Neurolymphomatosis: A Case Study of Diffuse Large B-Cell Lymphoma

Jessica N. Casselberry, OCN®, MSN, ANP-BC, and Alan D. Kritz, MD

Neurologic changes can be seen during treatment for hematologic malignancies such as lymphoma and leukemia. Differential diagnoses for neurologic changes remain vast, and etiologies may result from malignant, nonmalignant, and paraneoplastic syndromes. This article describes a case study of a man with neurolymphomatosis, a rare neurologic manifestation seen in B-cell and non-Hodgkin lymphoma and acute leukemias.

E xperiencing dyspnea and profound weakness, B.L., a 64-year-old man, presented to the emergency room in February 2011. He had a white blood cell count of 4,300 mcl, hemoglobin level of 5.3 g/dl, and platelet count of 16,000 mcl. The initial peripheral blood smear appeared to show acute lymphoblastic leukemia. However, the final pathology revealed high-risk, CD20-positive, stage IVB diffuse large B-cell lymphoma. B.L. also presented with high-risk features including bone marrow involvement, a palpable spleen, elevated lactate dehydrogenase, and poor performance status.

B.L. was treated with standard R-CHOP (rituxan, cyclophosphamide, vincristine, doxorubicin, and prednisone) chemotherapy for six cycles. Although the initial staging lumbar puncture was negative, with his aggressive leukemic phase presentation and bone marrow involvement, B.L.’s central nervous system was prophylaxed during treatment with intrathecal methotrexate biweekly.

Post-treatment positron-emission tomography/computed tomography (PET/CT) scan was consistent with complete remission, and cerebrospinal fluid analysis remained negative throughout treatment. B.L. then was seen at a local academic medical center for consideration of peripheral stem cell transplantation.

During pretransplantation evaluation, B.L. was noted to have evolving progressive new lower extremity weakness over three to four weeks, necessitating the use of a wheelchair. That new weakness delayed the transplantation as the next four months involved multiple hospitalizations for continued neurologic deterioration. His neurologic changes included development of left third cranial nerve palsy and severe bilateral motor neuropathy with a component of sensory neuropathy. Repeat PET/CT scan of the brain and spine and cerebrospinal fluid analysis remained negative. A magnetic resonance imaging (MRI) scan was not performed because B.L. had a permanent pacemaker.

Neurology was consulted and B.L. was diagnosed with an atypical Guillain-Barre syndrome and treated with high-dose steroids and IV gammaglobulin, despite no evidence of recurrent disease. B.L.’s condition continued to decline, and seven months after his initial diagnosis (three months after the onset of neurologic decline), he transitioned to palliative care, where he died.

Given the unusual neurologic manifestations, a postmortem examination was performed of the spinal cord and nerves, which showed diffuse infiltrates of his original diffuse large B-cell lymphoma within the peripheral nerves of the cauda equina, leading to paralysis and a final diagnosis of neurolymphomatosis (NL).

NL is a rare neurologic manifestation most often associated with B-cell non-Hodgkin lymphoma but also seen with leukemia where malignant cells infiltrate the nerve root, resulting in neurologic deterioration (Grisariu et al., 2010). The incidence of NL is unknown because a majority of the information available is based on case reports, with Grisariu et al. (2010) citing only 72 cases of NL occurring since 1980. The main characteristics associated with NL include painless or painful involvement of singular or multiple peripheral nerves, nerve roots, or cranial nerves (Baehring, Damek, Martin, Betensky, & Hochberg, 2003; Cheung et al., 2012; Grisariu et al., 2010).

Diagnostic Evaluation

Diagnosing NL often is challenging because the symptoms can fit a variety of diagnoses. Patients often present with diffuse disease, but single-site peripheral nerve involvement with no evidence of disease elsewhere, including the cerebrospinal fluid, has been reported (Baehring et al., 2003; Gan, Azad, Cher,
Gan et al. (2010) reported an overall response rate of 82% in 38 patients treated with chemotherapy alone with control of disease lasting only two weeks, as most responses do not remain durable. However, an unspecified number of rare patients who were treated with methotrexate were still living nine years after NL diagnosis (Gan et al., 2010). In contrast, Grisariu et al. (2010) reported an overall response in 46% of patients from their retrospective analysis (N = 50) during a 16-year period. Modern agents such as rituximab have not shown vast improvement in the treatment of NL. Because of the large size of the rituximab molecule, its ability to penetrate the central and peripheral nervous systems is poor (Gan et al., 2010). Methotrexate can penetrate the blood-brain barrier, and when given via IV every two weeks at a dose of 8 g/m², can provide therapeutic concentrations to the brain, cerebrospinal fluid, intradural and extradural nerves, and roots, with clinical improvement after six cycles (Baehring et al., 2003; Grisariu et al., 2010).

Baehring et al. (2003) also reported the use of radiation therapy with curative or palliative intent with sites including the craniospinal axis and lumbosacral roots. NL often involves nerve roots beyond the subarachnoid space, making the traditional treatments of craniospinal radiation and intrathecal chemotherapy ineffective (Baehring et al., 2003). Survival data and standard treatments do not exist and are not adequately outlined as systematic studies have not been conducted (Grisariu et al., 2010).

Discussion

Despite aggressive neurologic workup in the case of B.L., his NL remained undiscovered until autopsy. In addition, he developed NL despite six cycles of R-CHOP and four months of intrathecal methotrexate, with all of his cerebrospinal fluid cytologies remaining negative. His initial diagnosis of Guillain-Barre syndrome led to treatment with high-dose steroids and IV gammaglobulin, and he had transient response and minimal neurologic improvement after the first two treatments. According to Baehring et al. (2003), NL’s transient response to corticosteroids is “short-lived and does little other than to obscure the diagnosis” (pp. 111–112). Further neurologic evaluation was believed to be consistent with the diagnosis of chronic inflammatory demyelinating polyneuropathy but, unfortunately, additional treatment with high-dose steroids and IV gammaglobulin did not lead to neurologic improvement. Radiation to the lumbosacral nerve roots could have been effective if the diagnosis had been made antemortem.

Implications for Nursing and Conclusions

Diagnosis and treatment of NL remains elusive, and prognosis often is poor. NL is a rare manifestation associated most often with B-cell non-Hodgkin lymphoma, and patients often show no signs of disease via PET, CT, or MRI scan and cerebrospinal fluid analysis. Unfortunately, most patients will remain undiagnosed until time of postmortem examination. Of those diagnosed early enough to receive aggressive treatment, most will have disease progression and eventually die (Gan et al., 2010). Providers must remain vigilant and consider NL when patients with a history of aggressive diffuse large B-cell lymphoma develop unusual, progressive peripheral neurologic changes. Increased awareness with earlier diagnosis and appropriate treatment can lead to improved outcomes as healthcare providers learn more about this rare neurologic manifestation.

References