

# Primary Brain T-cell Lymphoma Concomitant with CNS Tuberculosis in a Kidney Transplant Patient

## Primer T-hücreli Beyin Lenfoması ile Santral Sinir Sistemi Tüberkülozunun Birlikte Bulunduğu Böbrek Transplantasyonlu Bir Olgunun Sunumu

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### Özet

Bu yazıda, böbrek transplantasyonu nedeniyle takipte olan ve immünsupresif tedavi alırken intrakranial kitle tespit edilen bir olgu sunulmuştur. Bu olguda primer santral sinir sistemi lenfoması ve santral sinir sistemi tüberküloz enfeksiyonu birlikte gözlenmiştir. Transplantasyon yapılan hastalarda, immünsupresif ilaçlar nedeniyle enfeksiyon ve malignite komplikasyonları artmaktadır ve atipik tutulumlar daha sık tespit edilmektedir.

Anahtar kelimeler: **Böbrek Transplantasyonu; Lenfoma, T-Hücreli; Tüberküloz, Merkezi Sinir Sistemi.**

### Abstract

In this article, a patient with intracranial mass which occurred during immunosuppressive therapy because of renal transplantation was reported. The patient had concomitant central nervous system tuberculosis and primary central nervous system lymphoma. The patient, who had had renal transplantation performed, had increased complications of infectious disease, malignancies and atypical manifestations because of immunosuppressive drugs.

Key words: **Kidney Transplantation; Lymphoma, T-Cell; Tuberculosis, Central Nervous System**

## Introduction

Organ transplant recipients are at an increased risk of infection and secondary malignant complications. Posttransplant lymphoproliferative disease (PTLD) is the most common neoplasia occurring in the early posttransplant course of graft recipients. PTLD affects approximately 1 % of renal transplant recipients (1). Extranodal localizations of PTLD are more frequent in transplant patients than in immunocompetent patients. The central nervous system (CNS) accounts for 24% of all extranodal PTLD (2). Primary central nervous system lymphoma (PCNSL) is defined as a diffuse lymphoma presenting in the brain or spinal cord in the absence of systemic lymphoma.

Tuberculosis is an important health problem in several developing countries, its prevalence being higher in immunocompromised patients. Solid organ transplant recipients requiring immunosuppressive therapy for continued allograft function are predisposed to mycobacterial infections. In different parts of the world, the incidence of tuberculosis in renal transplant recipients ranges from 0.2% to 15% (mean 3.7%) (3). CNS tuberculosis is clearly a significant cause of cerebral infection in patients with kidney transplant who must be given an immunosuppressive therapy. It may present with intracranial mass lesions.

An intracranial mass lesion is a diagnostic challenge in cases undergoing immunosuppressive therapy. We describe a patient who has concomitant CNS tuberculosis and PCNSL.

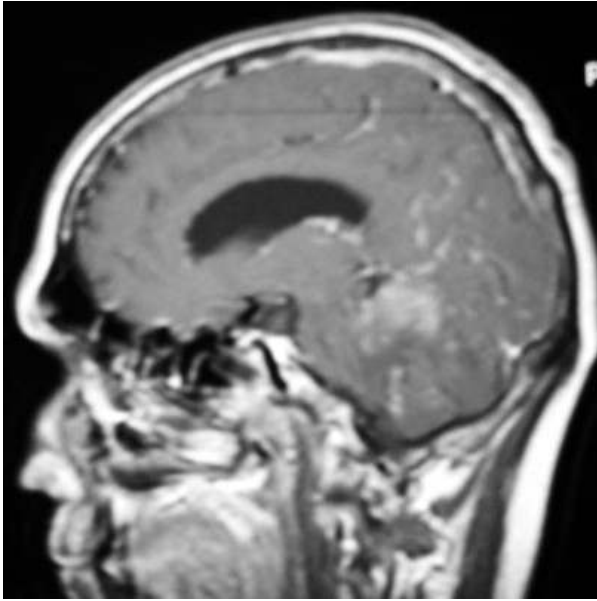
## Case Report

A 46-year-old Caucasian male with chronic renal failure of unknown origin, who had had an unrelated living renal transplantation 5 years earlier, was admitted with headache, vertigo, nausea, and vomiting. There was no previous or family history of tuberculosis. He was taking prednisone 10 mg qd, cyclosporine 100 mg bid, and mycophenolat mofetil 1 gr bid. On examination, the patient was afebrile; pulse was 92 beats/min, blood pressure was 130/90 mmHg, and respiratory rate was 16 breaths/min. Examination of the heart, lungs, and the abdomen was normal. Cranial nerves were intact, and muscle strength was within normal limits, including deep tendon reflexes. No meningismus or adenopathy was noted. Bilateral papilledema and ataxia were detected.

