

# Nivolumab induced colitis in a cancer patient: therapeutic dilemmas and patient-related factors

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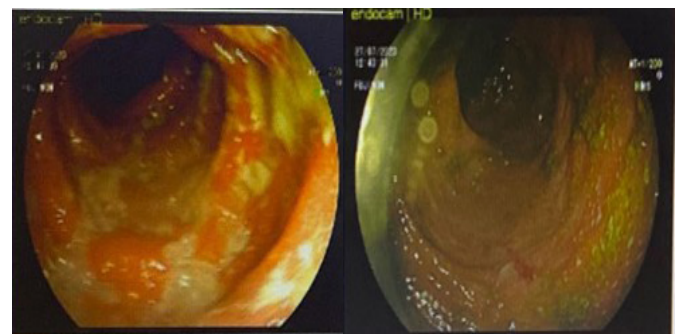
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## Dear Editor,

Nivolumab is a current type of monoclonal IgG4 antibody used to treat many types of cancer, including stomach cancer, lymphoma, malignant melanoma and non-small cell lung cancer.<sup>1</sup> Side effects associated with immune checkpoint inhibitors and tyrosine kinase inhibitors are increasingly recognized and presented as literature information.<sup>1,2</sup> One of the most commonly affected systems is the gastrointestinal system.<sup>1,3</sup> This case report presents a case of nivolumab-associated colitis in a patient with metastatic lung cancer, where treatment decisions were complicated by oncologic needs and patient compliance issues.

A 61-year-old male patient presented to our outpatient clinic with complaints of passing bloody, watery stools 8-10 times a day and fatigue. His medical history included hypertension and his treatment for metastatic lung cancer (liver metastases and lymph node metastases). He was receiving nivolumab therapy during his oncological treatment and reported that his symptoms began after five cycles of nivolumab. Blood tests revealed mild anemia (hemoglobin: 13.4 g/dl, hematocrit: 40%, WBC: 8.86 K/uL), elevated C-reactive protein level (39.38 mg/L), and elevated sedimentation rate (43 mm/h). Routine blood tests were within normal limits. Stool microscopy revealed abundant erythrocytes and leukocytes in all fields. Stool culture was negative for Salmonella, Shigella, and Aeromonas. Colonoscopy findings were consistent with pancolitis; there were widespread millimetric ulcers in the colon mucosa, submucosal vascular structures were obliterated (Figure), and multiple biopsies were taken. Biopsy findings were consistent with ulcerations, crypt abscesses, active severe inflammation, and inflammatory bowel disease. Immunohistochemical analysis of tissue samples taken for CMV colitis was negative. Because there was no history of inflammatory bowel disease or chronic colitis before nivolumab treatment, infectious causes of colitis had been excluded, and cases of nivolumab-induced colitis had been reported in the literature, a diagnosis of nivolumab-associated colitis was made based on our endoscopic and histopathological findings. Upon consultation with the



**Figure.** Endoscopic appearance of nivolumab induced colitis

patient's oncologist, discontinuation of nivolumab was not possible due to oncological necessity. Mesalazine was started as a first-line treatment, but the patient could not tolerate it. Systemic steroid therapy was considered, but the prednisolone-azathioprine combination was not approved by the oncology team. Budesonide, which has a more limited systemic effect and a lower risk of adverse outcomes, was started. The patient stated that he was feeling well on budesonide treatment and did not attend her outpatient clinic follow-ups despite phone calls. A few months later, our patient presented to our hospital's Emergency Department again with bloody diarrhea. He was informed that he had neglected his budesonide treatment because he was feeling well. A second colonoscopy revealed pancolitis, similar to the findings previously identified. No infectious or parasitic cause of pancolitis was identified, and the patient was started on methylprednisolone. However, the patient again failed to attend outpatient clinic follow-ups. A few months later, the patient underwent orthopedic surgery for a vertebral fracture and was subsequently admitted to intensive care. He was subsequently pronounced deceased due to complications from the surgery.

Immune checkpoint inhibitors have become a crucial component of cancer treatment, but they carry the risk of developing serious immune-related side effects, including colitis.<sup>4,5</sup> Nivolumab-induced colitis can mimic ulcerative colitis or infectious colitis endoscopically and

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histopathologically, but the clinical course can also be quite variable.<sup>3-5</sup> In this case, treatment options were limited by both oncological limitations and the patient's failure to attend regular outpatient clinic visits. Lack of follow-up and intolerance to standard therapy complicated disease management and contributed to the adverse clinical course. This case report clearly highlights the importance of a multidisciplinary approach, close follow-up, and patient compliance in the successful management of immune checkpoint inhibitor-associated colitis.

## ETHICAL DECLARATIONS

### Informed Consent

Written informed consent was obtained from the patient for the publication of this correspondence and any related clinical details.

### Peer Review Process

This letter was externally peer-reviewed.

### Conflict of Interest

The authors declare no conflicts of interest.

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