

Cerebral Post-Transplant Lymphoproliferative Disorder Occurring after Renal Transplantation: A Case Report

신 이식 후 발생하는 대뇌 림프증식성질환: 증례 보고

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Post-transplant lymphoproliferative disorder (PTLD) is a complication of organ transplantation and immunosuppression. A 36-year-old woman with a history of renal transplantation visited the hospital complaining of headache and on pathology was diagnosed with cerebral PTLD manifesting as multiple rim enhanced masses in both hemispheres. We report here a case of post-transplant lymphoproliferative disorder involving the cerebrum occurring after renal transplantation, and describe the MRI findings for this patient.

Index terms

Post-Transplant Lymphoproliferative Disorder
MRI
Central Nerve System

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INTRODUCTION

Post-transplant lymphoproliferative disorder (PTLD) is a disorder seen after organ transplantation in patients who have received immunosuppressive therapy. Lymphoid proliferation involves solid organs, bone marrow or stem cell allograft. Unlike primary central nerve system (CNS) lymphoma, hemorrhage, necrosis and rim enhancement are typical of cerebral PTLD (1). We present here a rare case of PTLD developing in the cerebrum after renal transplantation.

CASE REPORT

A 36-year-old woman visited the hospital with a complaint of headache and dizziness for 2 weeks. She had a history of renal transplantation due to chronic renal failure 15 years previously. After renal transplantation, she was treated with cyclosporine (200 mg/day), mycophenolate mofetil (1500 mg/day) and corticosteroid (6 mg/day) to achieve immunosuppression. Physical examination revealed she was afebrile with normal vital

signs. On laboratory testing, erythrocyte sedimentation rate was 5 mm/H (normal range, 0-25 mm/H) and c-reactive protein was 0.04 mg/dL (normal range, 0-0.5 mg/dL). Other tests revealed no signs of bacterial or fungal infection, and cerebral spinal fluid (CSF) study was negative on gram stain and acid fast bacilli stain. A human immunodeficiency virus antibody test was also negative. However CSF polymerase chain reaction (PCR) for John Cunningham virus was positive. Brain MR imaging was performed. Multiple masses with severe peritumoral edema were seen in the subcortical area of the parietal and temporal lobes of both hemispheres. These masses showed low to iso-signal intensity in the T1-weighted image and low-signal intensity in the T2-weighted image. On contrast study, these lesions showed rim enhancement (Fig. 1).

Brain biopsy was performed for diagnosis. Biopsy showed lymphoid cells infiltrating the brain parenchyma and perivascular areas. The lymphoid cells of the tumor were small in size, with mild atypia. On immunohistochemical staining, CD3+ T cells and CD20+ B cells were seen, but CD3+ cells were dominant (Fig. 2). A diagnosis of polymorphic PTLD was made, and the PCR for Epstein-Barr virus (EBV) was positive.

