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Cauda equina-conus medullaris syndrome as an isolated presenting symptom of intravascular large B-cell lymphoma: Case report and review of the literature

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Abstract

Intravascular large B-cell lymphoma (IVLBCL) is a rare non-Hodgkin lymphoma with variable clinical manifestations. Although neurological symptoms are common in patients with IVLBCL, isolated cauda equina-conus medullaris syndrome is rarely reported. We herein report a case of IVLBCL whose initial presentation was cauda equina-conus medullaris syndrome with neither dermatological nor hematological manifestations. A 54-year-old man without known immune-compromised state presented with progressive ascending numbness and weakness of bilateral legs and urine incontinence for 2 months. Lumbar-sacral magnetic resonance images showed gadolinium-enhanced conus medullaris and cauda equina nerve roots. Cerebrospinal fluid analysis revealed lymphocyte predominant pleocytosis and elevated protein level without malignant cells. Focal seizure and mental status changes followed several weeks later. Brain biopsy led to the diagnosis of IVLBCL.
Conclusions: IVLBCL should be included in the differential diagnosis of patients with isolated cauda equina-conus medullaris syndrome. A survey of previously published cases in the literature also showed that early initiation of chemotherapy has better outcome.

INTRODUCTION

Intravascular large B-cell lymphoma (IVLBCL) is a rare form of extranodal non-Hodgkin lymphoma. Disseminated disease with a variety of organ involvement complicates the clinical presentations and leads to diagnosis difficulty.[1] The nervous system and skin are the most frequently involved organs in western patients but are uncommon in Asians.[2] Asian patients with IVLBCL usually presents as bone marrow involvement with hematological manifestations.[3,4] The reasons for the ethnic difference in clinical presentation are unclear.[2-4] Isolated cauda equina or conus medullaris syndrome is rarely reported as the presenting symptom of IVLBCL.[5] We report an IVLBCL case whose initial presentation was cauda equina-conus medullaris syndrome without other system involvement. We also reviewed the previously reported cases reported in the literature.

CASE REPORT

A 54-year-old man had history of well-controlled hypertension, hyperlipidemia and polycystic kidney disease. He presented with a two-month history of progressive numbness, pain and weakness of bilateral legs and urine incontinence. There was no fever, preceding upper respiratory tract infection, history of vaccination, back pain or disturbed consciousness. Physical examinations did not reveal lymphadenopathy, hepatosplenomegaly or any skin lesion. Neurological examination revealed flaccid paraplegia, impairment of pinprick and light touch sensation over bilateral legs and over the perianal saddle area. There was urine incontinence, absent cremasteric reflex and loose anal sphincter tone. Laboratory investigation including peripheral blood hemogram was normal and HIV test was negative. However, elevated serum level of lactate dehydrogenase, 1604 U/L (reference level is 105-333), was noted. Magnetic resonance image (MRI) of lumbar and sacral spines showed diffuse gadolinium enhancement lesions over conus medullaris and cauda equina (Figure 1A and 1B). Cerebrospinal fluid (CSF) analysis showed lymphocyte pleocytosis (13 cells/μL) with two atypical lymphocytes, normal glucose (44 mg/dL) and elevated protein level (108.4 mg/dL). After admission, the muscle power of both legs further deteriorated and left upper limb weakness developed. His consciousness fluctuated and several episodes of seizures occurred. Brain T2-weighted MRI showed multiple hyperintensity

