Clinical and Experimental HEPATOLOGY

Clin Exp HEPATOL 2017; 3, 4: 215-217
DOI: https://doi.org/10.5114/ceh.2017.71447
Received: 06.05.2017, **Accepted:** 07.06.2017, **Published:** 14.11.2017

Case report

A rare cause of gastrointestinal bleeding in the post-transplant setting

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Abstract

Post-transplant lymphoproliferative disorder (PTLD) is a life-threatening complication noted after solid organ transplantation and is frequently related to Epstein-Barr virus infection. The present case highlights an unusual presentation of PTLD – gastrointestinal bleeding – in the absence of systemic symptoms.

Key words: liver, bleeding, transplant recipients.

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Introduction

Post-transplant lymphoproliferative disorder (PTLD) is a life-threatening complication noted after solid organ transplantation and is frequently related to Epstein-Barr virus (EBV) infection [1]. The frequency varies from 1.4% in liver transplant recipients to 6.2% in lung transplant recipients [2]. The risk of lymphomas in renal transplant recipients is 11.8-fold higher than in a matched nontransplanted population. First-year mortality in renal and heart transplant patients with lymphoma is approximately 40% and 50%, respectively [3]. Post-transplant lymphoproliferative disorder is classified, based on the WHO classification, as early lesions, polymorphic, monomorphic and classical Hodgkin lymphoma type PTLD [4]. The majority of cases of PTLD are of recipient origin, though donor-derived lymphomas can occur [5]. Although most cases of PTLD are associated with EBV infection, EBV-negative lymphomas have been reported. These typically occur late, more than 1 year after transplantation. Epstein-Barr virus latent membrane protein 1 (LMP1) has been implicated in the transformation of B lymphocytes through a receptor in the tumor necrosis factor receptor family [5, 6]. Immunosuppression, particularly with cyclosporine, OKT3, antithymocyte globulin and tacrolimus, is associated with increased risk of PTLD [7-9]. The clinical symptoms noted are fever and lymphadenopathy. Extranodal involvement and central nervous system involvement are noted in two thirds and one third of patients respectively [10, 11]. Poor performance status, monomorphic disease, EBV-negative status of the recipient, late onset of disease, disease involving multiple sites, advanced age, stage, elevated lactate dehydrogenase (LDH), severe organ dysfunction, CNS disease and grafted organ involvement are associated with poor prognosis [12-15].

Case report

A 63-year-old male patient presented to the emergency department with a history of painless, black tarry stools for two days. He was a known diabetic and had undergone DDLT (deceased donor liver transplantation) for nonalcoholic steatohepatitis (NASH) in 2014. He was on oral hypoglycaemics, tacrolimus 1.5 mg/day and mycophenolate mofetil 1 g/day. Apart from pallor and a well-healed abdominal scar, no major abnormality was noted on physical examination. After initial stabilization, the patient was taken up for endoscopic evaluation. Esophagogastroduodenoscopy was normal. Colonoscopy with ileal intubation showed a large,

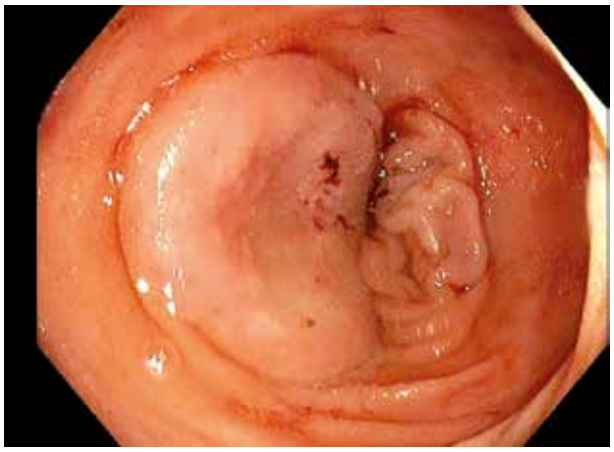

Fig. 1. Mass lesion in ileum with superficial ulceration

coffee bean shaped mass lesion with surface ulceration, obstructing 50% of the lumen in the terminal ileum (Fig. 1). Biopsy from the mass lesion (Fig. 2) showed sheets of malignant lymphoid cells that were pleomorphic with scanty cytoplasm and nuclear atypia. Mitosis and apoptosis were noted. Immunohistochemistry was positive for CD3, CD10, CD20, KI67 90% and negative for LMP1. A computed tomography scan showed ileal thickening; there was no lymph node enlargement.

