Ileal perforation in the setting of atezolizumab immunotherapy for advanced bladder cancer

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ZILLIOUX J, DILIZIA M, SCHAHEEN B, RUSTIN R, KRUPSKI TL. Ileal perforation in the setting of atezolizumab immunotherapy for advanced bladder cancer. *Can J Urol* 2018;25(5):9525-9526.

Atezolizumab is a promising immunotherapy for advanced urothelial carcinoma. Like other immune checkpoint inhibitors, it can produce rare immune-related adverse events (IRAEs). Here we present the recent case of a patient with metastatic bladder cancer who developed diarrhea and abdominal pain months after beginning atezolizumab therapy. He presented to our institution with an ileal perforation secondary to atezolizumab-induced enterocolitis. After surgical repair, the patient's condition improved, and he was discharged. We discuss the management of atezolizumab-induced enterocolitis, including the importance of early recognition and intervention to prevent more devastating complications.

Key Words: atezolizumab immunotherapy, ileal perforation advanced bladder cancer, urothelial carcinoma

Introduction

Atezolizumab is an effective new immunotherapy for advanced urothelial carcinoma.[1-4] Rare, serious immune-related adverse events (IRAEs) can develop, necessitating prompt recognition and intervention.[5-7] We present a case of a patient with an ileal perforation from atezolizumab-induced enterocolitis.

Accepted for publication August 2018

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Case report

A 79-year-old male with metastatic bladder cancer post palliative ileal conduit developed disease progression after gemcitabine-cisplatin therapy and was started on atezolizumab. Twenty weeks later, he developed severe abdominal pain. CT demonstrated pneumoperitoneum and mass-like bowel wall thickening, Figure 1. Urgent exploratory laparotomy revealed two punctate perforations of the distal ileum in a region of inflamed bowel but no evidence of ischemia, Figure 2. The area of perforated bowel was excised and repaired primarily without colostomy. Postoperatively, the patient's condition improved

TABLE 1. **Treatment algorithm of immune checkpoint inhibitor-induced enterocolitis.**[5]

Grade	Description	Treatment
1	Mild to moderate diarrhea.	Symptomatic treatment: loperamide, hydration, diet.
2	4-6 bowel movements per day above baseline, hematochezia and/or abdominal pain.	Methylprednisolone 0.5 mg/kg/d or equivalent. Check stool WBC, calprotein, C difficile antigen.
3	≥ 7 bowel movements per day above baseline, requirement of IV fluids, and/or fecal incontinence.	Methylprednisolone 1-2 mg/kg/d or equivalent. Dose delay of immunotherapy.
4	Symptoms refractory to high dose steroids.	Infliximab 5 mg/kg/d. Discontinue immunotherapy.

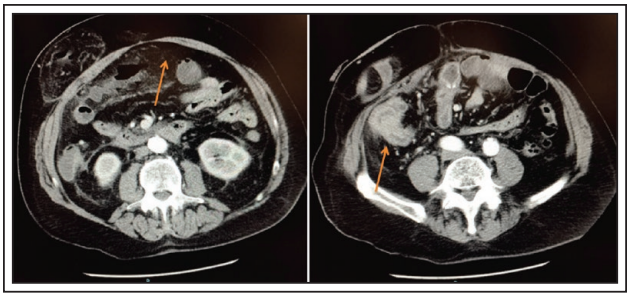

Figure 1. CT scan of the abdomen and pelvis with IV contrast demonstrating diffuse pneumoperitoneum (left) and thickening and enhancement of bowel wall near the ileoileostomy with associated fat stranding (right).

substantially, and he was discharged to subacute rehab. Initiation of steroid therapy is pending recovery from this event and persistence of enterocolitis symptoms.

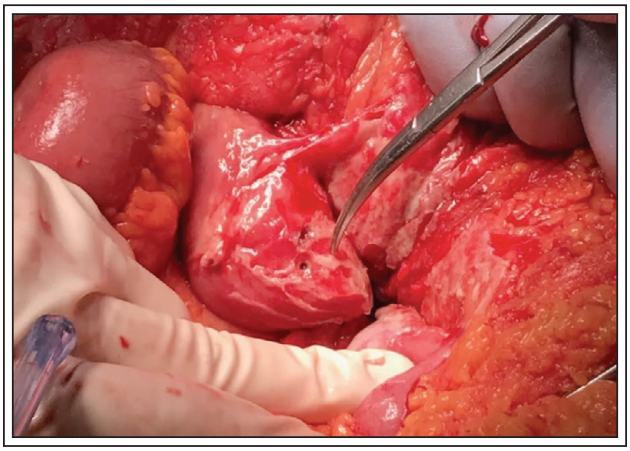

Figure 2. Ileal perforation observed during exploratory laparotomy. Multiple segments of inflamed bowel were also observed.

Comment

The estimated incidence of atezolizumab-induced enterocolitis is between 0.5%-1.5%, and bowel perforations are exceedingly rare.[8,9] Treatment for atezolizumab-induced enterocolitis, Table 1, follows algorithms developed for ipilumumab-induced enterocolitis.[5] Prompt recognition and treatment of IRAEs in patients receiving atezolizumab is crucial, as rapid steroid therapy is associated with earlier symptom regression and decreased morbidity.[9] □

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