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CASE REPORT | COLON

Brentuximab-Induced Colitis in a Non-Stem-Cell Transplant Patient

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ABSTRACT

Many chemotherapeutic agents have been associated with drug-induced colitis (DIC). With newer agents' expansion of approval as first-line therapy for common cancers, it is important to be cognizant of their association with DIC. We present a case of brentuximab-associated DIC in an elderly woman with CD30+ Hodgkin lymphoma. Brentuximab's association with DIC was suspected by others in the literature, but a history of stem-cell transplant in them would blur the association with graft-vs-host disease. Lack of stem-cell transplant in our patient makes the link between brentuximab and DIC unambiguous.

KEYWORDS: colon, colitis

INTRODUCTION

Drug-induced colitis (DIC) is a common adverse effect of many chemotherapeutic and anti-inflammatory drugs. As such, many cases of DIC go undiagnosed or misdiagnosed because of lack of knowledge of certain medications' association with DIC. Some of the commonly known medications that cause DIC are mycophenolate, anti-PD-1, and CTLA-4 inhibitors. Little is known about brentuximab's association with gastrointestinal adverse effects. Brentuximab is an anti-CD30 antibody that selectively targets tumor

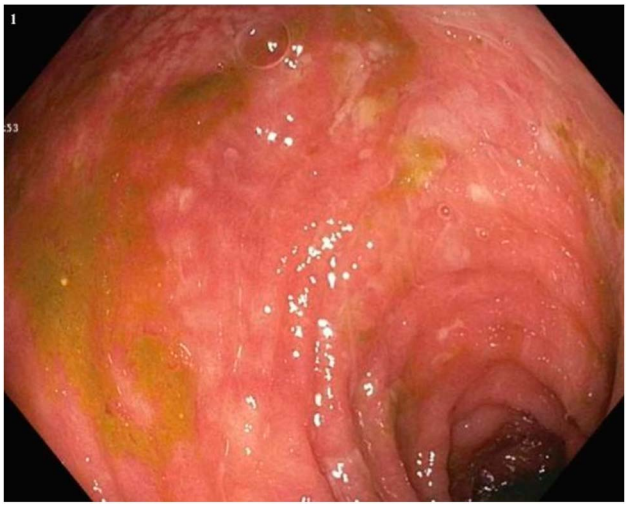

Figure 1. Left colon with erythema, loss of vascularity, and exudates.

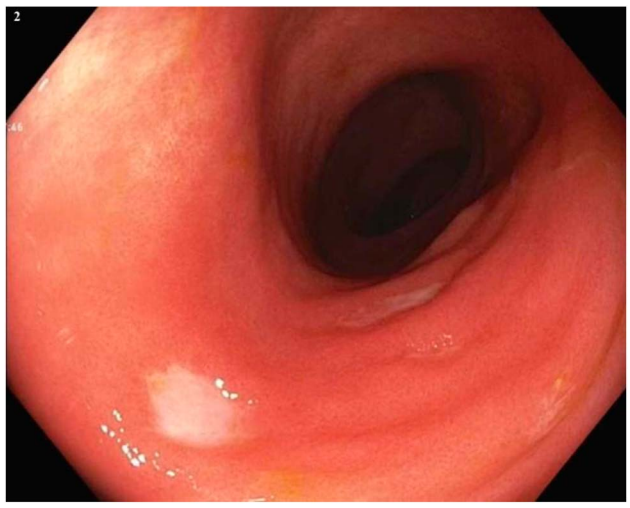

Figure 2. Discrete shallow ulcers at the rectosigmoid junction.

