B-Cell Lymphoma Intramedullary Tumor: Case Report and Systematic Review

Daniel Gregório Gonsalves¹  Paula Eduardo Albuquerque Zito Raffa¹  Gabriela Gerenutti de Sousa²
Melissa Esposito Gomes Rigueiral³  Iracema Araújo Estevão⁴  Cesar Cozar Pacheco⁴
Roger Thomaz Rotta Medeiros⁴  Paulo Roberto Franceschini⁵  Paulo Henrique Pires de Aguiar⁴,⁶,⁷

¹ Graduation Medicine at Faculty of Medicine of Catanduva, Catanduva, São Paulo, Brazil
² Graduation Medicine at Pontifical Catholic University of São Paulo, Sorocaba, Brazil
³ Graduation Medicine at Faculty of Medicine of ABC, Santo André, São Paulo, Brazil
⁴ Department of Neurosurgery, Santa Paula Hospital, São Paulo, Brazil
⁵ Department of Neurosurgery, University of Caxias do Sul, Rio Grande do Sul, Brazil

Address for correspondence  Daniel Gregório Gonsalves, Graduation Medicine at Faculty of Medicine of Catanduva, Rua dos Estudantes, 225, Catanduva, São Paulo, Brazil, 15.809-144
(e-mail: danielgregoriogonsalves@gmail.com).

⁶ Department of Research and Innovation, Laboratory of Cellular and Molecular Biology, Faculty of Medicine of ABC, Santo André, São Paulo, Brazil
⁷ Department of Neurology, School of Medicine of Pontifical Catholic University of São Paulo, Sorocaba, São Paulo, Brazil

AJNS 2023;18:231–245.

Abstract

Intramedullary tumors represent the major cause of spinal cord injuries, and its symptoms include pain and weakness. Progressive weakness may concomitantly occur in the upper and lower limbs, along with lack of balance, spine tenderness, sensory loss, trophic changes of extremity, hyperreflexia, and clonus. The study protocol was in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines. A systematic search of the MEDLINE electronic database was performed to identify the studies reporting the clinical features of children and adults who presented with an intramedullary lymphoma. Twenty-one studies were included, reporting 25 cases. Manuscripts were excluded if the full-text article was not available, original data were not reported (e.g., review articles), or if the main disease was not intramedullary lymphoma. A structured data extraction form was employed to standardize the identification and retrieval of data from manuscripts. To enlighten the discussion, a case is also presented. An 82-year-old woman with Fitzpatrick skin type II, diagnosed and treated for non-Hodgkin’s lymphoma 7 years ago, was admitted with mental confusion and memory loss for the past 2 months—evolving with recurring falls from her own height. One day before admission, she displayed Brown-Séquard syndrome. An expansive lesion from C2 to C4 in the cervical spinal cord was found and a hypersignal spinal cord adjacent was described at the bulb medullary transition to the C6–C7 level. A primary spinal cord tumor was considered, as well as a melanoma metastasis, due to the lesion’s flame pattern. The patient presented a partial recovery of symptoms and a reduction of the spinal cord edema after being empirically treated with corticosteroids, but the lesion

Keywords

► spinal cord neoplasms
► lymphoma
► large B cell
► diffuse
► neurosurgery

article published online: 2023-06-06

ISSN 2248-9614.

© 2023. Asian Congress of Neurological Surgeons. All rights reserved.

This is an open access article published by Thieme under the terms of the Creative Commons Attribution-NonDerivative-NonCommercial-License, permitting copying and reproduction so long as the original work is given appropriate credit. Contents may not be used for commercial purposes, or adapted, remixed, transformed or built upon. (https://creativecommons.org/licenses/by-nc-nd/4.0/)

Thieme Medical and Scientific Publishers Pvt. Ltd., A-12, 2nd Floor, Sector 2, Noida-201301 UP, India
maintained its extent. Subsequently, a large diffuse B-cell lymphoma with nongerminatal center was found in open body biopsy, infiltrating neural tissue. The main objective of the present study is to report a surgical case treated for a large diffuse B-cell lymphoma, in addition to presenting the results of a systematic review of primary intramedullary spinal cord lymphoma.

Introduction

Spinal tumors are divided into three groups, which are extradural, intradural–extramedullary, and intramedullary spinal cord tumors (IMSCT). They represent approximately 15% of all central nervous system (CNS) tumors. IMSCT is the most uncommon type of spinal tumor. It originates in the spinal cord itself, causing its invasion and destruction of white and gray matter. However, a spinal cord lesion can also be linked to a lymphoma. Primary intramedullary spinal cord lymphoma (PISCL) is one of the rarest spinal diseases, comprising 1% of all CNS lymphomas. It is characterized by a rapid progression in the first year after diagnosis, followed by a slower one after this period. PISCL is an aggressive condition and can emerge directly from CNS, involving the eye, leptomeninges, brain, and spinal cord. Primary CNS lymphoma (PCNSL) has a high possibility of relapse, with poor long-term survival, even though the assigned treatment has advanced. Currently, the treatment of choice in these cases is optimized therapy with high-dose methotrexate-based chemotherapy.

In Brown-Séquard syndrome, the lesion may be completely transverse, initially presenting with asymmetrical spinal cord signs. When an incomplete spinal cord injury (SCI) occurs, some neurologic function will be retained, and one of the syndromes related to that condition is Brown-Séquard syndrome (BSS). The symptoms of BSS, resulting from spinal cord hemisection, present themselves differently in each hemibody. These are weakness and paralysis on one side and painful and thermal sensory loss on the other, with causes ranging from traumatic to nontraumatic, such as tumors, vertebral disk herniation, and tuberculosis.

Individuals of all ages can be affected by spinal metastases. However, these are more frequently reported in patients between 40 and 70 years of age, with the thoracic spine the most affected site and the highest incidence of neurological deficit, followed by the lumbar and cervical spine.

