Primary Cranial Central Nervous System Lymphoma with Seeding Metastasis to the Spinal Cord

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INTRODUCTION

Primary cerebral nervous system lymphoma (Primary CNS Lymphoma, PCNSL) is an aggressive non-Hodgkin's lymphoma that originates from the central nervous system (CNS) without any other evidence of lymphoma at the time of diagnosis. These rare tumors account for 1% to 3% of CNS neoplasms (12). PCNSL may occur in all areas of the brain; however, primary lymphomas of the spinal cord are extremely rare.

We present a patient who developed a massive lymphoma encompassing the entire spinal cord that exhibited seeding metastasis after comprehensive treatment of a primary cerebral lymphoma and cerebral relapse.

CASE PRESENTATION

An 81-year-old male patient presented with progressive weakness in all extremities, complaining of back pain, as well as transient confusion and loss of consciousness. The patient's complaints had started two weeks before his admission to the hospital. The medical history of the patient was obtained from family members. The first complaint was headache and nausea starting 4 months before clinical presentation, when the patient was being followed up with a diagnosis of primary brain lymphoma. Cranial magnetic resonance imaging (MRI) revealed a frontal periventricular lesions. At that time, whole spinal cord MRI was normal. A positron emission tomography scanning (PET/CT) showed a pathological accumulation...
of 18-FluoroDeoxyGlucose (18-FDG) only on the lesion side of in the brain. A stereotactice brain biopsy was performed from the left frontal periventricular region of increased MRI signal intensity. Histological examination revealed a primary cerebral lymphoma (non-Hodgkin's diffuse B-cell lymphoma). Both radiotherapy and chemotherapy were refused by the patient's family, and he had only been treated palliatively with analgesics and corticosteroids prior to admission to the ward. Upon examination, vital signs were normal. He was confused and disoriented. The fundus examination showed bilateral papilledema. The clinical condition worsened with the development of quadripareisis and incontinence. Weakness in the lower extremities was more significant than in the upper extremities. Slit-lamp examination showed no ocular involvement. Whole-body computed tomography (CT) scans and bone marrow biopsy were also performed. There was no history suggestive of immunodeficiency disorders.

A cranial MRI showed traces of stereotaxic needle biopsy on the left frontal lobe. Lesions located within the genu of the corpus callosum and the anterior horn of lateral ventricle were isointense to slightly hypointense on T1-weighted studies, and iso- to slightly hyperintense on T2-weighted studies (Figure 1A,B). A whole spinal MRI demonstrated enlargement of the spinal cord, and an intramedullary lesion between C4 and D12 (Figure 2A,B). Cerebrospinal fluid (CSF) analysis determined protein levels up to 1500 mg/L and pleocytosis up to 50 cells/mL, without oligoclonal banding. Lymphoblast cells were seen in the CSF. The patient family members refused all further treatment. Only palliative treatment to resolve myelitis was given (500 mg/d prednisolone, i.v.). The patient died 4 months after diagnosis. A postmortem needle biopsy of the spinal cord showed lymphoblastic deposits (Figure 3).

DISCUSSION

Primary PCNSL is uncommon and accounts for approximately 1% to 3% of CNS neoplasms (12). Patients recommended for PCNSL staging include three risk groups: transplant recipients; those with congenital immunodeficiency disease syndrome; and patients infected with the Epstein-Barr virus. Age over 60 years appears as a strong negative prognostic factor in all series (1,3,9). It can affect any location in the neuraxis including the eyes, brain, leptomeninges, or spinal cord. Owing to the rarity of PCNSL the disease has been challenging to study and an effective standard of care has not been established (2,7). The clinical history of the presented case revealed none of the aforementioned risk groups, but the patient was over 60 years old.

The cerebral hemispheres, particularly the periventricular site, as well as the basal ganglia, thalamus, brain stem, and cerebellum, are the most commonly involved sites. The supratentorial structures are involved in 75% of patients. Up to 75% of lymphomatous masses are in contact with ependyma, meninges, or both (11,13).

Non-Hodgkin’s lymphoma of the spinal cord, as a form of PCNSL, is very rare. However, it is expected to be more common as a secondary lesion to the intracranial focus, probably after a seeding metastasis.
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for whom spinal cord or leptomeningeal spread is suspected (6). MRI presents intraspinal lymphoma as an intramedullary, contrast-enhancing lesion yielding a markedly high signal on T2-weighted images. These lesions are very similar to intracranial PCNSLs, with strong contrast enhancement without central necrosis in over 90% of cases and substantial edema in more than half of the cases. Characteristic imaging features should be suggestive of the diagnosis. Early neurosurgical consultation for stereotactic biopsy is very important with the avoidance of corticosteroids (7). It is clear that PCNSL may involve the brain, CSF and eyes. Therefore, diagnostic examination should also include evaluation of these regions (2, 7). In primary spinal lymphoma, these findings are not specific. Differential diagnosis includes malignant glioma, metastasis and inflammatory diseases and transverse myelitis (8). Therefore, a biopsy should be obtained when there is doubt about the nature of the process, or when steroid therapy has failed (4). However, leptomeningeal involvement is more likely in the presence of an intracranial lesion. In published reports, most intramedullary non-Hodgkin’s lymphoma lesions

Gadolinium-enhanced MRI of the brain serves as an important pretreatment baseline. Spinal MRI is not part of routine staging, but should be performed in patients

Figure 2: Sagittal T2-weighted A) cervical, B) thoracic spinal MRI demonstrated enlargement of the spinal cord, with thickening and an intramedullary lesion between C4 and D12.

Figure 3: Postmortem needle biopsy of spinal cord confirmed non-Hodgkin diffuse B-cell lymphoma. Section of intramedullary tumor showing diffuse infiltration by lymphoblasts (H&E x40) (white arrows).
are found in the upper thoracic or lower cervical (cervico-thoracic junction) regions of the spinal cord (1,8). Seeding metastasis to spinal cord after intracranial PCNSL is seen very rarely. However, Kawasaki suggested that spinal cord involvement was not a rare event in PCNSL and that there were two routes of spread: direct invasion from the medulla oblongata and dissemination via the CSF (10). The presented case highlights the unusual involvement of the entire spinal cord.

Clinical improvement was seen after treatment with an intrathecal chemotherapy, radiation therapy or a combination of both in more than 80% of the primary cranial CNS lymphoma patients (5,12). The median survival was 3.5 months; 32% of patients survived to 6 months. Progression of systemic disease was the most frequent cause of death (6). Resection provides no therapeutic benefit and should be reserved for the rare patient with neurological deterioration due to brain herniation (2).

In conclusion, PCNSL can spread as a seeding metastasis to the entire spinal cord. Gadolinium-enhanced MRI of whole spinal cord should be performed as part of the routine staging assessment in patients with PCNSL in order to avoid late diagnosis of spinal cord lymphoma and to prevent unsuccessful treatment.

REFERENCES