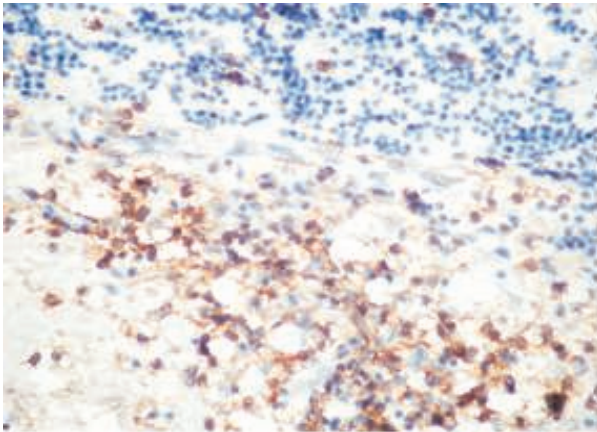
Laboratory analysis revealed: hemoglobin, 10.4 g/dl; white blood cells (WBC),  $5.1 \times 10^9/L$ , with 58% neutrophils; platelets,  $241 \times 10^9/L$ ; erythrocyte sedimentation rate (ESR), 60 mm/h; BUN, 38 mg/dL; creatinine, 2.3 mg/dl; sodium, 136 mmol/L; potassium, 3.8 mmol/L; chloride, 101 mmol/L; glucose, 115 mg/dL; albumin, 4.1 g/dL; total protein, 6.5 g/dL; uric ascite, 3.8 mg/dL; alanin transaminase (ALT), 20 U/L; aspartat transaminase (AST), 32 U/L, lactic dehydrogenase (LDH), 349 U/L; and total bilirubin, 0.3 mg/dL; A PPD was not performed. Serological tests including hepatitis A, B and C virus, EBV, CMV, HIV, rubella, toxoplasma were all negative.

Magnetic resonance imaging (MRI) (with gadolinium) of the brain revealed a mass of 2 cm in diameter in the right cerebellar hemisphere and an associated leptomeningeal enhancement (Figure Picture 1 and 2a). It was presumed to be a brain abscess; therefore, ceftriaxone 2x2 g, metronidazole 4x500 mg, and amphotericin B 1x200 mg (IV) were started empirically. A stereotactic brain biopsy was performed from the cerebellar mass on the 10<sup>th</sup> day of therapy, because the patient's complaints and papilledema increased. Surgical exploration revealed that the lesion was not an abscess, but had a solid nature. Pathologic examination revealed small neoplastic cells with tiny cytoplasm infiltrating cerebellar and neuroglial tissues. These cells were seen to concentrate especially around the vessels. On immunohistochemical examination, tumor cells reacted with CD45RO and CD3 (Picture 3). Small number of cells weakly reacted with CD20 and CD79a. Monoclonality tests confirmed that these cells were monoclonal in origin. Finally, diagnosis was established as small lymphocytic T-cell malignant lymphoma. Bone marrow examination, abdominal, and thoracic computerize tomography (CT) were normal.

Cranial radiotherapy was started. While radiotherapy was being continued acid-fast bacilli grew in automated blood culture (Myco-Bactec, Becton-Dickinson, Maryland, USA) bottles. Then, a quadruple anti-tuberculosis therapy (isoniazid 300mg/day, rifampin 600 mg/day, ethambutol 1000 mg/day, and pirazinamide 500 mg/day) was started. In addition to anti-tuberculosis therapy, a total radiotherapy dose of 6000cGy was administered. A cyclosporine blood level was monitored and the dose increased accordingly, because rifampicin lowered the blood level of cyclosporine by enhancing its hepatic metabolism. The doses of other immunosuppressive drugs were not change.

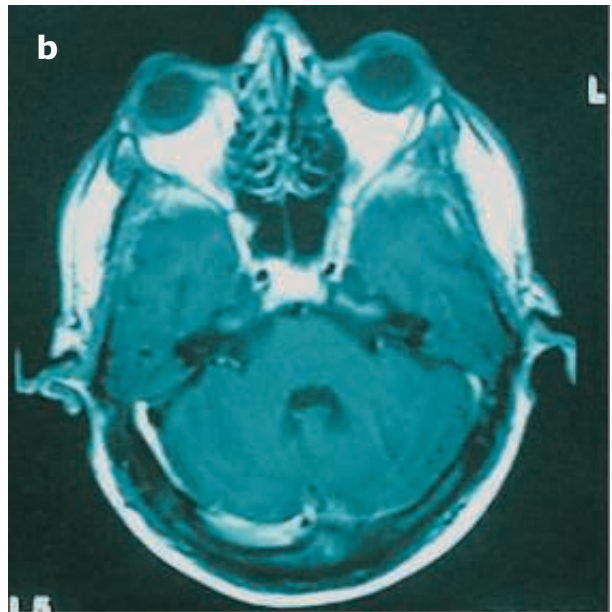


**Picture 1.** Sagittal contrast enhanced T1-weighted MR image; leptomeningeal enhancement.



**Picture 3.** CD3 immunostaining of lymphoma cells. Cerebellar cells are in the upper portion of the field.

Anti-tuberculosis therapy was continued for 12 months. Cranial MRI studies revealed the regression of the lesion (Figure Picture2b). During a follow-up period of 6 months after the completion of anti-tuberculosis therapy, the patient is doing well but his creatinine level continue to increase because of chronic rejection.



