

# Primary intradural Hodgkin lymphoma of the conus medullaris and cauda equina: case report

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Primary Hodgkin lymphoma of the central nervous system is an exceedingly rare condition with very few cases reported in the literature. Isolated intradural involvement of the spine is rarer still, with only two prior cases located in the extramedullary cervical and lumbosacral spine. We present a 48-year-old female who was presented with back pain, radiculopathy and a short history of sphincter disturbance and was subsequently found to have a lobulated homogeneously enhancing exophytic lesion involving the conus medullaris and cauda equina on magnetic resonance imaging. Histopathological examination demonstrated the features of classic Hodgkin lymphoma. In this report, we present a case of primary intramedullary Hodgkin lymphoma involving the conus medullaris and cauda equina.

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The identification and management of Hodgkin lymphoma (HL) has improved significantly since it was first characterized in 1832, with current 20-year survival rates around 70% [1–3]. The disease typically originates in the lymph nodes and may spread to any organ system, commonly displaying extra-nodal involvement including cardiac, pulmonary, hepatic, thymic, splenic and bone infiltration [4,5].

Central nervous system (CNS) involvement is relatively uncommon, reported to occur in 0.02–0.5% of cases [6–8]. Rarer still, a limited number of case reports describe the existence of primary CNS HL, although its existence remains controversial [9–20]. Primary intracranial HL has been previously documented in the literature [21], and spinal extradural lesions have also been reported [22–26]. Primary HL of the conus medullaris has been reported once previously [27]; however, this case was not isolated to the spine, with evidence of brainstem involvement found on neuroimaging.

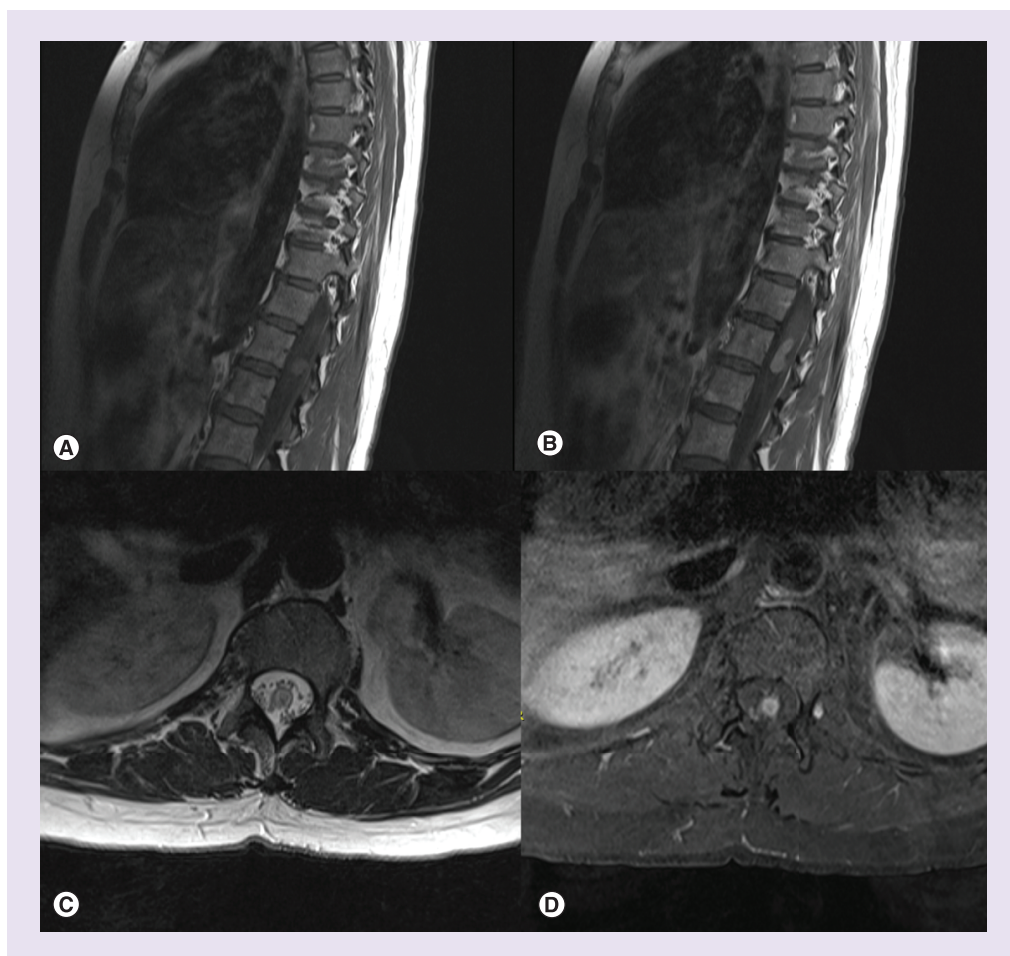
To our knowledge, there have been only two previous case reports demonstrating primary intradural HL, which was isolated to the spine, with one case in the cervical spine [28] and the other in the lumbosacral region [29]. Both cases were intradural extramedullary lesions.