All these concepts are necessary to understanding the following clinical case, in which an 82-year-old woman displays symptoms analogous to the BSS presentation, secondary to an intramedullary lesion. The aim of this investigation is to discuss this rare presentation and enlighten the diagnosis.

Methods

The study protocol was in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines.

Population: Adults and children, both genders, across the world.

Exposition: Diagnosed primary intramedullary lymphoma.

Comparison: Age, sex, interval of diagnosis, clinical features, diagnosis, localization, treatment, histological type.

Outcomes: Follow-up and mortality outcomes (alive, deceased).

Search Strategy and Data Sources

A systematic search of the MEDLINE electronic database from February 7 to September 31, 2022 was performed using PubMed’s MeSH Advanced Search Builder tool. The search commands can be referred to in Appendix 1.

The search was performed to identify studies reporting clinical features of children and adults who presented with an intramedullary lymphoma. The reference lists of identified studies were examined to identify further reports of interest.

Study Selection

Three reviewers independently screened the titles and abstracts of all citations for eligibility and retrieved those that met the inclusion criteria. If insufficient information was available in the abstract to decide on eligibility, the whole article was retrieved for review. Discrepancies were resolved by consensus and utilization of a fourth reviewer when necessary. Manuscripts reporting information on children and adults, both genders, were included when an intramedullary lymphoma was present and the article dated from the last 5 years. Manuscripts were excluded if the full-text article was not available, original data were not reported (e.g., review articles), or if the main disease was not intramedullary lymphoma.

Data Extraction

A structured data extraction form was employed to standardize the identification and retrieval of data from manuscripts. Data were organized into a standardized table, where each reviewer extracted the following data from the studies: age, sex, interval of symptom onset, clinical presentation, localization, treatment, histological type, follow-up, and outcome. Where manuscripts did not report the information we were evaluating, we displayed the information as not available.

Results

For the systematic literature review, of the 963 articles that were found, we selected those within 5 years of publication
date, excluding those that did not contain articles reporting primary data (e.g., isolated reviews, meta-analyses, or national database projects) and that were not written in English. In all, 148 articles were screened by the reviewers and articles that did not address lymphoma or were not case reports were excluded (102 articles). Then, 46 articles were screened for primary data and full-text information, including 21 studies to the review (Fig. 1).

The 21 selected studies7–27 that met the eligibility criteria are described in Table 1, reporting a total of 25 cases (20 male and 5 female patients), in the age range of 15 to 79 years (average: 52.72 years). Only 10 cases reported follow-up as 4 patients were lost to follow-up and 11 studies did not report it. The average follow-up was 1.73 years (range: 2 weeks–6 years). Three patients were deceased at the time of report, 7 did not report the information, and 15 patients were alive (6 free of infection, 1 in remission, 1 with remaining disease, and 7 unknown). In terms of location, 4 lesions were located above the cervical region, 5 cervical, 10 thoracic, 7 lumbar, and 7 unknown. In 7 cases, the lesion involved 1 cauda equina lesions (discriminated in the table), with 5 lesions located above the cervical region, 1 cervical, 4 thoracic, 4 lumbar, and 1 unknown. In terms of presentation, 4 lesions were reported as a partial recovery of symptoms and a reduction of the spinal cord edema after being empirically treated with corticosteroids, but the lesion maintained its extent (Fig. 2). Its dimension was $4.8 \times 0.8 \times 0.7$ cm, homogenous impregnation with gadolinium. There was also a hyperintensity in the spinal cord, from the bulb medullary transition to the C6–C7 level (Fig. 2), possibly corresponding with spinal cord edema. After being evaluated by the hematology, oncology, neurology, and neurosurgery teams, it was not possible to confirm or reject recidivated lymphoma, for a primary spinal cord tumor (ependymoma, astrocytoma, hemangioblastoma) was possible, as well as a melanoma metastasis, due to the lesion's flame pattern.

The patient presented a partial recovery of symptoms and a reduction of the spinal cord edema after being empirically treated with corticosteroids, but the lesion maintained its extent (Fig. 3). A frozen section body biopsy was performed, and the surgical material was sent to anatomopathological and immunohistochemical study (Table 2). A large diffuse B-cell lymphoma with nongerminal center infiltrating neural tissue was found in C2. Therefore, the primary hypothesis was confirmed: lymphoma.

Performed treatment included surgical resection, partial biopsy, chemotherapy, radiotherapy, biological therapy, and corticosteroids. Tumor resection was done in 13 patients, decompressive laminectomies was done in 9 patients, chemotherapy (CT) in 18 patients, corticosteroids in 6 patients, radiotherapy in 4 patients, and biological drugs in 2 patients. The following symptoms appeared recurrently in the case series and may help suspicion for lymphoma if present: constitutional symptoms, back pain, and lower motor neuron involvement.

Case Description

An 82-year-old woman, with Fitzpatrick type II skin, diagnosed and treated for non-Hodgkin's lymphoma 7 years ago, was admitted at the hospital with mental confusion and memory loss for the past 2 months, evolving with recurring falls from height in the last month. A day before hospital admission, her condition aggravated, now exhibiting loss of strength and hemiparesis in the right side of the body, associated with superficial hemiparesthesia in the left side, a clinical condition compatible with BSS, characterized by a spinal cord hemisection, which was confirmed by imaging tests. No other neurological findings were noted.

