Late Posttransplant Lymphoproliferative Disease: Report of a Rare Case and Role of Positron Emission Tomography-computed Tomography

P. Yadav, N. Kumar[1], N. Prasad[2], H. Lal[3]

Department of Urology and Renal Transplantation, SGPGIMS, [1]Department of Nuclear Medicine, SGPGIMS, [2]Department of Nephrology, SGPGIMS, [3]Department of Radiology, SGPGIMS, Lucknow, Uttar Pradesh, India

Abstract

Posttransplant lymphoproliferative disease (PTLD) is an uncommon complication of immunosuppression after solid organ transplantation. Early PTLD (<1 year after transplantation) is frequently found around the allograft, whereas late PTLD (>1 year after transplantation) does not have such a preference. 18-Fluorodeoxyglucose positron emission tomography-computed tomography (^{18}FDG PET-CT) has clinical significance in the evaluation of PTLD. ^{18}FDG PET-CT scan allows precise anatomic localization of FDG-avid lesions, hence helpful in staging of disease and evaluation of response to therapy. It can better characterize persistent lesions and differentiate residual tumor from fibrosis or necrosis. We present a rare case report of a perigraft PTLD developing 12 years after renal transplantation sparing the graft, in an Epstein–Barr virus-negative patient.

Keywords: *18-fluorodeoxyglucose positron emission tomography-computed tomography, chemotherapy, posttransplant lymphoproliferative disease*

Introduction

Posttransplant lymphoproliferative disease (PTLD) is an uncommon complication of immunosuppression after solid organ transplantation, reported first in 1984 by Starzl *et al*.[1] It is a heterogeneous group of lymphoproliferative disorders, ranging from abnormal lymphoid hyperplasia to frank neoplasia.[2] The usual site of presentation of PTLD depends on the time since transplantation. About 30% of renal transplant recipients who develop PTLD in the 1st year of transplantation have allograft localization of the disease, which is higher than the ones developing later.[3] 18-fluorodeoxyglucose positron emission tomography-computed tomography (^{18}FDG PET-CT) has significant role in the evaluation of PTLD. ^{18}FDG PET-CT scan allowsfunctional and precise anatomic localization of FDG-avid lesions, thus helpful in the staging of disease, evaluation of response to therapy, and better characterization of persistent lesions with FDG uptake differentiating residual tumor from fibrosis or tumor necrosis.[4] We present a rare case report of PTLD in perigraft location without involving the renal allograft, which developed 12 years after renal transplantation in the absence of Epstein–Barr virus (EBV) infection.

Case Report

An 18-year-old male underwent renal transplantation (in right iliac fossa) in 2003 for chronic interstitial nephritis-related renal failure with mother as donor. He received triple-immunosuppression therapy (cyclosporine, mycophenolate mofetil, and prednisolone). The patient was apparently normal till 2015, when he developed dull-aching, nonradiating right lower abdominal pain. There was no history of fever, hematuria, or passage of stones and the patient was able to carry out his daily activities normally. On palpation, a firm mass (approx. 15 cm × 10 cm) was palpable in the right iliac fossa under the surgical scar. Ultrasound of the abdomen revealed a large hypoechoic mass around the transplanted kidney, the vascularity and echogenicity of the graft were normal. Ultrasound-guided biopsy from the mass revealed monomorphic B-cell non-Hodgkin's lymphoma. Serum lactate dehydrogenase (LDH) level was 850 U/L (normal: 140–280 U/L). ^{18}FDG PET-CT revealed an intensely hypermetabolic (standardized uptake value [SUV] max - 23.9) ill-defined soft tissue density lesion in the right lumbar region, encasing the graft and invading

How to cite this article: Yadav P, Kumar N, Prasad N, Lal H. Late posttransplant lymphoproliferative disease: Report of a rare case and role of positron emission tomography-computed tomography. Indian J Nephrol 2018;28:393-6.

Address for correspondence:
Dr. H. Lal,
Department of Radiology, SGPGIMS, Lucknow - 226 014, Uttar Pradesh, India.
E-mail: hiralal2007@yahoo.co.in

Access this article online

Website: www.indianjnephrol.org

DOI: 10.4103/ijn.IJN_262_17

Quick Response Code:

adjacent colon, caecum, distal part of ileum, right-sided psoas muscle with extensive mesenteric fat stranding, and pulled-upper mesentery in right iliac fossa [Figure 1]. The lesion extended into the inguinal canal up to the testicular sac. Multiple hypermetabolic soft tissue lesions (largest SUV_{max} - 15.2) were also noted in the greater omentum infiltrating the anterior stomach wall and transverse mesocolon [Figure 1]. IgM assay for EBV was negative. Serum creatinine was 1.10 mg/dl.

