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Acute esophageal necrosis induced by immune checkpoint inhibitors

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Dear Editor,

A 73-year-old male with a history of chronic obstructive pulmonary disease and stage IV lung adenocarcinoma, being treated with the PD-1 inhibitor nivolumab, presented to the Emergency Room with a two-day history of coffee ground emesis and melena. On examination, he was tachycardic (130 per minute) and hypotensive (95/55 mmHg). Laboratory studies revealed anemia (6.9 g/dl), leukocytosis and hyper-lactatemia (lactate 6.3 mmol/l). Esophagogastroduodenoscopy was performed which showed diffuse circumferential blackish, necrotic-appearing mucosa of the first third of the esophagus (Fig. 1). These findings were consistent with a diagnosis of acute esophageal necrosis (AEN). A biopsy of the esophageal mucosa demonstrated fragments of necrotic tissue with predominant lymphocyte infiltration. He was managed with a strict restriction of oral intake, total parenteral nutrition, double-dose proton pump inhibitors and broad-spectrum antibiotics (piperacillin/tazobactam). Despite the measures adopted, the patient presented a progressive clinical deterioration and died of multiple organ failure 12 days after admission.

Discussion

AEN is a rare clinical entity and may have a poor prognosis. This syndrome mainly affects elderly men with multiple comorbidities such as hypertension, ischemic cardiopathy, diabetes mellitus and cancer (1). Most patients develop upper gastrointestinal bleeding symptoms (2,3). The diagnosis of AEN is made endoscopically by identifying diffuse circumferential progressive black discoloration of the distal third of the esophagus (1-3). The mortality rate is around 20-30 % (3).

Several upper gastrointestinal tract adverse events related to nivolumab, such as esophagitis or mucositis, have been described (4,5). However, this is the first case of AEN in association with immune checkpoint inhibitors. The severity of the clinical presentation, the involvement of the upper third of the esophagus and the predominant lymphocyte infiltration in the biopsy make us think about a relationship between treatment with nivolumab and the development of an AEN in this patient.

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Fig. 1. Esophagogastroduodenoscopy on admission showing continuous, circumferential, necrotic appearing mucosa of the proximal esophagus (15 cm from the dental arch). This was consistent with acute esophageal necrosis.