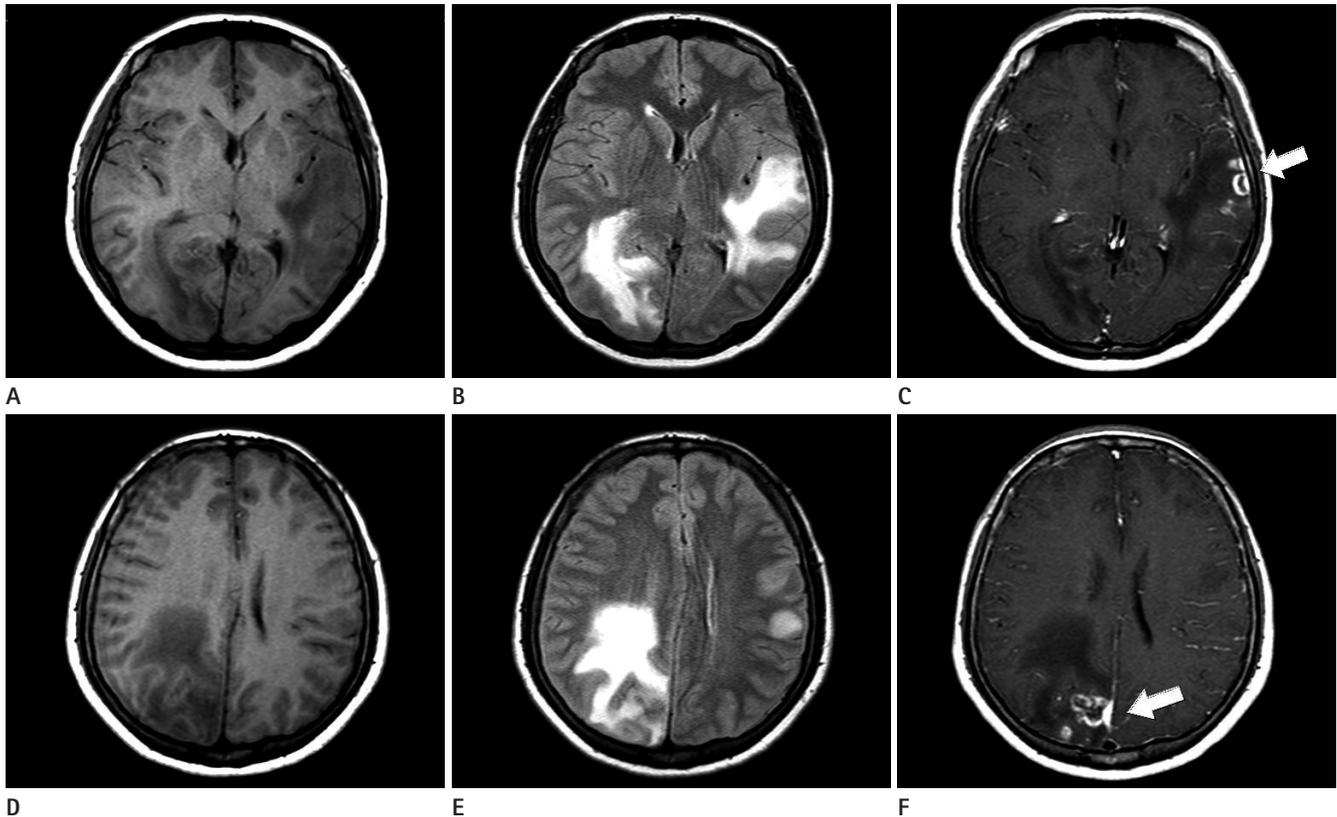


Fig. 1. A 36-year-old woman with cerebral post-transplant lymphoproliferative disorder.

A-F. Axial T1-weighted images (**A, D**), T2-weighted images (**B, E**) and contrast-enhanced T1-weighted images (**C, F**) show multiple masses with severe peritumoral edema in the subcortical white matter of the parietal and temporal lobes of both hemispheres. On contrast study, these masses show rim enhancement (arrow).

After diagnosis, the immunosuppressive regimen was changed. The dose of cyclosporine was reduced from 200 mg/day to 150 mg/day, and mycophenolate mofetil was stopped. Whole-brain irradiation was performed.

A follow-up MRI was obtained after three months. The size of the masses and the extent of the peritumoral edema had decreased in the subcortical white matter of the parietal and temporal lobes (Fig. 3).

DISCUSSION

PTLD is a heterogeneous group of diseases that is an uncommon complication of transplantation and can lead to significant morbidity and mortality (1).

Lymphoid growth proceeds in an uncontrolled fashion as a result of the immunocompromised state. EBV infection or reactivation of this infection is thought to play a role, and EBV seronegativity at the time of the transplant is a well-known risk factor for developing PTLD (2).

The pathologic classification systems for PTLD by the Society of Hematology and the World Health Organization have four major categories: A) hyperplastic lesions; B) polymorphic lesions; C) monomorphic lesions, which are further subcategorized along recognized lines of B-cell, T-cell, or natural killer cell neoplasia; and D) other lymphoproliferative disorders, including Hodgkin lymphoma (3).

The overall frequency of post-transplant lymphoproliferative disorder has been reported to range between 1% and 10% (4). Renal transplant recipients generally have lower risks than recipients of liver, lung and heart transplants.

Central nervous system involvement is relatively uncommon today. Miller et al. (9) found that with the introduction of newer more potent immunosuppressants, such as cyclosporine, there has been a shift in the sites of involvement. When azathioprine was the primary immunosuppressant, the central nervous system was the predominant site of involvement. With the introduction of cyclosporine, however, isolated central nervous system involvement has become relatively uncommon (9).