Computed tomography (CT) scan and magnetic resonance imaging (MRI) showed an expansive lesion from C2 to C4 in the cervical spinal cord (Fig. 2). Its dimension was $4.8 \times 0.8 \times 0.7$ cm, homogenous impregnation with gadolinium. There was also a hyperintensity in the spinal cord, from the bulb medullary transition to the C6–C7 level (Fig. 2), possibly corresponding with spinal cord edema. After being evaluated by the hematology, oncology, neurology, and neurosurgery teams, it was not possible to confirm nor reject recidivated lymphoma, for a primary spinal cord tumor (ependymoma, astrocytoma, hemangioblastoma) was possible, as well as a melanoma metastasis, due to the lesion's flame pattern.

The patient presented a partial recovery of symptoms and a reduction of the spinal cord edema after being empirically treated with corticosteroids, but the lesion maintained its extent (Fig. 3). A frozen section body biopsy was performed, and the surgical material was sent to anatomopathological and immunohistochemical study (Table 2). A large diffuse B-cell lymphoma with nongerminal center infiltrating neural tissue was found in C2. Therefore, the primary hypothesis was confirmed: lymphoma.

The neurosurgical team performed an excision of the intramedullary cervical lesion (Fig. 4), through a lateral intermediate sulcus approach. The patient was neuromonitored intraoperatively and afterward motor rehabilitation was initiated (Fig. 5). A discreet improvement of muscle strength on the right hemibody was perceived. Vital signs were stable, besides a few hypertension episodes. The next step was urgent radiotherapy, followed by chemotherapy.

Unfortunately, the patient developed sepsis during chemotherapy 2 weeks after surgical resection and succumbed to the disease.
Table 1 Relevant lymphomas cases from the literature in the past 5 years

<table>
<thead>
<tr>
<th>Title</th>
<th>Year</th>
<th>DOI</th>
<th>Authors</th>
<th>Age/sex</th>
<th>Interval (onset-diagnosis)</th>
<th>Clinical features</th>
<th>Diagnosis</th>
<th>Localization</th>
<th>Treatment</th>
<th>Histological type</th>
<th>Follow-up</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>A conservative approach to the treatment of a rare case of cervical spine double expressor diffuse large B-cell lymphoma: a case report</td>
<td>2022</td>
<td>10.7759/cureus.21208</td>
<td>Chen W, Hika B, Smith CJ, Parrett TJ, Mesfin F</td>
<td>58/M</td>
<td>1 y</td>
<td>Chronic neck pain and spasm</td>
<td>Diffuse large B-cell lymphoma</td>
<td>Retropharyngeal mass extending through the bilateral neuroforamina, into the epidural space, and involving the posterior elements of the cervical spine at C2–C3 (1.8 x 4.7 x 4.5 cm)</td>
<td>Posterior decompresion and excisional biopsy without resection of the tumor, CT (systemic and intrathecal), RT</td>
<td>Double expressor DLBCL with anaplastic features. Small lymphocytes and large atypical cells with prominent nucleoli and large cytoplasm, positive for CD20, cyclin D1, and Pax5. KI67 revealed a substantial level of proliferative activity</td>
<td>Not available</td>
<td>Alive</td>
</tr>
<tr>
<td>A rare entity in the lumbar epidural region: T-cell lymphoblastic lymphoma</td>
<td>2021</td>
<td>10.14444/71655</td>
<td>Erdem MB, Kale A, Yaman ME, Emmez H</td>
<td>38/F</td>
<td>1 mo</td>
<td>Weakness in the lower extremities and newly developed urinary incontinence</td>
<td>T-lymphoblastic lymphoma</td>
<td>L2-L4 levels</td>
<td>L3 total, and L2 and L4 bilateral partial decompressive laminectomies, CT, donor lymphocyte</td>
<td>Lymphoblastic cell infiltration in the bone marrow biopsy, positive for cytoplasmic CD3 expression and TdT</td>
<td>5 mo</td>
<td>Deceased</td>
</tr>
<tr>
<td>Primary cauda equina T-cell lymphoblastic lymphoma</td>
<td>2020</td>
<td>10.1016/j.jnee.2020.06.184</td>
<td>De Vries J, Oterdoom MD, Den Dunnen Wf, Eerling RH, Kloet RW, Roeslofzen WW, Jeltema HR</td>
<td>54/F</td>
<td>8 mo</td>
<td>Progressive back pain radiating to both legs and deteriorating neurologic deficits</td>
<td>Primary cauda equina TLBL, (T-cell lymphoblastic lymphoma)</td>
<td>L1-L4 and a central mass at L3-L4</td>
<td>Laminectomy of L3 and L4, Corticosteroids, CT (intrathecal and venous), RT</td>
<td>Small blue round tumor cells in hematoxylin and eosin staining. Microscopic analysis showed a vague, nodular growth pattern. The tumor cells were polymorphic and had hyperchromatic nuclei and a nucleus in some cells. There was hardly any cytoplasm. Multiple mitotic figures were spotted as well as small, thin-walled vessels. Focal points of necrosis were apparent. The lesion mainly consisted of CD3-positive cells. Further analysis showed positive results for TdT (terminal deoxynucleotidyl transferase) and for the following clusters of differentiation (CD): CD1a, CD99, CD4, and CD8. Weakly positive were T-cell markers CD2, CD5, and CD7. The lesion showed a Ki67 proliferation fraction of 90%. EBV in situ hybridization came out negative. These findings are compatible with T-EBL</td>
<td>6 wk</td>
<td>Deceased</td>
</tr>
<tr>
<td>Title</td>
<td>Year</td>
<td>DOI</td>
<td>Authors</td>
<td>Age/sex</td>
<td>Interval (onset-diagnosis)</td>
<td>Clinical features</td>
<td>Diagnosis</td>
<td>Localization</td>
<td>Treatment</td>
<td>Histological type</td>
<td>Follow-up</td>
<td>Outcome</td>
</tr>
<tr>
<td>-------</td>
<td>------</td>
<td>-----</td>
<td>---------</td>
<td>---------</td>
<td>---------------------------</td>
<td>-------------------</td>
<td>-----------</td>
<td>-------------</td>
<td>-----------</td>
<td>-------------</td>
<td>-----------</td>
<td>---------</td>
</tr>
<tr>
<td>Primary central nervous system lymphoma mimicking longitudinally extensive transverse myelitis</td>
<td>2020</td>
<td>10.1177/1941874420967560</td>
<td>Natteru PA, Shukhar S, Nair LR, Uschmann H</td>
<td>59/W</td>
<td>4 wk</td>
<td>Progressive tetraparesis and bowel and bladder incontinence</td>
<td>Large B-cell lymphoma</td>
<td>T1–T9 levels</td>
<td>CT, Corticosteroids</td>
<td>Immunohistochemical staining and flow cytometric analysis was positive for CD-20, BCL-6, and MUM1, and negative for CD-10 and cyclin D1</td>
<td>Not available</td>
<td>Alive</td>
</tr>
<tr>
<td>A rare case of primary ventricular lymphoma presented on FDG PET/CT</td>
<td>2020</td>
<td>10.1097/RLU.0000000000002876</td>
<td>Wang D, Su M, Xiao J</td>
<td>51/W</td>
<td>4 mo</td>
<td>Unsteady gait and progressive decline in memory</td>
<td>Diffuse large B-cell lymphoma</td>
<td>Multiple space-occupying lesions in the ventricles</td>
<td>Not available</td>
<td>Diffuse growth pattern of large, dysplastic lymphocytes with vesicular nuclei, positive for CD20 and MUM1 immunostaining. Ki67 demonstrated high proliferative index</td>
<td>Not available</td>
<td>Not available</td>
</tr>
<tr>
<td>Primary central nervous system lymphoma with diffuse neurolymphomatosis involving multiple cranial and spinal nerve roots</td>
<td>2020</td>
<td>10.1097/RLU.0000000000003018</td>
<td>Singh SS, Mittal BR, Kumar R, Singh H, Babani N, Goyal M</td>
<td>23/M</td>
<td>4 mo</td>
<td>Intermittent fever, headache, vomiting, loss of weight and appetite, and progressive weakness of all 4 limbs, which subsequently progressed to quadriparesia associated with urinary incontinence. Evolved with altered sensorium, decreased hearing in both ears, decreased sensation in lateral upper and lower limbs and trunk, difficulty in swallowing, change in voice, and nasal regurgitation</td>
<td>B-cell non-Hodgkin’s lymphoma</td>
<td>Brainstem, cerebellum, spinal cord, craniopharyngeal plate, bilateral foramen ovale and foramen rotundum, multiple spinal nerve roots, lateral ventricles, bilateral jugular foramen, and carotid canal, bilateral Meckel’s cave</td>
<td>Antitubercular therapy, Corticosteroids,</td>
<td>High-grade B-cell non-Hodgkin’s lymphoma</td>
<td>Not available</td>
<td>Not available</td>
</tr>
<tr>
<td>Primary diffuse large B-Cell non-Hodgkin’s lymphoma of the thoracic spine presented initially as an epigastric pain</td>
<td>2020</td>
<td>10.4103/ajns.AJNS_300_19</td>
<td>Falkhoury F, Shoumal N, Obeid B, Alkhoder A</td>
<td>60/M</td>
<td>4 days</td>
<td>Acute nonsaturating epigastric pain. Two days later, the pain started to radiate toward the back, and the patient started to suffer from severe thoracic back pain. Four days later, the pain started to radiate toward both lower limbs with subtle beginning of</td>
<td>Large B-cell lymphoma</td>
<td>T6/T7 level</td>
<td>Partial laminectomy with total resection of the extradural mass, CT</td>
<td>Diffuse malignant infiltration of large atypical lymphoid cells, large vesicular nuclei, prominent nucleoli, and coarse chromatin. Numerous mitotic cells were also present, and immune stains were positive for CD20 and leukocyte common antigen</td>
<td>2 y</td>
<td>Alive, free of infection</td>
</tr>
</tbody>
</table>

