DOI: 10.2478/romneu-2018-0069

Primary intramedullary spinal cord non-Hodgkin lymphoma - case report and review of the literature

Aurelia Mihaela Sandu[1], M.A. Fürtös[1], G. Petrescu[1], Anamaria Gheorghiu[1], B.I. David[1], F.M. Brehar[1, 2], A. Giovani[1], M.R. Gorgan[1,2]

[1]"Bagdasar-Arseni" Department of Neurosurgery, Emergency Clinical Hospital, Bucharest, ROMANIA
[2]"Carol Davila" University of Medicine and Pharmacy, Bucharest, ROMANIA

Abstract: Introduction: Primary intramedullary spinal cord lymphomas are extremely rare, occurring mainly in immune compromised patients. *Case report:* We report a case of a 43 years old patient admitted with spinal cord compression. Spinal MRI revealed two thoracic intramedullary tumours. The patients underwent surgery and we performed resection of both primary intramedullary tumours, with favourable neurological outcome. The histopathologic exam was non-Hodgkin lymphoma. The patient underwent adjuvant radiotherapy. Two months later the patient presented thoracic and cerebellar drop metastases, confirmed histopathologically. *Conclusions*: The diagnosis of primary intramedullary spinal lymphoma must be kept in mind in patients with myelopathy. Surgery is needed to provide histopathological samples for positive diagnosis and spinal decompression. Primary intramedullary spinal lymphomas have a propensity to disseminate along the neuraxis.

Key words: intramedullary lymphoma, non-Hodgkin lymphoma

Introduction

Spinal cord lymphomas are rare. Spinal lymphomas are usually extradural, occurring in vertebral bodies or in epidural tissue.

Primary intramedullary spinal cord lymphomas are very rare and accounts for 1% of CNS lymphomas.[1,2] The majority of intramedullary lymphomas are secondary drop metastases. Some studies found them most commonly located in cervical and thoracic spinal segments[3], while other considered that conus medullaris and cauda equina are more affected[4].

They usually occur in the fifth or the sixth decades of life.[1,3,4] Men are more commonly affected compared with women are white race is more affected.[1,4] Risk factors for occurrence of lymphomas are immune depression, such as: AIDS, congenital immune deficiency, cancer, organ transplant related immune

suppression, infection with Epstein-Barr virus, etc.

Intramedullary lymphomas usually appear as a solid, homogenously enhancing mass, isointense in T1W and hyperintense in T2W.[5] CSF cytology shows increased cellularity.[3]

Treatment of spinal lymphomas usually consists of surgical biopsy to establish a positive diagnosis, followed by adjuvant radiotherapy. Chemotherapy is controversial.

Prognosis is poor, 2 years survival rate is 32-36%.[1,4]

Case report

A 43 years old man was admitted in our department with spinal cord compression with neurological level T1, Frankel C severe right > left and loss of consciousness. The patient was immune competent and had no relevant medical history.

Neurologic exam showed paraparesis, right L2 ASIA 2, right L3 ASIA 2, right L4 ASIA 1+, right L5 ASIA 1+, right S1 ASIA 3-, left L2 ASIA 3-, left L3 ASIA 3-, left L4 ASIA 3-, left L5 ASIA 3- and left S1 ASIA 3. Total motor score on the right side was 34 and on the left was 40. We also found hypoesthesia with level T1, bilateral diminished osteotendinous reflexes, bilateral Babinski sign and urinary incontinence.

Spinal MRI revealed two solid intramedullary tumours hyperintense in T1W and isointense in T2W, contrast enhancing. The first intramedullary tumour was located right posterolateral at T1 level, had an important exophytic expansion sizing 27/13/12.5 mm, compressing and pushing the spinal cord to the left. It had an associated syringomyelia extending upwards to C4 and inferiorly to T7. The second tumour was also intramedullary exophytic, located left posterolateral at level T3 and measured 5/4 mm. (Figure 1)

Thoracic spine X-ray showed no radiological changes of vertebral bodies.

Cerebral MRI showed a right temporo-mesial infiltrative tumour.

Blood workout, EKG and pulmonary X-ray showed no relevant changes.

