

## **Ipilimumab-Induced Colitis with Colon Ulcers**

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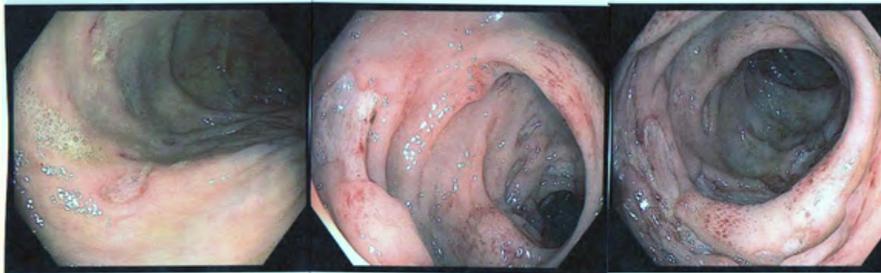
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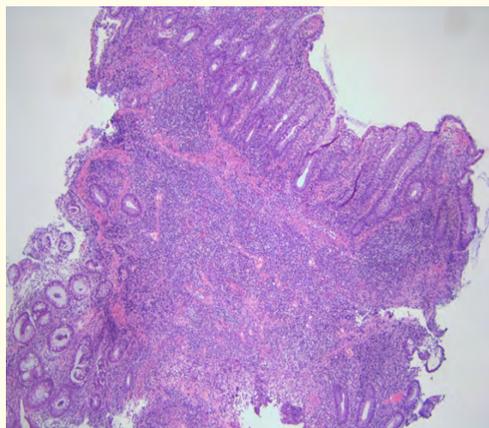
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A 69-year-old white male presented with bloody diarrhea and proctalgia after receiving two doses of Ipilimumab for his melanoma of the right arm, metastatic to lungs. His colonoscopy showed (Figure 1) mucosal friability and multiple punched out ulcers throughout the colon from rectum to cecum. Random colon mucosal and ulcer biopsies showed (Figure 2) markedly increased lamina propria and submucosal inflammation with aphthous ulcer formation and acute cryptitis (H&E, 40x). Immunohistochemical stains for CMV and HSV were negative. The clinical, endoscopic and histological findings were consistent with immune-mediated colitis with colon ulcers due to Ipilimumab.



**Figure 1**



**Figure 2**

Multiple colon ulcers are not uncommon in our clinical practice. There are a variety of causes which include inflammatory bowel disease, non-steroidal anti-inflammatory drugs, ischemic colitis, radiation colitis, stercoral ulcers, solitary rectal ulcer syndrome, infections due to cytomegalovirus, amebiasis and tuberculosis [1]. Colon ulcers have also been reported following administration of chemotherapy with bevacizumab for the treatment of metastatic colon cancer [2]. Gastrointestinal vasculitis due to Behcet's disease and Churg-Strauss syndrome [3] can also lead to colon ulcers [4]. Ipilimumab is used for the treatment of metastatic melanoma [5]. It is an anti-cytotoxic T-lymphocyte-4 antigen (CTLA-4) monoclonal antibody. About 20% of patients may develop diarrhea. It has been associated with immune mediated colitis, enterocolitis and intestinal perforation [6]. The histologic features of ipilimumab associated colitis consist of three patterns: neutrophilic infiltrates only (46%), lymphocytic infiltrates only (15%), or mixed infiltrates (38%) [7]. Ipilimumab-induced colitis is characterized by endoscopic and histological findings similar to what is found in inflammatory bowel disease. Multiple colon ulcers as part of colitis has been shown in our case.

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