

# Primary CNS T-Cell Lymphoma of the Spinal Cord: Case Report and Literature Review

Melissa Guzzetta, DO,<sup>1</sup> Steven Drexler, MD,<sup>2\*</sup> Brian Buonocore, MD,<sup>3</sup> Virginia Donovan, MD<sup>2</sup>

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## ABSTRACT

Primary central nervous system lymphoma (PCNSL) accounts for 1% of all lymphoma diagnoses and as many as 6% of all central nervous system (CNS) tumors. Most cases of PCNSL are of B-cell type; few are of T-cell lineage. PCNSL mainly occurs intracranially; primary spinal-cord lymphoma only occurs rarely. Moreover, intramedullary

presentation without intracranial lesions is virtually unknown. Herein, we present a case of primary T-cell CNS lymphoma limited to the intramedullary spinal cord in an 82-year-old white man, along with a review of the literature on this condition and similar conditions.

**Keywords:** Primary CNS lymphoma, primary intramedullary spinal cord lymphoma, CNS T-cell lymphoma

Primary central nervous system lymphoma (PCNSL) accounts for only 1% of all lymphoma diagnoses and between 0.8% to 6.6% of all central nervous system (CNS) neoplasms.<sup>1</sup> Most CNS tumors involve the supratentorial space (60%); in these tumors, the posterior fossa (13%) is less commonly involved and the spinal cord (1%) is rarely involved.<sup>1,2</sup> Moreover, spinal cord neoplasms are generally uncommon. These lesions are classified as *intramedullary* (occurring within the spinal cord parenchyma) or *extramedullary* (occurring outside the spinal cord). Intramedullary spinal tumors account for 5% to 10% of spinal tumors, most of which are glial in origin; an extremely small percentage of these are lymphomas.<sup>3</sup> This finding contrasts with that of spinal involvement in systemic lymphoma, in which diffuse leptomeningeal involvement and extradural nodules are usually present.<sup>4</sup>

Most lymphoma diagnoses are of B-cell lineage and are seldom of T-cell lineage. There are only a few reported cases of T-cell PCNSL.<sup>1,5</sup> For instance, approximately 20 years ago, Memorial Sloan Kettering Cancer Center in New York City reported 200 cases of PCNSL, of which only 2 were of T-cell origin.<sup>6</sup>

## Case Report

An 82-year-old white man reported progressive lower back pain and weakness of the lower extremities over a period of 1 year. Magnetic resonance imaging (MRI) of the thoracic and lumbar spine showed a signal abnormality from T7, the conus medullaris, with clumping and enhancement of the cauda equina. The patient had a full neurological workup, including lumbar punctures that tested negative for malignant neoplasms but positive for acute inflammatory cells consistent with meningitis. We also performed a head computed tomography (CT) scan that revealed no evidence of acute intracranial abnormality or acute territorial infarction. The patient underwent nerve-conduction studies and needle electromyography (EMG) for both lower extremities. The findings showed an absence of nonspecific lower-extremity motor responses. In isolation, the significance of these findings was unknown; however, we observed them in a central spinal cord lesion, as demonstrated by the MRI findings (**Image 1**). Over the course of the 12-day

### Abbreviations:

PCNSL, primary central nervous system lymphoma; CNS, central nervous system; MRI, magnetic resonance image; CT, computed tomography; EMG, electromyography; GMS, Grocott-Gomori methenamine-silver stain; PAS, periodic acid–Schiff stain; AFB, acid-fast bacillus; CSF, cerebrospinal fluid; TCR, T-cell receptor; NHL, non-Hodkin lymphoma; PCR, polymerase chain reaction

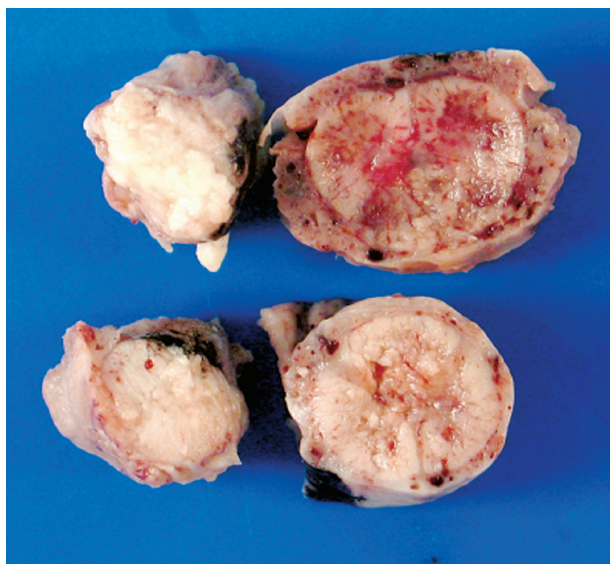
<sup>1</sup>Department of Pathology, Hofstra North Shore–LIJ Health System, Hempstead, NY, and Departments of <sup>2</sup>Pathology and <sup>3</sup>Radiology, Winthrop-University Hospital, Mineola, NY