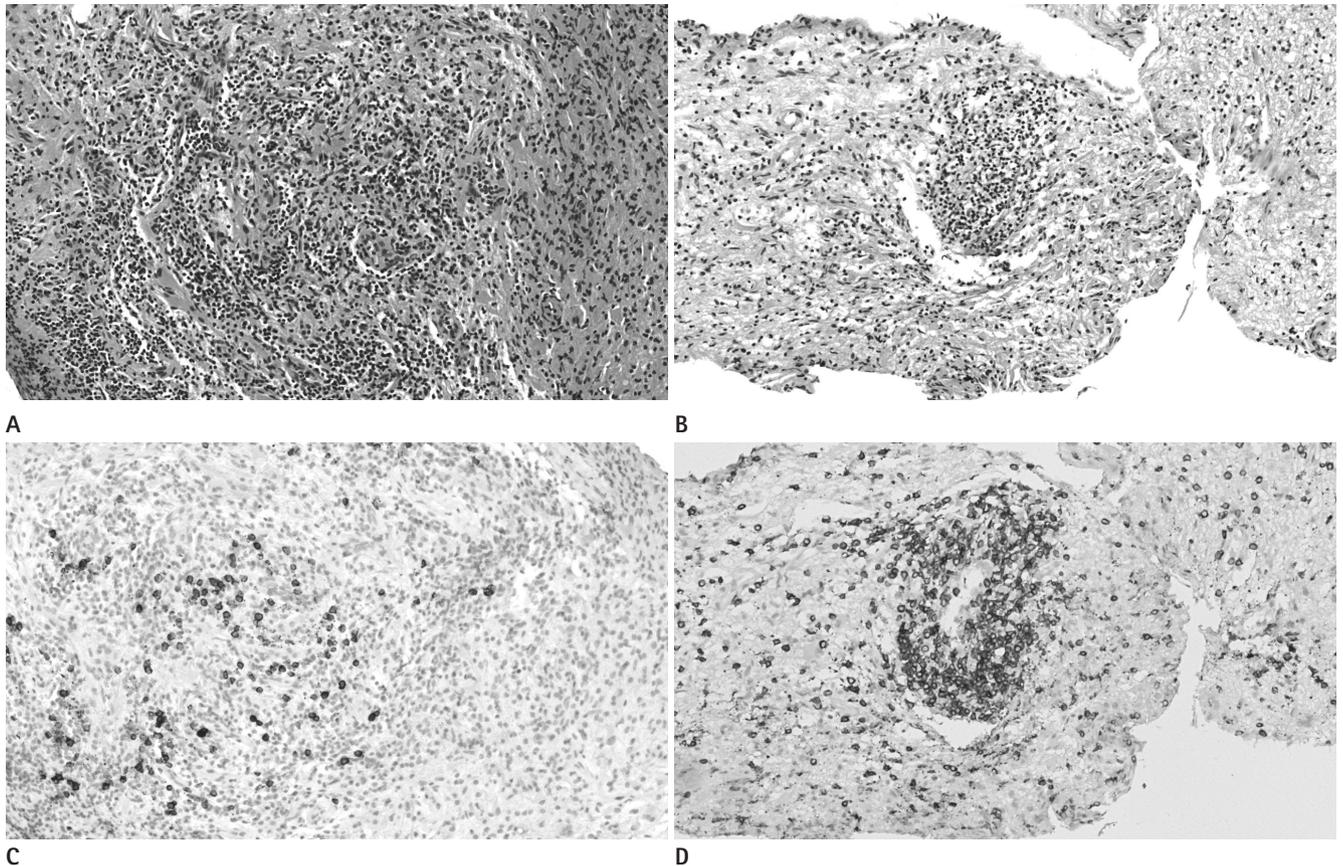


Fig. 2. Histological features of cerebral post-transplant lymphoproliferative disorder in a 36-year-old woman.
A, B. Histological findings show lymphoid cells infiltrating the brain parenchyma and perivascular area (hematoxylin-eosin stain, $\times 100$).
C, D. Immunohistochemical staining shows a positive reaction with CD20+ B cells and CD3+ T cells (immunohistochemical stain, $\times 100$).