The patient underwent surgery. We performed a longitudinal midline skin incision, from C5 to T5 and bilateral subperiosteal skeletonization of paravertebral muscle from C7 to T4. We performed T1-T3 laminectomies and midline dural incision. We found two intramedullary infiltrative tumours with exophytic components, one located right paramedian at level T1, measuring 2.5/1.5 cm in diameter and another located left paramedian at level T3, measuring 0.5/0.5 cm. We performed total resection of T1 tumour and near total resection of T3 tumour. Haemostasis. Dural closure. Epidural external drainage. Wound closure.

Histopathological exam from both spinal tumours found malignant non-Hodgkin lymphoma. (Figure 2)

Postoperative outcome was favourable, without any additional neurological deficits.

He received dexamethasone 24 mg / d. He began rehabilitation the second day after surgery. He underwent adjuvant radiotherapy.

Two months later, the patient was readmitted with seizures, headache and diplopia. Neurological exam showed paraparesis, right L2 ASIA 3+, right L3 ASIA 3+, right L4 ASIA 3, right L5 ASIA 3, right S1 ASIA 4-, left L2 ASIA 4, left L3 ASIA 4, left L4 ASIA 4 and left L5 ASIA 4. Total motor score on the right side was 41 and on the left was 46. He also had pain and temperature hypoesthesia with level T3 and full sphincter control.

Spinal MRI showed dural contrast enhancement from C3 to T8 and numerous micronodular lesions from T2 to T10, suggestive for drop metastases. The largest lesion sizing 7/8 mm was located at T3 level. (Figure 3)

Thoracic spine X-ray showed T1-T3 laminectomies and no radiological changes of vertebral bodies.

Cerebral MRI showed bilateral cerebellar drop metastases, measuring 0.98 cm on the right and 0.92 cm on the left and right temporo-mesial tumour hypointense in T1W and hyperintense in T2W and FLAIR, without contrast enhancement. (Figure 4)

The patient underwent second surgery and we performed stereotactic biopsy of the right temporo-mesial tumour. Histopathological exam revealed diffuse infiltrative astrocytoma grade II WHO.

For the third surgery, performed under the same general anaesthesia, we performed a minimal left suboccipital craniectomy. Dural mater was cut in X. We found a cortical tumour located immediately inferior to the transverse sinus. We performed total resection of a tumour 1 cm in diameter. Haemostasis. Dural closure. Epidural drainage. Wound closure. Histopathological exam revealed malignant non-Hodgkin lymphoma.

Postoperative outcome was favourable; the patient presented no additional neurological deficits. Under antiepileptic therapy (carbamazepin 200 mg x 3 / d) the patient presented no seizures.

At 6 months follow-up the patients had paraparesis right L2 ASIA 4-, right L3 ASIA 4-, right L4 ASIA 4, right L5 ASIA 4, left L2 ASIA 4+, left L3 ASIA 4+ and left L4 ASIA 4+.

