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Treatment of steroid-refractory immune checkpoint Inhibitor-induced intestinal pseudo-obstruction with infliximab

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Dear Editor,

Immune checkpoint inhibition therapy using targeted monoclonal antibodies is a relatively new therapeutic approach for patients with several cancer types including non-small cell lung cancer¹. Targeted monoclonal antibodies based drugs can activate anti-tumor immunity by blocking immune checkpoint receptors (CTLA-4, PD-1 receptor and its ligand PD-L1), in order to restore T-cell effector function^{2,3}. However, the use of immune checkpoint inhibitors can lead to a unique side effect profile termed as immune-related adverse events (irAEs). Loss of T-cell inhibition results in an enhanced immune response driven by T-cell activation and is capable of inducing an autoimmune-related inflammation in normal tissue as a consequence of impaired self tolerance⁴. These irAEs can potentially involve every organ system including gastrointestinal, dermatologic, hepatic, and endocrine toxicities. For example, Fernandez-Gordon Sanchez *et al* reported a patient with immune-mediated colitis and nonimmune-mediated cholestatic injury induced by pembrolizumab that was successfully treated with Ustekinumab⁵. We report a steroid-refractory case of lung adenocarcinoma patient with an unusual irAE (intestinal pseudo-obstruction) during the treatment with immune checkpoint inhibitors that could be successfully managed by the administration of infliximab.

A 56-year-old man with recurrent lung adenocarcinoma treated with nivolumab was admitted in our hospital with abdominal pain, distension, and vomiting for the last two weeks. He had received 6 cycles of nivolumab at 3 mg/kg every two weeks with the last dose administered four days before the onset of his symptoms. Clinical examination revealed a moderate abdominal distension painful to palpation without signs of peritoneal irritation and low back pain. His temperature was normal. Subsequent laboratory findings were as follows: White blood cells (WBC) $10.08 \times 10^9/L$, C-Reactive Protein (CRP) 26.5 mg/L, Albumin (ALB) 24.8 g/L, and Hemoglobin (Hb) 87 g/L. The abdominal contrast-enhanced Computed Tomography

(CT) revealed bowel distention (Figure 1). Patient received nasogastric tube and bowel rest treatment with intravenous fluid hydration. After four days of conservative management with no improvement, the patient's state deteriorated and the small bowel was significantly distended. There were no signs of metastatic disease including lymphadenopathy. After thorough investigation and exclusion of other factors, suspicion was raised toward the adverse effect of the immune checkpoint inhibition therapy occurred in this patient. Then steroid treatment (intravenous prednisone 2 mg/kg/day) was initiated, but the patient's condition did not improve after high-dose steroid. After infliximab was added, the clinical manifestations and imaging were significantly improved. He has continued an immunotherapy starting two months after his discharge. Patient remains in a stable clinical status during his follow-up eight months after infliximab therapy and has not presented any similar symptomatology.

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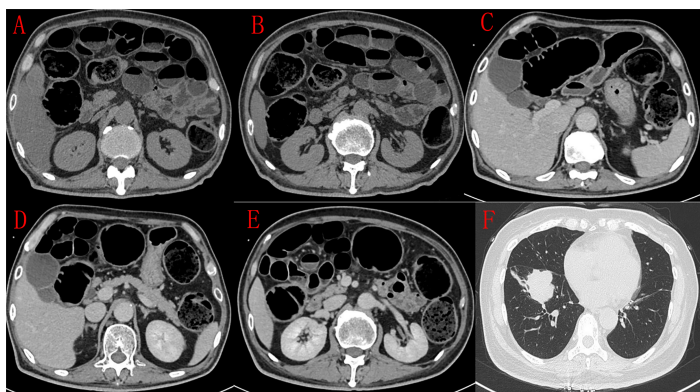


Figure 1 A-E: Abdominal computed tomography (CT) showed bowel distention; F: Lung CT showed right lung space-occupying lesions.