We present a case report of a patient with a primary intradural intramedullary classical HL, with immunohistochemical analysis. Informed written consent was gained from the patient to publish this case report.

## Case description

### History & examination

A 48-year-old female presented with a 2-month history of lower back pain and a 4-week history of right L5-S1 radiculopathy with associated perianal paresthesia. For the few days prior to her admission, she developed anal and urinary sphincter dysfunction with incomplete emptying of her bowels and occasional urinary incontinence. She was systemically well with no history of fevers, weight loss, night sweats or fatigue. Her medical history included alopecia areata treated previously with corticosteroids. On physical examination, she had preserved motor function with loss of sensation to S3–5 dermatomes and preserved reflexes. Routine blood workup was normal.



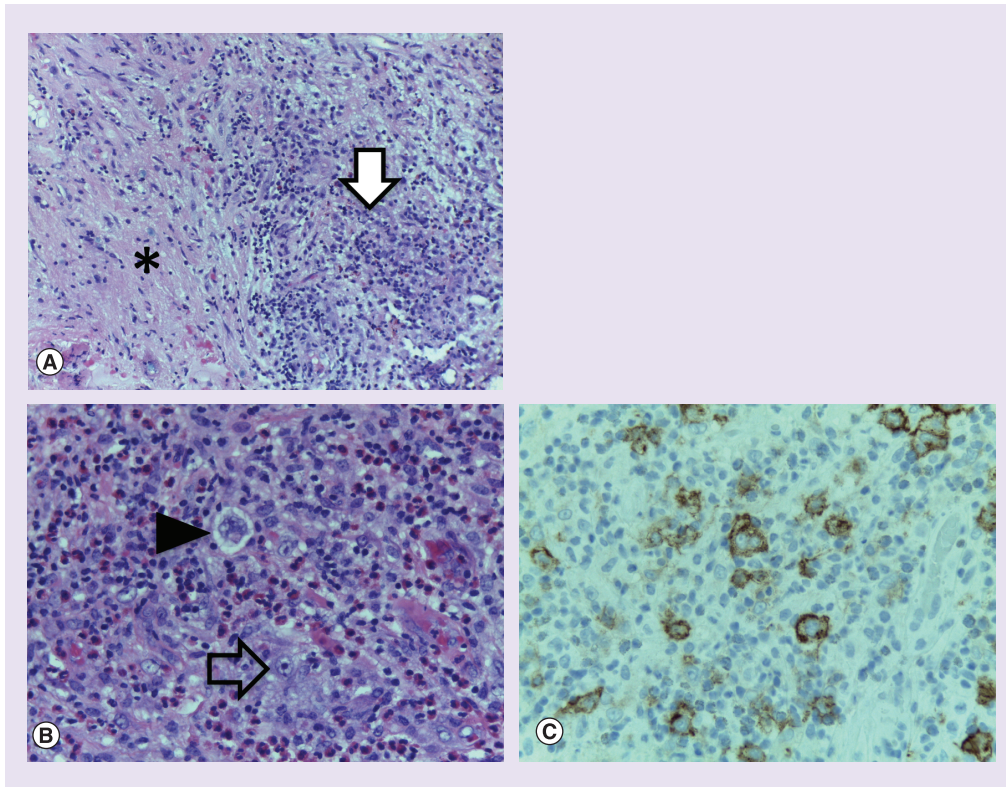
**Figure 1.** Preoperative sagittal T1-weighted precontrast and postcontrast images (A & B) and axial T2- and T1-weighted postcontrast images (C & D). Intramedullary lesion involving conus medullaris with larger lobulated component extending into the cauda equina measures  $13 \times 14 \times 22 \text{ mm}^3$ , is intermediately hyperintense on T2-weighted and iso- to hyperintense on T1-weighted relative to paraspinal muscles and avidly enhances. Subtle enhancement of the descending nerve roots on the right is present. Nonenhancing expansion of the cord from conus to mid T10 vertebral level is consistent with edema.