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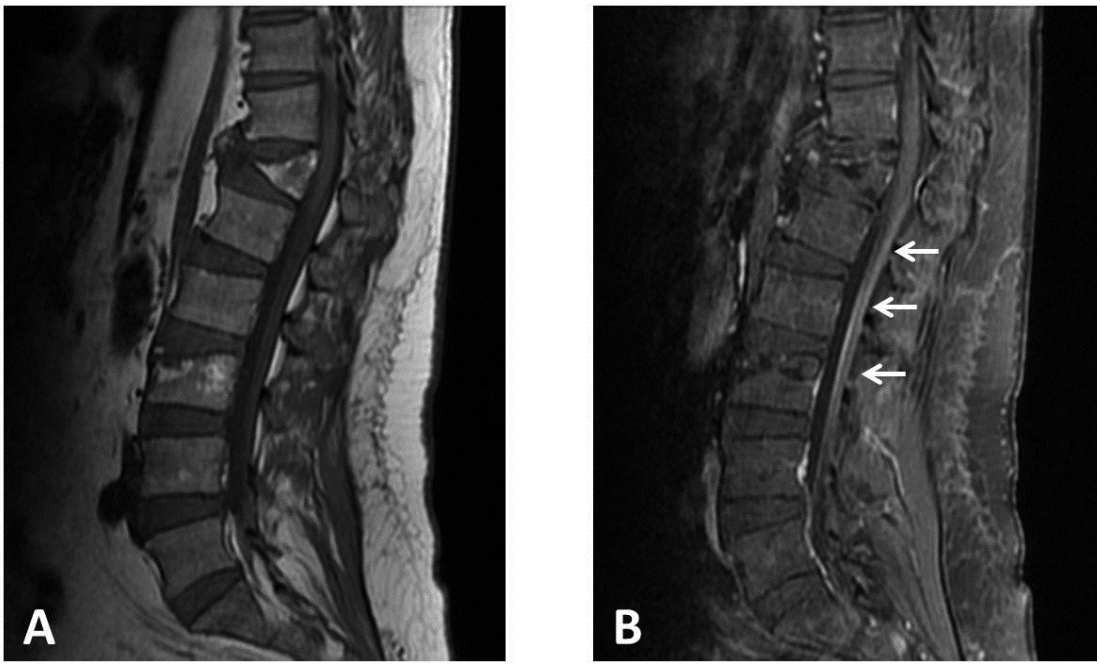

Figure 1. Lumbar-sacral spine MRI without (A) and with (B) gadolinium contrast with arrows to indicate gadolinium contrast enhanced lesions of the conus medullaris and cauda equina nerve roots.

lesions at left frontal, bilateral subcortical white matter areas, cerebellum, and pons. Some of these showed contrast enhancement (Figure 2A). Open brain biopsy at the left frontal pole was performed. Pathology showed neoplastic lymphoid cells lodged within the lumen of small or intermediate vessels with scanty extravascular involvement (Figure 3A). The tumor cells were immunopositive for CD20, CD79a and focally for MuM-1 but negative for CD138 (Figure 3B), and confirmed IVLBCL. Chemotherapy was started with Methotrexate, Ara-C and Rituximab.

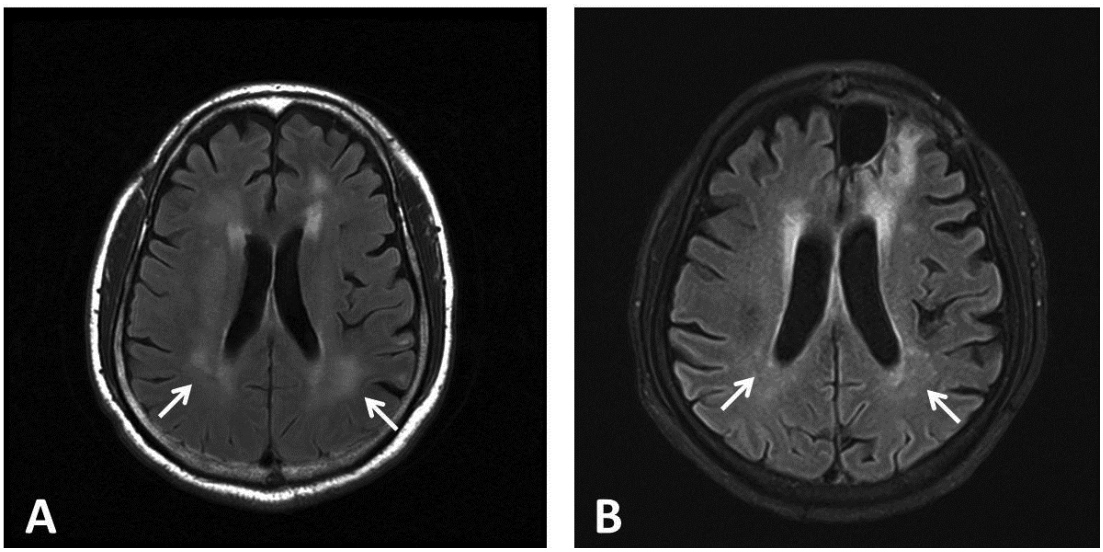

Figure 2. FLAIR Brain MRI of the patient on admission and two months after chemotherapy. (A) On admission, FLAIR showed multiple abnormal T2 hyperintense lesions over bilateral subcortical white matter, with some of the lesions showing mild diffusion restriction and contrast enhancement. (B) Two months after chemotherapy, the follow-up brain image showed left medial frontal post-operative change from the open-brain biopsy, and mild regression of bilateral subcortical white matter lesions as compared to (A).

