



Primary Central Nervous System Lymphoma in a Renal Transplant Recipient With Bardet-Biedl Syndrome

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ABSTRACT

Bardet-Biedl syndrome (BBS) is a rare autosomal recessive disorder. End-stage renal failure has been reported as the most frequent cause of death in this disorder. There are few reports of kidney transplantation in these patients. Renal transplant patients are known to be at increased risk for the development of malignancies. Although a few patients with BBS have been described to develop malignant disease, there was no previous association with lymphoma. We report a 20-year-old patient in whom primary central nervous system lymphoma was diagnosed 20 months after renal transplantation.

BARDET-BIEDL SYNDROME (BBS) is an autosomal recessive disorder characterized by polydactyly, obesity, mental retardation, pigmentary retinopathy, hypogonadism, and renal disease.¹ BBS and Laurence-Moon syndrome (LMS) have a similar phenotype.² They are differentiated by the presence of spasticity and the absence of polydactyly in LMS.¹⁻³ BBS is more common than LMS.² Chronic renal failure has been reported in 30% to 60% of patients.^{3,4} Renal transplantation has been performed successfully in some cases.⁵⁻⁸ We present a renal transplant recipient with BBS who developed primary central nervous system lymphoma.

CASE REPORT

A 12-year-old female was diagnosed with BBS in 1996 due to complaints of amenorrhea, obesity, blindness, and polydactyly. She underwent successful preemptive renal transplant from a living relative in our center in April 2003 because of end-stage renal disease. Her immunosuppressive treatment consisted of prednisolone, mycophenolate mofetil, sirolimus, and daclizumab. In the postoperative period she experienced a ureteral leak that required a reanastomosis operation. In her follow-up, she had two rejection episodes, namely at 1 week and 5 months post-transplant which responded to steroids. The creatinine level after the last episode was 1.3 mg/dL. After 17 months, she complained of pain localized to the outer aspects of both thighs and legs. Osteonecrosis was diagnosed in both hips and distal tibias, as well as the right talus, navicular, and cuneiform bones. She commenced paracetamol, was advised to rest as much as possible, and to perform weight-bearing exercises. Then she had numbness in her legs. Her neurological examination was normal. Twenty months after transplant, she was admitted to the emergency department with syncope, convulsions, and severe leg pain. The serum creatinine level was 1.6 mg/dL. The cranial computerized tomography (CT) examination showed a mass lesion of 5 × 6 cm extending from the left cerebral hemi-

sphere to the superior left lateral ventricular corpus that contained patchy hypodense areas in the center and hyperdense areas at the periphery with surrounding edema. Upon subtotal resection, the specimen showed large-cell Non-Hodgkin's lymphoma (NHL) of B-cell origin with CD20-positive immunohistochemical staining (Fig 1). Abdominal, thoracic, pelvic, and neck CTs were normal and the bilateral iliac crest bone marrow biopsies were normocellular. The cerebrospinal fluid contained no malignant cells. Her serological tests were negative for cytomegalovirus, Epstein-Barr virus, and HIV. With these findings the patient was diagnosed as having a primary central nervous system (CNS) lymphoma confined to the CNS. Her immunosuppression continued except the mycophenolate mofetil. Six courses of chemotherapy (high-dose, intravenous and intrathecal methotrexate by 1-week intervals) were started with field radiation therapy planned.

DISCUSSION

In recent years, the nephrological community has become aware of the fact that renal impairment is an important feature of BBS. Renal abnormalities have been described in up to 100% of BBS patients. Renal function anomalies include urine concentration and acidification defects.⁹ Renal failure is the major cause of morbidity and early mortality in BBS.^{3,4,9} Although the etiology of end-stage renal disease in our case is unknown, chronic glomerulopathy and cystic tubulointerstitial disease in BBS and LMS may progress to chronic renal failure.¹⁰ Renal transplants

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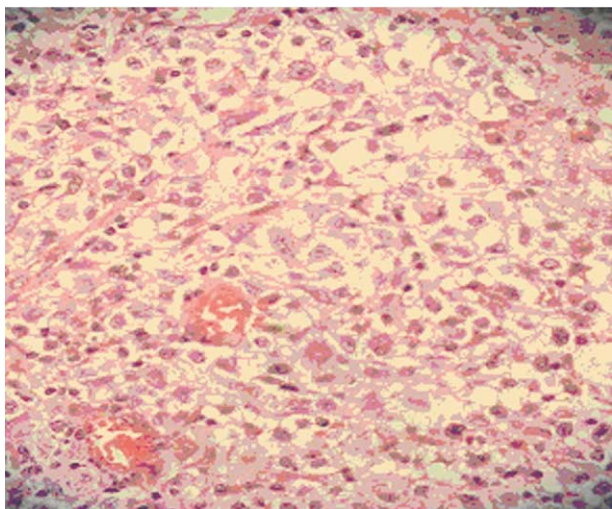


Fig 1. Photomicrograph showing diffuse malignant lymphoid cell infiltration of between glial tissues (Hematoxylin-eosin, original magnification $\times 400$).

have been performed in some cases, most of whom had morbid obesity after transplant.^{6–8} Our case had no weight gain.

Renal transplant patients are known to be at increased risk for the development of malignancies. Nonmelanotic skin and lip cancers, solid tumors, and malignant lymphomas account for the majority of these malignancies.¹¹ Lymphomas are mostly large B-cell type NHL with extranodal involvement. NHLs are also the most common primary intracranial neoplasms encountered in organ allograft recipients.¹² Currently, primary CNS lymphomas represent 4% to 7% of newly diagnosed primary CNS tumors, with an incidence rate of approximately 30 cases per million person years.^{13,14} BBS is a highly heterogenous genetic disorder. Six of the eight causative genes have been cloned, encoding proteins of largely unknown function.¹⁵ BBS genes have been suggested to play a role in renal malformations and renal cancer.¹⁶ Endometrial and common bile duct carcinomas have also been observed in patients with LMS or BBS.^{17,18} A recent report described new syndrome-tumor associations in several entities, including BBS (acute lymphoblastic leukemia).¹⁹ Only a few reports concerning the coincidence of intracranial tumor-related conditions associated with LMS or BBS: namely, pituitary eosinophilic adenoma, hypothalamic hamartoma, meningioma, diffuse brainstem glioma, and craniopharyngioma have been described in the literature.^{2,20–23} Whether the cause of primary CNS-NHL in our case is immunosuppressive therapies or a possible relation between cancer and BBS remains uncertain.

The diagnosis of CNS lymphoma is difficult. The diagnosis is suspected in renal transplant patients with mental status changes or new neurologic findings. There was no marked symptom indicating CNS lymphoma when our case was admitted to the emergency department because of

convulsions except for numbness in her legs starting a month prior. Untreated primary CNS lymphomas have a rapidly fatal course, with a survival of approximately 1.5 months from the time of diagnosis. Survival after radiation therapy ranges from 10 to 18 months, increasing to an average of 44 months following chemotherapy plus radiation, or chemotherapy alone.^{24,25} In treated patients who had disease confined to the CNS, the complete remission rate was 26% (29 of 111). Ten patients survived more than 5 years, among them six survived more than 10 years.¹² In conclusion, we have reported an interesting case presenting the first association of BBS and isolated CNS-NHL. Patients with BBS should be managed considering the possibility of the development of malignancies.

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