The patient was offered the reduction of immunosuppression along with rituximab, cyclophosphamide, vincristine, and prednisolone (R-CVP)-based chemotherapy.[5] His mycophenolate mofetil was stopped, and the dose of cyclosporine was reduced after explaining the risk of graft rejection. Interim ^{18}FDG PET-CT (after 4 cycles) showed a complete response to the treatment with a gradual clearance of the physiological retention of the tracer in calyceal system of graft [Figure 2a and b]. Two additional cycles of R-CVP were given followed by ^{18}FDG PET-CT after 4 weeks, which revealed the same findings as the interim ^{18}FDG PET-CT [Figure 2c and d]. At 1 year of follow-up, the patient is asymptomatic, his serum creatinine is 1.34 mg/dl, and serum LDH is 199 U/L.

Discussion

PTLD is a heterogeneous group of lymphoproliferative diseases ranging from hyperplastic lesions to polymorphic and monomorphic lesions that occur in the setting of solid organ or allogeneic hematopoietic cell transplantation. Risk factors include EBV infection, human leukocyte antigen mismatching, and T-cell depletion. It is the most common malignancy in pediatric population and second most common malignancy in adults following solid organ transplantation. The highest incidence occurs after lung and small bowel transplantation (5%–20%), whereas only 1%–3% patients undergoing renal transplantation develop PTLD.[6] The average onset time of PTLD is approximately 6 months in solid organ transplant patients and 2–3 months in hematopoietic stem cell transplantation patients, but in few cases, PTLD has been reported as soon as 1 week and as late as 10 years after transplant.[7] PTLD occurring within a year of renal transplantation is often associated with EBV infection. Furthermore, early PTLD has a predilection for allograft localization.[8] However, the same is not true for late PTLD, the majority of which are away from the allograft.[9] The present case is unusual as it occurred 12 years after transplantation and yet was primarily localized in perigraft location. The importance of location of PTLD was highlighted by Khedmat and Taheri, who found that renal allograft involvement was associated with higher rate of partial and complete remission of PTLD after anticancer therapy.[8]

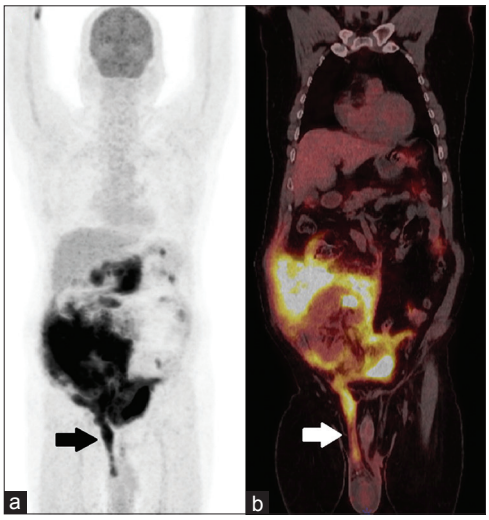

Figure 1: Baseline (a) 18-fluorodeoxyglucose positron emission tomography-computed tomography maximum intensity projection reconstruction of computed tomography attenuation corrected image and (b) 18-fluorodeoxyglucose positron emission tomography-computed tomography (fused) coronal reconstruction image revealing intensely fluorodeoxyglucose-avid primary lesion encasing the transplanted kidney, invading the adjacent ascending colon, cecum, and distal part of ileum. The lesion is also extending in right inguinal canal (arrow)

The clinical presentation of PTLD is usually nonspecific with symptoms such as fever and abdominal pain or mass accounting for nearly 50% of the cases.[9] Moreover, over 80% of the patients may have a primarily extranodal disease.[9] Hence, imaging plays an important role not only in the diagnosis of PTLD but also the staging, treatment response evaluation, and surveillance in these patients. Given the frequent extranodal and multiorgan involvement associated with PTLD, ^{18}FDG PET-CT has emerged as a sensitive tool for early diagnosis of PTLD.[10] In some patients, perigraft PTLD may be misdiagnosed as hematoma/infected collection/abscess, especially when there is no associated lymphadenopathy or lesion in the graft itself.[11] Being a functional or metabolic study in addition to anatomical study (with the incorporation of CT), ^{18}FDG PET-CT is more sensitive and specific than CT alone for the diagnosis and follow-up of patients with PTLD.[6,12,13] The reported sensitivity and specificity of ^{18}FDG PET-CT for detecting PTLD is 90% and 89%, respectively.[14] Early relapses may not be picked on any investigation but ^{18}FDG PET-CT.[15] Another advantage of ^{18}FDG PET-CT is that it can predict the biological behavior of the malignant lesion based on the maximum SUV. SUV <6 suggests a high likelihood of indolent lymphoma whereas SUV >13 has a high likelihood of aggressive histology.[16] In case of transplanted kidney, possibility of contrast-induced nephropathy remains a major issue; hence, noncontrast ^{18}FDG PET-CT serves as a safe and effective imaging modality. Contrast-enhanced ultrasound is also emerging as a noninvasive technique to diagnose PTLD, which shows enhancement with persistent hypovascularity.[17] However, its role for the same is not defined at present. A high index of suspicion and judicious use of imaging can ensure early biopsy since the diagnosis