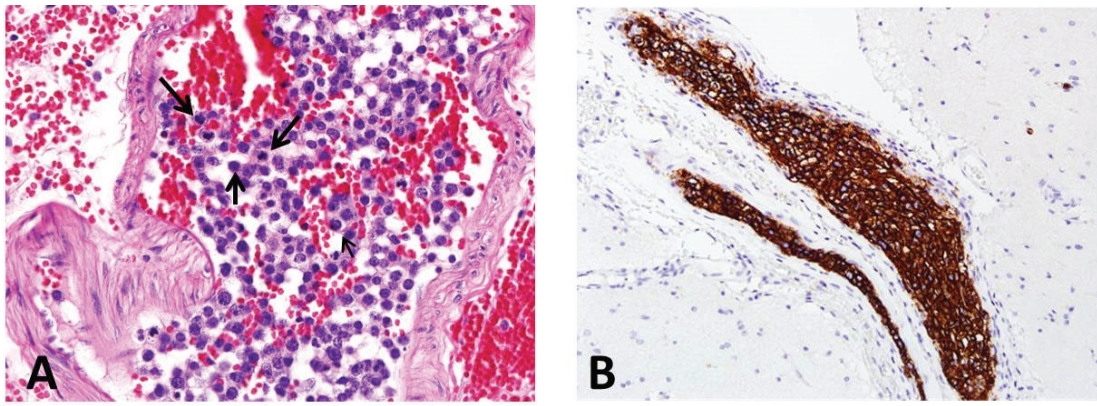

Figure 3. Left frontal lobe open-brain biopsy of the patient. (A) Arrows indicate IVLBCL neoplastic lymphoid cells with large nucleoli and mitosis lodged within lumina of vessels (hematoxylin and eosin stain, original magnification × 200). (B) Immunohistochemical staining show numerous CD20+ lymphoma cells filled in the lumen of small vessels (original magnification × 100).

Consciousness improved and follow-up brain MRI 2 months later demonstrated diminished cerebral white matter lesions (Figure 2B). However, pancytopenia developed after a high dose of methotrexate and he died from sepsis 8 months after the onset of symptoms.

DISCUSSION

We report a patient with IVLBCL presenting as cauda equina-conus medullaris syndrome without evidence of hepatosplenomegaly or bone marrow involvement.

Isolated neurological symptoms are estimated to be less than 30% in CNS IVLBCL.[1-3,6] Cauda equina/conus medullaris syndrome accounts for only 5%.[7] Deficits are caused by invasion of the lymphoid tumor cell into the small vessels of either the central nervous system or the peripheral nerves, and lead to microcirculatory dysfunction and subsequent neuronal damage.

Given that isolated cauda equina or conus medullaris syndrome is a rare presenting symptom in patients with IVLBCL, we searched MEDLINE for previously published cases. The terms we used for keyword search included intravascular lymphoma, cauda equina, conus medullaris, spinal cord, and paraplegia. A total of 23 related cases were identified from 1991 to 2013 (Table 1). When combined with our index patient, the median onset age of neurological symptoms was 64.4 years old (range 41-86 years) and mostly were men. Most cases had paraparesis with sensory and sphincter dysfunction. Notably, 9 patients (38%) had pain as part of their initial symptoms, either radicular pain or low back pain, which is probably related to ischemic change of nerve root caused by tumor cell thrombosis.[1] Among these 24 IVLBCL patients, 10 patients showed isolated cauda equina or conus medullaris involvement (42%), 5 patients had isolated thoracic cord involvement (21%), 6 had long segment involvement from the thoracic region to the conus medullaris/cauda equina level (25%). None had cervical cord involvement. With disease progression, 3 of the 5 patients (60%) with initial thoracic cord lesion reported subsequent involvement of conus medullaris or cauda equina. In contrast, among the 10 patients with initial conus medullaris or cauda equina involvement, only 2 patients (20%) had subsequent thoracic cord involvement. These observations suggest that IVLBCL has a predilection for the lower spinal cord invasion with subsequent caudal-rostral involvement of the adjacent spinal cord.