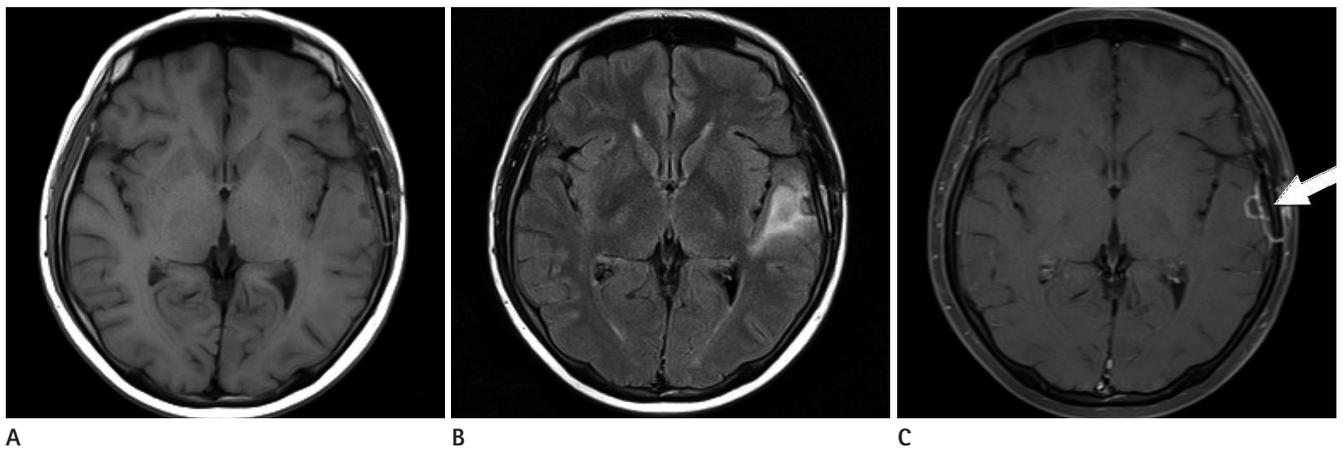


Fig. 3. A follow-up MRI was performed after three months.
A-C. Axial T1-weighted image (**A**), T2-weighted image (**B**) and contrast-enhanced T1-weighted image (**C**) show a decrease in the size of the masses and the extent of the peritumoral edema in the subcortical white matter of the temporal lobe (arrow).

Castellano-Sanchez et al. (5) reported that the monomorphic type was more predominant than the polymorphic type in CNS PTLDs. But our case was confirmed on pathology to be of the polymorphic type.

Hemorrhage, necrosis and rim enhancement, which are un-

common in patients with intact immune systems, are typical of cerebral PTLD. The findings on imaging closely resemble those seen in AIDS-related CNS lymphoma (6). Lesions typically affect the deep supratentorial structures, especially the periventricular region. Subcortical white matter involvement is also common,

whereas cerebellum and brainstem involvement are uncommon. Multiple lesions occur more commonly in PTLTD than in primary CNS lymphoma in immunocompetent patients (7).

On unenhanced CT, the lesion has high attenuation secondary to hypercellularity or hemorrhage. The lesion is typically low to iso-signal intense in T1-weighted MR images, with high-signal intensity reflecting areas of hemorrhage. In T2-weighted images, the lesion appears low-signal intense, presumably due to hypercellularity, although focal high-signal intensity can be seen, a finding that reflects an area of necrosis. The lesion is usually surrounded by vasogenic edema. Rim enhancement following contrast material administration is typical (6). In our case, hemorrhage was not seen, but multiple rim-enhanced lesions with massive peritumoral edema in the subcortical white matter were manifested.

Reduction of immunosuppression is considered first-line therapy for PTLTD, with a response usually seen within 2-4 weeks of treatment (8). But complete remission is rarely obtained through using this method solely. Most cases obtaining complete remission were treated with other therapeutic modalities, including surgical resection, chemotherapy and radiotherapy (8).

In conclusion, we report here on a case of cerebral PTLTD occurring after renal transplantation. Cerebral involvement of PTLTD is rare, but if a patient has a history of transplantation with immunosuppressive treatment and has multicentric rim-enhanced lesions on contrast MRI, cerebral PTLTD should be considered in the differential diagnosis.

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신 이식 후 발생하는 대뇌 림프증식성질환: 증례 보고

서장호 · 변우목 · 김홍철 · 황미수

이식 후 림프증식성질환은 장기 이식과 면역억제의 결과로 발생하는 림프증식성질환이다. 신장 이식을 받은 36세 여자 환자가 두통을 주소로 내원하였다. 영상검사에서 양쪽 대뇌에 다수의 변연부 조영증강을 보이는 병변들이 관찰되었고, 병리적으로 이식 후 림프증식성질환으로 진단되었다. 저자들은 신장 이식 후 대뇌에 발생한 이식 후 림프증식성질환의 증례를 자기공명영상 소견과 함께 보고하고자 한다.

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