

# Posttransplant Lymphoproliferative Disorder Involving the Gastrointestinal Tract

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## Abstract

### Keywords

- ▶ Epstein–Barr virus
- ▶ hematopoietic stem-cell transplantation
- ▶ posttransplant lymphoproliferative disorder
- ▶ solid-organ transplantation

Posttransplant lymphoproliferative disorder (PTLD) is a rare and life-threatening complication of both solid organ transplantation and hematopoietic stem cell transplantation. In most cases, PTLD develops in Epstein–Barr virus (EBV)-seropositive individuals in the setting of chronic immunosuppression and decreased T-cell surveillance. Clinical manifestations of PTLD may be nonspecific, resembling primary EBV infection (fever, night sweats, malaise, and cervical lymphadenopathy), or it can involve the central nervous system, bone marrow, kidneys, liver, lungs, and gastrointestinal tract. Gastrointestinal symptoms in the posttransplant setting may indicate underlying PTLD, and it is important for physicians to be able to recognize its appearance on endoscopy.

## Introduction

Gastrointestinal symptoms in the posttransplant setting may reflect multiple etiologies. However, posttransplant lymphoproliferative disorder (PTLD) being life-threatening should always be considered in the differential diagnosis, and a positive stool test for a pathogen does not rule out PTLD if clinically suspected.

## Case Report

A 70-year-old man presented with diarrhea of 3 weeks' duration, 2 months following an allogeneic-matched unrelated stem cell transplant for acute myeloid leukemia. Abdominal examination revealed no tenderness or organomegaly. Stool studies were positive for *Clostridium difficile* and norovirus GI/GII (Genotype I/Genotype II). He was treated with oral vancomycin with suboptimal response to therapy. At this point, esophagogastroduodenoscopy and flexible sigmoidoscopy were performed to evaluate for graft versus host disease (GVHD). Endoscopy showed nodular

lesions with ulcerations throughout the gastrointestinal tract including the stomach, duodenum, and rectum (▶Fig. 1A and B).

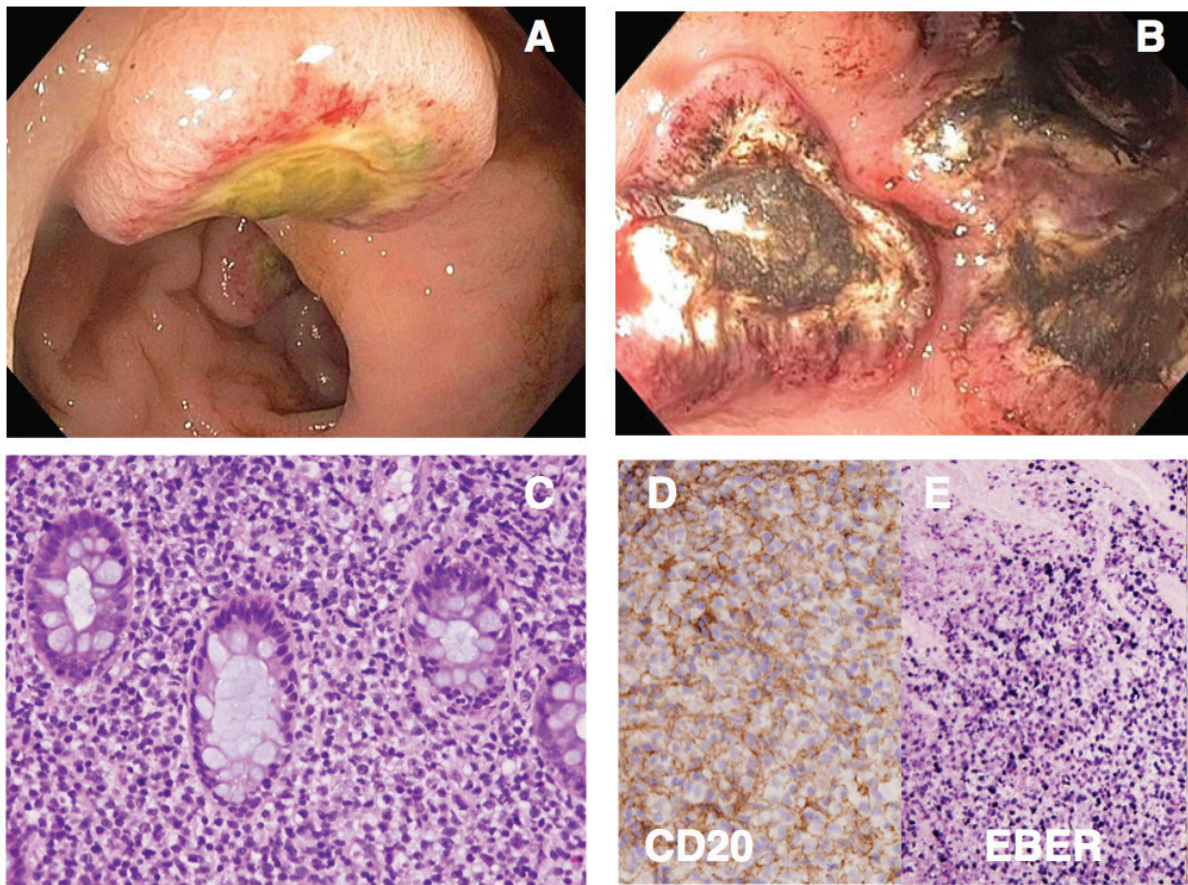
Tissue biopsy showed a diffuse lesion composed of large lymphoid cells positive for CD20 (▶Fig. 1C and D) and negative for CD3, CD34, and myeloperoxidase. The cells were uniformly positive for Epstein–Barr virus (EBV)-encoded small RNA (▶Fig. 1E). A diagnosis of EBV + PTLD (monomorphic type), best classified as diffuse large B-cell lymphoma was established. Polymerase chain reaction (PCR) studies performed on plasma detected 3,711 copies of EBV DNA at the time of initial diagnosis. The patient was on immunosuppression for the prophylaxis of GVHD with tacrolimus and mycophenolate mofetil. The immunosuppressants were tapered and stopped, and four cycles of rituximab were administered. No antiviral treatment was given for the EBV infection. After treatment with rituximab, plasma EBV levels were found to be undetectable and gastrointestinal lesions had resolved. The patient was then discharged, with the plan of regular outpatient follow-up with EBV-PCR testing and interval positron emission tomography-computed