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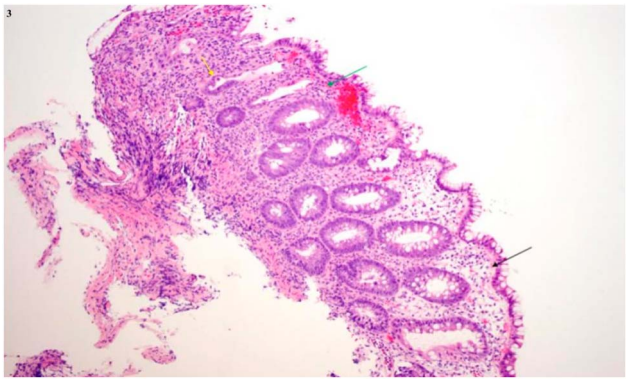

Figure 3. Photomicrograph of colonic mucosa with edematous lamina propria (black arrow), acute and chronic inflammatory cell infiltrate (green arrow), and neutrophilic cryptitis (yellow arrow).

cells expressing CD30 on their cell surface. Several studies performed on efficacy and tolerability of brentuximab have shown its effectiveness against refractory or relapsed CD30+ Hodgkin lymphoma. The most commonly reported adverse effects were peripheral sensory neuropathy, nausea, and fatigue.[1] We present the first case of brentuximab-induced colitis in a non-stem-cell transplant patient who was treated with brentuximab as part of a first-line regimen for CD30+ Hodgkin lymphoma.

CASE REPORT

A 71-year-old woman who was recently diagnosed with CD30+ Hodgkin lymphoma presented with cramping abdominal pain, nausea, vomiting, and diarrhea. She was receiving chemotherapy with brentuximab, doxorubicin, vinblastine, and dacarbazine (AAVD) and had completed the second cycle 10 days before presentation. Laboratory studies were negative for neutropenia. The abdominal and pelvic computed tomography (CT) revealed a thickened and edematous left colon and rectum with gaseous distention

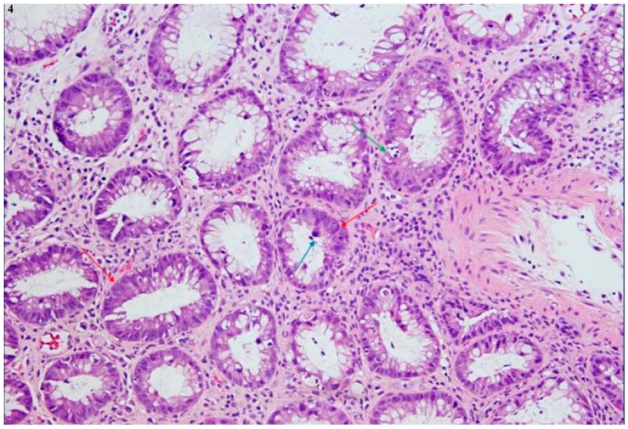

Figure 4. Higher magnification showing crypts with crowded enlarged nuclei with mucin loss (red arrows), mitotic figure (blue arrow), and apoptotic bodies (green arrow).

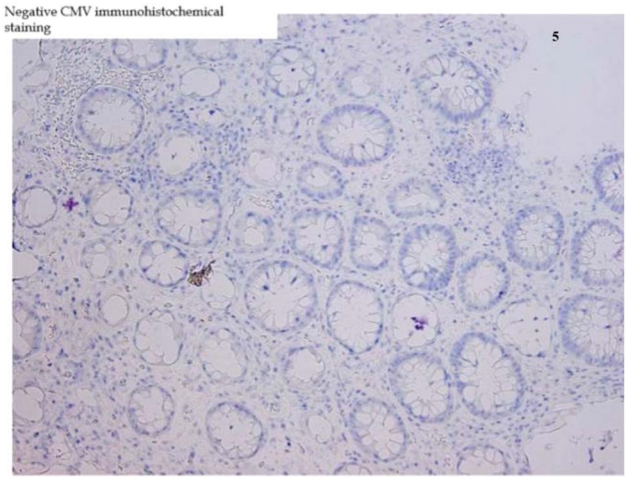

Figure 5. Negative cytomegalovirus stain.

involving the proximal colon. She had presented 2 weeks prior with similar symptoms shortly after the first cycle of AAVD, and at that time, the abdominal and pelvic CT angiography demonstrated patent mesenteric vessels. To further evaluate thickening in the colon, colonoscopy was performed and revealed patchy mild inflammation with linear and aphthous ulcerations throughout the entire colon in addition to a few 10-mm ulcers in the sigmoid colon. Biopsies from the ulcers revealed fragments of colonic mucosa with focal acute and chronic inflammation, acute cryptitis, crypt microabscesses, and scattered apoptotic bodies. Immunohistochemical statins were negative for cytomegalovirus. Differential diagnosis included DIC and