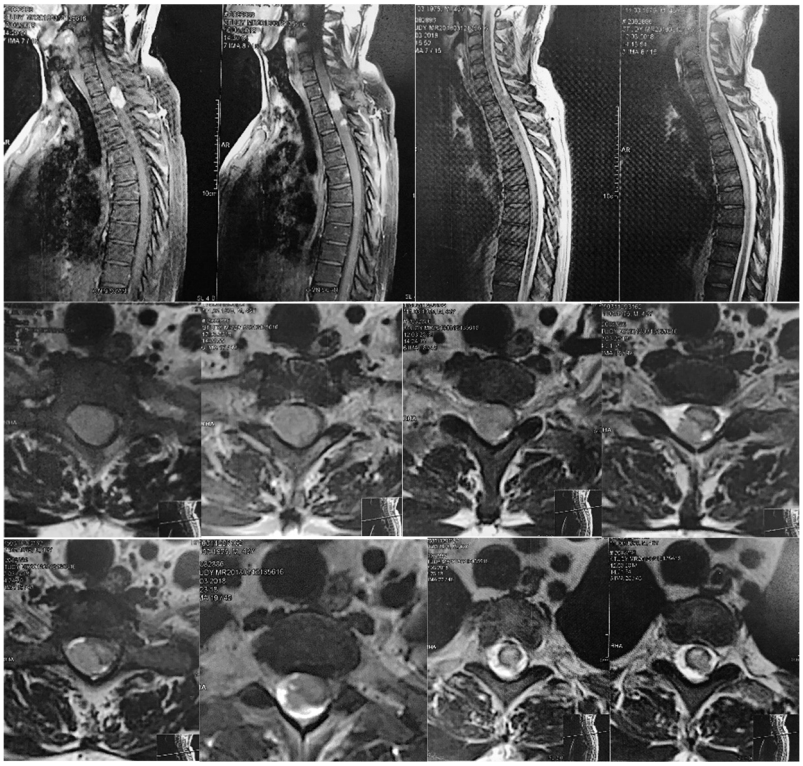

Figure 1. Spinal MRI. Right posterolateral T1 intramedullary with exophytic mass; polar syringomyelia from C4 to T7; left posterolateral T3 intramedullary tumour with exophytic component

Figure 2. Histopathological exam. Malignant B-cell non-Hodgkin lymphoma. (HE stain, 20x)

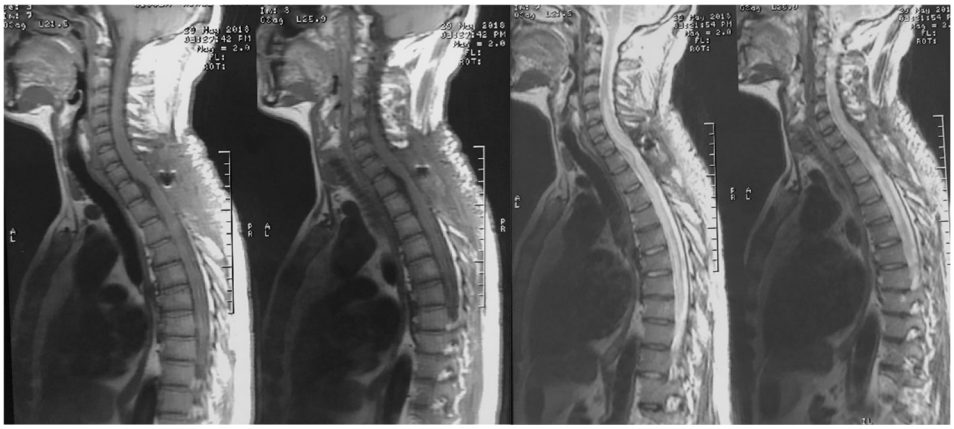

Figure 3. Spinal MRI. Dural contrast enhancement from C3 to T8; micronodular drop metastases micronodular T2 to T10