### Neuroimaging

A computed tomography (CT) scan revealed no abnormality; however, magnetic resonance imaging (MRI) of the lumbosacral spine revealed a lobulated homogeneously enhancing exophytic lesion involving the conus medullaris and filum terminale (Figure 1). The lesion, measuring  $13 \times 14 \times 22 \text{ mm}^3$  and located at the level of the L1/2 lamina was associated with cord edema extending to the level of T11. A further small lesion of 5 mm was also noted in the cauda equina at the L5/S1 level. Subsequent imaging of the remainder of the cranio-spinal axis revealed no abnormality, with no leptomeningeal enhancement. On neuroradiological grounds, an ependymoma was favored with metastases and lymphoma thought less likely.

### Operation

The role of surgery was discussed with the patient and, given the presumptive diagnosis of ependymoma, complete resection of the lesion was planned. A L1/2 laminectomy was subsequently undertaken with midline dural opening. The tumor was identified within the conus and seen tracking down the filum terminale. Separate to the conus, tumor was found encasing the right side of the cauda equina and, when dissected apart, the affected nerve roots contained intraneural tumor. No clear tumor–conus interface was seen. Therefore, the conus component was debulked in a piecemeal fashion and sent with biopsies of the cauda equina component for histopathological analysis.



**Figure 2. Histological features and CD30 immunohistochemistry at tumour diagnosis. (A)** Hematoxylin and eosin stain photomicrographs (20 × objective) showing spinal cord parenchyma (\*) infiltrated by Hodgkin lymphoma (white arrow). **(B)** Hematoxylin and eosin stain (40 × objective) shows a lacunar cell (arrow head) and a Hodgkin cell (arrow) surrounded by a mix of small lymphocytes, histiocytes and eosinophils. **(C)** CD30 immunohistochemistry (40 × objective) demonstrates membrane staining of Hodgkin cells.

