Lyme Meningoradiculitis and Myositis after Allogeneic Hematopoietic Stem Cell Transplantation

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We describe a patient with a history of allogeneic hematopoietic stem cell transplantation complicated by chronic graft-versus-host disease who developed painful meningoradiculitis and myositis due to Lyme borreliosis. To our knowledge, this is the first report of such an infection occurring after allogeneic hematopoietic stem cell transplantation in the United States.

Case report. A 44-year-old man with a history of chronic lymphocytic leukemia was in remission after receiving a non-myeloablative allogeneic hematopoietic stem cell transplant (HSCT) 2 years before admission, but he developed chronic cutaneous and mucosal graft-versus-host disease (GVHD) that required ongoing immunosuppression with mycophenolate mofetil and topical tacrolimus and dexamethasone. His past medical history was also remarkable for hypothyroidism, type II diabetes mellitus, recurrent sinusitis, and hypogammaglobulinemia treated with intravenous immunoglobulin supplementation every other month.

Eighteen days prior to admission in June 2004, the patient noted fever (temperature, 38.6°C) and was treated with levofloxacin. Six days later, he developed sudden onset excruciating lower-back pain radiating to both legs and pain between his shoulder blades. One day prior to admission, he developed progressive proximal leg weakness without bowel or bladder symptoms. On examination, he had an erythematous rash on the face and trunk with secondary lichenification and changes in his oral mucosa attributed to chronic GVHD. Numerous resolving papular lesions were also noted on his arms and legs; the patient attributed these to insect bites from a recent wild turkey-hunting trip in south central Maine. The findings of a neurological examination were significant for mild nuchal rigidity with meningismus, extreme pain on straight-leg raise to 10 degrees, bilateral 4/5 strength in hip and knee flexion, and ankle dorsiflexion. The patient was areflexic in his lower extremities and had flexor plantar responses bilaterally; the findings of his sensory examination were normal.

The patient’s blood leukocyte count was 3100 cells/μL, and his platelet count was 168,000 platelets/μL. The patient’s serum creatine kinase level was elevated at 437 U/L (normal range, 41–266), his aldolase level was 7.6 U/L (normal range, 1.5–8.1), and his thyroid-stimulating hormone level was 6 μU/L; the results of a screening antinuclear antibody test were negative. The patient’s IgG level was 731 mg/dL (normal range, 700–1600 mg/dL). A spinal MRI revealed subtle, homogenous enhancement of multiple nerve roots. Initial examination of CSF samples demonstrated a protein level of 283 mg/dL, a glucose level of 79 mg/dL, and 2 leukocytes and 1 erythrocyte per milliliter of CSF. Nerve conduction studies revealed reduced amplitudes of bilateral sural sensory nerve action potentials. Bilateral peroneal compound muscle action potentials and the left tibial compound muscle action potentials had normal amplitudes, mildly prolonged distal latencies, and moderate slowing of conduction velocities (33–34 m/s; normal value, >42 m/s). Tibial F waves were slightly prolonged (minimal latency, 65 m/s). The findings of nerve conduction studies of the arms were normal except for mildly prolonged median F waves (minimal latency, 37.4 m/s). Electromyography demonstrated fibrillation potentials and positive sharp waves in proximal and distal muscles of the left arm and leg and early recruitment of small motor unit action potentials in proximal muscles. The findings of the study were interpreted as showing evidence of mild polyneuropathy and superimposed necrotizing myopathy. A deltoid muscle biopsy specimen demonstrated many scattered necrotic and regenerating fibers, perifascicular atrophy, and perivascular inflammatory cell infiltrate centered around blood vessels and in the perimysial connective tissue. The patient started receiving 1 mg/kg per day of methylprednisolone and systemic tacrolimus for treatment of possible GVHD involving muscle or some other inflammatory myopathy. He also received 2 g/kg of intravenous immunoglobulin.

Two weeks into his hospital stay, the patient’s weakness progressed, and he was nearly plegic in both legs, although arm strength remained at 4/5. He experienced continued pain that
required intravenous hydromorphone and transdermal fentanyl for control. The findings of additional nerve conduction studies were essentially unchanged from those of the initial study. Electromyography continued to demonstrate widespread fibrillation potentials and positive sharp waves in the left arm and leg. Small-amplitude, short-duration motor unit action potentials that were recruited early were evident in the left arm. In the legs, however, there was reduced recruitment of motor unit action potentials.

Because of the history of a recent exposure in an area where Lyme disease is endemic, testing for Borrelia burgdorferi was performed. The results of a Western blot test of the initial CSF specimen were positive for B. burgdorferi IgG (MarDx Diagnostics; testing was performed at Associated Regional and University Pathologists, Salt Lake City, UT) (table 1) [1, 2], whereas the results of a peripheral blood EIA were negative. The patient initiated treatment with 2 g/day of ceftriaxone. An additional lumbar puncture demonstrated a protein level of 177 mg/dL, a glucose level of 144 mg/dL, and 2 leukocytes/μL CSF. The results of PCR of the CSF sample for B. burgdorferi were negative, but the sample was positive for IgG by Western blot analysis (table 1). The results of PCR of the CSF sample for the presence of herpes simplex virus, varicella-zoster virus, cytomegalovirus, Epstein-Barr virus, human herpes virus type 6, and enterovirus were negative. The results of Veneral Disease Research Laboratory and EIA testing of CSF for the presence of West Nile virus, eastern equine encephalitis virus, and lymphocytic choriomeningitis virus were negative.

The radicular and back pain resolved after 4 days of ceftriaxone treatment. The patient’s muscular strength also started to improve. Corticosteroid therapy was tapered to 20 mg of prednisone per day for treatment of chronic GVHD. The patient went to a rehabilitation facility for 1 month, where he completed 28 days of ceftriaxone therapy, with demonstrated full recovery of his strength at a follow-up examination 6 weeks later. Silver staining of the muscle biopsy specimen did not demonstrate spirochetes. The patient continues to do well a year after treatment.