(Continued)
<table>
<thead>
<tr>
<th>Authors</th>
<th>Year</th>
<th>DOI</th>
<th>Title</th>
<th>Age/sex</th>
<th>Interval</th>
<th>Localization</th>
<th>Diagnosis</th>
<th>Clinical features</th>
<th>Treatment</th>
<th>Histological type</th>
<th>Follow-up</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pandey S, Gokden M, Kazemi NJ, Post GR</td>
<td>2019</td>
<td>Not available</td>
<td>Hematological malignancies presenting with spinal epidural mass and spinal cord compression: a case series</td>
<td>61/M</td>
<td>3 wk</td>
<td>Lower back and leg pain, numbness, incontinence</td>
<td>Diffuse large B-cell lymphoma, not otherwise specified</td>
<td>L1 mass with extension from T12 to L3 with compression</td>
<td>Tumor resection</td>
<td>Large neoplastic cells with prominent eosinophilic cytoplasm, large irregular nuclei, frequent mitoses, with scattered eosinophils</td>
<td>Not available</td>
<td>Alive with disease</td>
</tr>
<tr>
<td>Gonsalves et al.</td>
<td>2023</td>
<td>Not available</td>
<td>Asian Journal of Neurosurgery Vol. 18 No. 2/2023 © 2023. Asian Congress of Neurological Surgeons. All rights reserved.</td>
<td>49/M</td>
<td>2 wk</td>
<td>New back pain, left leg weakness, numbness</td>
<td>Diffuse large B-cell lymphoma, not otherwise specified</td>
<td>T2 vertebral body mass with epidural extension at T16-17</td>
<td>Tumor resection, CT</td>
<td>Large neoplastic cells with prominent eosinophilic cytoplasm, large irregular nuclei, frequent mitoses, with scattered eosinophils</td>
<td>Not available</td>
<td>Alive, free of infection</td>
</tr>
<tr>
<td>23/M</td>
<td>1 mo</td>
<td>Progressive back pain and difficulty walking</td>
<td>Anaplastic large cell lymphoma</td>
<td>T7-T8 vertebral body mass with epidural compression at T6-17</td>
<td>Tumor resection, CT</td>
<td>Pleomorphic population of highly atypical cells with eosinophilic polymorphonuclear leukocytes, with scattered CD45, CD5, and CD30</td>
<td>Not available</td>
<td>Alive, free of infection</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>55/F</td>
<td>3 mo</td>
<td>Mid-back pain (3 mo), bilateral lower extremity weakness (2 wk), and complete sensorimotor loss (2 d)</td>
<td>Anaplastic large cell lymphoma</td>
<td>T4 vertebral mass with T3-T5 soft-tissue component and cord compression. Additional lesions in T12 vertebra, left ilium, right femur, bilateral pleural effusions, multiple lung nodules, and left frontal extra-axial mass</td>
<td>Tumor resection, CT</td>
<td>Pleomorphic population of highly atypical cells with eosinophilic polymorphonuclear leukocytes, with scattered CD45, CD5, and CD30</td>
<td>Not available</td>
<td>Alive, free of infection</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15/M</td>
<td>1 mo</td>
<td>Back pain, tingling, and numbness of legs</td>
<td>B-lymphoblastic lymphoma</td>
<td>T9 vertebral body mass with epidural compression at T8-T10</td>
<td>Tumor resection, CT</td>
<td>B-lymphoblastic lymphoma</td>
<td>Not available</td>
<td>Alive, free of infection</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Table 1 (Continued)

