An Interesting Case of PTLD After Kidney Transplantation

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Introduction

Post-transplant lymphoproliferative disorders (PTLD) are proliferations of lymphoid and/or plasmacytic cells that occur due to therapeutic immunosuppression after solid organ or allogeneic hematopoietic stem cell transplantation. PTLD is the most common malignancy, with the exception of skin cancer, after solid organ transplant in adults and occurs in up to 10% of patients. In most cases, PTLD is associated with Epstein Barr Virus (EBV) infection of B cells, either as a consequence of reactivation of the virus post-transplantation or from primary EBV infection. More than half of PTLD cases present with extra-nodal masses. Involvement of the allograft itself accounts for almost 25% of the cases of PTLD. Other involved organs include the gastrointestinal tract, lungs, skin, liver, and central nervous system. In this case report, we present a 62-year-old recent renal transplant recipient who presented with hyperkalemia and acute kidney injury, and was found to have a large peri-hilar mass infiltrating his right lower abdominal kidney allograft.

Case Presentation

A 62-year-old male with ESRD due to hypertension, with history of a benign bladder tumor in 1992 underwent successful deceased donor renal transplantation. He was induced with basiliximab, an IL2 receptor blocker. His post-transplant course was complicated by low-level cytomegalovirus (CMV) viremia, which responded to three weeks of valganciclovir therapy, and BK viremia, which resolved following reduction in the dose of mycophenolate mofetil. Throughout this time, patient’s renal function remained excellent with his baseline creatinine in the 1.1-1.3 range.

Seven months after transplantation, the patient presented to clinic with complaints of fatigue and decreased appetite. He noted right lower abdominal pain that was intermittent and not associated with activity. He denied any vomiting or diarrhea, but did complain of nausea. He was found to have acute kidney injury with a creatinine of 1.8 and hyperkalemia with a K+ of 6.4. Given the degree of his electrolyte abnormalities, he was admitted for a renal transplant biopsy and acute management of his hyperkalemia. The patient had an ultrasound of his kidney allograft prior to biopsy, which showed evidence for a slightly distented collecting system with a slightly thickened urethelium. A focus of the soft tissues in the renal hilum of uncertain significance was seen. After discussion with Urology regarding this questionable hilar mass, the decision was made to proceed with allograft biopsy. The patient underwent allograft biopsy which showed acute cellular rejection 1a based on Banff criteria. There was also no evidence of BK nephropathy. The patient was treated with intravenous steroids for a three days. His renal function improved slightly and after discussion with Radiology, the patient underwent an MRA abdomen/pelvis with and without contrast to better evaluate the questionable peri-hilar mass seen on ultrasound at the time of kidney biopsy. The MRA revealed a hilar enhancing mass infiltrating the allograft and surrounding tissues that measured up to 9.5 cm, which likely represented post-transplant lymphoproliferative disease (Figure 1). A dedicated CT guided biopsy of the peri-hilar mass was then performed by Radiology. The biopsy revealed a monomorphic post-transplant lymphoproliferative disorder, plasmablastic lymphoma type (Figure 2a). Immunohistochemical stains demonstrated that the lymphoma cells were positive for CD20, PAX5 (weak), BCL2, BCL6, MUM1, CD138, CD45, and EBV EBER with lambda light chain restriction and a Ki67 proliferative index of 60-70% (Figure 2b). Flow cytometry demonstrated a small population of large B-cells with lambda light chain restriction. Serum EBV PCR was negative. A PET scan was then done showing a large heterogeneous mass with intense FDG uptake (7.824 Max SUV) in the transplant kidney located in the right pelvis. This was consistent with the biopsy proven lymphoma. No FDG uptake was seen in the urinary bladder.