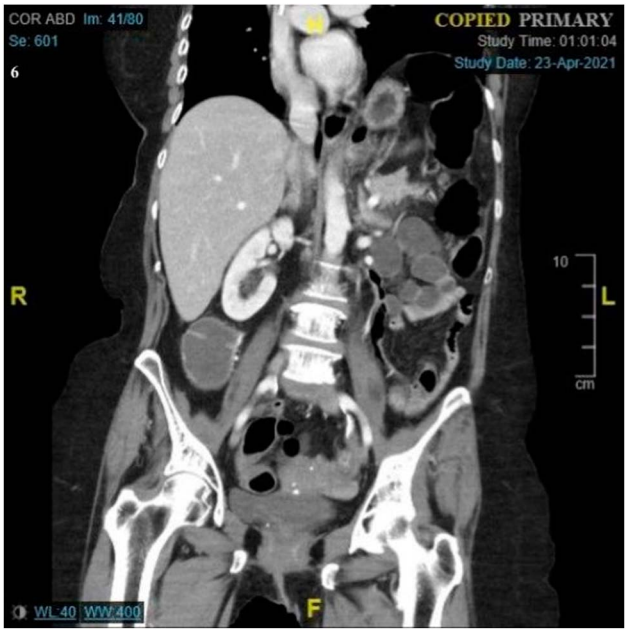

Figure 6. Contrast-enhanced computed tomography demonstrating partially collapsed descending and sigmoid colon with mild wall thickening.

ischemic colitis. The chronological relationship between symptom onset, chemotherapy, and the recent normal CT angiography made the latter less likely. DIC was believed to be the cause of her symptoms. Since brentuximab was the newer chemotherapeutic agent in the AAVD regimen with limited research regarding association with colitis, it was held during the subsequent cycles. She reported complete resolution of symptoms on holding brentuximab from the AAVD regimen and did not experience recurrence with the following cycles (Figures 1–6).

DISCUSSION

Brentuximab is an anti-CD30 antibody that selectively targets cancer cells expressing CD30 on their cell surface. Some of the commonly reported adverse effects of brentuximab include peripheral neuropathy, neutropenia, fatigue, anemia, upper respiratory tract infection, thrombocytopenia, and cough.[1] Adverse effects of brentuximab on the gastrointestinal tract include nausea, vomiting, abdominal pain, and diarrhea. Initially, brentuximab was approved for Hodgkin lymphoma that had relapsed or failed stem-cell transplant (SCT).[2] However, based on ongoing research, brentuximab is now approved as a first-line agent for stage III or IV Hodgkin lymphoma.[3] Parente et al[4] reported 1 case of possible brentuximab-associated colopathy. However, that patient had undergone SCT before receiving brentuximab, and as such, it is difficult to differentiate the colopathy findings from graft-vs-host disease and brentuximab-associated colopathy. Our patient did not undergo SCT, and complete resolution of symptoms after removing brentuximab from the treatment regimen strongly suggests DIC due to brentuximab. Another tool that can aid in determining the likelihood of brentuximab causing this reaction is the Naranjo score. This scale was created to determine the likelihood of a particular drug causing an adverse reaction. Scores range from −4 to 13; if the score is 9 or higher, the reaction is definite. Scores of 5–8 are probable, and 1–4 is possible. A score of 0 or less is doubtful for this drug to cause a reaction.[5] For this patient, the Naranjo score for brentuximab is 7 (probable). With expansion of approval as a first-line agent, DIC due to brentuximab is more likely to be encountered. It is imperative to familiarize ourselves with its association with DIC.

DISCLOSURES

Author contributions: S. Ali, S. AbdulMujeeb, and A. Khattab contributed to writing and editing manuscript. N. Asado provided the images. M. Fine contributed to editing manuscript. S. Ali is the article guarantor.

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Informed consent was obtained for this case report.

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