<table>
<thead>
<tr>
<th>Title</th>
<th>Year</th>
<th>DOI</th>
<th>Authors</th>
<th>Age/sex</th>
<th>Interval (onset-diagnosis)</th>
<th>Clinical features</th>
<th>Diagnosis</th>
<th>Localization</th>
<th>Treatment</th>
<th>Histological type</th>
<th>Follow-up</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary intraspinal non-Hodgkin’s lymphoma: case report and review of literature</td>
<td>2019</td>
<td>10.1016/j.jocn.2018.11.046</td>
<td>Beume LA, Wolf K, Urbach H, Klingler JH, Staszewski O, Marks R, Weller C, Rauer S, Hosp JA</td>
<td>67/F</td>
<td>6 wk</td>
<td>Inability to walk, reduced sensitivity in the lower extremities, and bowel and bladder dysfunction. Severe weakness of the right (MRC muscle scale: 1/5) and left leg (2/5), and loss of sensation below Th6. Deep tendon reflexes of the legs were absent while Babinski’s sign was positive on both sides</td>
<td>Primary intraspinal B-cell non-Hodgkin’s lymphoma</td>
<td>Upper border of C6: upper border of T12. Intramedullary T3–T9. Retinal infiltration</td>
<td>CT/BT</td>
<td>Pleomorphic partially lymphoid, partially blastic tumor cells with increased mitotic and proliferative activity and immunohistochemical positivity for CD20 and CD79a, with a MIB1 of 90%</td>
<td>Not available</td>
<td>Alive</td>
</tr>
<tr>
<td>Primary peripheral gamma delta T-cell lymphoma of the central nervous system: report of a the intramedullary spinal cord and presenting with myelopathy</td>
<td>2019</td>
<td>10.4132/jptm.2018.08.21</td>
<td>Yim J, Song SC, Kim S, Choi JH, Lee RC, Bae JM, Jeon YK</td>
<td>75/W</td>
<td>3.5 mo</td>
<td>Back pain and lower extremity weakness</td>
<td>Primary peripheral gamma delta T-cell lymphoma</td>
<td>Multiple enhancing intramedullary nodular lesions in the spinal cord at T9–T10, T11, and L5 levels</td>
<td>T11 laminectomy and tumor removal</td>
<td>Diffuse infiltration of monotonous, medium-to-large atypical lymphocytes with round nuclei, condensed chromatin, pale-to-eosinophilic cytoplasm, and small inconspicuous nucleoli. Immunohistochemically, the atypical cells were CD3(−), CD20(−), TCRβ(−), TCRγ(−), CD30(−), CD4(−), CD8(−), CD10(−), BCL-6(−), MUM1(−), CD56(−), TIA-1(−), granzyme B(−), and CD103(−). The Ki-67 index was about 80%</td>
<td>Lost to follow-up</td>
<td>Not available</td>
</tr>
<tr>
<td>Spinal primary central nervous system lymphoma: case report and literature review</td>
<td>2018</td>
<td>10.1016/j.jocn.2018.01.034</td>
<td>Li Feng, Dingbang Chen, Hongyan Zhou, Cunzhou Shen, Haiyan Wang, Xunli Sha, Xiulin Liang, Ling Chen</td>
<td>45/M</td>
<td>1 y</td>
<td>Progressive tremor in the left limbs and slight dysarthria as well as 3-mo history of paraparesis, tinnitus, and insomnia. Severe dysarthria, salorhea, incontinent closure of the eyelids, constipation, atrophy in the left limbs, as well as paralysis and numbness in the left lower limb in 2 mo</td>
<td>Spinal primary central nervous system lymphoma</td>
<td>Cerebellum and cauda equine</td>
<td>First tuberculosis was suspected, treatment with isoniazid, rifampicin, pyrazinamide, and ethambutol was performed, in addition to intrathecal injections of isoniazid and dexamethasone</td>
<td>Cytological examination of CSF revealed an abundant of lymphocytes with macronuclei</td>
<td>2 wk</td>
<td>Deceased</td>
</tr>
<tr>
<td>Title</td>
<td>Year</td>
<td>DOI</td>
<td>Authors</td>
<td>Age/sex</td>
<td>Interval (onset-diagnosis)</td>
<td>Clinical features</td>
<td>Diagnosis</td>
<td>Localization</td>
<td>Treatment</td>
<td>Histological type</td>
<td>Follow-up</td>
<td>Outcome</td>
</tr>
<tr>
<td>----------------------------------------------------------------------</td>
<td>--------</td>
<td>--------------------------------------</td>
<td>--------------------------------------</td>
<td>---------</td>
<td>-----------------------------</td>
<td>--------------------------------------------------------------------------------</td>
<td>-----------------------------------------------</td>
<td>--------------</td>
<td>-----------------------------------------</td>
<td>---------------------</td>
<td>--------------------</td>
<td>------------------</td>
</tr>
<tr>
<td>Wrap-around appearance: underrecognized radiologic feature of spinal lymphoma</td>
<td>2018</td>
<td>10.1016/j.wneu.2018.04.051</td>
<td>Patel M, Wu OC, Kaishwal MK</td>
<td>71/M</td>
<td>Not available</td>
<td>Neck and upper back pain</td>
<td>Non-Hodgkin's lymphoma</td>
<td>T2</td>
<td>T2 laminectomy and decompression, CT</td>
<td>Not available</td>
<td>Not available</td>
<td>Not available</td>
</tr>
<tr>
<td>Primary spinal lymphoma masquerading as meningioma: preoperative and postoperative magnetic resonance imaging findings</td>
<td>2018</td>
<td>10.1016/j.wneu.2018.04.129</td>
<td>Arslan H, Yavuz A, Aycan A</td>
<td>55/M</td>
<td>Not available</td>
<td>Back pains with the complaints accompanied by increasing weakness in the lower extremities</td>
<td>Diffuse large B-cell non-Hodgkin's lymphoma</td>
<td>Thoracic area, the anterior epidural space and paravertebral area, approximately 55 x 9 mm</td>
<td>Tumor removal</td>
<td>Diffuse large B-cell non-Hodgkin's lymphoma</td>
<td>Not available</td>
<td>Not available</td>
</tr>
<tr>
<td>Primary central nervous system lymphoma of T-cell origin: an unusual cause of spinal cord disease</td>
<td>2017</td>
<td>10.1007/s13730-016-0726-y</td>
<td>Sophie Fastré, Frédéric London, Julie Leteille, Alessandra Camboni, Anne Jolyon</td>
<td>45/M</td>
<td>Over weeks</td>
<td>Progressive paraparesis and numbness of his lower limbs over weeks, with bladder dysfunction, Generalized hyperreflexia and bilateral extensor planter response</td>
<td>Lymphoma of T-cell origin</td>
<td>Hypermagnetic images in the left cerebellum and intramedullary cervical spinal cord with rostral extension to the brainstem</td>
<td>Corticosteroids, CT</td>
