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Management of cytomegalovirus reactivation in patient with immunotherapy-induced gastritis

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Dear Editor,

We present the case of a 52-year-old woman diagnosed with stage IV clear cell renal cell carcinoma who received combination of surgery and systemic therapy with nivolumab (anti-PD1) and ipilimumab (anti-CTLA-4). During treatment, patient presented oral intolerance, vomiting and abdominal pain. Computed tomography (CT) and gastroscopy (EGD) were performed, identifying findings suggestive of severe gastro-duodenitis with friability and diffuse oedema of the mucosa and deep ulcers (Fig 1A).

A gastrointestinal immunotherapy-induced toxicity was suspected so patient was managed with proton pump inhibitors (PPIs) and intravenous corticosteroids 1mg/Kg. Three weeks

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later, corticosteroid treatment failed. EGD was repeated and gastric biopsies were taken for histological and microbiological tests. Gastric biopsies revealed the presence of cytomegalovirus (CMV) inclusion bodies by immunohistochemistry (IHC). CMV viral load by quantitative PCR in plasma was 2,000 IU/mL so intravenous ganciclovir was prescribed. These findings suggested cytomegalovirus reactivation instead of previous CMV serology (IgG positive, IgM negative) before starting immunotherapy.

Then, the patient presented poor clinical course with persistent vomiting due to a failure of first-line corticosteroid and antiviral treatment. Another EGD was performed. Last IHC reveals a low CMV viral load. Second-line treatment with Anti-TNF was performed using a single-dose regimen of intravenous infliximab 5 mg/Kg. Finally, the patient presented a clinical and endoscopic response (Fig. 1B) and a negative CMV DNA test in the blood after completing the antiviral treatment.

Gastrointestinal toxicity by immune checkpoint inhibitors (ICI) are recorded in approximately one third of all patients, especially with anti-CTLA-4 and anti-PD1 monoclonal antibodies (1). These encompass hepatitis, colitis and upper digestive tract symptoms varying from 2% to 40% (2).

Gastroscopy with biopsies has been proposed as the gold standard diagnostic tool for patients with suspicion of ICI-induced gastritis. However, therapeutic management is not well established. The use of PPIs and intravenous corticosteroids treatment are recommended in patients with moderate and severe cases. Moreover, biological therapy (Infliximab 5mg/kg) is recommended in patients with corticosteroids-refractory ICI-induced gastritis (persistence of symptoms within 3-5 days) such as this case (3).

CMV viral reactivation is common in immunocompromised patients, treated with corticosteroid, biological or ICI therapy (2). However, an initial screening must be performed, to achieve an early therapeutic approach.

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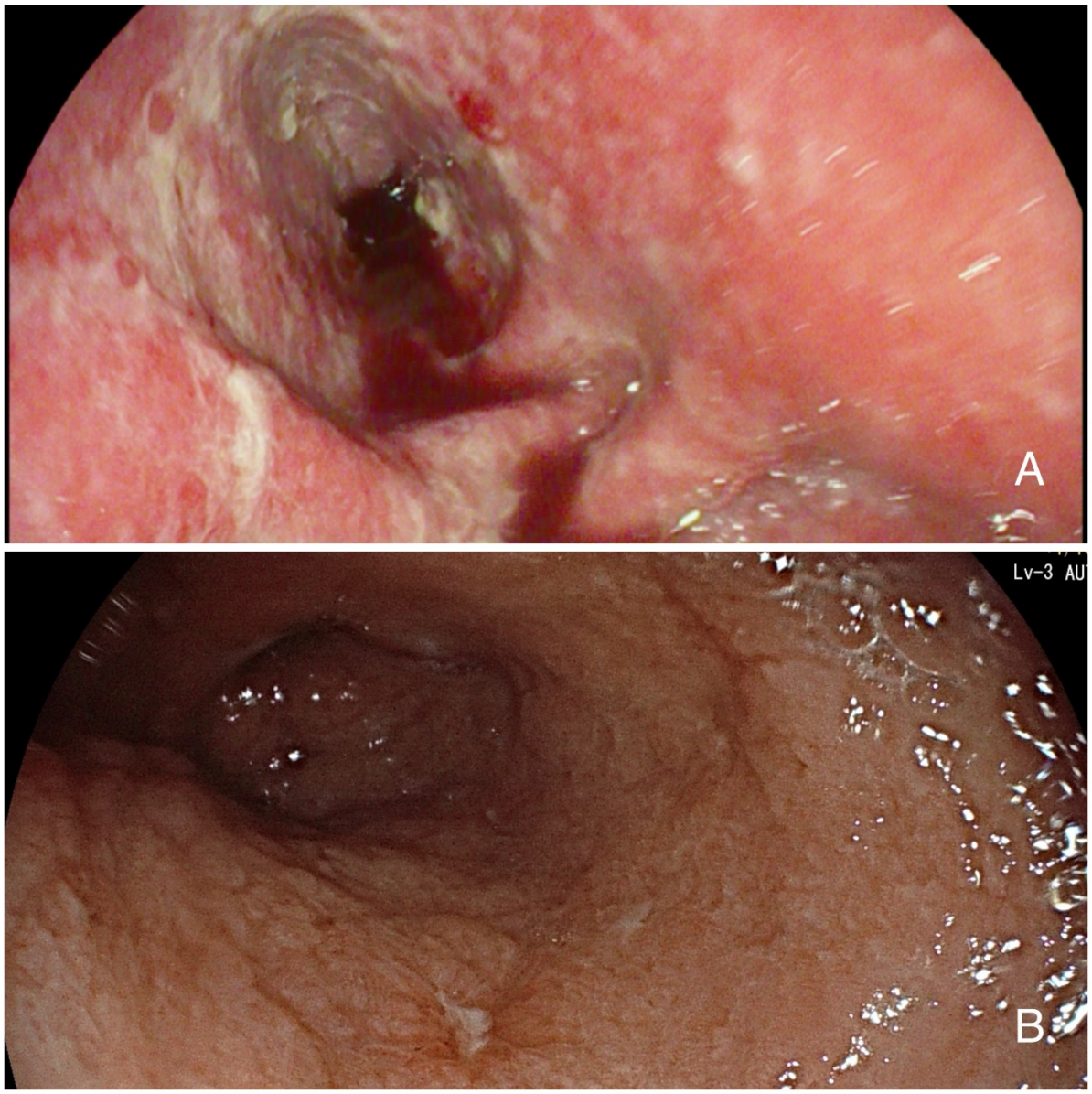

Figure 1A: Gastrointestinal endoscopic image after immune checkpoint inhibitor administration. Diffuse erythema, erosions, ulcers, and white exudate from the gastric antrum to the body were observed. 1B: Endoscopic examination after Infliximab and ganciclovir treatment showed the disappearance of mucosal redness, ulcers and white exudate