**Picture 2.** a. Axial contrast enhanced T1-weighted MR image; the right cerebellar lesion with a ring-like enhancement. b. Right cerebellar lesion has disappeared after completed radiotherapy

## Discussion

PCNSL may be a cause of intracranial mass lesions in patients with in renal allograft recipient treated by immunosuppressive therapy. In PCNSL, focal motor and/or sensitive neurological deficits are frequent, with manifestations of intracranial hypertension, personality disturbances, and behavioral changes when the frontal lobe is affected (4).

The optimal neuroimaging of PCNSL is gadolinium-enhanced MRI. Most lesions are supratentorial and periventricular, often involving deep structures such as the corpus callosum and basal ganglia. Lesions may be hypo- or hyper-intense on pre-contrast T<sub>1</sub> imaging. On T<sub>2</sub> weighted, most of the lesions appear hyperintense (5).

A stereotactic needle biopsy is the procedure of choice to establish a histopathologic diagnosis in patients with intracranial mass lesion. Microscopically, PCNSL is a diffuse lesion with an angiocentric growth pattern; some tumors may even invade the blood vessel wall (6). Morphologically, 98% of these tumors are large B-cell (CD 20+), diffuse, lymphomas categorized as high-grade non-Hodgkin's type. T-cell lymphomas (CD3+, CD45RO+) constitute only approximately 2% of all PCNSL. T-cell lymphomas occur more frequently in posterior fossa locales, particularly in the cerebellum, and also show a propensity to arise in the leptomeninges. (6)

PCNSL is a radiosensitive tumor, and whole-brain radiotherapy (RT) was the standard treatment for many years. Most treatment regimens now incorporate high-dose MTX (1 to 8 g/m<sup>2</sup>) alone or in combination with other chemotherapeutic agents followed by whole-brain RT. (7)

*Mycobacterium tuberculosis* infection of the CNS is an uncommon disease manifestation, but immunocompromised patients and solid organ transplant recipients involve a high rate of CNS tuberculosis. Three main forms have been described: cerebral tuberculoma, meningitis and spinal meningitis. Tuberculous involvement of the brain occurs during the hematogenous spread of mycobacteria from a primary pulmonary infection or, less frequently, during the course of chronic tuberculosis (8)

The pathologic features of tuberculosis are the result of the degree of hypersensitivity and the local concentration of antigen. When the degree of hypersensitivity is very

low, tissue reaction may be nonspecific, consisting of a few polymorphonuclear leukocytes and mononuclear cells with the huge numbers of tubercle bacilli, a condition termed nonreactive tuberculosis (9).

In CNS tuberculosis, clinical signs and symptoms generally change due to the nature of the involvement. In the cases with tuberculoma, symptoms may be related to mass effect, depending on the location and size. Intracranial hypertension may be present (e.g. papilledema/headache). Constitutional symptoms such as fever, night sweats, and weight loss are usually absent (10). In cases with tuberculous meningitis, the clinical spectrum is very broad, ranging from subtle headache or change in mentation over many weeks to sudden and severe meningitis. It is important to emphasize, however, that in 25% or more of such cases there is no clinical or historical evidence of either active or quiescent tuberculosis (9).

Our patient was admitted with nonspecific symptoms such as nausea, vomiting, headache, and vertigo. These features were attributed to the increased intracranial pressure and mass effect of the lesion. However, no clinical features favored tuberculosis.

Although radiological studies give invaluable information about intracranial masses, diagnostic evidence is generally obtained by histopathological and microbiological studies, which entails a brain biopsy. Our case had involvement in cerebral, cerebellar, and meningeal structures and brain biopsy surprisingly yielded both lymphoma and tuberculosis by histopathological and microbiological examinations respectively. The absence of typical histological features of tuberculosis can be explained by both obtaining a very small amount of tissue during the intervention and failure of the currently immunosuppressed patient to express a typical immune response.

Since the transplantation recipients are at an increased risks of developing malignancy and infection, CNS lesions should raise the suspicion of primary CNS lymphoma and tuberculosis. Although very rare, both disorders may complicate the same patient simultaneously.

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