Cauda equina syndrome secondary to intravascular lymphoma

Ahmad Abuzinadah, MBBS

Yaser Almalik, MBBS

Meer-Taher Shabani-Rad, MD, FRCPS

Chester H. Ho, MD

David George, MD

Jacob Alant, FRCS

Douglas Zochodne, MD, FRCP

Intravascular lymphoma (IVL) is an extranodal B-cell lymphoma that involves the lumina of small and medium size vessels.¹ Neurologic presentations are varied and include encephalopathy, myelopathy, and polyradiculoneuropathy, among other features.^{1,2} Cauda equina syndrome (CES) with IVL has been identified late, either at autopsy or after complications such as flaccid paraplegia.^{2–4} Early diagnosis and treatment before disease dissemination is difficult but increases progression-free survival and remission.¹ We describe a patient with isolated CES and subtle non-nodular MRI nerve root enhancement, who was identified to harbor IVL by cauda equina biopsy.

A 70-year-old man presented with a 4-week history of perineal, patchy lower limb numbness and urinary retention. Neurologic examination disclosed absent ankle reflexes and sensory alterations in the back of his thighs and perineal region in an S2–S5 distribution. He had an absent anal wink.

Normal investigations included complete blood count, electrolytes, creatinine, urea, thyroid-stimulating hormone, B12, hepatic enzymes, serology for hepatitis B and C and HIV 1 and 2, and paraneoplastic antibodies. Lactate dehydrogenase was elevated (460 U/L; normal 100–235). Serum protein electrophoresis identified an immunoglobulin G (IgG) κ monoclonal protein (1.3 g/L). CSF had an elevated protein (0.53 g/L, normal 0.15–0.45 g/L), normal glucose, and elevated leukocytes (6.7×10^6 /L) without erythrocytes. Negative CSF studies included fungal and bacterial cultures, PCR for herpes simplex virus, varicella zoster virus, Epstein-Barr virus, enterovirus, and flow cytometry. CSF protein electrophoresis disclosed oligoclonal bands and an IgG κ monoclonal protein.

Electrophysiologic studies identified declines in peroneal compound muscle action potential amplitudes bilaterally with preserved tibial motor, sural, and superficial peroneal sensory conduction. EMG showed fibrillation potentials and positive sharp waves in the right medial gastrocnemius and enlarged motor unit potential amplitudes in the right tibialis anterior and left medial gastrocnemius muscles. Lumbar spine MRI showed smooth, diffuse enhancement of the nerve roots in the cauda equina (figure, A and B). The appearance was interpreted as

University of Calgary, Calgary, Canada.

Correspondence to: dzochodn@ucalgary.ca

Figure Lumbar spine MRI and S2 nerve root biopsy

Noncontrast T1 lumbar spine imaging shows normal intensity signals in the cauda equina nerve roots (A); however, the contrast-enhanced images highlight abnormal diffuse smooth enhancement (arrows) (B). Large atypical lymphoid cells are seen within intravascular spaces as well as severe, active, and chronic axonal degeneration of the spinal root (C; hematoxylin & eosin and Luxol fast blue staining with enlarged lymphomatous cells within the inset). Intravascular large B-cells are positive for CD20 (D) as well as CD5 (E). The latter finding is seen in 30%-40% of cases of intravascular large B-cell lymphoma. The neoplastic B-cells are also positive for MUM-1 (F). C bar = 100 μ m, D-F bar = 20 μ m.

inflammatory. Enhanced CT scan of chest, abdomen, and pelvis, bone marrow biopsy, liver biopsy, and skeletal survey were normal.

Given the inflammatory MRI appearance without systemic tumor, the patient was treated with a 5-day course of methylprednisolone, with transient benefit. Neurologic decline ensued, however, with diffuse loss of lower limb muscle power, loss of his ability to walk or self

transfer, and the development of bowel and bladder dysfunction. Five months after initial presentation, the patient underwent a cauda equina S2-nerve root biopsy that identified intravascular large B-cell lymphoma. The intravascular large neoplastic lymphoid cells were positive for CD5, CD20, BCL-2, MUM-1, and Ki67 (figure, C–F).

The patient received radiotherapy 3,000 Gy over 10 fractions directed to the lumbar spine and 2 doses of rituximab (325 mg/m²/dose), 1 dose of methotrexate (5 g/m²/dose), and 1 cycle of CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone).

His course was complicated by increased lower limb weakness, peripheral facial paralysis, hearing loss, radiation-related colitis, and aspiration pneumonia with sepsis requiring a 13-day intensive care unit admission. Despite the development of additional cranial symptoms, likely from IVL, no imaging correlate by enhanced brain MRI was identified. At his request, additional chemotherapy was withheld. Seven months after diagnosis, he had made significant recovery in muscle power and assisted ambulation. The patient was self catheterizing and bowel incontinence had resolved.

DISCUSSION

Our patient had CES as an initial presentation of IVL. MRI showed diffuse nerve root enhancement. The diagnosis was made through a cauda equina nerve root biopsy, an uncommon diagnostic approach toward CES. IVL may cause neurologic deficits through either ischemia or infiltration,⁵ and generally has a rapidly fatal outcome, with a reported median survival of 5–7 months.⁶ However, IVL could potentially carry a better prognosis if therapy is instituted early, before irreversible damage.⁵

Of 3 cases of IVL presenting with CES, 2 were diagnosed at autopsy^{3,4} and 1 on muscle biopsy after flaccid paraplegia.² The consistent features in these patients and our patient were elevated CSF protein and serum LDH. When rituximab was added to the chemotherapeutic regimen in systemic IVL, the progression-free survival at 2 years increased from 27% to 56%. Additional methotrexate may be necessary to improve the outcome when there is CNS involvement.¹

In a patient with an isolated CES, cauda equina root biopsy may allow a targeted diagnosis given that IVL may be only one possibility. Diffuse nerve and nerve root enhancement has been reported in 17% of patients with neurolymphomatosis.⁷ Patients with suspected IVL or neurolymphomatosis may have subclinical systemic involvement—not seen in our patient—and supporting a suggestion that random nerve, skin, and other biopsies can be considered. Alternatively, PET scan may identify subclinical involvement.⁸ In our patient, the sural nerve action potential was normal, arguing against its potential value in diagnosis. Elevations of LDH, CSF protein, and the presence of a monoclonal protein may support a diagnosis of IVL.

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DISCLOSURES

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