Total Abdominal Colectomy for Management of Refractory Immune Checkpoint-Induced Colitis

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Introduction

Immune checkpoint inhibitors, such as ipilimumab and nivolumab are changing treatment paradigms and improving overall survival for a myriad of cancers. As with all treatments, adverse side effects become more apparent with greater exposure. Ipilimumab activates the immune system by targeting CTLA-4, a protein receptor that downregulates the immune system. Nivolumab is a human IgG4 monoclonal antibody that blocks PD-1. The combination of both is commonly used in metastatic melanoma. Using both increases the rate of immune-mediated colitis (1).The reported incidence of colitis is about five times greater with ipilimumab than nivolumab and is 13.6% with combination therapy (1). We present a case of a 69-year-old male with metastatic melanoma who developed extensive colitis after starting combination therapy with failure of medical management leading to a total abdominal colectomy.

Case Description

The patient was a 69-year-old Caucasian male with a past medical history significant for atrial fibrillation on Eliquis (apixaban), Obstructive Sleep Apnea, Prostate cancer, Morbid obesity, hypertension, and hyperlipidemia. He had a diagnosis of Stage IIIC melanoma for which underwent a wide local excision and sentinel lymph node biopsy of a right upper arm melanoma on 4/3/19. The sentinel lymph node was positive and later had a completion axillary lymphadenectomy on 4/26/19. He declined immunotherapy but continued to be followed by Oncology. Hilar lymphadenopathy was found on imaging in 2021. A subsequent biopsy was consistent with melanoma. He started ipilimumab and nivolumab in June 2022.

He was admitted to an OSH due to diarrhea on 7/21/22. Sigmoidoscopy showed severe inflammation characterized by adherent blood, congestion, erythema, friability, loss of vascularity, mucus, and deep ulcerations found in a continuous pattern from the rectum to sigmoid colon. Colonic biopsies were consistent with the clinical impression of immune checkpoint inhibitor colitis. Treatment with steroids and infliximab resulted in improvement of symptoms. The patient was discharged. He was hospitalized for similar symptoms on 08/16/22, treated effectively with steroids, and discharged on 08/24/22.

He presented to our hospital on 09/03/22 for significant abdominal pain. A CT Abdomen and Pelvis demonstrated a significant amount of free air, primarily around the stomach in the upper abdomen, concerning for perforated viscus, and sigmoid colon diverticulosis with mild focal colonic wall thickening of the sigmoid colon. Noted to be hemodynamically unstable and was taken to OR and underwent Exploratory laparotomy with total abdominal colectomy, creation of end ileostomy and drainage of peritoneal abscesses.

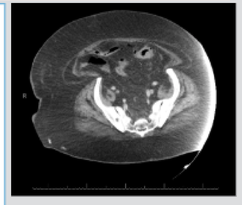


Figure 1 Above :CTAP mild focal colonic wall thickening of the sigmoid colon.
Figure 2 Below: Presence of pneumoperitoneum



Surgical Management

We began with an exploratory laparotomy. The remainder of the case progressed as follows:

1. Large amount of purulent fluid was encountered upon entry into the abdomen, and cultures were taken.
2. Upon inspecting the descending and sigmoid colon, there was a large perforation in the sigmoid colon and few smaller perforations beside it with active spillage from the perforation sites. The splenic flexure, transverse colon, and hepatic flexure were friable and with patchy areas throughout the whole colon.
3. The peritoneum of the sigmoid mesentery was incised at the level of the sacral promontory. The sigmoid colon was mobilized by incising the white line of Toldt. Next, using a TA stapler, the sigmoid colon was stapled at the rectosigmoid junction. The descending colon was mobilized by taking down the white line of Toldt to the splenic flexure. Enseal was used to take down the sigmoid and descending mesentery. The descending and sigmoid colon were mobilized medially, separating them from the retroperitoneum. Splenic flexure was taken down by taking down the splenocolic ligament. The greater omentum was separated off the transverse colon, and the lesser sac entered using Enseal. The gastrocolic ligament was taken down with the Enseal. Next, the right colon was mobilized in a similar fashion by incision the white line of Toldt, and the mesentery taken down with Enseal from terminal ileum to the hepatic flexure, and the right colon mobilized medially separating from the retroperitoneum. Care was taken to protect both ureters throughout the whole procedure. At this point, the entire colon was mobilized and mesentery taken down. TA stapler was used to staple the terminal ileum, and the entire colon was taken out as one specimen and sent to pathology.
4. Attention was turned to the RLQ, a circular skin incision made and deepened until the fascia was encountered. The fascia was incised vertically, the rectus muscle split and peritoneum entered vertically also. We dilated the incision So that it was sufficient to pass two fingers. The terminal ileum was passed through this opening without tension or torsion. 3-0 Vicryl stitches were placed through the skin and terminal ileum wall to anchor it in place.
5. Drains were placed.
6. Midline incision was closed.
7. The ileostomy was matured at this point and an ostomy appliance was placed. Wound vac was applied to the abdominal midline wound and placed to suction.

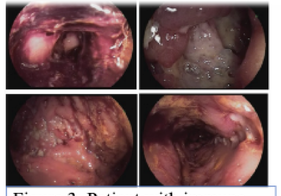


Figure 3: Patient with immune checkpoint inhibitor colitis. (2)

Conclusion

The risk factors for such extensive colitis including failure of appropriate medical management, greater likelihood of immune-mediated colitis in Caucasian/white patients, those treated with an anti-CTLA4 based regime, NSAID use, and those with prior history of checkpoint inhibitor induced colitis (3). We identify the need for additional studies in which patients will likely fail medical management of immune mediated colitis caused by checkpoint inhibitors. As these medications become the standard of care, it is important to determine which patients may be refractory to conservative management of their immune mediated colitis as in the case of our patient.

References

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Disclosures

The authors have no disclosures.