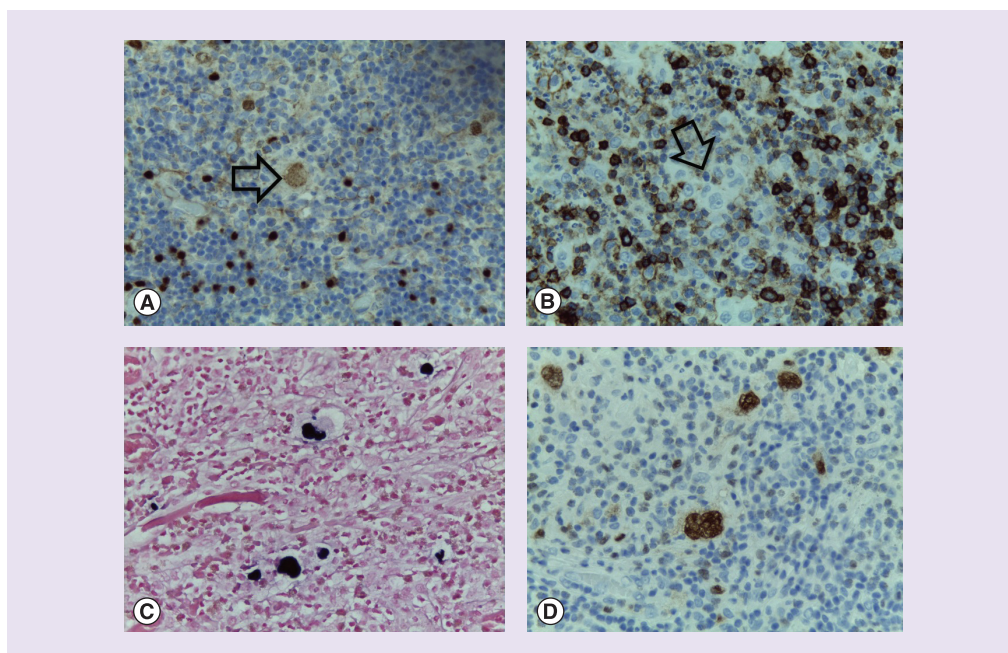
### Histopathological examination

Histology demonstrated features of classic HL involving spinal cord parenchyma and peripheral nerve fascicles. The tumor tissue was composed of scattered Hodgkin cells, Reed–Sternberg cells and lacunar cells surrounded by a mix of small lymphocytes, histiocytes, eosinophils and occasional neutrophils (Figure 2). No prominent fibrous bands were present and, therefore, the mixed cellularity subtype was favored. On immunohistochemistry, the tumor cells showed membrane staining for CD30. They showed weak-positive staining for CD20 and PAX5 and were also positive for MUM1 and EBV-encoded RNA (EBER) *in-situ* hybridization (ISH; Figure 3). Other differentials such as T-cell histiocyte-rich large B cell lymphoma, nodular lymphocyte-predominant HL and peripheral T-cell lymphoma were excluded on the basis of CD45 negativity.

### Postoperative course

Following this histopathological diagnosis, nuclear medicine whole body positron emission tomography (PET)/CT was organized and proved negative for further CNS involvement or systemic disease. Bone marrow trephine and serological screening, including for Epstein–Barr virus, was also normal. The patient was staged as according to the Ann Arbor lymphoma staging system [30] as Stage IE HL of the CNS. The patient subsequently completed radiotherapy to the residual tumor with a dose of 36 Gy in 20 fractions to T10–sacrum, delivered with intensity modulated radiation therapy. Following a discussion with the patient, chemotherapy was not given as primary treatment, yet reserved in the event of either local or systemic relapse of the disease.

On follow-up review at 10 months postoperatively, the patient was well with no motor deficit and normal bowel and bladder function. MRI showed complete resolution in the area of enhancement at the L1/2 level as well as resolution of the nodule of enhancement at L5/S1 postradiotherapy. No further disease was seen on follow-up imaging of the remainder of the cranio-spinal axis.



**Figure 3.** Additional tumour immunohistochemistry and EBER *in situ* hybridization stains. (A) Hodgkin cell (arrow) showing weak PAX5 staining relative to background small B cells. (B) Hodgkin cells demonstrating negativity for CD45. (C) EBER *in situ* hybridization was positive. (D) MUM1 was positive in Reed–Sternberg and Hodgkin cells.

### Conclusion

Primary HL of the CNS is an exceedingly rare condition with few cases reported in the literature. Furthermore, according to our research, there have only been two other cases of intradural HL isolated to the spine, both extramedullary [28,29].

Due to the absence of lymphoid tissue in this area, it is difficult to determine the cancer-initiating cell as there is no evidence of systemic disease burden or extradural disease. The role of regulatory T cells has been hypothesized in CNS HL pathogenesis, as there has been an associated high number of these cells present in affected tissue [31].

There are several approaches for treatment following a histological diagnosis, including good responses seen using CNS penetrating chemotherapy and/or radiation therapy [22,29,32]. Standard chemotherapy options for systemic HL Adriamycin, Bleomycin, Vinblastine, and Dacarbazine (i.e., ABVD) do not penetrate the CNS, so there is no role for addition of these agents. Radiation therapy alone, postresection, was chosen in this case given the lack of widespread systemic involvement and the potential toxicities of the CNS penetrating chemotherapeutic agents (e.g., high-dose methotrexate). Although radiotherapy alone is not often the primary treatment option in CNS lymphoma, this decision was guided by the few similar reports of isolated CNS HL [11].

Prognosis of this condition is also difficult to ascertain, as there is very limited data about its presentation and natural history. From the limited case reports, primary HL of the spine generally tends to be associated with very low risk of systemic relapse and overall, there is a better prognosis with HL isolated to the CNS, compared with systemic disease [7,33]. However, long-term remission rates are largely unknown and further cases are required to gain insight into this rare condition.

