

Primary Spinal Epidural Non-Hodgkin's Lymphoma: A Case Report

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Abstract

Introduction: Non-Hodgkin's lymphomas (NHLs) are a varied group of malignancy originating in the lymphatic system. As a subset of lymphomas, primary spinal epidural lymphomas are diagnosed when there are no other recognizable sites of lymphomas at the time of diagnosis. It mimics other spinal diseases making the diagnosis difficult to establish as well as in obtaining tissue diagnosis. We present an atypical case of a 45-year-old female who presented initially with back pain then eventual loss of sensory and motor function of the lower extremities, further work up showed primary spinal epidural NHL.

Case: This is a case of a 45-year-old female with chief complaint of back pain. Magnetic resonance imaging (MRI) of the thoracic spine showed nonspecific epidural soft tissue mass at T5 to T6 level compressing the spinal cord. Operative procedure was done with histopathology of the epidural lesion consistent of NHL. Immunohistochemical staining showed CD20 (+), thus a diagnosis of diffuse large B cell

lymphoma (DLBCL) was made. Patient underwent six cycles of cyclophosphamide, doxorubicin, vincristine, prednisone (CHOP) regimen.

Conclusion: Signs and symptoms of primary spinal epidural NHL often overlaps its manifestations with other spinal diseases. A high index of clinical suspicion warrants inclusion of such neoplastic condition in determining the exact and definitive diagnosis of cases manifesting spinal compression.

Keywords: case report, primary spinal epidural non-hodgkin's lymphoma, spinal cord compression, lower extremity weakness, back pain, epidural mass

Introduction

Primary spinal lymphoma arises from the paraspinal lymphoid tissue. It is a rare form of extranodal lymphoma that invades the spinal cord. This is to report a case of a patient presenting with a compressive tumor in the spinal epidural area and its unique behavior. Due to the atypical clinical presentation of primary spinal lymphoma, its diagnosis is challenging to health care practitioners. Spinal cord compression occurs in 0.1% to 3.3% of patients with non-Hodgkin's lymphoma (NHL) and is a rare presentation. NHL may infrequently arise subdurally or within the spinal cord.⁵ Spinal cord compression typically presents with back pain, leg numbness and tingling, radicular pain followed by extremity weakness, paresis and paralysis, but can also be asymptomatic at presentation.

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Case

A 45-year-old female was admitted due to increasing severity of her back pain. Patient noted a gnawing lower back pain about three months ago, intermittent in duration with a pain score of five out of 10. Around this time she did not experienced any bladder or bowel changes and felt she was well and hardly noticed any problems. Since she assumed the pain was not worrisome she did not attempt to visit her physician.

A week before confinement, she again complained but of severe gnawing pain on the lower back, this time it was associated with lower extremity numbness. She was seen by a private physician, worked up and claimed to have been managed with bacterial pneumonia., was given cefuroxime 500mg two times a day for a week together with an unrecalled pain medication. There was no improvement of the pain and was followed a few days after with difficulty in urination and bowel movement including both lower extremity paresis. With the increasing severity of the pain, and the obvious neurologic insult, she decided in her incapacity

to have herself admitted to the hospital. Patient has no co-morbid conditions, and denies no past surgeries. A devoted housewife with no history of any vices. Heredofamilial diseases include breast cancer, hypertension and diabetes on maternal side.

She was seen at the emergency room awake, a bit anxious, but not in any type distress, with a blood pressure of 110/80 mmhg, heart rate of 89 beats per minute with a regular rhythm, respiratory rate of 20 bpm and was afebrile. There were no pertinent physical examination finding except distention of the hypogastric region and laxity of the sphincter tone on rectal examination. Neurologic evaluation revealed patient was alert, attentive and oriented in three spheres. She had intact cranial nerve findings with no nuchal rigidity. There was no pronator drift, muscle bulk and tone were normal yet strength on both lower extremities were noted to be 0 out of five, the rest of the upper extremities were normal (5/5). Symmetric hyporeflexia (patellar and achilles tendon) was evident at both knees and ankles. Babinski reflex was positive. Sensory mapping by light touch and pinprick showed loss of sensation from the umbilicus to both lower extremities. With the prominent finding of low back pain associated with loss of function ON both lower extremities, similar pathologic conditions considered as differential diagnosis includes pott's disease, guillane barre syndrome, spinal abscess and transverse myelitis. She had a normal blood count, liver function test, and electrolytes but with an elevated ESR. Radiographic imaging both chest and thoracolumbar views did not reveal any pertinent findings. The prominence of a full bladder and the patient's inability to void prompted insertion of a urinary catheter draining 700 cc of urine. Patient was given tramadol 50 mg intravenously every eight hours to address her lower back pain with afforded relief. She was referred to a neurologist and requested for a magnetic resonant imaging (MRI) on the thoracic spine with spinal survey. The scan (Figure 1) reported an increased signal intensity of the spinal cord extending from T3 to T10 attributed to edema. An epidural soft tissue mass finding located at the level of T5, T6 and T7. It measures 10x 18x 39 mm with signal abnormalities in the dorsal and visualized upper lumbar spine with signs of spinal cord compression. Considerations of an inflammatory or neoplastic lesion was entertained.

