A Case of Diffuse Large B-Cell Lymphoma Presenting as Transverse Myelopathy

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Background: In patients with lymphoma, transverse myelopathy can be induced by direct infiltration of tumor cells into spinal cord, ischemic cord change secondary to intravascular infiltration of tumor cells or immunogenic paraneoplastic syndrome. We report an unusual case of diffuse large B-cell lymphoma presenting as transverse myelopathy. Case Report: A 78-year-old woman was presented with paraparesis and hypoesthesia below T6 level. C-T-L spine magnetic resonance image (MRI) showed multiple bulging discs without signal change on spinal cord. Brain MRI and CSF study showed no specific finding. After steroid pulse therapy, paraparesis was partially improved. Two months after the onset, papaparesis and hypoesthesia were aggravated. Spine MRI showed increased signal intensities on T2-4 level without contrast enhancement. Ultrasonography-guided lymph node biopsy confirmed diffuse large B-cell lymphoma. Conclusion: Our patient presented with only clinically suspected transverse myelopathy, which turned out to be paraneoplastic. Underlying lymphoma could be revealed by unusual clinical courses and careful physical examination.

Introduction

Lymphoma may be associated with neurological symptoms in various ways such as direct metastasis to central nervous system (CNS), opportunistic infection or paraneoplastic syndrome. Paraneoplastic neurological diseases (PNDs) are a rare group of syndromes that occur in patients with cancer and which are not due to the presence of metastases or direct infiltration of the tumor into the nervous system. Most of PNDs are associated with lung cancer, lymphoma and gynecological tumors. The anatomical distributions of PNDs include muscle (polymyositis), neuromuscular junction (Lambert-Eaton myasthenic syndrome, myasthenia gravis and neuromyotonia), peripheral nerves (neuropathies and polyradiculopathies) and CNS. PNDs involving CNS can clinically present as subacute cerebellar degeneration, encephalomyelitis (limbic encephalitis, brainstem encephalitis, myelitis) or opsoclonus-myoclonus syndrome. But, there are few reports available on lymphoma primarily causing neurological signs, especially with paraneoplastic myelopathy. We report a 78-year-old woman presenting with transverse myelopathy in whom lymphoma was discovered at lymph node biopsy after 2 months.

Case

A 78-year-old woman presented with 18 days history of ascending sensory loss, progressive weakness of both legs and dysuria. She didn’t complain back pain, weight loss or night sweating. Her medical history was unremarkable except hypertension under control. On neurological examination, higher cortical function and cranial nerve functions were normal. Motor power was MRC grade II at both legs and sensory level was present at T6 level. Deep tendon reflexes were hyperactive at both knee and ankle joint, but Babinski’s sign was absent. Magnetic resonance imaging (MRI) study was performed on C-T-L spine areas. There were postero-central disc herniations and bulging discs at many cervical and lumbar areas without cord compression, and there was no evidence of spinal cord lesion (Fig. 1A, B). Nerve conduction studies showed decreased amplitude but normal conduction velocity on left sural nerve. Somatosensory-evoked potentials of the median and posterior tibial nerves showed normal latencies and amplitudes. Studies of biochemical profiles including thyroid function, urine analysis, antinuclear antibody, antiphospholipid antibodies, anti-SS-A/SS-B anti-
bodies were not remarkable. Vitamin levels including vitamin B₆ (53.6 nmol/L, normal range: 21.6–104.1 nmol/L), B₁₂ (1,912 pg/mL, normal range: 211–911 pg/mL), E (0.99 mg/dL, normal range: 0.75–1.41 mg/dL) and folate (14.75 ng/mL, normal range: 3.45–13.77 ng/dL) were within normal ranges. The patient was seronegative for syphilis serology, human T-cell lymphotrophic virus-I, human immunodeficiency virus (HIV), IgM for HSV and CMV, and paraneoplastic antibodies including anti-VGCC (voltage-gated calcium channels), antiHu, anti-Ri and anti-Yo. Serum lactate dehydrogenase was 1,028 U/L (normal range: 200–470 U/L). Cerebrospinal fluid (CSF) examination showed normal protein level (38 mg/dL) without pleocytosis. No malignant cell was found on cytological examination. Myelin basic protein was elevated by 7.20 ng/mL (normal range: 0–2.0 ng/mL). IgG index was within normal range (0.47) and no oligoclonal band was detected from CSF. She was treated with a five-day course of intravenous steroid therapy of 1.0 gram/day and there were partial improvement of motor (MRC grade III) and sensory symptoms.