The patient had not received OKT3 or antithymocyte globulin at any point of time. He had no documented acute rejection and his tacrolimus level at presentation was 4.3 µg/dl. His serological tests for EBV and cytomegalovirus (CMV) were negative prior to transplantation. He had received the organ from a healthy 36-year-old man who had been declared brain dead after a road traffic accident. The donor serological tests were negative for EBV and CMV.

After confirmation of the diagnosis, the tacrolimus dose was reduced and everolimus was added. The patient was counseled regarding the disease and its prognosis. He was advised to undergo CT scans of the chest, brain and neck to determine the disease severity. However, the patient refused any further medical treatment and left the hospital against medical advice.

Discussion

There have been reports of endoscopic detection of PTLD lesions in the small intestine [16]. In a large series reported by Cruz *et al.*, it was noted that patients with gastrointestinal PTLD were of late onset, often involved the lower gastrointestinal tract and were monoclonal in origin. In the author's series, intestinal obstruction was the commonest indication for surgery; bleeding or perforation carried a worse prognosis [17].

Our patient was more than 60 years of age and three years after the transplant. He had been on tacrolimus since the transplant. He had no documented episodes of acute rejection. The patient and his donor were both EBV negative. He presented with melena and there was no history of systemic symptoms such as fever and no lymphadenopathy was noted. Computed tomography of the abdomen did not reveal any abdominal lymph nodes. On histopathology, he had pleomorphic PTLD as per the WHO classification.

Treatment strategies that could benefit such patients include decreasing cyclosporine or tacrolimus by 50% and discontinuing azathioprine or mycophenolate mofetil [18], use of antiviral agents in patients with early or polymorphic disease [19], chemotherapy with or without rituximab [20, 21] and hematopoietic transplantation in recurrent cases [22].

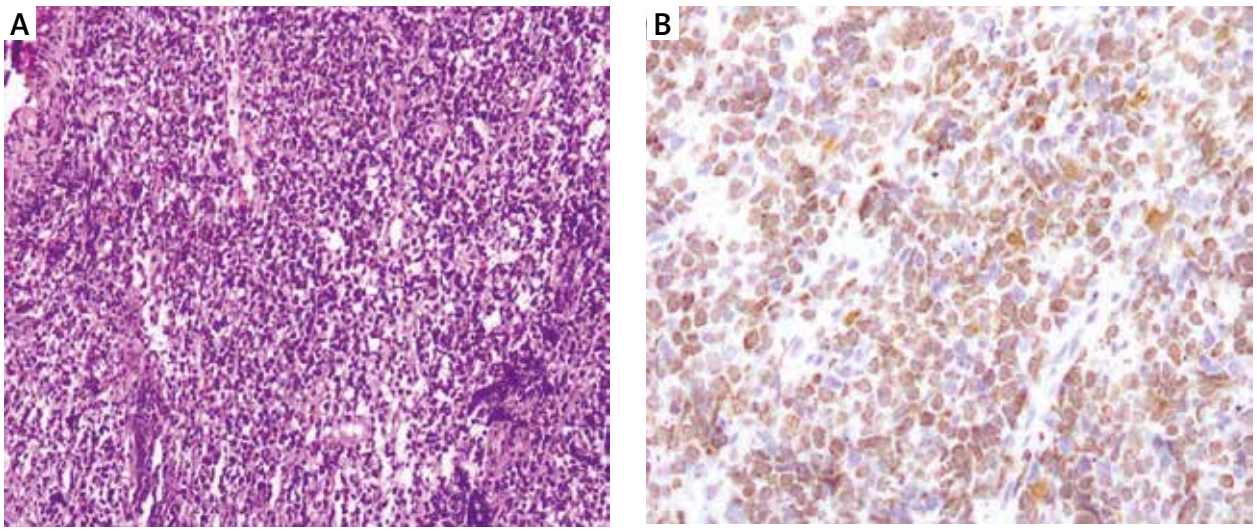

Fig. 2. Terminal ileal biopsy showing malignant lymphoid cells **(A)** and high Ki-67 activity **(B)**

Preventive strategies are also being investigated to prevent PTLD. Vaccination against EBV may provide protection, particularly in EBV-naïve pediatric patients. A vaccine directed against gp350, a viral membrane protein, is currently under trial [23]. Antiviral prophylaxis in EBV negative recipients has also been tried with variable results [24, 25]. To conclude, the present case highlights an unusual presentation of PTLD in an EBV negative recipient. PTLD should be kept as a differential diagnosis for varied gastrointestinal manifestations such as obstruction, perforation and bleeding in solid organ transplant recipients.

Disclosure

Authors report no conflict of interest.

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