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Tumor Discovery

CASE REPORT

Chemotherapy-induced ileus and gastrointestinal hemorrhage following therapy with BrECADD for Hodgkin lymphoma: A case report

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Abstract

A 62-year-old male with newly diagnosed advanced-stage Hodgkin lymphoma (HL) developed life-threatening gastrointestinal (GI) complications during brentuximab vedotin, etoposide, cyclophosphamide, doxorubicin, dacarbazine, and dexamethasone chemotherapy. He presented with chemotherapy-induced enteritis and jejunal ileus, followed by severe GI bleeding requiring two consecutive laparotomies and segmental jejunal resections. Histology revealed ulcerative jejunitis without signs of lymphoma infiltration. His medical course was further complicated by acute renal failure requiring dialysis. Although the patient temporarily stabilized with intensive care management, he subsequently developed Candida sepsis. At the time of submission, his outcome remains uncertain. This case underscores a rare but serious occurrence of GI toxicity associated with intensive chemotherapy for HL.

Keywords: Ileus; Enteritis; Hemorrhage; BrECADD; Hodgkin lymphoma

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1. Background

Hodgkin lymphoma (HL) is a highly curable malignancy with a range of effective chemotherapeutic regimens. While hematological and infectious complications are well-documented, gastrointestinal (GI) complications such as chemotherapy-induced ileus remain poorly characterized. This report presents a rare case of enteritis complicated by ileus, GI hemorrhage, and renal failure, following brentuximab vedotin (BV), etoposide, cyclophosphamide, doxorubicin, dacarbazine, and dexamethasone (BrECADD) chemotherapy.[1]

2. Case presentation

A 62-year-old male patient with a medical history of arterial hypertension, obesity, and hypothyroidism presented for evaluation of prolonged coughing. Imaging studies revealed extensive mediastinal tumor mass, bilateral pleural effusions, and a pericardial effusion. A computed tomography-guided biopsy confirmed the diagnosis of HL. The patient was then referred to our oncology department for treatment initiation.

Staging workup revealed advanced-stage HL with a large mediastinal mass and associated pleural and pericardial effusions (Figure 1). Before initiating chemotherapy, right-sided pleural drainage and pericardial drainage were necessary. The patient was then started on systemic therapy according to the BrECADD protocol in accordance with the German Hodgkin Study Group recommendations for patients up to 75 years of age.[2]

On day 5 of chemotherapy, the patient developed diarrhea consistent with chemotherapy-induced enteritis. Stool cultures were negative. Several days later, he experienced abdominal pain and vomiting. Imaging revealed a mechanical ileus caused by jejunal stenosis (Figure 2). The patient had no prior history of abdominal surgery, and there was no radiological evidence of abdominal lymphoma involvement. Although surgical intervention was indicated, it was not performed as it was deemed unfeasible due to chemotherapy-induced aplasia. Conservative management with a nasogastric tube, prokinetic agents (neostigmine and metoclopramide), fluid replacement, parenteral nutrition, and antibiotic therapy (meropenem) led to resolution of the ileus over the next several days.

Subsequently, the patient experienced acute GI bleeding resulting in hemorrhagic shock. The patient had to be transferred to the intensive care unit for vasopressor support. Emergency laparoscopy identified a bleeding jejunal ulcer, requiring segmental small bowel resection. A second laparotomy with additional jejunal resection was necessary a few days later due to recurrent bleeding. Histopathological analysis of the resected jejunal segments revealed severe ulcerative jejunitis without evidence of lymphoma infiltration.

The patient also developed dialysis-dependent acute tubular necrosis and transient hyperbilirubinemia. The renal failure was attributed to both the cytotoxic effects of chemotherapy and the neutropenic enteritis.

Following a prolonged intensive care unit stay, the patient was eventually transferred to the general ward. After a brief period of recovery, he unfortunately developed Candida sepsis, requiring catecholamine support and endotracheal intubation. At the time of manuscript submission, his outcome remains uncertain. In the event of sufficient recovery, a de-escalated treatment regimen for his HL is planned, most likely incorporating nivolumab.