### Author contributions

TJ Williamson worked on the conception and design. TJ Williamson, M Wang, J Williams and J Clark drafted the article. TJ Williamson and M Wang critically revised the article. TJ Williamson, M Wang, J Williams, J Clark and A Drnda reviewed the submitted version of the manuscript. A Drnda supervised the study.

### Financial & competing interests disclosure

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

No writing assistance was utilized in the production of this manuscript.

### Ethical conduct of research

The authors state that they have obtained verbal and written informed consent from the patient for the inclusion of their medical and treatment history within this case report.

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### Executive summary

- Primary Hodgkin lymphoma (HL) of the central nervous system (CNS) is an exceedingly rare condition with few cases reported in the literature.
- There have been very few reports of primary CNS HL isolated to the spine.
- Diagnosis is via histopathological examination demonstrating Hodgkin and Reed–Sternberg cells with tumor cell membranes staining for CD30 on immunohistochemistry.
- There is a paucity of literature regarding optimal treatment; however, good results have been seen with CNS penetrating chemotherapy and/or radiotherapy.
- From the limited case reports, primary HL of the spine generally tends to be associated with very low risk of systemic relapse.
- There is a better prognosis with HL isolated to the CNS, compared with systemic disease.

### References

Papers of special note have been highlighted as: ● of interest

1. Mauch PM, Kalish LA, Marcus KC *et al*. Long-term survival in Hodgkin's disease relative impact of mortality, second tumors, infection, and cardiovascular disease. *Cancer J. Sci. Am.* 1(1), 33–42 (1995).
2. Jemal A, Ward E, Thun M. Declining death rates reflect progress against cancer. *PLoS ONE* 5(3), e9584 (2010).
3. Brenner H. Long-term survival rates of cancer patients achieved by the end of the 20th century: a period analysis. *Lancet* 360(9340), 1131–1135 (2002).
4. Mauch PM, Kalish LA, Kadin M, Coleman CN, Osteen R, Hellman S. Patterns of presentation of Hodgkin disease. Implications for etiology and pathogenesis. *Cancer* 71(6), 2062–2071 (1993).
5. Guermazi A, Brice P, Kerviler Ed *et al*. Extranodal Hodgkin disease: spectrum of disease. *Radiographics* 21(1), 161–179 (2001).
6. Blake PR, Carr DH, Goolden AW. Intracranial Hodgkin's disease. *Br. J. Radiol.* 59(700), 414–416 (1986).
7. Gerstner ER, Abrey LE, Schiff D *et al*. CNS Hodgkin lymphoma. *Blood* 112(5), 1658–1661 (2008).
8. Re D, Fuchs M, Schober T, Engert A, Diehl V. CNS involvement in Hodgkin's lymphoma. *J. Clin. Oncol.* 25(21), 3182 (2007).
9. Foo WC, Desjardins A, Cummings TJ. Primary intracerebral Hodgkin lymphoma with recurrence. *Clin. Neuropathol.* 30(2), 75–79 (2011).
10. de Castro AF, Junior AS, de Lins e Horta H *et al*. Primary intracerebral Hodgkin lymphoma. *Br. J. Haematol.* 138(5), 562 (2007).
11. Kresak JL, Nguyen J, Wong K, Davis R. Primary Hodgkin lymphoma of the central nervous system: two case reports and review of the literature. *Neuropathology* 33(6), 658–662 (2013).
- **A good case report and review of the literature with information on treatment and follow-up.**
12. Sharaf N, Lobo B, Lee J, Prayson RA. Primary Hodgkin lymphoma of the central nervous system. *J. Clin. Neurosci.* 21(7), 1271–1273 (2014).
13. Shivane A, Smith ME, Lewis D, Berei T. A rare case of primary intracerebral Hodgkin lymphoma. *Clin. Neuropathol.* 35(6), 389–392 (2016).
14. Ashby MA, Barber PC, Holmes AE, Freer CE, Collins RD. Primary intracranial Hodgkin's disease. A case report and discussion. *Am. J. Surg. Pathol.* 12(4), 294–299 (1988).

