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LETTER TO THE EDITOR

Primary central nervous system lymphoma of T-cell origin: an unusual cause of spinal cord disease

Sophie Fastré[1] · Frédéric London[1] · Julie Lelotte[2] · Alessandra Camboni[2] · Anne Jeanjean[1]

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Introduction

Less than 1% of lymphomas are primary central nervous system lymphomas (PCNSL) [1]. Most of them are B-cell lineage and involve the supratentorial space, whereas T-cell origin and involvement of spinal cord are extremely rare [1]. Despite its rarity, primary spinal cord lymphoma (PSCL) of T-cell origin requires a meticulous diagnosis, because delayed treatment can shorten survival. However, there are no typical clinical features or radiological findings and it is always necessary to perform biopsy to obtain accurate pathological diagnosis so as to guide therapeutical decisions and avoid severe neurological sequelae.

Case report

A 45-year-old Caucasian man without relevant medical history developed progressive paraparesis and numbness of his lower limbs over weeks, with bladder dysfunction. He had no systemic symptoms or fever. Clinical examination also revealed generalized hyperreflexia and bilateral extensor plantar response. Brain and spinal cord magnetic resonance imaging (MRI) showed hypersignal on T2/FLAIR images in left cerebellum and intramedullary cervical spinal cord with rostral extension to the brainstem and Gadolinium enhancement (Fig. 1a–d). Antinuclear, SSA, SSB, and anti-aquaporin-4 antibodies were negative and angiotensin-converting enzyme was normal. Infectious serologies, including human immunodeficiency virus (HIV), were negative. Cerebrospinal fluid (CSF) analysis revealed lymphocytic pleocytosis (30 cells/mm^3), but protein and glucose level were normal. Although CSF oligoclonal IgG bands were negative, a demyelinating disease was suspected and he was first treated with intravenous methylprednisolone 1 g daily for 7 days. Despite initially significant favourable outcome, clinical worsening was observed with paraplegia and complete urinary and faecal incontinence. Significant longitudinally extension of T2/FLAIR spinal cord hyperintensities (Fig. 1e–g) and presence of a pachymeningitis in cauda equina (Fig. 1h–j) were observed on MRI follow-up 3 months later. Whole body positron emission computed tomography did not reveal any non-CNS abnormalities, especially no hilar adenopathy. Significant increase of protein level (353 mg/dl) and lymphocytic pleocytosis (101 cells/mm^3) observed on new CSF examination, performed 3 months after the first analysis, led us to consider lymphoma and the patient underwent stereotactic needle biopsy of the left cerebellar lesion. Histopathology analysis on microscopic evaluation showed infiltration of cerebellar

S. Fastré and F. London contributed equally to the work.

✉ Frédéric London
londonfrederic@gmail.com

Sophie Fastré
fastre.sophie@gmail.com

Julie Lelotte
julie.lelotte@uclouvain.be

Alessandra Camboni
alessandra.camboni@uclouvain.be

Anne Jeanjean
anne.jeanjean@uclouvain.be

[1] Department of Neurology, Cliniques Universitaires UCL St-Luc, 10 Avenue Hippocrate, 1200 Brussels, Belgium

[2] Department of Pathology, Cliniques Universitaires UCL St-Luc, 10 Avenue Hippocrate, 1200 Brussels, Belgium

