Intravascular lymphoma presenting as progressive paraparesis

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Abstract

We present a patient with subacute progressive paraparesis secondary to intravascular lymphoma restricted to the spinal cord where initial laboratory and imaging studies were inconclusive. We emphasise the importance of a systematic approach to the diagnosis and highlight the utility of spinal cord biopsy to establish the definitive diagnosis of this rare but treatable illness.

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1. Introduction

Intravascular lymphoma is a rare subtype of extranodal diffuse large B cell lymphoma. The disease is characterised by the presence of malignant lymphoma cells in small vessel (especially capillary) lumina, with subsequent small vessel occlusion.¹ Intravascular growth and dissemination of the

malignancy is generally not accompanied by the formation of extravascular visceral lymphomatous masses. The clinical and pathological manifestations of intravascular non-Hodgkin lymphoma (IV-NHL) relate to the intravascular growth and spread of the malignant cells, which result in secondary thrombo-occlusive and haemorrhagic events. It is usually widely disseminated at presentation and notoriously difficult to diagnose. Presenting features are highly variable as the small vessel pathology may affect a variety of organs.¹ Central nervous system (CNS) involvement ranks second to cutaneous disease as the principal site of

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involvement at presentation. The neurological manifestations of IV-NHL have been categorised into four broad groups. These include progressive multifocal cerebrovascular events, spinal cord and nerve root vascular syndromes, subacute encephalopathy and peripheral or cranial neuropathies. Neurological symptoms including focal lesions, subacute encephalopathy, multi-focal cerebrovascular events, seizures and dementia have been described as presenting features.² This subtype of lymphoma is reported to have a poor prognosis, attributable in part to delay in diagnosis.¹ If this disorder is considered, early diagnosis is possible and allows potentially curative treatment.

2. Case report

A 65-year-old left-handed Caucasian man presented with bilateral lower limb weakness and sensory loss, thigh and lumbar back pain and urinary incontinence, with gradual onset over a 6-week period. There were no upper limb or cranial nerve symptoms and there was no history of weight loss.

Examination revealed pyramidal pattern lower limb weakness, mild hypertonia and reduced reflexes in the lower limbs. Plantar reflexes were flexor. There was hypo-algesia to L2 and pallanesthesia to the anterior superior iliac spine bilaterally. The remainder of the neurological and general examination was normal.

MRI of the spine and brain at presentation was unremarkable. Cerebrospinal fluid (CSF) examination showed protein 0.61 g/L, normal glucose and 4 leukocytes/ μ L. Cytology was normal. Polymerase chain reaction (PCR) on CSF was negative for cytomegalovirus, herpes simplex virus and varicella zoster virus. Oligoclonal bands were not detected.

Full blood picture, renal function, erythrocyte sedimentation rate, c-reactive protein (CRP), vitamin B₁₂, red cell folate and serum angiotensin-converting enzyme were normal. Anti-nuclear antibodies (ANA), extractable nuclear antigens (ENA), anti neutrophil cytoplasmic antibodies (ANCA), anti-GM1 ganglioside antibodies and HIV1/2 serology were negative. Electromyograph (EMG) and nerve conduction studies (NCS) were unrewarding.

Empirical corticosteroid therapy produced equivocal improvement in symptoms, including return of bladder control.

Three weeks later the patient represented with bilateral anterior thigh pain, bladder dysfunction and difficulty walking. Examination showed normal tone, with 4/5 power at the hips and knees and 3/5 power at the ankles bilaterally. Reflexes remained depressed, with flexor plantar responses. Sensation was reduced to the L1 level bilaterally.

Repeat MRI of the spine and lumbar puncture findings were unaltered. Visual evoked potentials were normal. Whole body CT scan did not demonstrate any mass lesions, lymphadenopathy or hepatosplenomegaly. Repeat EMG and NCS were unhelpful. Serum and urine electrophoresis, plasma copper and tumour markers were normal, except for

CA19–9, which was mildly elevated (56 kU/L, normal <40). Syphilis serology, glutamic acid decarboxylase (GAD) antibodies and Purkinje cell antibodies were negative.

Further intravenous corticosteroids produced an unstained improvement in lower limb strength. There was progressive deterioration over the following 4 weeks with flaccid lower limb weakness, bilateral sensory loss to T10 level and faecal and urinary incontinence. The plantar response became extensor on the left. There was progressive respiratory muscle dysfunction and the onset of upper limb weakness.

Repeat MRI demonstrated subtle lumbar enlargement and signal alteration within the spinal cord at T2–T3, T5–T7 and conus levels. This was mainly central, with some eccentric white matter changes. No enhancement was seen following gadolinium.

Spinal cord biopsy confirmed the diagnosis of intravascular B cell lymphoma. Subsequent positron emission tomography (PET) did not identify other sites of disease and bone marrow aspiration and trephine did not show evidence of lymphoma. The patient completed six cycles of R-CHOP chemotherapy. The changes on MRI have not progressed and he remains in complete remission 15 months post-completion of chemotherapy. He remains paraplegic.

3. Discussion

There was a wide differential diagnosis in this case. Detailed neurological examination revealed evolving mixed upper and lower motor neuron signs. Repeated imaging and CSF examination were initially unrewarding. The mixed features were not typical of more common diagnoses such as multiple sclerosis, and other disorders such as CNS vasculitis, lymphoma and paraneoplastic conditions were considered.

Ultimately spinal cord biopsy was required to establish the diagnosis. Biopsy of the spinal cord will almost invariably result in neurological deficit, so thorough and systematic investigation is required prior to biopsy. The recognition of systemic manifestations may allow diagnostic specimens to be obtained from outside the CNS. Skin and adrenal glands are commonly reported sites of involvement. Conversely, there are many reported cases in which there is no evidence of systemic disease.³ In these cases brain or spinal cord biopsy remains the only means of obtaining a tissue diagnosis.

A case series of 38 spinal biopsies found that pre-operative laboratory and imaging studies were often diagnostically inconclusive in spinal cord lesions with non-specific features. Specific treatment was based on biopsy results in 26% of cases.⁴ In this case, biopsy was crucial to guide management and prevent further neurological deterioration. Evidence of lymphoma was not found outside of the CNS, even after the diagnosis was confirmed.

This case highlights the importance of early accurate diagnosis. There is no consensus on the optimal therapy for intravascular lymphoma; however, various systemic chemotherapy regimens have been used with demonstrable

complete and partial responses. It is recognised that less intensive treatments, such as corticosteroids, intravenous immunoglobulin and plasmapheresis have little efficacy.⁵ Treatment with these agents may result in unsustained improvement, perhaps by suppressing a paraneoplastic syndrome or anti-inflammatory effects. This may mask evolution of the underlying disease and delay diagnosis.

Intravascular lymphoma is a rare but important cause of myelopathy as it is a treatable diagnosis. This is an aggressive form of lymphoma, which often results in death a short time after presentation.¹ The reported poor prognosis is due in part to the frequent delay in diagnosis, secondary to the extremely variable clinical presentations. A large proportion of patients with intravascular lymphoma are diagnosed in the postmortem setting.¹ In patients such as

this, in which the diagnosis is made early, aggressive chemotherapy can be curative.

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