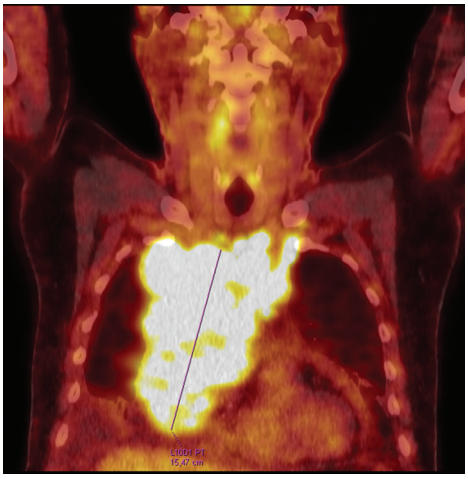


Figure 1. Positron emission tomography scan showing the large mediastinal tumor mass

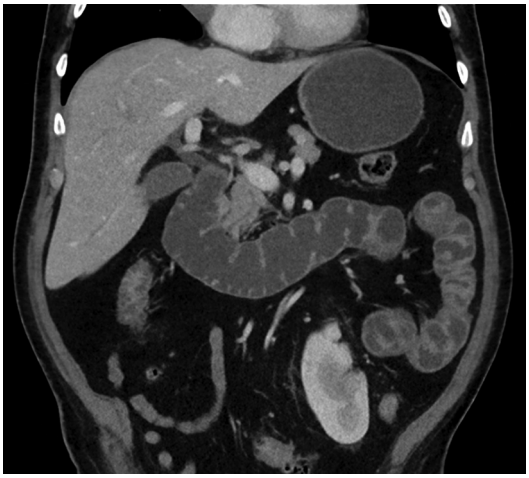


Figure 2. Computed tomography scan showing high ileus with distention of the stomach and a jejunal bowel segment

3. Discussion

3.1. Chemotherapy-induced ileus

Chemotherapy-induced (GI) toxicity encompasses a spectrum of adverse effects, including nausea, vomiting, diarrhea, constipation, and mucositis. Among these, bowel obstruction is a rare but potentially life-threatening complication. The pathophysiology involves direct cytotoxic effects on enteric neurons and smooth muscle cells, leading to impaired motility. In addition, chemotherapy-induced mucosal injury can disrupt the gut barrier, promoting bacterial translocation and systemic inflammation, which may exacerbate ileus and contribute to sepsis.[3]

Reports of chemotherapy-induced ileus are quite rare in the scientific literature. Published case reports exist for a variety of chemotherapeutic agents and most patients were successfully managed without surgery.[4-9]

BV has been associated with a range of GI complications, including intestinal obstruction, (neutropenic) enterocolitis, erosion, ulceration, perforation, and hemorrhage, some of which have resulted in patient deaths.[10] A meta-analysis of four lymphoma trials involving over 2,000 patients found an increased incidence of GI adverse events in the

BV treatment group.[11] In addition, a review of the Food and Drug Administration adverse event reporting system indicated that antibody-drug conjugates, including BV, may elevate the risk of a broad spectrum of GI adverse events.[12]

In our patient, neutropenic enteritis likely led to mucosal compromise, stenosis, and eventual bleeding. The absence of prior surgeries and lymphoma involvement suggests a direct link to chemotherapy toxicity. Our patient was initially managed conservatively with nasogastric decompression, prokinetic agents, intravenous fluids, parenteral nutrition, and antibiotics. Despite initial resolution, the patient experienced severe GI bleeding, necessitating surgical intervention and intensive care support.

3.2. Chemotherapy-associated GI hemorrhage

GI bleeding is a well-recognized complication in cancer patients undergoing chemotherapy. However, massive GI hemorrhage resulting in hemodynamic compromise is a rare and serious event. The management of GI bleeding in this population involves a multidisciplinary approach that combines supportive care with targeted interventional procedures.[13]

Initial treatment typically includes transfusion of blood products such as red blood cells, platelets, fresh frozen plasma, and coagulation factors to stabilize the patient and correct any underlying coagulopathies. Endoscopic techniques play a central role in controlling bleeding and may include argon plasma coagulation, hemoclipping, or epinephrine injection, depending on the source and severity of the hemorrhage.[13]

In cases where endoscopic therapy is either unsuccessful or not feasible, trans-arterial embolization has emerged as an effective alternative.[14] Surgical intervention remains a last resort, reserved for refractory cases, but it is associated with a significantly higher risk – particularly in patients with advanced malignancies or poor performance status.