While in the ward, febrile episodes were noted ranging from 37.8 °C to 38.4 °C. Medical service planned to start antibacterial empiric treatment. She was started with ceftriaxone 2g IV q12H with vancomycin 1 g IV OD after blood culture and sensitivity were taken. CBC showed normal wbc count with lymphocytopenia (12%). The medical service did not pursue the plan for steroid treatment due to the febrile nature of the patient's condition and tuberculosis of the spine was part of the differential consideration.

Eventually, she was then referred to neurosurgery service due to the intermittent lower back pain and MRI findings.

Patient underwent thoracic laminectomy at T5-T6 level. Intraoperative finding showed a 30.0 mm brown irregular epidural mass impinging the spinal cord. Pre-operative diagnosis was pott's disease with spinal cord compression. After surgery, the post operative diagnosis was epidural granuloma with probable pott's disease. Specimen was sent to laboratory for histopathology together with AFB and gram stain. Acid fast bacilli (AFB) stain came out to be negative.

Histopathology came out after a few days, the epidural mass in question was consistent with NHL. Microscopic features of the mass showed loose cohesive sheets of medium to large cells demonstrating oval to round vesicular nuclei with fine chromatin pattern. Some of the cells showed prominent nucleoli. The cytoplasm is moderate to scant and basophilic. Mitosis activity was brisk. (See Figure 2).

To confirm the diagnosis of NHL, immunohistochemical staining for CD3, CD20 and CD30. CD3 and CD30 were both negative. CD3 is usually confers T-cell lymphoma and T-cell chronic lymphocytic leukemia while CD30 has reference to classic hodgkin's lymphoma. Patient showed positivity to CD20. A diagnosis of NHL of a diffuse large B cell lymphoma (DLBCL) type was made based on the histochemical staining report. An ultrasound of the whole abdomen did not reveal any metastasis during confinement. Patient was then referred to a hematologist-oncologist where an ultrasound of the abdomen was further ordered which revealed no



Figure 1. MRI of the thoracic spine showing an epidural soft tissue mass at the level of T5, T6 and T7 with evidence of spinal cord compression shown by arrow marks.

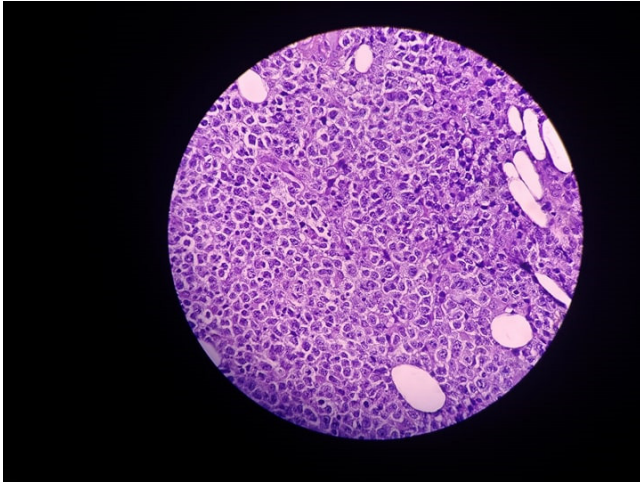


Figure 2. Histopathology of the epidural mass showing NHL. loose cohesive sheets of medium to large cells demonstrating oval to round vesicular nuclei with fine chromatin pattern. Some of these cells show prominent nucleoli. The cytoplasm is moderate to scant and basophilic. Several mitotic figures are seen as shown by the arrows.