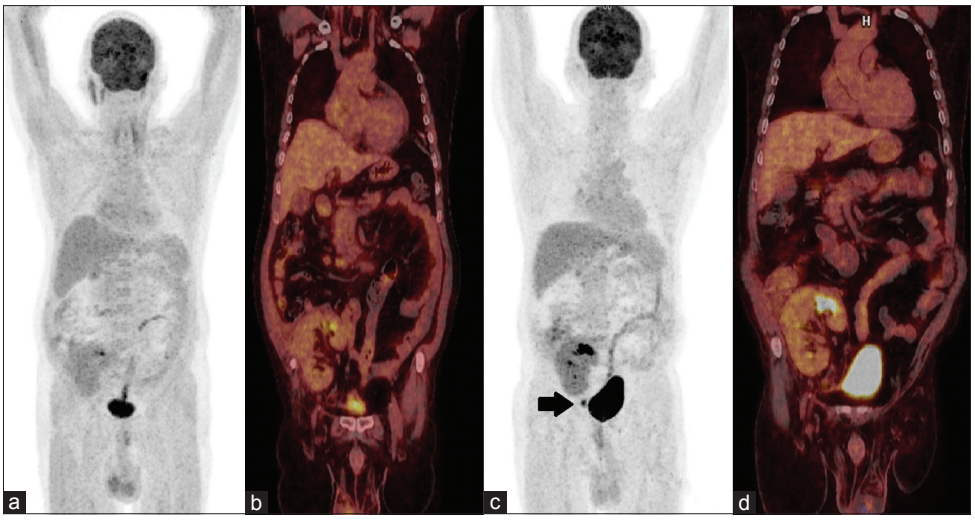

Figure 2: Interim (a) 18-fluorodeoxyglucose positron emission tomography-computed tomography maximum intensity projection reconstruction of computed tomography attenuation corrected image and (b) 18-fluorodeoxyglucose positron emission tomography-computed tomography (fused) coronal reconstruction image after four cycles of chemotherapy do not show any abnormal 18-fluorodeoxyglucose accumulation suggestive of a complete metabolic response to chemotherapy. Only holdup of tracer in calyx of transplanted kidney at the upper pole is seen. (c) 18-fluorodeoxyglucose positron emission tomography-computed tomography maximum intensity projection reconstruction and (d) 18-fluorodeoxyglucose positron emission tomography-computed tomography (fused) coronal reconstruction image after six cycles of chemotherapy show similar findings as in interim positron emission tomography-computed tomography except urine hold up in mid ureter (arrow)

of PTLD is established on histopathological examination. In the present case, PTLD was not suspected initially when ultrasonography was done. It was only when biopsy proved the diagnosis, the patient underwent ^{18}FDG PET-CT to look for the extent of the disease. ^{18}FDG PET-CT helped in this case by defining the baseline disease burden and assessing response to treatment as seen by disappearance of the FDG avid lesion seen in the baseline study.