Clinical outcome of IVLBCL was dismal before the use of chemotherapy, especially rituximab. Patients receiving chemotherapy had a longer survival duration and less systemic dissemination of the disease than patients who did not receive chemotherapy.[9] Shimada *et al.* reported a retrospective analysis of 106 patients with IVLBCL and found that the 2-year survival rate was 66% and 46% in patients receiving and not receiving rituximab, respectively.[3] These findings suggest that rituximab-containing chemotherapy was crucial for patients with IVLBCL. In the case series reviewed, the survival duration of patients with and without chemotherapy was 17 months and 6 months, respectively. The most common chemotherapy regimens were anthracycline-based chemotherapy, CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisolone) and rituximab (Table 1). Thus, early chemotherapy

Table 1. Summary of published cases of IVLBCL with initial presentation of spinal cord dysfunction or cauda equine-conus medullaris syndrome

Case number	Authors	Age/ gender	Initial symptoms	CSF findings	Biopsy site & pathology cell type	Level of spinal cord involvement	Chemotherapy regimen	Outcome
1	Nakahara *et al*., 1999[5]	63/M	Paraplegia, dysthesia & urine retention	Pleocytosis, elevated TP	Muscle, B-cell	Cauda equina-conus medullaris	CHOP	Survived >16 months
2	Davis TS, 2003[10]	86/M	Paraplegia, pain & incontinence	N/A	Muscle, B-cell	Cauda equina	R-CHOP+ Etoposide	Survived >8 months
3	Piyatonont *et al*., 2010[11]	77/M	Paraplegia	Pleocytosis, elevated TP	Skin, B-cell	Cauda equina	Methotrexate	Expired, 9months
4	Viali *et al*., 2000[12]	53/M	Paraplegia	Elevated TP	Autopsy, B-cell	Conus medullaris	Nil	Expired
5	Savard *et al*., 2008[13]	61/F	Paraplegia & urine incontinence	Elevated TP	Autopsy, B-cell	T11,12, conus medullaris	Mitoxantrone	Expired, 18 months
6	Debiais *et al*., 2004[14]	71/F	Paraplegia & urine incontinence	Pleocytosis, elevated TP	Brain, B-cell	Conus medullaris	MBVP	Survived, >21 months
7	Liu *et al*., 2009[15]	78/M	Paraplegia	Pleocytosis, elevated TP	Autopsy, B-cell	Conus medullaris	Nil	Expired, 5 months
8	Grove *et al*., 2008[16]	65/M	Paraplegia & urine incontinence	Elevated TP	Spinal cord, B-cell	T2-T7, conus medullaris	CHOP	Survived, 21 months
9	Lee *et al*., 2011[17]	70/M	Paraplegia & urine retention	Elevated TP	Lacrimal gland, B-cell	T7-8	R-CHOP	Survived
10	Amagasaki *et al*., 1999[18]	55/M	Paraplegia, hypothesia below umbilicus	N/A	Autopsy, B-cell	Low T level	Nil	Expired, 18 months
11	Kumar *et al*., 2011[19]	82/F	Paraplegia & neurogenic bladder	Elevated TP	Autopsy, B-cell	T7-T11	Nil	Expired
12	Szots *et al*., 2008[20]	62/M	Paraplegia & pain	Elevated TP	Autopsy, B-cell	T7 to conus medullaris	Nil	Expired, 50 days
13	De Fino *et al*., 2012[21]	76/F	Paraplegia & urinary dysfuction	Elevated TP	Autopsy, B-cell	Suspect low T lesion but MRI was normal	Nil	Expired, 9 months
14	Legeais *et al*., 2004[22]	71/F	Paraplegia & urine incontinence	Normal	Brain, B-cell	Conus medullaris	MBVP	Survived, 22.5 months