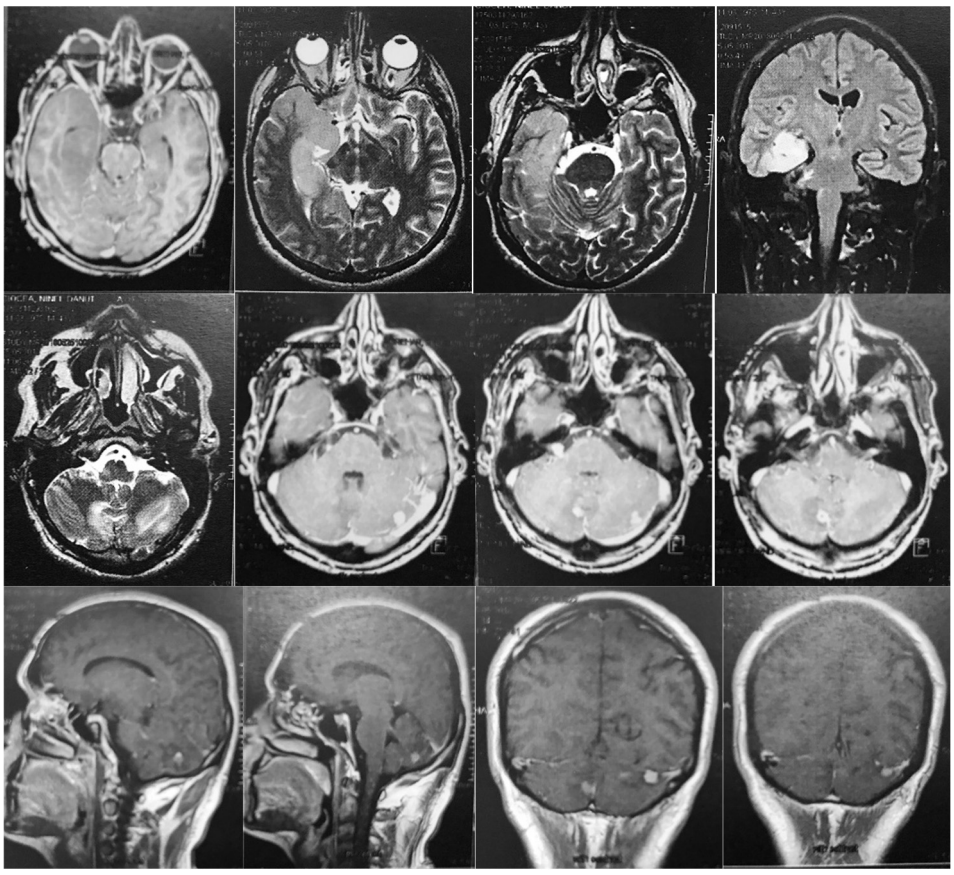

Figure 4. Cerebral MRI. Right temporo-mesial non-enhancing tumour; cerebellar drop metastases

TABLE I

Primary intramedullary lymphomas

No.	*Author, year of publication*	*No. of cases*
1	Bruni J et al., 1977 [10]	1
2	Mitsumoto H et al, 1980 [11]	1
3	Hautzer NW et al., 1983 [3]	1
4	Itami J et al., 1986 [12]	1
5	Landan I et al., 1987 [13]	1
6	Slowik F et al., 1990 [14]	1
7	Wong Chung ME et al., 1991 [15]	1
8	McDonald AC et al., 1995 [16]	1
9	Urasaki E et al., 1996 [8]	1
10	Caruso PA et al., 1998 [17]	1
11	Bekar A et al., 2001 [18]	1
12	Nakamizo T et al, 2002 [5]	2
13	Peltier J et al., 2007 [19]	1
14	Machiya T et al., 2007 [20]	1
15	Matsuyama Y et al., 2009 [21]	3
16	Flanagan EP et al., 2011 [4]	14
17	Lin YY et al., 2012 [22]	1
18	Bhushanam TV et al., 2014 [23]	1
19	Sivri M et al., 2015 [2]	1
20	Guzzetta M et al., 2015 [6]	1
21	Yang W et al., 2017 [1]	346
22	Our case, 2018	1

Discussions

Primary intramedullary lymphomas are rare. So far, besides the two clinical studies reported by Yang et al.[1] and Flanagan et al.[4], only case reports have been described in the literature. (Table 1)

Being so rare, the diagnostic of patients without spinal cord compression syndrome is often delayed[4], so we must keep in mind this diagnosis to insure a prompt diagnosis and initiate appropriate therapy. Spinal lymphomas must be always suspected in immunocompromised patients.

Histopathologic diagnosis is made after surgery (tumour resection or biopsy) or at autopsy. According to WHO classification, the vast majority are B-cell non-Hodgkin lymphomas, with subgroups diffuse large B-cells and follicular being the most frequent.[1] T-cell lymphomas are extremely rare, representing only 1.4% of primary intramedullary spinal lymphomas.[1,6-8] Other histopathological types that can be found are small B-cell, Burkitt, precursor cells and unspecified. Primary intramedullary Hodgkin lymphoma is exceptionally rare.[1]

Nowadays the diagnosis is made on MRI. Spinal lymphomas are hyperintense in T2W, in contrast with cranial lymphomas which are isointense. Multifocal lesions with contrast enhancement are pathognomonic for spinal lymphomas. CSF increased cellularity have no specific pattern. Even though MRI was suggestive for a subdural extramedullary tumour, intraoperative findings showed that the tumour was in fact intramedullary with massive exophytic component. The exophytic mass was contiguous with an intramedullary tumour and presented no other attachment to any structure.

Differential diagnosis is made with other intramedullary tumours: astrocytomas, ependymomas, epidermoid and dermoid tumours, metastases, hemangioblastomas, spinal embryonal tumours, multiple sclerosis.

Treatment consists from surgery, for establishing positive diagnosis and spinal cord decompression, concomitant high-dose corticosteroids, followed by adjuvant radiotherapy and chemotherapy.

