Research Article

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Post-Transplant Lymphoproliferative Disorder Presenting as a Small Bowel Obstruction in Two Patients with Kidney Transplantation

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Abstract

Solid organ transplant recipients are at an increased risk for developing malignant neoplasms. Post transplantation lymphoproliferative disorder (PTLD) is a polyclonal or monoclonal lymphoid proliferation occurs in the severe immunosuppression after solid organ transplantation.

Epstein-Barr virus infection is one of the most important risk factors for PTLD, even though 40% of PTLD cases in concurrent series are not Epstein-Barr virus-associated. The overall level of immunosuppression seems to be the most important stimulant of the increased occurrence of PTLD in solid organ transplant recipients.

Herein, we report two cases of polymorphic PTLD presenting with isolated gastrointestinal involvement in an Epstein-Barr virus negative in one patient with decead-donor kidney transplantation, 6 months after receiving the transplant, and the others Epstein-Barr, CMV virus and covid 19 positive with decead-donor kidney transplantation, 1 year after transplantation. Although rare, gastrointestinal PTLD can lead to small bowel obstruction or perforation in patients with a history of solid-organ transplantation. However typical symptoms may be indefinable in the immunocompromised setting, clinicians should be careful for underlying PTLD with isolated gastrointestinal involvement.

Keywords: Kidney transplantation; Small bowl; PTLD

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Case Report

Case 1

An 11-year-old girl was admitted with an abdominal pain. The patient had undergone deceased donor kidney transplantation due to secondary FSGS, predisposition of mitochondrial myopathies disease. Six months after the transplantation, she presented to our hospital with two weeks of intermittent preomblical and epigastric pain, anorexia. Physical examination was normal without abdominal tenderness, with normal bowl sounds and vital signs were stable. The patient was admitted. The studies were done, blood work, amylase, lipase, CMV PCR and EBV PCR was normal. The average creatinine during the six months was 0.5 mg/dL. Abdominal and pelvic sonography was normal. Because of no improvement in symptoms, upper endoscopy performed that demonstrated mild esophagitis, mild gastritis. Biopsies of the gastric and duodenal were normal and negative for cytomegalovirus, H. pylorei. Because of no responsing *to* parentral PPI, abdominal and pelvic CT scan and surgical consultation was done, that were normal. Gradually improved symptoms and the patient were discharged in good general condition. Three days after discharge, the patient was re-hospitalized due to severe abdominal pain, vomiting, anorexia and generalized abdominal tenderness. Abdominal ultrasound was performed again, that was reported dilated bowel loops containing liquid and gas .*Abdominal CT scan with contrast revealed* band adhesion and volvulus in treitz ligament.

She underwent laparotomy, division of band adhesion and 10 cm of small bowel resected due to ischaemic necrosis with an end-to-end anastomosis.

Open surgical biopsy revealed a diagnosis of EBER-positive, polymorphic PTLD [**Figure 1**].

Her immunosuppressant regimen was adjusted according to the diagnosis, and tacrolimus changed to cyclosporine. She was started rituximab 375 mg/m^2 weekly, for four doses. Improvement of the patient was pleasant. The patient also was assessed by hematology, which advised rituximab and carrying out The PET scan at the end of the treatment, that it was normal.

Case 2

A 14-year- old boy who presented to the office with a history

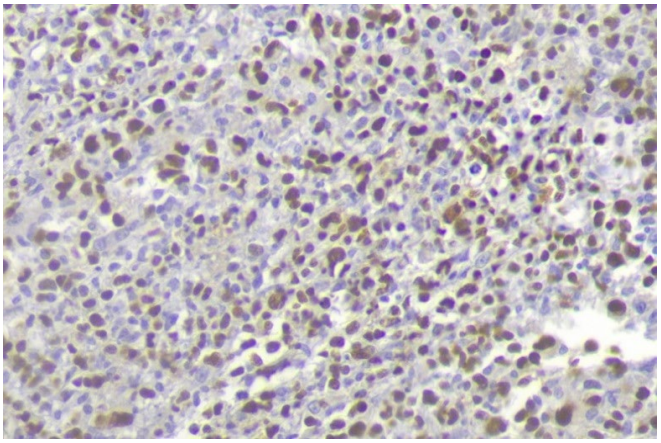

Figure 1 Open surgical biopsy revealing a diagnosis of Epstein-Barr encoding region (EBER)-positive, polymorphic post-transplant lymphoproliferative disorder (PTLD).

of anorexia, abdominal pain and nausea from two months ago. The pain was intermittent in his egigasteric and preombliacal. The patient denied other symptoms including fevers, and chills. He underwent deceased donor kidney transplantation due to primary FSGS about one year ago. His immunosuppressive regimen consisted of cellcept, Tacrolimus and Prednisone. Physical examination was normal. The first evaluation including lab test, PCR covid, H1N1 and the ultrasound of the abdomen and pelvis was normal except for a non-mobile echogenic lesion in the wall of the gallbladder and the possibility of a polyp. PPI for patient was prescribed. The patient was discharged after 3 days due to improvement in symptoms.