**Discussion.** We describe a patient who developed Lyme meningoarachiditis and myositis after HSCT. To our knowledge, this is the first reported case of Lyme borreliosis in a transplant recipient in the United States.

The syndrome of lymphocytic meningoarachiditis (Garin-Bujadoux-Bannwarth syndrome) is a well-recognized complication of Lyme disease and is its most common neurologic manifestation in Europe [3]. This presentation seems to be less common in the United States, where facial palsy is the most frequently reported neurologic finding [3, 4]. In patients with borrelial polyradiculoneuropathy, radicular pain is characteristic. Other symptoms include back pain, dysesthesias, sensory loss, focal weakness, autonomic dysfunction, and loss of reflexes [5]. Lyme polyradiculoneuropathy can mimic other entities and has been misdiagnosed as disc herniation or lymphoma [6, 7]. Typical findings in the CSF include lymphocytic pleocytosis with elevated protein levels. Glucose level and opening pressure are usually normal. The detection of intrathecal synthesis of B. burgdorferi–specific antibodies is the best indicator of Lyme neuroborreliosis [2, 8, 9]. B. burgdorferi PCR of CSF has a reported median sensitivity of 38% [2, 9]. Case series have reported patients with neuroborreliosis whose blood samples had negative serological test results and whose CSF samples had positive antibody responses, as was the case for our patient [4, 5, 9, 10].

Our patient had evidence of polyradiculoneuropathy and a superimposed inflammatory myopathy that deserves special mention, given its rarity in cases of Lyme borreliosis. Diffuse myalgia and muscle stiffness are common in early infection, but frank myositis has rarely been associated with Lyme disease [10–13]. These patients usually report muscle pain and weakness. Physical examination can reveal muscle tenderness, edema, weakness, and atrophy. The distribution varies from generalized myositis to localized muscle pain. Patients can have concomitant manifestations such as rash, arthritis, myocarditis, or neurologic syndromes. The serum levels of creatine kinase are normal or slightly elevated for the majority of patients; very high levels are rare [10]. Myopathic findings with concomitant polyradiculoneuropathy have occasionally been identified [10, 11].

Reported histological findings of Lyme disease–associated myositis have not been uniform and include focal nodular myositis, interstitial myositis, and necrotizing myopathy [10, 14, 15]. Diffuse mononuclear infiltration and fiber degeneration are usually not seen. Interstitial lymphohistiocytic infiltrates with plasma cells are found predominantly in the vicinity of small endomysial vessels. Immunohistological examination shows infiltrates that mainly consist of CD4+ T lymphocytes and macrophages and fewer CD8+ T cells and B cells. Occasionally, the organisms can be seen after silver staining [10, 12, 14]. The perifascicular atrophy and perivascular, perimysial inflammation are characteristic of dermatomyositis. Cases of Lyme disease presenting as dermatomyositis [16] and rehab-

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**Table 1. Western blot analysis of IgG antibodies against Borrelia burgdorferi in CSF samples from a patient with a history of allogeneic hematopoietic stem cell transplantation complicated by chronic graft-versus-host disease.**

<table>
<thead>
<tr>
<th>Date of CSF sampling</th>
<th>Result, by B. burgdorferi protein band in kDa</th>
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<tbody>
<tr>
<td>5 Jun 2004</td>
<td>++++ + + + + + + + + + + + + + + + + +</td>
</tr>
<tr>
<td>19 Jun 2004</td>
<td>+ + + + + + + + + + + + + + + + + +</td>
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**NOTE.** An assay with ≥5 positive bands was considered to have positive results [1, 2].
domyolysis complicating severe myositis have been reported [13].

It is surprising that only 2 case reports of Lyme borreliosis involving transplant recipients have been published to date (both of them from Europe), despite the fact that Lyme borreliosis is the most common tick-borne illness in the United States [17, 18]. Our patient had typical symptoms and signs of polyradiculopathy and myopathy. The clinical course and laboratory and biopsy findings were similar to those described for immunocompetent patients, although the tempo of the presentation seemed to be accelerated. The renal transplant recipient described by Chochon and colleagues presented with a focal rash and painful radiculoneuritis that progressed to encephalitis [17]. The heart transplant recipient with recurrent Lyme carditis described by Habedank and colleagues had diffuse interstitial fibrosis and areas of fiber necrosis on myocardial biopsy [18]. Both patients recovered after receiving adequate antimicrobial treatment. The negative serological test results for our patient may have been explained by his receipt of chronic immunosuppressive treatment for GVHD and intravenous IgG supplementation. This highlights the difficulty in confirming a diagnosis of Lyme borreliosis in chronically immunosuppressed HSCT recipients with use of the current serological approach.

On the other hand, the presence of B. burgdorferi IgG in CSF samples was diagnostic, given the clinical presentation. Although we could not demonstrate spirochetes during analysis of the muscle biopsy specimen, the patient’s clinical course worsened despite the receipt of high-dose steroids, tacrolimus, and intravenous IgG; however, his response to antimicrobial therapy was dramatic, suggesting that Lyme borreliosis caused both the myositis and the painful polyradiculopathy.

It is important to consider Lyme disease in the differential diagnosis of rheumatologic and neurologic problems when evaluating transplant recipients who are living in areas of endemicity, especially after obvious exposures. These patients should be carefully reminded of how to avoid or minimize the risks of tick-borne illnesses. Antimicrobial treatment against Lyme borreliosis should be considered for chronically immunocompromised patients who present with typical signs and symptoms, even when serological test results are uninformative.

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References