<td>Infiltration of cerebellar tissue with histiocytes and lymphocytes. Lymphoma of T-cell origin; strongly positive for CD3, CD2, CD5, and CD4, and weakly positive for CD7</td>
<td>3 mo</td>
<td>Alive</td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma of the cauda equina: a rare entity</td>
<td>2017</td>
<td>10.1080/0268869.2016.12243121</td>
<td>Ghevaaghcheh R, Marcus K, Aizpurua M, Aizpurua J, Aizpurua S, Aizpurua K</td>
<td>46/M</td>
<td>3 mo</td>
<td>Gradually worsening lower back pain, radiating to both legs (worse on the right) accompanied with paresthesia over the genital area, lack of sensation on passing urine and stools</td>
<td>Follicular grade I-II lymphoma</td>
<td>L4/L5 to the mid-S2 level</td>
<td>L4–5 decompression and debulking, corticosteroids, CT, IMB</td>
<td>Positive for CD20 and a low proliferative index (Ki67, 10%)</td>
<td>2.5 y</td>
<td>Alive, free of infection</td>
</tr>
<tr>
<td>A case report of primary central nervous system lymphoma with intestinal obstruction as the initial symptom</td>
<td>2018</td>
<td>10.1097/MD.0000000000010080</td>
<td>Li X, Qi S, Jiao Y, Gao J, Du H</td>
<td>50/M</td>
<td>8 d</td>
<td>Lack of defecation for 8 d and with symptoms of abdominal distention, intermittently suffered from backache</td>
<td>Diffuse large B-cell lymphoma</td>
<td>Right of centers of T9–T11</td>
<td>Tumor removal, CT</td>
<td>Immunohistological analyses showed the following: AE1/AE3 (–), Bcl-2 (–), Bcl-6 (+), CD10 (–), CD30 (Ki-1) (–), CD31 (–), CD34 (–), CD5 (marginally +), HMB45 (–), K-67 (index; 40%), Mum-1 (–), and PAX-5 (–)</td>
<td>Lost to follow-up</td>
<td>Alive, free of infection</td>
</tr>
<tr>
<td>Primary cauda equina lymphoma diagnosed by nerve biopsy: a case report and literature review</td>
<td>2018</td>
<td>10.3892/ol.2018.8629</td>
<td>Suzuki K, Yasuda T, Hiraiwa T, Kanamori M, Kimura T, Kawaguchi Y</td>
<td>65/M</td>
<td>5 mo</td>
<td>Gait disturbance due to motor palsy in the bilateral lower extremities, and severe numbness in his left sole</td>
<td>Diffuse large B-cell lymphoma, non-germinatal center type</td>
<td>L1–S1</td>
<td>Cauda equina biopsy, CT</td>
<td>Atypical cells with irregular large nuclei and little cytoplasm had infiltrated into the nerve, positive for cluster of differentiation (CD)20, B-cell lymphoma 2 (BCL-2), BCL-6, multiple myeloma oncogene 1 (MUM-1), and negative for CD3, CD5, and CD10</td>
<td>6 y</td>
<td>Alive, free of infection</td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma of the cauda equina: a rare entity</td>
<td>2017</td>
<td>10.1080/0268869.2016.12243121</td>
<td>Ghevaaghcheh R, Marcus K, Aizpurua M, Aizpurua J, Aizpurua S, Aizpurua K</td>
<td>46/M</td>
<td>3 mo</td>
<td>Gradually worsening lower back pain, radiating to both legs (worse on the right) accompanied with paresthesia over the genital area, lack of sensation on passing urine and stools</td>
<td>Follicular grade I-II lymphoma</td>
<td>L4/L5 to the mid-S2 level</td>
<td>L4–5 decompression and debulking, corticosteroids, CT, IMB</td>
<td>Positive for CD20 and a low proliferative index (Ki67, 10%)</td>
<td>2.5 y</td>
<td>Alive, free of infection</td>
</tr>
<tr>
<td>Title</td>
<td>Year</td>
<td>DOI</td>
<td>Authors</td>
<td>Age/sex</td>
<td>Interval (onset-diagnosis)</td>
<td>Clinical features</td>
<td>Diagnosis</td>
<td>Localization</td>
<td>Treatment</td>
<td>Histological type</td>
<td>Follow-up</td>
<td>Outcome</td>
</tr>
<tr>
<td>-------</td>
<td>------</td>
<td>-----</td>
<td>---------</td>
<td>---------</td>
<td>---------------------------</td>
<td>------------------</td>
<td>-----------</td>
<td>-------------</td>
<td>-----------</td>
<td>----------------</td>
<td>-----------</td>
<td>---------</td>
</tr>
<tr>
<td>Primary spinal marginal zone lymphoma: an unusual cause of spinal cord compression</td>
<td>2017</td>
<td>10.11604/pamj.2017.27.171.11947</td>
<td>Alaya Z, Achour B</td>
<td>67/M</td>
<td>2 mo</td>
<td>Progressive paralysis, concerned with the lower limbs</td>
<td>Marginal zone lymphoma</td>
<td>Extensive posterior epidural tissue process from T6 to T8 in continuity with left pleural neoplastic thickening through the intervertebral homolateral foramens</td>
<td>Laminectomy with resection of the intraductal lesion, CT</td>
<td>Heterogeneous group of B-cell lymphomas derived from marginal zone cells found in the spleen's white pulp and surrounding germinal centers</td>
<td>Not available</td>
<td>Alive, free of infection</td>
</tr>
<tr>
<td>Primary intramedullary malignant lymphoma in the cervical cord with a presyrinx state</td>
<td>2017</td>
<td>10.7759/cureus.2006</td>
<td>Chida K, Sugawara A, Koji T, Rogou T, Mure Y, Sugai T, Ogawa K</td>
<td>79/M</td>
<td>6 mo</td>
<td>Left hemiparesis with 2/5 in his upper limb and 3/5 in his lower limb and hypoesthesia in his left side from the neck to the foot. The deep tendon reflexes were increased in his left upper limb</td>
<td>Diffuse large B-cell lymphoma</td>
<td>C1–C2</td>
<td>Tumor removal</td>
<td>Diffuse proliferation of large atypical lymphocytes, positive for CD20 and CD79a, and negative for CD3</td>
<td>2 y</td>
<td>Alive</td>
</tr>
<tr>
<td>Primary spinal epidural lymphoma as a cause of spontaneous spinal anterior syndrome: a case report and literature review</td>
<td>2017</td>
<td>10.1055/s-0036-1597692</td>
<td>Córdoba-Morquenda ME, Guerra-Mosa JR, Sánchez-Silva MC, Vicuña-González RM, Torre AI</td>
<td>45/M</td>
<td>2 mo</td>
<td>High intensity thoracic pain limiting his movements; a month later, he was accompanied by decrease in the strength of the left pelvic limb; after 2 mo, he started with weakness of both lower limbs and impaired urinary sphincter control</td>
<td>Diffuse large B-cell lymphoma</td>
<td>T1–T2</td>
<td>Neural decompression by posterior way and biopsy of the extradural spinal lesion, CT, RT</td>
<td>CD20, BCL-2, CD3, CD5, CD10, CD30, and I667 positive in 20% of neoplastic cells</td>
<td>Not available</td>
<td>Not available</td>
</tr>
</tbody>
</table>
Discussion

