic abscesses (green arrows) within attenuated glands, and within the surface epithelium, which is also attenuated. There is also a marked increase in intraepithelial lymphocytes (red arrows). Occasional lymphoid aggregates are seen. There is depletion of mucin, and no specialised glands are seen in the biopsies from the body of the stomach. There is no intestinal metaplasia, dysplasia or malignancy. No *H. pylori* organisms are seen, and the appearances are not typical of an NSAID-induced gastritis. Immunostaining for CMV and HSV, and for *H. pylori* were negative.

159x99mm (300 x 300 DPI)