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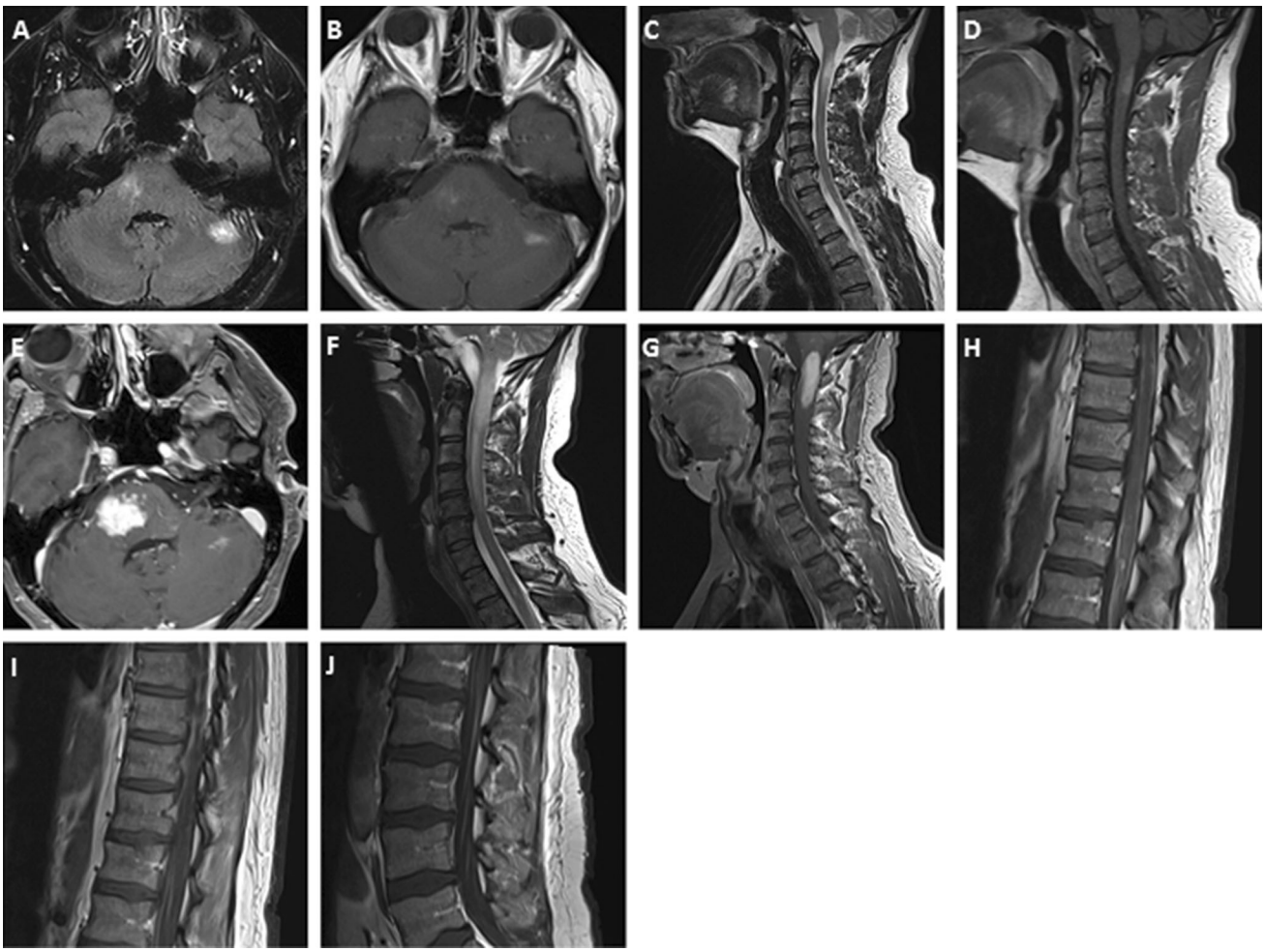

Fig. 1 Brain and spinal cord MRI. First MRI assessment showing left cerebellar T2/FLAIR hyperintensity (**a**) with Gadolinium enhancement (**b**) and upper cervical spinal cord T2 hyperintensity (**c**) with rostral extension to the brainstem and Gadolinium enhancement on post-contrast T1-weighted images (**d**). Brain and spinal cord MRI follow-up (at 3 months from baseline) after clinical worsening, revealing extension of brain stem hyperintensity and Gadolinium enhancement (**e**) and an extensive cervical spinal cord T2 hyperintensity (**f**) with intense Gadolinium enhancement on post-contrast T1-weighted images (**g**). Diffuse leptomeningeal lymphomatosis is observed on post-contrast sagittal T1-weighted images (**h–j**)

tissue with histiocytes and lymphocytes (Fig. 2a, b). Lymphoma of T-cell origin was confirmed by immunohistochemical stainings which were strongly positive for CD3, CD2, CD5, CD4 as well as focally and weakly positive for CD7 (Fig. 2c). A positive clonal T-cell receptor gamma gene rearrangement was observed by polymerase chain reaction of the cerebellar tissue. The proliferation index was increased (Fig. 2d). Flow cytometry of CSF detected a population of T cells expressing surface CD3, CD2, CD5, and CD7; B-cells were absent.

Chemotherapy was started promptly but despite good radiological outcome and almost complete disappearance of leptomeningeal lymphomatosis after two cycles of chemotherapy, and the patient had severe disability as he remained paraplegic with marked weakness in left arm, persistent bladder dysfunction, and sensory level T8.

