CNS Post-Transplant Lymphoproliferative Disorder in a Heart Recipient: A Case Report

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ABSTRACT

Solid organ recipients have increased risk of malignancy in comparison with general population. Although post-transplant lymphoproliferative disorders are the second most common cancer in transplanted patients, primary CNS lymphoma is a rare presentation of these disorders. Among the wide range of neurologic complications in post- transplant period, some characteristics could be helpful for diagnosing of this disorder. Rarity of CNS lymphoma may lead to late diagnosis of this disease while early detection has utmost importance for better management of it. Here, we describe a heart recipient young woman with focal neurologic symptoms 14 months after transplantation and some features that could be helpful for on-time diagnosis.

KEYWORDS: Heart transplant; CNS; Lymphoma

INTRODUCTION

Solid organ recipients have a 2-3 fold increased risk of cancer in comparison with the general population [1].

Post-transplant lymphoproliferative disorders (PTLD) are the second most common malignancies after skin cancer, however CNS involvement is rare. Some factors have been proposed that increase the risk of PTLD including the type of transplantation. It has been shown that the incidence is higher in lung and intestinal transplantation recipients. It may be due to the severity of immunosuppression or lymphoid tissue quantity [2].

In a retrospective study including transplanted patients, during a 47 year period, CNS PTLD comprised only 7% of all PTLD cases, and presented late from the transplant time with diffuse large B-cell lymphoma (DLBCL) histology and Epstein-Barr virus (EBV) positivity [3].

Although there are several reports on PTLD patients, due to rarity of CNS-PTLD, there are insufficient data in these patients. Here, we report a young female heart recipient who presented with CNS-PTLD.

CASE PRESENTATION

A 29-year female underwent heart transplantation 20 months prior to her last admission due to end-stage heart failure without obvious cause. Immunosuppressive drugs were tacrolimus and mycophenolate mofetil (MMF). Six months after transplantation, she presented with left shoulder and neck pain diagnosed as herpes zoster infection and received parenteral acyclovir and then oral valacyclovir. Repeated surveillance endomyocardial biopsies were grade 0 (no rejection). Approximately 14 months after transplant, she referred with reduced forced and paresthesia of the left upper extremity. The patient was taking tacrolimus 3.5 mg daily, mycophenolate

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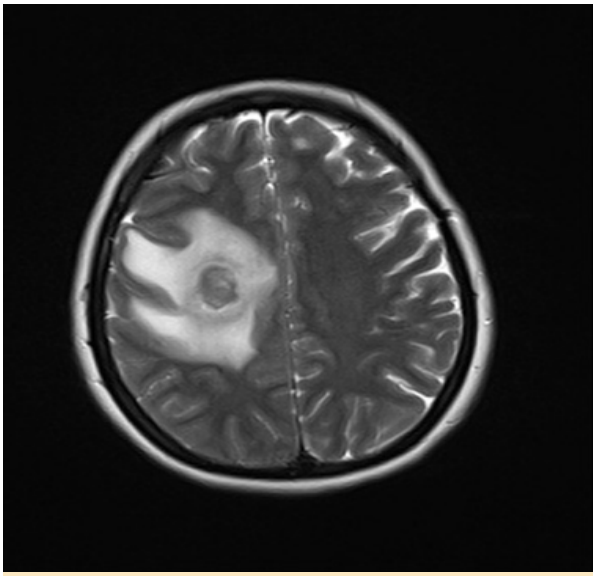

Figure 1: Brain MRI without contrast, showing right parietal lobe lesion.

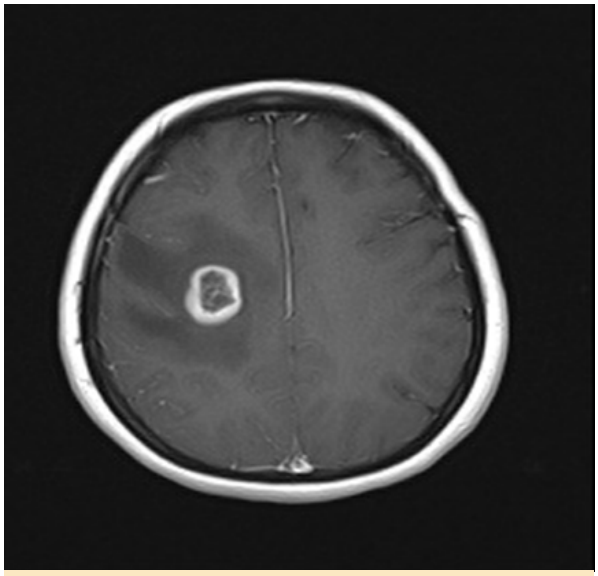

Figure 2: Brain MRI with contrast, showing right parietal lobe mass with ring enhancement.