Treatment of PTLD varies and depends on the subtype, disease staging, and the type of transplanted organ; multiple treatment strategies exist to treat PTLD. The various treatment modalities include reduction or withdrawal of immunosuppressant therapy and/or antiviral agents such as acyclovir, and chemotherapy as R-CVP, R-CHOP, etc.[18-20] At times, it is difficult to decide whether a patient should be prescribed rituximab monotherapy or a combination therapy. Choquet *et al*. proposed three factors to help make this decision: (a) age >60 years, (b) Eastern Cooperative Oncology Group performance status 2–4, and (c) raised LDH.[21] Further, three risk groups were proposed: low, intermediate, and high based on the presence of 0, 1, and >1 risk factors, respectively. The patients in intermediate- and high-risk groups have a poor survival and would not be benefited with rituximab monotherapy. Hence, rituximab should be given in combination with other chemotherapeutic agents in these patients. Our patient belonged to the intermediate group and was treated with 6 cycles of R-CVP chemotherapy.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Starzl TE, Nalesnik MA, Porter KA, Ho M, Iwatsuki S, Griffith BP, *et al.* Reversibility of lymphomas and lymphoproliferative lesions developing under cyclosporin-steroid therapy. Lancet 1984;1:583-7.
2. Taylor AL, Marcus R, Bradley JA. Post-transplant lymphoproliferative disorders (PTLD) after solid organ transplantation. Crit Rev Oncol Hematol 2005;56:155-67.
3. Bakker NA, van Imhoff GW, Verschuuren EA, van Son WJ, Homan van der Heide JJ, Veeger NJ, *et al.* Early onset post-transplant lymphoproliferative disease is associated with allograft localization. Clin Transplant 2005;19:327-34.
4. von Schulthess GK, Steinert HC, Hany TF. Integrated PET/CT: Current applications and future directions. Radiology 2006;238:405-22.
5. Parker A, Bowles K, Bradley JA, Emery V, Featherstone C, Gupte G, *et al.* Management of post-transplant lymphoproliferative disorder in adult solid organ transplant recipients - BCSH and BTS guidelines. Br J Haematol 2010;149:693-705.
6. Bakker NA, van Imhoff GW, Verschuuren EA, van Son WJ. Presentation and early detection of post-transplant lymphoproliferative disorder after solid organ transplantation. Transpl Int 2007;20:207-18.
7. LaCasce AS. Post-transplant lymphoproliferative disorders. Oncologist 2006;11:674-80.

8. Khedmat H, Taheri S. Early onset post transplantation lymphoproliferative disorders: Analysis of international data from 5 studies. Ann Transplant 2009;14:74-7.
9. Sakhuja V, Ramachandran R, Kohli HS, Jha V, Gupta KL, Rathi M, *et al.* Spectrum of lymphoproliferative disorders following renal transplantation in North India. Indian J Nephrol 2013;23:287-91.
10. Lal H, Yadav P, Dey M, Kumar N. Postrenal transplant metastatic colonic neoplasm: Posttransplant lymphoproliferative disorder or adenocarcinoma? Indian J Nephrol 2017;27:218-21.
11. Sandhu MS, Kalra N, Sidhu R. Posttransplant lymphoproliferative disorder (PTLD) localized near the allograft mimicking a collection. Indian J Radiol Imaging 2002;12:132-3.
12. Hicks RJ, Mac Manus MP, Seymour JF. Initial staging of lymphoma with positron emission tomography and computed tomography. Semin Nucl Med 2005;35:165-75.
13. Bianchi E, Pascual M, Nicod M, Delaloye AB, Duchosal MA. Clinical usefulness of FDG-PET/CT scan imaging in the management of posttransplant lymphoproliferative disease. Transplantation 2008;85:707-12.
14. Dierickx D, Tousseyn T, Requilé A, Verscuren R, Sagaert X, Morscio J, *et al.* The accuracy of positron emission tomography in the detection of posttransplant lymphoproliferative disorder. Haematologica 2013;98:771-5.
15. Blaes AH, Cioc AM, Froelich JW, Peterson BA, Dunitz JM. Positron emission tomography scanning in the setting of post-transplant lymphoproliferative disorders. Clin Transplant 2009;23:794-9.
16. Juweid ME, Cheson BD. Role of positron emission tomography in lymphoma. J Clin Oncol 2005;23:4577-80.
17. Lampe A, Duddalwar VA, Djaladat H, Aron M, Gulati M. Contrast-enhanced ultrasound findings of post-transplant lymphoproliferative disorder in a transplanted kidney: A case report and literature review. J Radiol Case Rep 2015;9:26-34.
18. Benkerrou M, Durandy A, Fischer A. Therapy for transplant-related lymphoproliferative diseases. Hematol Oncol Clin North Am 1993;7:467-75.
19. Milpied N, Vasseur B, Parquet N, Garnier JL, Antoine C, Quartier P, *et al.* Humanized anti-CD20 monoclonal antibody (Rituximab) in post transplant B-lymphoproliferative disorder: A retrospective analysis on 32 patients. Ann Oncol 2000;11 Suppl 1:113-6.
20. Muti G, Cantoni S, Oreste P, Klersy C, Gini G, Rossi V, *et al.* Post-transplant lymphoproliferative disorders: Improved outcome after clinico-pathologically tailored treatment. Haematologica 2002;87:67-77.
21. Choquet S, Leblond V, Herbrecht R, Socié G, Stoppa AM, Vandenberghe P, *et al.* Efficacy and safety of rituximab in B-cell post-transplantation lymphoproliferative disorders: Results of a prospective multicenter phase 2 study. Blood 2006;107:3053-7.