Spine tumors can be branched between extradural, intradural extramedullary, and intradural intramedullary, the latter being (IMSCIs) rare neoplasms that can be subdivided into gliomas (ependymomas and astrocytomas) and hemangioblastomas, all of which may be responsible for neurologi-
cal dysfunction and deterioration. The pathophysiology of these lesions varies: ependymomas are encapsulated tumors, mostly benign; spinal astrocytomas are less aggressive than when developed in the brain, but nerve fiber stretching can cause pain and neurologic defects; hemangio-
blastomas are highly vascular tumors and can cause mass effect due to capillary hyperpermeability. Also, metastatic intramedullary tumors can occur, usually arising from primary neoplasms such as of the lung and breast. Intramedullary spinal cord metastasis (ISCM) can also be secondary to malignant melanoma, since it can present with paraparesis, quadripareisis, and urinary and/or fecal incontinence, but it is an extremely difficult diagnosis of exclusion.

The primary malignant melanoma is also an intramedul-

ary tumor that can occur in the spinal cord, but it is still little
described. It accounts for 1% of all cases of melanoma,
indicating the lesion is extremely unique, with the diagnosis requiring histopathological confirmation and excluding metastatic spread from other areas. This diagnosis was considered especially because of the patient’s Fitzpatrick type II classification.