Given his newly diagnosed malignancy his immunosuppression was reduced. Mycophenolate was discontinued altogether and patient was switched from tacrolimus to low dose sirolimus. He was also received chemotherapy in the form of rituximab, cyclophosphamide, and prednisone. This was followed by 6 cycles of dose adjusted R-EPOCH.
EBV infected B cells that give rise to PTLD can lymphoproliferative disorders such as PTLD. With immunosuppression, this can give rise to B cells persist, and if T cell immunity wanes such as escapes immun. However, a small subpopulation of the infected B cells express viral antigens which elicit a T cell response and expansion of B cells (EBV) and 90% to 95% containing the Epstein-Barr virus. Approximately 90% of PTLD are of B cell or T/NK cell lymphomas recognized in immunocompetent patients. Monomorphic PTLD - monoclonal lymphoid proliferations that meet the criteria for one of the B cell or T/NK cell lymphomas recognized in immunocompetent patients and/or abnormal imaging studies. Laboratory testing in patients with PTLD may show one or more of the following: 1) unexplained anemia, thrombocytopenia, or leukopenia 2) elevated level of serum lactate dehydrogenase 3) hypercalcemia 4) hyperuricemia and/or abnormal imaging studies. The primary risk factors associated with developing PTLD are related to the degree of immunosuppression and the EBV status of the recipient. Additional risk factors include recipient age less than 25 and Caucasian race. T cell immunity, particularly, is thought to play a major role in the development of PTLD. Interestingly, it is during the first year after transplantation when immunosuppression is the strongest, when the incidence of PTLD is the highest. Highlighting the importance of T cell immunity, it has been shown that induction agents that suppress T cell activity (such as thymoglobulin) are associated with higher rates of PTLD. There is an increased risk of PTLD among EBV-negative recipients receiving organs from EBV-positive donor organs as well, as was the case in our patient. The clinical presentation of PTLD is heterogeneous - depending on the degree of PTLD, location of involvement, and other co-morbidities affecting the patient. The most common presenting symptoms include fever, weight loss, and fatigue. An unexplained infectious syndrome in a transplant recipient should raise the suspicion of a PTLD. More than half of PTLD presents with extra-nodal masses – namely the stomach, intestine, lungs, skin, liver, central nervous system, and the allograft itself. Often times, if the allograft is involved, it can lead to ultimate failure or dysfunction of the allograft. In general, EBV negative tumors tend to present much later (after 6 years) and have an overall more aggressive course.

Diagnosing PTLD is usually dependent on the clinicians’ level of suspicion based on patient history. Reasons to suspect PTLD include constitutional symptoms, lymphadenopathy, allograft dysfunction, and/or abnormal imaging studies. Laboratory testing in patients with PTLD may show one or more of the following: 1) unexplained anemia, thrombocytopenia, or leukopenia 2) elevated level of serum lactate dehydrogenase 3) hypercalcemia 4) hyperuricemia and/or 5) monoclonal protein in the serum or urine. If PTLD is suspected, imaging of the area in question is recommended as well as consideration of a positron.
emission tomography (PET) scan if the diagnosis is highly suspected. EBV viral load should be tested. To definitively make the diagnosis, a tissue biopsy is necessary in which the morphology, immunophenotype, EBER, and molecular genetic studies and antigen receptor genes are suggested.

Management of PTLD varies significantly according to the type of lymphoproliferative disease present. Reduction of immunotherapy is the primary and most immediate focus of therapy. For most patients with early lesions, reduction of immunosuppression alone is usually all that is necessary. In CD20 positive patients who cannot tolerate a reduction of immunosuppression or for those who have residual disease, rituximab may be considered as an option. In polymorphic PTLD (CD20+), the use of rituximab in addition to reduction of immunosuppression is the cornerstone of therapy. Our patient had evidence of monomorphic CD20+ PTLD. Such cases are treated with rituximab in combination with chemotherapy, and reduction of immunosuppression. Our patient was able to control his aggressive PTLD, with 6 cycles of rituximab, chemotherapy (EPOCH) and a reduction of his immunosuppression to low dose Sirolimus and prednisone. Patients whose tumors do not express CD20 are not candidates for rituximab therapy and are therefore treated with combination chemotherapy plus immunosuppression reduction. Surgery is reserved for patients with complications such as perforation or obstruction. Lastly, for most patients with classical Hodgkin lymphoma-like PTLD, management with chemotherapy plus/minus radiation therapy according to protocols used for classical Hodgkin lymphoma is suggested.

Post-transplant lymphoproliferative disorders remain one of the most adverse consequences following both solid organ and stem cell transplantation. We present a remarkable case of a kidney transplant recipient who developed a large peri-hilar mass infiltrating into the allograft that was found to be a monomorphic type of PTLD, which was effectively treated with rituximab and chemotherapy. We highlight the importance of having a clinical suspicion of such a diagnosis, and provide a better understanding of the evaluation and management of post-transplant lymphoproliferative diseases.

![Figure 1](image1.png)

**Figure 1:** MRI of abdomen/pelvis

![Figure 2](image2.png)

(A. H & E stain of hilar mass showing significant inflammation  
B. EBV EBER stain positive showing involvement of EBV virus)

![Figure 3](image3.png)

**Figure 3:** Repeat MRI Abdomen/Pelvis shows significantly decreased size of the peri-hilar mass
REFERENCES


Submitted on August 8, 2014