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Case number	Authors	Age/ gender	Initial symptoms	CSF findings	Biopsy site & pathology cell type	Level of spinal cord involvement	Chemotherapy regimen	Outcome
15	Scully *et al.*, 1995[23]	43/M	Paraplegia & urine incontinence	Pleocytosis, elevated TP	Brain, B-cell	T cord, conus medullaris	Methotrexate	Expired
16	Schwarz *et al.*, 2002[24]	41/M	Perineal sensory loss & urine incontinence	Pleocytosis, elevated TP	Autopsy, B-cell	Conus medullaris	Cyclophosphamide	Expired, 13 months
17	Clark *et al.*, 1991[25]	63/M	Paraplegia & voiding difficulty	N/A	Autopsy, B-cell	T8 level	Nil	Expired
18	Yang *et al.*, 2008[26]	70/M	Paraplegia & sphincter dysfunction	Elevated TP	Autopsy, B-cell	Suspect low T lesion but MRI was normal	Nil	Expired, 3 months
19	Abbasi *et al.*, 2014[27]	58/M	Paraplegia & urine retention	Elevated TP	Renal, B-cell	T6-T10	R-CHOP	Survived, 3 years
20	Waring *et al.*, 1999[28]	74/M	Urine retention	Elevated TP	Autopsy, B-cell	Lower T to upper L spinal cord	Nil	Expired, 3 months
21	Takizawa *et al.*, 2007[29]	52/M	Paraplegia, pain & urine incontinence	Elevated TP	Muscle, B-cell	Lower T to conus medullaris	R-CHOP	Survived, 3.5 years
22	Abuzinadah *et al.*, 2012[30]	70/M	Perineal numbness with urine retention	Pleocytosis, elevated TP	S2 nerve root, B-cell	Cauda equina	R-CHOP+ Methotrexate	Survived, 12 months
23	Lozsadi *et al.*, 2005[7]	62/M	Paraplegia & sensory level at T6	Elevated TP	Brain, B-cell	T5	Nil	Expired, 4.5 months
24	Current report	54/M	Paraplegia & urine incontinence	Pleocytosis, elevated TP	Brain, B-cell	Cauda equine-conus medullaris	Methothrexate+ Cytarabine+Rituximab	Expired, 8 months

CSF: cerebral spinal fluid; TP: Total protein (mg/dL); N/A: not available; T:Thoracic; CHOP: cyclophosphamide, doxorubicin, vincristine and prednisone; R-CHOP: Rituximab, cyclophosphamide, doxorubicin, vincristine and prednisone; MBVP: methotrexate, carmustine, Etoposide and methylprednisolone

treatment in patients with IVLBCL appear to have better outcome.

In conclusion, we report a case of IVLBCL whose initial presentation was isolated cauda equina-conus medullaris syndrome. Review of literature showed that patients with isolated spinal cord dysfunction as the leading symptom are mostly men and there is a predilection of the lymphoid tumor to affect the conus medullaris and cauda equina. Early initiation of chemotherapy is associated with better outcome.