\*To whom correspondence should be addressed. sdrexler@winthrop.org



**Image 1**

Spinal magnetic resonance imaging (MRI) scan of thoracolumbar region of the patient, an 82-year-old white man, demonstrating T2 hyperintensity.



**Image 2**

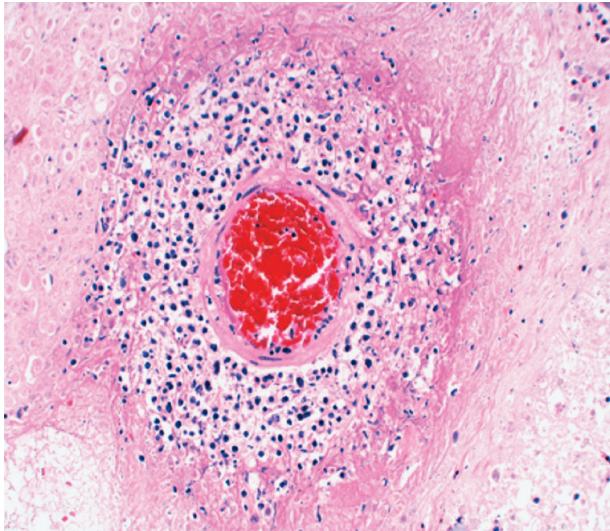
Cross-sections of the spinal cord of the patient, an 82-year-old white man, showing white fleshy neoplasm with necrosis (obtained during autopsy).

hospitalization of the patient, his health declined rapidly; the patient developed areflexia and then died. At the time of autopsy, the most significant abnormal findings were those from the spinal cord.

Gross examination revealed that the upper half of the spinal cord was extremely necrotic and friable. The distal 15 cm of the cord was congested, and the subarachnoid space was completely encased by firm, white, fleshy tissue (**Image 2**). On microscopic examination, we observed widespread perivascular large atypical lymphocytes with an associated necrotizing vasculitis (**Image 3**). We ruled out microorganisms because of the negative results that we obtained via several stains (Grocott-Gomori methenamine-silver stain [GMS], periodic acid–Schiff stain [PAS], acid-fast bacillus [AFB], Warthin-starry, and gram stain) and the negative results of blood and cerebrospinal fluid (CSF) cultures. Immunohistochemical staining of these cells proved that they were T cells. Immunohistochemical staining results were positive for CD3, CD30, CD5, and CD2, and negative for AE1/AE3, EMA, CD20, CD7, PAX5, and CD68 (**Image 4**). T-cell receptor (TCR) gamma gene rearrangement analysis of the spinal cord tissue by polymerase chain reaction (PCR) demonstrated a positive clonal TCR gamma gene rearrangement. These findings are consistent with the diagnosis of T-cell PCNSL and, more specifically, primary intramedullary spinal cord lymphoma.

## Discussion

PCNSL accounts for less than 1% of lymphoma diagnoses, and the T-cell phenotype is found in less than 1% of PCNSL cases.<sup>3,5</sup> Hence, there are few reported cases in the literature of PCNSL of T-cell type. Moreover, primary spinal involvement is exceptionally rare, occurring in less than 1% of patients with PCNSL.<sup>3-6</sup> From a histological standpoint, T-cell lymphomas are a heterogeneous group of neoplasms that may be difficult to diagnose using morphologic and immunophenotypic criteria.<sup>7,8</sup> Some of these less common lymphomas do not bear the obvious cytologic atypia of malignancy, or the malignant cytology is obscured by an abundance of nonneoplastic inflammatory cells. A spectrum of cell sizes and types are typically found in these lymphomas, including nonneoplastic cells, making it problematic to differentiate T-cell lymphomas from reactive



**Image 3**

Staining of perivascular large atypical lymphocytes with an associated necrotizing vasculitis in the patient, an 82-year-old white man (hematoxylin-eosin, original magnification  $\times 200x$ ).