15. Clark WC, Callihan T, Schwartzberg L, Fontanesi J. Primary intracranial Hodgkin's lymphoma without dural attachment. Case report. *J. Neurosurg.* 76(4), 692–695 (1992).
16. Doorly TP, Farrell MA, Phillips J. Primary intracerebral Hodgkin's lymphoma. *J. Neurol. Neurosurg. Psychiatry* 50(8), 1048–1050 (1987).
17. Schrickler JL Jr, Smith DE. Primary intracerebral Hodgkin's disease. *Cancer* 8(3), 629–633 (1955).
18. Sickler GK, Hanson SK, Hsu SM, Papisozomenos SC. Primary intracerebral Hodgkin's disease: a case report. *Clin. Neuropathol.* 9(3), 143–147 (1990).
19. Sparling HJ Jr, Adams RD. Primary Hodgkin's sarcoma of the brain. *Arch. Pathol. (Chic.)* 42, 338–344 (1946).
20. Klein R, Mullges W, Bendszus M, Woydt M, Kreipe H, Roggendorf W. Primary intracerebral Hodgkin's disease: report of a case with Epstein–Barr virus association and review of the literature. *Am. J. Surg. Pathol.* 23(4), 477–481 (1999).
21. Nagashima K, Mori S, Yoshimasu N, Takahashi K. Primary Hodgkin's disease of the falx cerebri. *Acta Neuropathol.* 51(2), 161–163 (1980).
22. Higgins SA, Peschel RE. Hodgkin's disease with spinal cord compression. A case report and a review of the literature. *Cancer* 75(1), 94–98 (1995).
23. Samadian M, Vahidi S, Khormae F, Ashraf H. Isolated, primary spinal epidural Hodgkin's disease in a child. *Pediatr. Neurol.* 40(6), 480–482 (2009).
24. Al-Khayat H, Al-Khayat H, Al-Baker O *et al.* Cervical radiculopathy secondary to Hodgkin's lymphoma. *Surg. Neurol.* 67(5), 540–543 (2007).
25. Yaman O, Ozdemir N, Sevin IE, Ozer FD, Unlüoğlu S. Primary spinal epidural Hodgkin's lymphoma. *J. Surg. Case Rep.* 2013(10), rjt090 (2013).
26. Citow JS, Rini B, Wollmann R, Macdonald RL. Isolated, primary extranodal Hodgkin's disease of the spine: case report. *Neurosurgery* 49(2), 453–457 (2001).
27. Martinez DL, Gujrati M, Geoffroy F, Tsung A. Isolated CNS Hodgkin's lymphoma: implications for tissue diagnosis. *CNS Oncol.* 3(6), 383–387 (2014).
- **A well-written review on the implications for tissue diagnosis in central nervous system primary Hodgkin lymphoma.**
28. Heran NS, Yong RL, Heran MS, Yip S, Fairholm D. Primary intradural extraarachnoid Hodgkin lymphoma of the cervical spine. Case report. *J. Neurosurg. Spine* 5(1), 61–64 (2006).
29. Chotai N, Dutta R. Primary intradural Hodgkin's lymphoma in lumbosacral spine: a rare location. *Clin. Neuroradiol.* 20(4), 247–249 (2010).
30. Cheson BD, Fisher R, Barrington S *et al.* Recommendations for initial evaluation, staging, and response assessment of Hodgkin and non-Hodgkin lymphoma: the Lugano classification. *J. Clin. Oncol.* 32(27), 3059–3067 (2014).
31. Alfaseh A, Rajeh MN, Hamed G. Primary central nervous system Hodgkin lymphoma: A case discussion and hypothesis on the aetiology. *Avicenna J. Med.* 9(1), 28–31 (2019).
- **A good case review with an interesting hypothesis on the role of regulatory T cells in the etiology of this condition.**
32. Kushwaha VS, Srivastava K, Husain N, Singh S. Unusual case of Hodgkin lymphoma presenting as soft tissue mass with intracranial metastasis and review of literature. *Clin. Cancer Investig. J.* 4(3), 419–421 (2015).
33. Van Blydenstein SJ, Patel M, Philip P *et al.* Classical Hodgkin lymphoma involving the central nervous system (brain) – an unusual presentation. *Clin. Case Rep.* 2(3), 88–92 (2014).