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**Fig. 1** (A) Multiple well-defined raised and ulcerated nodular lesions in the rectum. (B) Nodular raised posttransplant lymphoproliferative disorder lesions in gastric body. (C) The neoplastic cells are large and have abundant eosinophilic cytoplasm and vesicular nuclear chromatin (H and E,  $\times 200$ ). (D) The neoplastic cells are positive for CD20 (immunohistochemistry with hematoxylin counterstain). (E) The neoplastic cells are uniformly positive for Epstein-Barr virus-encoded small RNA (EBER) (in situ hybridization with eosin counterstain). H and E, hematoxylin and eosin.

tomography (PET-CT) scans. The PET-CT scan 12 days after discharge showed complete remission.

## Discussion

PTLD is a rare but life-threatening complication of both solid-organ transplantation and hematopoietic stem cell transplantation.<sup>1,2</sup> The pathogenesis of PTLD in most cases is related to EBV-induced proliferation of B-lymphocytes, in the setting of chronic immunosuppression and decreased T-cell surveillance, although EBV-negative cases have also been reported.<sup>3,4</sup> Factors influencing PTLD include time since transplantation, type of transplant, age of recipient, type, and duration of immunosuppressive therapy. Higher incidence of PTLD is seen in the first year after transplantation, in intestinal and lung transplants and in the pediatric population due to higher number of EBV-seronegative recipients.<sup>4,5</sup> Clinical manifestations of PTLD can be nonspecific, resembling primary EBV infection, such as fever, night sweats, malaise, and cervical lymphadenopathy, underscoring the need for a high index of suspicion in making the diagnosis. PTLD can also involve other organs such as the central nervous system, bone marrow, kidneys, liver, lungs, small intestine, and spleen. Often, diffuse disease mimics acute GVHD or sepsis.<sup>1</sup>

This case demonstrates that gastrointestinal symptomatology in posttransplant patients may reflect multiple etiologies, and a positive stool study for a pathogen should not preclude further testing for PTLD if clinically suspected.

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### Conflicts of Interest

There are no conflicts of interest.

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