Discussion

Primary spinal cord lymphoma of T-cell lineage mostly occurs in middle-aged patients and is so rare that it is frequently under-recognized and misdiagnosed [2]. We found less than ten reported cases [1, 2]. The main differential diagnosis is inflammatory disorders of the CNS, especially demyelinating diseases and spinal cord sarcoidosis (SCS) and establishment of the proper diagnosis remains challenging. If distinguishing PSCL from demyelinating diseases and SCS is highly needed for optimal treatment, its clinical presentation (B or T-cell origin) is unspecific and consists in a progressive myelopathy, which is consistent with our observation [2]. Constitutional symptoms are frequently reported in PSCL, but it is not a discriminating factor, since they can be

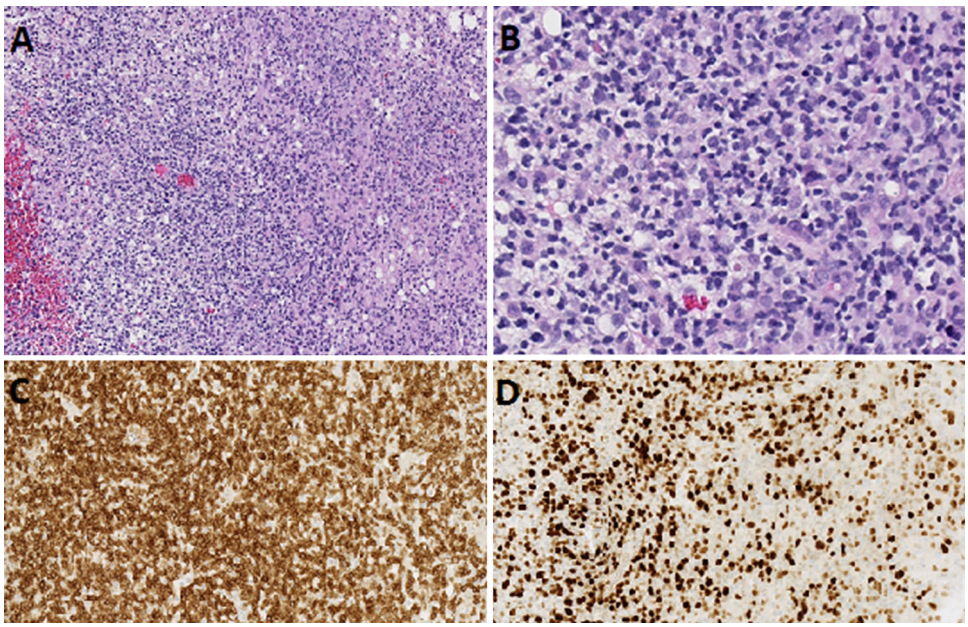

Fig. 2 Histopathological findings. The cerebral tissue is largely infiltrated by small, nonatypical, lymphocytes, and histiocytes (**a**, **b**). The lymphocytes showed a positive immunostaining for CD3 (**c**), CD5, CD4, and CD2 (not showed), but they showed a partially loss of expression of CD7 (not showed). The proliferation index was increased (**a**) (**a** HE 10×; **b** HE 40×; **c** CD3 20×; and **d** Ki67 20×)

observed in sarcoidosis too [3]. MRI findings in spinal cord lymphomas are nonspecific, with a predominant involvement of the lower cervical and upper thoracic spine [3], and are mostly indistinguishable from SCS or a demyelinating disorder. In our case, the T2 lesion length on MRI follow-up makes multiple sclerosis less likely, but it cannot distinguish PSCL from SCS and neuromyelitis optica which commonly cause spinal cord lesion spanning ≥3 vertebral segments. Persistent Gadolinium enhancement over 2 months following steroid therapy makes a demyelinating disease unlikely, but does not rule out SCS and PSCL.

Moreover, transient but dramatic clinical improvement after empiric use of corticosteroids is very common in CNS lymphomas, which may further obscure or delay diagnosis. Medical history of immunosuppressive drugs and HIV must be systematically sought because of the known link between immunosuppression and malignancy.

Due to the lack of typical clinical and radiological features, and of a sensitive and specific blood or CSF marker, in the absence of evident diagnosis, CSF flow cytometry and biopsy with immunostaining must be promptly considered to obtain correct diagnosis and provide the best current treatment. Management of CNS lymphoma is based on chemotherapy regimens with systemic methotrexate and/or radiotherapy according to published protocol [4]. Long-term prognosis remains unpredictable, but early diagnosis is essential so as not to hamper successful outcome.

Compliance with ethical standards

Conflict of interest The authors declare no conflict of interest related to this publication.

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Ethical standard This article does not contain any study with human participants or animals performed by any of the authors.

Informed consent The patient provided written consent for publication of the report.

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