lesions.<sup>5,8</sup> T-cell lymphomas are known colloquially to be accompanied by a mixture of inflammatory cells that closely simulates vasculitis or encephalitis. Further complicating the diagnosis, immunophenotyping may not be definitive because T cells do not express clonal markers as B cells do immunoglobulin light chains.<sup>5,8</sup> Immunohistochemical staining is useful to determine the cell lineage, in which these atypical lymphoma T cells are immunoreactive for CD3 and for any combination of CD2, CD4, CD5, CD7, and/or CD8. Also, TCR gene rearrangement by PCR analysis may demonstrate a clonal TCR gene rearrangement and has been shown to be a useful method for determining the clonality of neoplastic cells.<sup>5,8</sup>

When primary spinal cord involvement of lymphoma occurs, the lesions are almost always intramedullary spinal cord lesions. This finding contrasts with spinal involvement in systemic lymphoma, in which there is usually diffuse leptomeningeal involvement and extradural nodules.<sup>4-6</sup>

Clinically, patients usually display progressive myelopathic manifestations; the pattern of weakness and sensory loss will depend on the localization and extent of the lesion. Most reported cases of primary spinal lymphoma have involved the lower cervical and upper thoracic regions.<sup>6</sup>

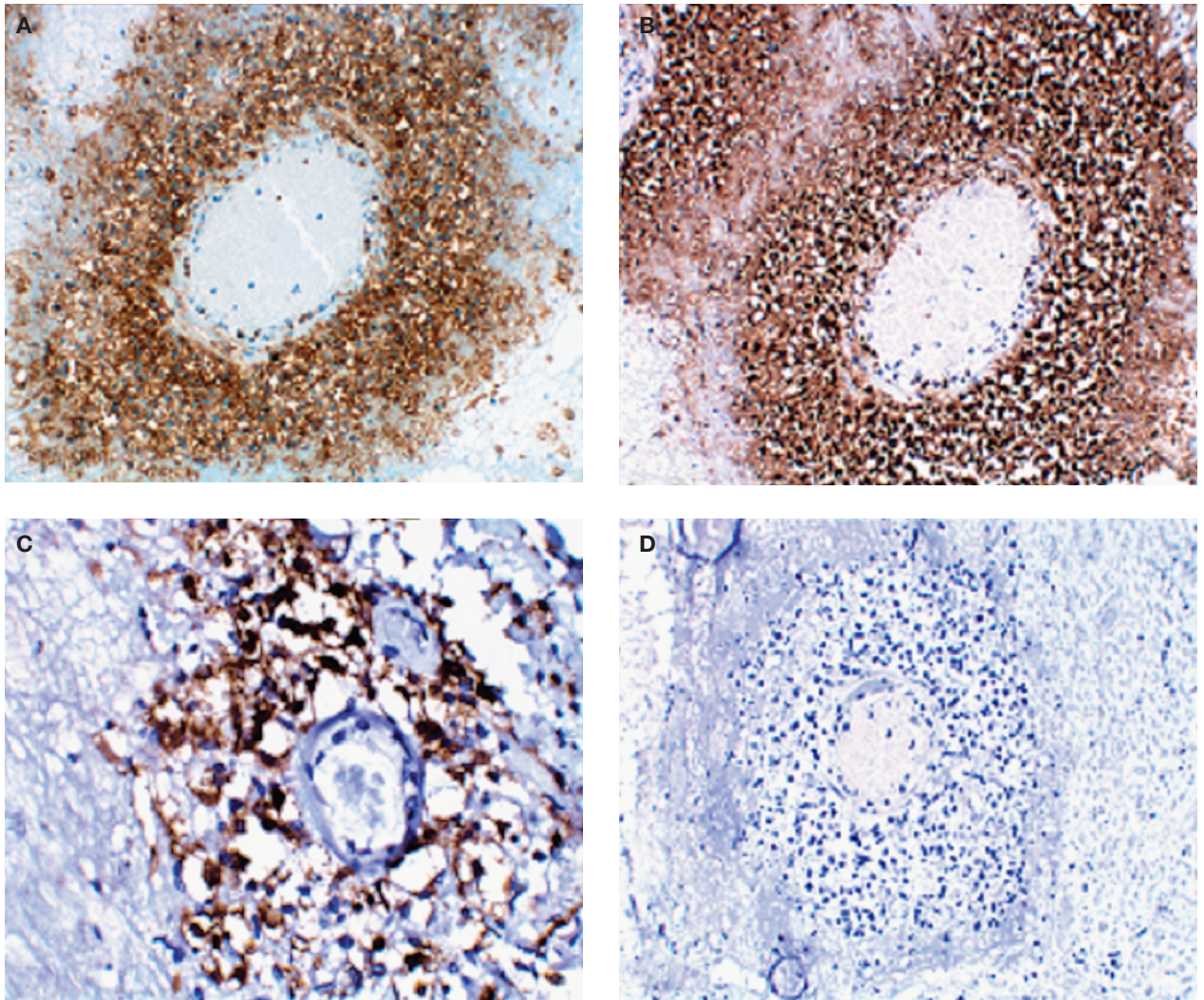
A retrospective analysis performed by the Mayo Clinic<sup>6</sup> showed that most patients with primary intramedullary spinal cord lymphoma displayed multifocal and persistently enhancing lesions on spinal MRI. Also, more than half of these patients had involvement of the conus medullaris and/or cauda equina. Spinal cord expansile lesions have been noted in many of these patients. Also, it has been reported that all patients initially harbored progressive myelopathic manifestations.<sup>6</sup> The diagnosis of primary intramedullary spinal cord lymphoma is often delayed due to the broadness of the differential diagnoses for myelopathy as well as the rarity of this condition.<sup>2,3,6</sup> A high percentage of patients have additional signs and symptoms that include systemic B symptoms, back pain, and evidence of lower-body motor-neuron involvement.<sup>6-9</sup>