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DISCLOSURE

Conflicts of interests: None

REFERENCES

1. Shimada K, Kinoshita T, Naoe T, Nakamura S. Presentation and management of intravascular large B-cell lymphoma. *Lancet Oncol* 2009; 10:895-902.
2. Ferreri AJ, Campo E, Seymour JF, *et al*. Intravascular lymphoma: clinical presentation, natural history, management and prognostic factors in a series of 38 cases, with special emphasis on the 'cutaneous variant'. *Br J Haematol* 2004; 127:173-83.
3. Shimada K, Matsue K, Yamamoto K, *et al*. Retrospective analysis of intravascular large B-cell lymphoma treated with rituximab-containing chemotherapy as reported by the IVL study group in Japan. *J Clin Oncol* 2008; 26:3189-95.
4. Shimada K, Murase T, Matsue K, *et al*. Central nervous system involvement in intravascular large B-cell lymphoma: A retrospective analysis of 109 patients. *Cancer Sci* 2010; 101:1480-6.
5. Nakahara T, Saito T, Muroi A, *et al*. Intravascular lymphomatosis presenting as an ascending cauda equina conus medullaris syndrome: Remission after biweekly CHOP therapy. *J Neurol Neurosurg Psychiatry* 1999; 67:403-6.
6. Glass J, Hochberg FH, Miller DC. Intravascular lymphomatosis: A systemic disease with neurologic manifestations. *Cancer* 1993; 71:3156-64.
7. Lozsadi DA, Wieshmann U, Enevoldson TP. Neurological presentation of intravascular lymphoma: report of two cases and discussionof diagnostic challenges. *Eur J Neurol* 2005; 12:710-4.
8. Ponzoni M, Ferreri AJ, Campo E, *et al*. Definition, Diagnosis, and Management of Intravascular Large B-Cell Lymphoma: Proposals and Perspectives From an International Consensus Meeting. *J Clin Oncol* 2007; 25:3168-73.
9. DiGiuseppe JA, Nelson WG, Seifter EJ, Boitnott JK, Mann RB. Intravascular lymphomatosis: a clinicopathologic study of 10 cases and assessment of response to chemotherapy. *J Clin Oncol* 1994; 12:2573-9.
10. Davis TS. Intravascular Lymphoma Presenting with Cauda Equina Syndrome: Treated with CHOP and Rituxan. *Leukemia & Lymphoma* 2003; 44:887-8.
11. Piyatanont K, Bamrungrak K, Watcharananan S, *et al*. Intravascular B-cell lymphoma presenting with cauda equina syndrome: the role of skin biopsy. *Eur J Dermatol* 2010; 20:821-2.
12. Viali S, Hutchinson DO, Hawkins TE, *et al*. Presentation of intravascular lymphomatosis as lumbosacral polyradiculopathy. *Muscle Nerve* 2000; 23:1295-300.
13. Savard M, Verreault S, Gould PV, *et al*. Intravascular lymphoma with conus medullaris syndrome followed by encephalopathy. *Can J Neurol Sci* 2008; 35:366-71.
14. Debiais S, Bonnaud I, Cottier JP, *et al*. A spinal cord intravascular lymphomatosis with exceptionally good outcome. *Neurology* 2004; 63:1329-30.
15. Liu H, Koyanagi I, Chiba H, *et al*. Spinal cord infarct as the initial clinical presentation of intravascular malignant lymphomatosis. *J Clin Neurosci* 2009; 16:570-3.
16. Grove CS, Robbins PD, Kermode AG. Intravascular lymphoma presenting as progressive paraparesis. *J Clin Neurosci* 2008; 15;1056-8.
17. Lee BS, Frankfort BJ, Eberhart CG, Weinberg RS. Diagnosis of intravascular lymphoma by a novel biopsy site. *Ophthalmology* 2011; 118:586-90.
18. Amagasaki K1, Yamazaki H, Ohmori K, Koizumi H, Hashizume K, Sasaguchi N. Malignant intravascular lymphomatosis associated with venous stenosis. Case report. *J Neurosurg* 1999; 90:355-8.
19. Kumar N, Keegan BM, Rodriguez FJ, Hammack JE, Kantarci OH. Intravascular lymphoma presenting as a longitudinally-extensive myelitis: Diagnostic challenges and etiologic clues. *J Neurol Sci* 2011; 303:146-9.
20. Szots M, Szomor A, Kover F, *et al*. Intravascular lymphomatosis of the nervous system. *J Neurol* 2008; 255:1590-2.
21. De Fino C, Arena V, Hohaus S, Di Iorio R, Bozzoli V, Mirabella M. Intravascular large B-cell lymphoma presenting as slowly progressive paraparesis with normal MRI features. *J Neurol Sci* 2012; 314:171-4.
22. Legeais M, Gallas S, Cottier JP, Herbreteau D. Paraplegia and sensory deficit caused by angiotropic large cell lymphoma. *Am J Neuroradiol* 2004; 25:1831-5.
23. Scully RE, Mark EJ, McNeely WF, *et al*. Case records of the Massachusetts General Hospital: Case 31-1995. A 43-year-old man with multifocal neurologic problems and confusion. *N Engl J Med* 1995; 333:992-9.
24. Schwarz S, Zoubaa S, Knauth M, Sommer C, Storch-Hagenlocher B. Intravascular lymphomatosis presenting with a conus medullaris syndrome mimicking disseminated encephalomyelitis. *J Neurooncol* 2002; 4:187-91.
25. Clark WC, Dohan FCJr, Moss T, Schweitzer JB. Immunocytochemical evidence of lymphocytic derivation of neoplastic cells in malignant angioendotheliomatosis. *J Neurosurg* 1991; 74:757-62.
26. Yang T, Tian L, Li Q, *et al*. A case of intravascular

B-cell lymphoma presenting as myelopathy and diagnosed post mortem. *J Neurol Sci* 2008; 272:196-8.
27. Abbasi H, Bell SL, Stewart W, Neelakantan A, Webb S. A mystery solved. *Pract Neurol* 2014; 14:107-9.
28. Waring WS, Wharton SB, Grant R, McIntyre M. Angiotropic large B-cell lymphoma with clinical features resembling subacute combined degeneration of the cord. *Clin Neurol Neurosurg* 1999; 101:275-9.
29. Takizawa S, Shirasugi Y, Nakamura N, *et al*. An Atypical Form of Asian Variant of Intravascular Large B-cell Lymphoma Presenting with Myelopathy Alone for 4 Months Prior to Pancytopenia. *Intern Med* 2007; 46:1879-80.
30. Abuzinadah A, Almalik Y, Shabani-Rad MT, *et al*. Cauda equina syndrome secondary to intravascular lymphoma. *Neurol Clin Pract* 2012; 2:158-61.