mofetil 1000mg bid, prednisolone 5mg daily, itraconazole 1000mg bid, Co-trimoxazole, aspirin, statin, alendronate, calcium, vitamin D, metformin and amlodipine. Laboratory data were as follows, WBC: 5700 with 60% PMN, Hb:10g/dL, platelet count: 218000 and ESR: 20mm/hr. Echocardiography showed normal findings without vegetation or mass. Brain CT without contrast showed, low attenuated area in right parietal lobe with round lesion in the center measured 17mm, suspicious of brain abscess or mass. Brain MRI with and without contrast showed, abnormal signal intensity of edema and round lesion in the center measured 17*16mm in right parietal lobe with peripheral ring enhancement suggestive of abscess formation or mass lesion. Cytomegalovirus (CMV) polymerase chain reaction (PCR) and toxoplasma serology were negative. Antibiotic and antifungal drugs were administered due to probability of brain abscess. Due to lack of response to medical therapy, control MRI was done 23 days later which showed the following results: ring enhancing lesion measured 23*19 mm in right parietal lobe with vasogenic edema which showed mild enlargement compared to previous study, furthermore mild compressive effect was noted on the right lateral ventricle (Fig 1 & Fig 2).

The findings suggested the possibility of brain mass. Biopsy of the lesion using stereotactic guide, revealed brain tissue infiltration by a highly necrotic neoplasm composed of highly atypical cells with clear cytoplasm and vesicular irregular nuclei. Immunohistochemistry study showed, CD45 and CD20 were positive while CD3, synaptophysin and pan-cytokeratin (PanCK) were negative. The final diagnosis was diffuse large B-cell lymphoma, CD20 positive.

EBV serology was positive for IgG before transplant. The patient underwent treatment with methotrexate, rituximab and temozolomide (an alkylating agent). Dose of mycophenolate mofetil was reduced to 50%. She is now under chemotherapy sessions. Her symptoms have been improved relatively but not completely.

DISCUSSION

Out of 225 heart transplants that have been performed during 10 years in our center, this is the first case of CNS-PTLD. Due to low prevalence, diverse manifestations and importance of early diagnosis of this disorder, we aimed to report this case with some explanations regarding discrimination of CNS-PTLD among other differential diagnosis with neurologic findings.

Neurologic events are among the most common complications after solid organ trans-

plantation. In a survey, these events occurred in 85% of heart recipients during an 18 years follow-up. Although the spectrum of neurologic complications are wide from postoperative delirium and peri-transplant stroke to drug toxicity, CNS infections and lymphoma, some clues could be helpful in differentiating these entities, especially in challenging cases. Theses clues include, type of transplanted organ, time interval between transplant and event occurrence, type of immunosuppressive drugs, clinical signs and symptoms, imaging modalities and further diagnostic work-ups like cerebrospinal fluid (CSF) analysis and electroencephalography (EEG). In contrast with other complications that have peak incidence of 6 months or earlier after transplantation, CNS lymphoma has peak incidence of 6 months and later after transplant [4].

Occurrence of neurologic symptoms 14 months after transplantation in our patient, was in favor of CNS lymphoma.

Evidences have shown an association between MMF and PTLD, while calcineurin inhibitors (CNI) like tacrolimus may have protective effects [5]. Although our patient was receiving tacrolimus but consumption of MMF in our patient may be considered as a risk factor for PTLD.

From imaging point, some clues could be helpful for distinguishing CNS-PTLD from other lesions. These lesions tend to have ring enhancement, ill-defined margins with lobar and supratentorial location [6]. Imaging findings of our patient had all of these findings which support the possibility of CNS-PTLD.

Role of primary EBV infection in association with primary CNS lymphoma (PCNSL) is supported by higher incidence of PCNSL in EBV seronegative patients and also the increased incidence of this malignancy 1.5 years after transplantation. Despite these evidences, prophylactic antiviral treatment is not recommended in EBV-seronegative recipients from EBV positive donors but close EBV viral load monitoring at least during the first post-transplant period is recommended [7]. Our patient was EBV seropositive, so viral load monitoring was unnecessary in this patient.

In a large series on heart and lung recipients, bone marrow involvement and hypo-albunemia were poor prognostic markers. Five-year survival rate was 29%. In this study, there was a reduced incidence of PTLD in recent years probably due to the change in immunosuppression protocols, especially avoidance of cytolytic agents like anti-thymocyte globulin (ATG). Late onset PTLD (>1 year after transplant) was more common in heart recipients and approximately 80% of tumor cells were EBV positive [8].

Treatment strategy in CNS PTLD consists of immunosuppression reduction, methotrexate, aracytine and rituximab addition and radiotherapy. In a study, response rate was about 60% with 3-year survival rate of 43%. A promising treatment is cell therapy which is now available only in study protocols. It is based on recruitment of T-cells against EBV antigens, so it is useful only in EBV positive patients [9].

In conclusion, CNS-PTLD is among the rare malignancies after organ transplantation. It usually occurs relatively late after transplant (6 months or later), is more common in MMF consumers, has somewhat distinguishing imaging findings like ring enhancement, ill-defined margins and lobar location.

ACKNOWLEDGMENTS

We would like to thank the staff of Rajaie Cardiovascular, Medical and Research Center who supported our work.

CONFLICTS OF INTEREST: None declared.

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