Additionally, the patient also had a medical history of a non-Hodgkin’s lymphoma from 7 years ago, which hinted to a possible recidivistic lymphoma. Intramedullary lesions can therefore be subdivided into glial tumors, nonglial tumors such as lymphomas and benign lesions, exemplified by epidermoid cysts, lipomas, and, rarely, abscesses.

Lymphomas develop from progressive mutations in the deoxyribonucleic acid (DNA), namely, amplification, deletion, and, or chromosomal translocations. Non-Hodgkin’s lymphomas arise from mature B lymphocytes and may have small portions of T lymphocytes or natural killer cells. Some subtypes may also be associated with infections, such as Epstein–Barr virus, *Helicobacter pylori*, and hepatitis C virus. Primary central nervous system lymphoma (PCNSL) is an extranodal non-Hodgkin’s lymphoma whose known causes can commonly be human immunodeficiency virus (HIV), chronic immunosuppression, and organ transplantation. Studies show that the human T-lymphotropic virus type 1 (HTLV-1) virus can also be associated with the appearance of T-cell lymphomas of the spinal cord. According to Urasaki et al, the virus probably migrates from blood to the parenchyma of the CNS, but does not proliferate. Thus, parainfectious myelitis is believed to occur. However, this disease can develop in immunocompetent patients, as already seen in association with rheumatoid arthritis and systemic lupus erythematosus. These relations could not be found in the patient’s history.

The most conclusive sign of intramedullary lesion was the presentation of BSS, which is little described in the literature as a PCNSL manifestation. BSS is a result of hemisection of the spinal cord and manifests with weakness or paralysis and ipsilateral proprioceptive deficits and loss of pain and temperature sensation on the contralateral side of the lesion, indicating a diverse severity. Partial hemisection is more evident and includes nerve tracts in the injured area. Therefore, the sensory sensations affected depend on the site of the lesion (Table 3).

### Table 3 Sensory sensation loss depending on the nerve tract involved (Brown-Séquard syndrome [BSS])

<table>
<thead>
<tr>
<th>Nerve Tract</th>
<th>Sensory Sensation Loss</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dorsal columns</td>
<td>Fine touch, vibration, two-point discrimination, and conscious proprioception ipsilaterally affected</td>
</tr>
<tr>
<td>Spinothalamic tract</td>
<td>Pain, temperature, and crude touch contralaterally affected</td>
</tr>
<tr>
<td>Dorsal and ventral spinocerebellar tracts</td>
<td>Dorsal: ipsilateral dystaxia and involvement Ventral: contralateral dystaxia</td>
</tr>
<tr>
<td>Horner’s syndrome (lesion at or above T1)</td>
<td>Ptosis, miosis, and anhidrosis (due to ipsilateral loss of sympathetic fibers), facial redness (due to vasodilation)</td>
</tr>
<tr>
<td>Corticospinal tracts</td>
<td>At the site of the lesion: ipsilateral loss of movements, presenting flaccid paralysis, lower motor neuron lesion like loss of muscle mass, fasciculations, and decreased power and tone</td>
</tr>
</tbody>
</table>

Below the level of lesion: paralysis with hypertonia clasp knife type, hyperreflexia, and positive Babinski’s sign.

Source: Shams and Arain.

The most common intramedullary location is the cervical cord, as seen in our case, followed by the thoracic, then the lumbar cord. It is common to observe a delay on its diagnosis, due to its rarity, similarity to other causes of myelopathy, and the difficulties in obtaining viable histological samples and pathologic diagnosis. Intramedullary spinal cord lymphoma is very rare. It is seen in less than 1% of primary CNS lymphomas. Longitudinally extensive transverse myelopathy (LETM) is common and is usually inflammatory, demyelinating, related to connective tissue disease, due to sarcoidosis or paraneoplastic causes, but uncommon on lymphomas. The presentation of LETM may be associated with brain lesions, and other differentials such as neuromyelitis optica (NMO) spectrum disorders is considered, leading to delay in diagnosis and may be fatal if not suspected or detected. Two case series of LETM showed that none of the patients evaluated had lymphoma as diagnosis although our patient and one other reported case presented it.

Even though spinal cord expansion is usually present, some patients may have minimal enlargement. Lesions are generally poorly defined, syringomyelia is rare, hemorrhagic component usually does not appear as a component, and cysts are not usually present. Involvement of the brain is reported, within the brainstem, cerebellum, deep gray matter, or cerebral cortex. Peripheral nerve involvement has been described as well.

Reported signal characteristics include T1: isointense to the spinal cord/T2: hyperintense (contrasts with the characteristic low T2 signal intensity that is seen in intracranial lesions)/T1 C+ (Gd): usually solid and homogeneous enhancement.

The patient evolved with loss of strength and hemiparesis on the right side of the body and superficial hemiesthesia on the left side, thus suggesting BSS, which was confirmed by imaging tests.

**Conclusion**

Intramedullary lesions can be related to several pathologies, such as tumors and lymphomas. Even if the etiology is different, most of the time the clinical presentation is similar.
Occurrence of BSS is commonly concurrent to the intramedullary lesions and is valuable evidence of a spinal cord herniation. Therefore, it is difficult to differentiate the two conditions. In this case, the patient’s medical history played a major role in the diagnosis, but the etiology and treatment of the disease could be elucidated only after a biopsy. Thus, it is important to stress the value of surgical procedures to conclude neurological diagnosis.

Funding
None.

Conflict of Interest
None declared.

References
4. Löw S, Han CH, Batchelor TT. Primary central nervous system lymphoma. Ther Adv Neurol Disord 2018;11:175628641879362
19. Arslan H, Yavuz A, Aycan A. Primary spinal lymphoma masquerading as meningo: a preoperative and postoperative magnetic resonance imaging findings. World Neurosurg 2018;118:86–87