The clinical appearance and findings on MRI of primary intramedullary spinal cord lymphoma are nonspecific; other intracranial processes, such as multiple sclerosis, sarcoidosis, and occasionally gliomas, have a similar appearance on MRI.<sup>3,9</sup> MRI findings are usually isointense to hypointense on T1-weighted images and hypointense on T2-weighted images. Further, the CSF test results are usually inconclusive.<sup>3-5,9</sup> This raises the question of when to suspect the diagnosis of PCNSL of the spinal cord because biopsy is required for proper pathologic diagnosis and delayed treatment usually results in death.<sup>9-11</sup>

PCNSL is sensitive to chemotherapy and radiotherapy; however, the overall response rates and long-term survival are significantly inferior to the results achieved in similar subtypes of extranodal non-Hodgkin lymphoma (NHL).<sup>8-11</sup> Patients should be encouraged to enroll in a clinical trial for PCNSL and should seek histopathologic confirmation of their diagnosis.<sup>9</sup> Histopathologic confirmation of the diagnosis is critical because in a subset of patients, a presumptive but incorrect diagnosis of PCNSL is given based on MRI appearance and tumor response to corticosteroids. However, tissue diagnosis is essential because of other intracranial processes that yield similar MRI findings and also result in a transient response to corticosteroids.<sup>8-11</sup>

The recommended diagnostic procedure for PCNSL is a stereotactic needle biopsy because patients derive no additional clinical benefit from surgical resection. Also, the deep-seated nature of most lesions makes resection impossible or increases the risk of surgical complications.<sup>5,8-11</sup>





**Image 4**

Immunohistochemical staining of large, atypical cells from the patient, an 82-year-old white man, showing cells positive for CD3 (A), CD5 (B), and CD2 (C) and negative for CD20 (D).

The optimal treatment of PCNSL is unclear; there is variation in clinical practice treating this condition. Since 1978, there have been more than 40 prospective clinical trials and large institutional series published that report a variety of treatment algorithms.<sup>8</sup> Numerous prospective and retrospective case series have evaluated different treatment options.<sup>8-9</sup> Only 2 randomized trials have been completed. However, the results of completed phase II trials are difficult to compare directly due to differences in response definitions and follow-up.<sup>8,9</sup> Data from several retrospective and prospective trials indicate an improvement in survival for patients treated initially with

chemotherapy, compared with those treated only with radiation. Chemotherapy regimens that use high-dose systemic methotrexate appear to be more effective against PCNSL than regimens that do not contain methotrexate.<sup>9-11</sup>

In conclusion, it is imperative to closely investigate the clinical and radiological findings of patients with progressive myelopathic manifestations that are refractory to treatment because a biopsy could be prudent to patient care. Also, patients diagnosed with PCNSL should be encouraged to participate in clinical trials when available because no effective treatment options currently exist. **LM**

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