A retrospective analysis of 156 patients with pancreatic cancer undergoing chemoradiation found that approximately 25% experienced GI bleeding, most commonly from the upper GI tract. Among these, there were eight fatal cases. Management strategies in that cohort included transfusion support, pharmacologic measures, and endoscopic therapy, which demonstrated a high success rate in most patients.[15]

3.3. Contemporary treatment strategies for advanced-stage HL: Spotlight on BrECADD and Nivo-AVD

The BrECADD regimen – comprising BV, etoposide, cyclophosphamide, doxorubicin, dacarbazine, and dexamethasone – was developed to improve the treatment of advanced-stage classical HL (AS-cHL) by enhancing efficacy while reducing toxicity. The phase 3 HD21 trial, a multicenter, open-label, randomized study, compared BrECADD with the escalated bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, and prednisone (BEACOPP) regimen in patients aged 18 – 60 years with newly diagnosed AS-cHL.[1] The trial demonstrated that BrECADD was superior to BEACOPP in terms of progression-free survival (PFS) and had a more favorable safety profile. At a median follow-up of 48 months, the 4-year PFS was 94.3% for BrECADD compared to 90.9% for BEACOPP (hazard ratio: 0.66; p=0.035). Furthermore, treatment-related morbidity was significantly lower in the BrECADD group (42%) compared to the BEACOPP group (59%; p<0.0001). Notably, the BrECADD regimen was associated with a lower incidence of severe sensory polyneuropathy and improved recovery rates of gonadal function compared to BEACOPP. The reported rate of severe GI adverse events was 8% for the BrECADD cohort, apparently without any cases of bowel obstruction.

A single-arm cohort within the phase II HD21 trial, examining the BrECADD protocol in adults up to 75 years of age, concluded that the regimen is feasible and safe in older patients, although it requires more frequent dose adjustments.[16]

Historically, patients older than 60 years received ABVD (doxorubicin, bleomycin, vinblastine, and dacarbazine) therapy.[2] This treatment standard has since evolved – first to BV, doxorubicin, vinblastine, and dacarbazine (BV-AVD) and more recently to nivolumab, doxorubicin, vinblastine, and dacarbazine (Nivo-AVD).[17,18] The phase III S1826 study demonstrated significantly improved outcomes and a more favorable safety profile with six cycles of Nivo-AVD compared to BV-AVD.[18] The complete remission rate at the end of treatment with Nivo-AVD was 83.1%, which is similar to the 82% reported with BrECADD. After a median follow-up of 2.1 years, the 2-year PFS for the overall cohort, as well as for the subgroup of patients aged 18 – 60 years, was 92%. Although numerically slightly lower than the PFS reported for BrECADD, direct comparison of these results is not appropriate due to significant differences in trial design and populations. For instance, the S1826 trial included patients younger than 18 years and those aged 60 and above, and enrolled a racially and ethnically diverse population. Nevertheless, the safety profile of Nivo-AVD is clearly more favorable, with fewer severe adverse events and treatment discontinuations due to toxicity compared to BrECADD.[1,18]

3.4. Clinical considerations of chemotherapy selection in our patient

In our patient, we opted to administer BrECADD due to the highly aggressive and symptomatic nature of the disease. Before diagnosis, the patient was in excellent

physical condition, with an ECOG performance status of 0. His comorbidities were considered clinically insignificant. Therefore, despite his age being over 60 years, we elected to proceed with the more intensive BrECADD regimen.

As this case illustrates, careful patient selection is critical when considering intensive chemotherapy in older or comorbid individuals, to minimize the risk of excessive toxicity, as was unfortunately observed in our patient. Based on this experience, we will adopt a more conservative approach moving forward, reserving intensive regimens such as BrECADD for younger patients with adequate performance status and minimal comorbidity burden.

4. Conclusion

This case report highlights the rare but potentially life-threatening complication of chemotherapy-induced ileus in a patient with AS-cHL treated with the BrECADD regimen. Although GI toxicity, including diarrhea and mucositis, is well documented in chemotherapy, bowel obstruction remains an uncommon manifestation. In this case, chemotherapy-induced enteritis likely triggered ileus, which was further complicated by GI hemorrhage and acute renal failure. Despite initial conservative management, the patient required surgical intervention due to recurrent bleeding. Our case demonstrates that careful patient selection is essential when considering intensive chemotherapy regimens such as BrECADD. Close monitoring for GI symptoms is crucial during treatment.

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Conflict of interest

The authors declare they have no competing interests.

Author contributions

Conceptualization: Karl Mayrhofer
Investigation: Karl Mayrhofer
Writing – original draft: Karl Mayrhofer
Writing – review & editing: Simon Udovica

Ethics approval and consent to participate

Not applicable.

Consent for publication

Informed consent was obtained from the patient for the publication of this case report and any accompanying images. The patient agreed to the use of clinical details for academic and publication purposes. All data have been fully anonymized to protect the patient's identity.

Availability of data

Not applicable.

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