The patient was readmitted three weeks later due to vomiting, left lower quadrant pain, diarrhea and fever. He had tachycardia with normal blood pressure upon admission, and was observed generalized abdominal tenderness.

The laboratory tests reveal leukocytosis with left shift, anemia, increased ESR, CRP, hypokalemia and serum Cr of 1.5. Other tests were reported normal. A positive PCR covid, with high viral load of PCR CMV (18982) and EBV (13258 copies) were reported.

The abdominal and pelvic ultrasound report, indicated a collection of approximately 200 cc containing gas foci in the LLQ, along with a hypo Echoic heterogeneous area without vascularity. Additionally echogenic foci are noted in the intraluminal space within the LLQ suggestive of a collection.

The abdominal CT scans with and without contrast enhancement reveals a collection measuring 109*60*56 cm in the left side of the abdomen adjacent to the jejunal loops and reactive lymph nodes.

The dosage of immunosuppressive drugs was decreased. The patient was placed on broad-spectrum antibiotics. Remdesivir and gancyclovire were initiated based on the positive test result of covid and CMV.

The patient underwent laparotomy, several days after receiving antibiotics, Remdesivir and gancyclovire.

A 50 cm of the ligament of Treitz an abscess was observed, that extending up to 70 cm. Due to perforation, 20 cm of the jejunum was resected. Open surgical biopsy revealed diagnosis of polymorphic PTLD.

The patient's immunosuppression drugs were decreased. He was started rituximab 375 mg/m^2 weekly, for four doses. Improvement of the patient was pleasant. Positron emission tomography–computed tomography was done at the end of the treatment, that it was normal.

Discussion

The incidence of PTLD varies depending on the type of transplant, and is estimated to be 0.8-20%. There is a known association between EBV infection and PTLD with an estimated 70-80% of cases being EpstinBarr positive [1]. An average time period between transplantation procedure and the diagnosis of PTLD is approx. 5.5 years. GI PTLD mostly occurred late, from the 6th to the 10th post-transplant year. There are multiple factors which appear to have a role in incidence of PTLD such as, the degree of immunosuppression, EBV serostatus, and time of post-transplant, recipient age, type of allograft, sex, and ethnicity. EBV seroconversion is one of the most important risk factors, especially in pediatric transplant recipients and in early onset PTLD [2].

Diagnosis of PTLD can be problematic because the clinical range and diagnostic tests are nonspecific.

The illness finding of small bowl PTLD is highly variable ranging from nonspecific abdominal symptoms to overt hemorrhage, perforation, or obstruction. The stomach and small intestine are the most frequently involved organs in the GI tract making clinical investigation and question of symptoms which may represent pathology in these organs important [3].

PTLD with isolated GI involvement is less common. O'Connor et al described 6 pediatric liver-transplant patients presenting with nonspecific GI symptoms, anemia, and failure to thrive. Additionally, a few pediatric cases were reported to present with GI bleeding [4].

Like other lymphomas, PTLD is aggressive and mortality rates improve with early treatment. Prognosis and treatment are dependent on time of disease presentation, morphological subtype of PTLD, and concomitant systemic disease. The most important step in management is reduce IS; which is usually effective. Rituximab and chemotherapy based on morphologic subtype have been found to be effective [5].

Because PTLD treatments are most effective in the early stage, prior to the occurrence of progression, not only the early detection of PTLD, but also the determination of the clonality of PTLD, is of importance in planning of treatment.

In these cases, the patients were treated successfully with laparotomy, small bowel resection and primary fixed side to side anastomosis, reduction in immunosuppression, and rituximab. Fortunately, both of them were able to complete treatment without complication of perforation.

Conclusion

However small bowl PTLD in kidney transplantation is rare, but it is necessary to be included in the differential diagnoses for any transplant patient presenting with unspecified GI signs and symptoms, ranging from mild diarrhea to diffuse peritonitis, and aggressive investigation for PTLD. Like other lymphoma variants, PTLD can be very aggressive, making early diagnosis key to prognosis. Initial treatment is reduction of immunosuppression which is effective in more than 50% of cases; however, additional therapy including rituximab, chemotherapy, and surgery may also be required.

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