Surgery is the first step in treatment of patients with spinal cord tumours. The goals of surgery are obtaining tissue for histopathological diagnosis, achievement of maximum tumour removal without inducing new neurological deficits and preservation of spinal stability. In lymphomas, if the tumour is small and does not cause spinal cord compression, there is no need to perform total resection, a biopsy being sufficient. If the tumour is large and compresses the spinal cord, surgical cytoreduction immediately reduces compression. Tumoral cytoreduction may also be beneficial for adjuvant therapy. Surgical decompression improves neurological outcome and survival.[9]

We performed a posterior approach, through T1, T2, T3 laminectomies. In this way we were able to gain access to both lesions. Although the patients had bipolar syringomyelia extending from C4 to T7, there is no need to address it, because it is secondary, and after tumour resection the syrinx will regress.

There are several ways to resect an intramedullary tumour. The most used surgical route is posterior midline myelotomy. This is a safe anatomic area. Keeping the midline does not induce neurological damage to surrounding structures. This approach is widely used in all intramedullary tumours, especially in those who have no expression on the cord surface. In some cases, when the tumour causes cord distortion keeping within the midline may be challenging. Tumours that come in contact with the cord surface and are not infiltrative display normal structures and can be approach through this safe zone. Exophytic tumours have an important part situated outside the cord. This part is resected first and then the approach can be done through the area where exophytic part of the tumour exited the cord. Intramedullary tumours can be either well-defined or infiltrative. In well-defined tumours the resection is made within the cleavage plane and complete resection is possible, in infiltrative lesions there is no such plane of demarcation and only subtotal or near-total resection is possible. We choose to resect the exophytic component and then enter the cord through this safe area and resect the intramedullary part from inside out. The larger the tumour, and more precisely the larger the area of effraction of the cord, the bigger is the surgical corridor, this is why the bigger tumour could be totally resected and the small one cannot. However, total resection is not needed in lymphomas and the tumour situated at T3 level was not causing compression on the spinal cord.

Intraoperative somatosensory and motor evoked potentials are very useful to monitor the effects on spinal cord induced by surgical gestures.

We did not consider necessary to perform osteosynthesis of the spinal column because the spinal thoracic column is stable and we performed only three laminectomies, with complete preservation of articular facets.

Lymphomas have a high sensibility to corticosteroids and immediately after initiating the therapy neurological improvement occurs. Combined adjuvant oncologic therapy with radio and chemotherapy is more effective than either of

them used alone. Chemotherapy consists of cyclophosphamide, vincristine, doxorubicin, methotrexate, cytarabine, rituximab, vincristine.

Lymphomas of the CNS display a highly aggressive behaviour, are prone to disseminate and drop metastases can be found along the neuraxis, intracranial or spinal. Two months after surgery, our patient came with two drop metastases in the posterior fossa and numerous at the spinal level. Despite radiotherapy and chemotherapy, the prognosis is poor. Median survival rate is 6-9 months, and 2 years survival is 32-36%.[1,4] Young age, early diagnosis, low stage, follicular histologic type are positive prognostic factors.[1]

Conclusions

The diagnosis of primary intramedullary spinal lymphoma must be kept in mind in patients with myelopathy. Surgery is needed to provide histopathological samples for positive diagnosis and spinal decompression. Rapid surgical decompression, corticosteroids and adjuvant radiotherapy improve neurological outcome. Primary intramedullary spinal lymphomas have a propensity to disseminate along the neuraxis.

Correspondence
Aurelia Mihaela Sandu
Address: Fourth Department of Neurosurgery, Emergency Clinical Hospital Bagdasar-Arseni, No. 10-12, Berceni Road, District 4, Bucharest, Romania, postcode 041902
E-mail: aurasandu@gmail.com