Two months after the onset, paraparesis was aggravated and she had to be hospitalized again. Neurological examination showed MRC grade 0 on both legs and sensory level at T4. Physical examination revealed 1.5 cm sized palpable mass on right lower abdomen and right axillary region. Repeated spinal MRI scans revealed poorly delineated increased signal intensity in spinal cord of T2-T4 level on T2WI. There was neither enhancement nor mass effect in that lesion (Fig. 1C, D). Ultrasound assisted needle biopsy was performed on a 1.5×1.4×0.9 cm sized mixed echoic nodule within the subcutaneous fat layer of the abdominal wall. Biopsy specimens of the lymph nodule revealed that the infiltration was composed of large lymphoid cells. Immunohistochemical investigations demonstrated that the majority of large lymphoid cells strongly expressed the L26 and CD79a antigen, and partial composition of them expressed the CD43 and CD5 antigen (Fig. 2). The patient did not consent to chemotherapy and she died four months after the symptom onset.

**FIGURE 1.** Spinal cord MRls at first presentation and 2-months later. A, B: There is no abnormal signal intensity on cervico-thoracic spinal cord at initial MRI (A: T2WI, B: T1WI). C, D: After two months later, there is increased SI without enhancement in the spinal cord of T2-T4 level (C: T2WI, D: Enhancement study).

**FIGURE 2.** Ultrasonography on abdominal wall and pathological findings. A: About 1.5×1.4×0.9 cm sized mixed echoic nodule exists within the subcutaneous fat layer of the abdominal wall on RLQ area. B, C: Pathological study of abdominal lymph node shows diffuse large B-cell lymphoma (A: H-E stain, B: CD20 immunohistochemical stain).
A postmortem examination was not performed.

**Discussion**

Current WHO modification of the REAL classification recognized three major categories of the lymphoid malignancies based on morphology and cell lineage: B-cell neoplasms, T-cell/natural killer-cell neoplasms, and Hodgkin’s lymphoma. Among B-cell neoplasms, diffuse large B-cell lymphoma (DLBC) is the most common type. It is also the most common type of the aggressive lymphoma. The international prognostic index for aggressive non-Hodgkin’s lymphoma identifies five significant prognostic factors of overall survival: age, serum lactate dehydrogenase (LDH), performance status, stage, and extranodal site involvement. This patient had all of the risk factors (age over 60 years, high serum LDH level, completely disabled performance status, advanced stage and extranodal site involvement) to show poor prognosis.

In lymphoma, neurological symptoms of myelopathy can be caused by two ways of direct involvement of the spinal cord. One mechanism is tumor cell invasion of spinal cord proper. Epidural, intradural-extradural, and intramedullary spinal cord metastasis of lymphoma was previously documented. Primary intramedullary lymphoma of the spinal cord is an uncommon neoplasia, and hyperintensities on T2WI could be the key to diagnosis of ALCL. Another characteristic clinical findings of ALCL were lymphadenopathy and skin rash. Compared to our case, transverse myelopathy, negative cerebrospinal fluid and elevated serum LDH were compatible findings. However, lymphadenopathy and lack of skin rash in our patient were against ALCL. Most of all, direct spinal cord involvement of above mechanisms is not suggested because initial MRI findings was negative in our patient. Intradural-extradural leptomeningeal involvement could also be excluded by negative CSF findings including cytology, protein and glucose levels, and opening pressure.

Immunogenic paraneoplastic syndrome can appear as myelopathy, and underlying pathological findings are variable including inflammation, demyelination and necrosis. MRI may be normal or show spinal cord swelling regardless of contrast medium enhancement. The absence of epidural mass or discrete intramedullary enhancement rules out metastatic myelopathy, which is more common. It is suggested that PNDs including myelopathy come from the disturbance of immunologic reaction, and antigen-derived oligoclonal cytotoxic T-cell response may be involved. It may also be caused by the overproduction of cytokines and ectopic hormone production in patients with lymphoma. Treatment is usually unsuccessful; however, there are some reports to have responded to steroid or underlying malignancy therapy. We assume that the response to treatment is inconsistent because of these variable pathogenesis and pathologic findings in paraneoplastic myelopathy.

In general, investigation of a patient suspected of having paraneoplastic syndrome might fail to reveal the tumor until it becomes symptomatic, typically 3—13 months later. Our patient showed myelopathy as presenting symptom of DLBC, which finally diagnosed after two months. We could not confirm the pathology of the spinal cord and find a paraneoplastic antibody in our case. However, because this patient had steroid responsiveness, normal serum and CSF findings, initially normal spinal cord images, and progressive clinical deficit, immune-mediated paraneoplastic process is probable pathophysiology in this patient.

**REFERENCES**

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