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Toxic Injury to the Gastrointestinal Tract After Ipilimumab Therapy

To the Editor:

We read with interest the recent case report by Shepard et al¹ entitled "Toxic Injury to the Gastrointestinal Tract after Ipilimumab Therapy for Advanced Melanoma." We congratulate the authors on their description of an interesting case and on their informative review of available literature.

We report a similar case that complements that of Shepard et al. Our patient was a 63-year-old man with hormone-refractory metastatic prostate cancer. He received ipilimumab in a phase 2 clinical trial. Three weeks after ipilimumab administration, he presented to the emergency department with fever, abdominal pain, and bloody bowel movements. Stool studies at that time were negative for infectious bacteria, ova and parasites, and *Clostridium difficile*. Results from abdominal computed tomography revealed pancolitis. The colonic mucosa was friable on sigmoidoscopy. Biopsy results demonstrated focal active colitis without chronicity,

ischemic injury, or viral infection. Steroids and mesalamine were administered for suspected ipilimumab enterocolitis. Frequency of bowel movements decreased, and the patient was discharged and directed to take prednisone.

One week after discharge, he was re-admitted with abdominal pain and persistent diarrhea. Laboratory results were notable for leukocytosis, and stool studies were negative for infectious bacteria, ova and parasites, and *C difficile*. The patient's symptoms improved with administration of intravenous steroids. Prior to discharge, the patient underwent repeated sigmoidoscopy, after which worsening abdominal pain developed. Results from repeated abdominal computed tomography revealed free intraperitoneal air, and he underwent a subtotal colectomy with end ileostomy and debridement. The surgical specimen was notable for ischemia and necrosis with multiple perforations, all of which were proximal to the sigmoid colon. His postoperative course was complicated by venous thrombosis, aspiration pneumonia, retroperitoneal hematoma, and persistent peritonitis. He was transitioned to home hospice care and died shortly thereafter.

We believe that our case, along with the case of Shepard et al,¹ adds to the growing body of literature describing the scope of potential immune-related adverse events associated with the use of ipilimumab. Although it is certainly possible that diffuse toxic injury to the gastrointestinal tract represents a stronger intolerance to self-antigens, our case and others demonstrate that devastating complications can occur from toxic injury localized to the colon.² Colonic ulcerations may also predict steroid refractory disease.³ A recent meta-analysis also found a statistically significant increase in ipilimumab-related fatal adverse events when used in patients with prostate cancer.⁴

We thank the authors for their interesting case and comprehensive review of the available literature on this topic. (doi:10.7556/jaoa.2018.118)

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