References

1. Yang W, Garzon-Muvdi T, Braileanu M, Porras JL, Caplan JM, Rong X, Hunag J, Jallo GI. Primary intramedullary spinal cord lymphoma: a population-based study. Neuro Oncol 2017; 19:414-421.
2. Sivri M, Erdogan H, Allahverdiyev I, Koplay M, Temizoz O. A rare cause of spinal mass: primary intramedullary spinal cord lymphoma. Spine J 2015; 15:e43-e44.
3. Hautzer NW, Aiyesimoju A, Robitaille Y. "Primary" spinal intramedullary lymphomas: a review. Ann Neurol 1983; 14:62-66.
4. Flanagan EP, O`Neil BP, Porter AB, Lanzino G, Haberman TM, Keegan BM. Primary intramedullary spinal cord lymphoma. Neurology 2011; 77:784-791.
5. Nakamizo T, Inoue H, Udaka F, Oda M, Kawai M, Uemura K, Takahashi M, Nishinaka K, Sawada H, KAmeyama M, Koyama T. Magnetic resonance imaging of primary spinal intramedullary lymphoma. J Neuroimaging 2002; 12:183-186.
6. Guzzetta M, Drexler S, Buonocore B, Donovan V. Primary CNS T-cell lymphoma of the spinal cord: case report and literature review. Lab Med 2015; 46:159-163.
7. Gijtenbeek JM, Rosenblum MK, DeAngelis LM. Primary central nervous system T-cell lymphoma. Neurology 2001; 57:716-718.
8. Urasaki E, Yamada H, Tokimura T, Yokota A. T-cell type primary spinal intramedullary lymphoma associated with human T-cell lymphotropic virus type I after a renal transplant: case report. Neurosurgery 1996; 38:1036-1039.
9. Chang CM, Chen HC, Yang Y, Wang RC, Hwang WL, Teng CL. Surgical decompression improves recovery from neurological deficit and may provide a survival benefit in patients with diffuse large B-cell lymphoma-associated spinal cord compression: a case-series study. World J Surg Oncol 2013; 11:90.
10. Bruni J, Bilbao JM, Gray T. Primary intramedullary malignant lymphoma of the spinal cord. Neurology 1977; 27:896-898.
11. Mitsumoto H, Breuer AC, Lederman RJ. Malignant lymphoma of the central nervous system: a case of primary spinal intramedullary involvement. Cancer 1980; 46:1258-1262.
12. Itami J, Mori S, Arimizu N, Inoue S, Lee M, Uno K. Primary intramedullary spinal cord lymphoma: report of a case. Jpn J Clin Oncol 1986; 16:407-412.

13. Landan I, Gilroy J, Wolfe DE. Syringomyelia affecting the entire spinal cord secondary to primary spinal intramedullary central nervous system lymphoma. J Neurol Neurosurg Psychiatr 1987; 50:1533-1535.
14. Slowik F, Mayer A, Afra D, Deak G, Havel J. Primary spinal intramedullary malignant lymphoma. A case report. Surg Neurol 1990; 33:132-138.
15. Wong Chung ME, van Heesewijk JP, Ramos LM. Intramedullary non-Hodgkin's lymphoma of the spinal cord; a case report. Eur J Radiol 1991; 12:226-227.
16. McDonald AC, Nicoll JA, Rampling R. Intramedullary non-Hodgkin's lymphoma of the spinal cord: a case report and literature review. J Neurooncol 1995; 23:257-263.
17. Caruso PA, Patel MR, Joseph J, Rachlin J. Primary intramedullary lymphoma of the spinal cord mimicking cervical spondylotic myelopathy. AJR Am J Roentgenol 1998; 171:526-527.
18. Bekar A, Cordan T, Evrensel T, Tolunay S. A case of primary spinal intramedullary lymphoma. Surg Neurol 2001; 55:261-264.
19. Peltier J, Cretu I, Fichten A, Toussaint P, Desenclos C, Le Gars D. Primary intramedullary lymphoma. Case report. Neurochirurgie 2007; 53:375-378.
20. Machiya T, Yoshita M, Iwasa K, Yamada M. Primary spinal intramedullary lymphoma mimicking ependymoma. Neurology. 2007;68(11):872-872. Neurology 2007; 68:872.
21. Matsuyama Y, Sakai Y, Katayama Y, Imagama S, Ito Z, Wakao N, Sato K, Kamiya M, Yukawa Y, Kanemura T, Yanase M, Ishiguro N. Surgical results of intramedullary spinal cord tumor with spinal cord monitoring to guide extent of resection. J Neurosurg Spine 2009; 10:404-413.
22. Lin YY, Lin CJ, Ho DMT, Guo WY, Chang CY. Primary intramedullary spinal cord lymphoma. Spine J 2012; 12:527-528.
23. Bhushanam TV, Rajesh A, Linga VG, Uppin MS, Malik M. Primary intramedullary non-Hodgkin's lymphoma in an immunocompetent child. Spinal Cord 2014; 52 Suppl:S21-S23.