metastasis. She was advised for chemotherapy of six cycles of CHOP (cyclophosphamide, doxorubicin, vincristine, prednisolone) regimen which she had as outpatient. She had an initial first chemocycle done in the hospital wherein few episodes of nausea and vomiting was noted. She underwent physical rehabilitation which consistently was followed from her hospital stay and as outpatient as well. Emphasis on bed sore prevention was part of the preventive education given to the patient and family members. Consultation with her oncologist was made in the context of her prognosis, and the likelihood of return of her motor and sensory function. Patient was advised to have good to intermediate prognosis with four to five year survival if with proper adherence to chemotherapy treatment with follow up. Patient was then discharged well after her initial chemotherapy yet with neurologic deficits.

After her six cycles of chemotherapy, patient had her follow up with her oncologist and was advised increasing caloric intake. She had the same neurologic deficit presented as seen during her discharge from the hospital.

Discussion

The patients presentation of severe lower back pain associated with neurologic condition would provide a clue that it is of spinal cord origin. The symptoms associated with, by neurologic assessment, could be compressive in nature. The findings of NHL in this setting was unlikely to be a primary suspect. An infrequent presentation of about 0.1% of patients with primary epidural NHL presents with spinal cord compression.¹ Metastatic tumors from any primary site are most common conditions with neoplastic spinal cord compression (ESCC) presentations with approximately half of the cases came from prostate, lung, breast.¹²

Non-Hodgkin's lymphomas (NHLs) are a diversified group of lymphoid malignancies that involve less commonly in the spinal epidural tissue. This incidence accounts to about 0.1 to 3.3%.^{2,3} Cases on review were commonly caused by extradural disease, either due to an isolated deposit within the spinal canal or by an extension from an adjacent nodal mass or bone involvement. Less commonly would NHL arises subdurally or within the spinal cord.¹

Epelbaum et al. described two phases of its presentation. Starting with the prodromal phase presenting with a localized back pain with occasional radicular pain lasting for months to a year. The second phase would present over two to eight weeks with a rapid neurological deterioration due to spinal cord compression.⁴ The features of the second phase correlates to the patient's manifestation during her confinement. The occurrence of spinal lymphoma appears to be of male predominance with 1.6:1 male to female ratio with a median age of 70 years of age.^{5,11} A completely opposite demographic form the patients profile in this case.

The most common site of occurrence of primary spinal epidural lymphoma is the thoracic spine in 69% of cases.² This is due to its superior length, a concentrated lymphatic drainage system and its plasticity, which permits the formation of the bulky disease.⁵

Magnetic resonance imaging (MRI) as the least invasive is the preferred modality of choice. It has several advantages. It is capable to portray the extent of the epidural lesion compared to myelography. It is most sensitive technique for the detection of multiple epidural lesions and a sensitive technique for the detection of vertebral metastases (T1-weighted images).⁶

Histopathological examination would show atypical lymphoid cell proliferation. Tumor cells on immunohistochemistry are positive for LCA and CD20 and is negative for CD138, CD30, and CD3. Diffuse Large B cell lymphoma (DLBCL) is the common type at this site. DLBCL involving spinal epidural space (SEDLCL) constitutes 1.8% of all DLBCLs in a study by Wada et al.⁷

Spinal lymphomas invade the spine in a peculiar way. Tumorigenesis is thought to arise from paravertebral ganglions or the epidural lymphoid tissues. It is then thought to enter the epidural space through the vertebral foramen without causing bony erosion. This invasion method is likely to be unique in contrast to other tumors where cord invasion is achieved through vertebral bone destruction.

A conflicting evidence on the role of primary surgical decompression in primary spinal epidural lymphoma due to the tumor's sensitivity to radiation and chemotherapy. primary surgical decompression in other studies improved neurological outcomes, however in a study by Peng et al, due to a higher post-operative mortality rates, non-surgical

management of cord compression was recommended.⁸ Conducting thoracic laminectomy in the case at hand at the T5 –T6 level did not improve outcomes neurologically.

As lymphomas are highly chemosensitive and radiosensitive, chemo-radiotherapy remains the main stay of treatment with CHOP regimen as the gold standard of treatment. Hyper-CVAD (cyclophosphamide, vincristine, doxorubicin, and dexamethasone) or CHOP regimens have shown favorable outcomes.⁵ A five-year survival rate of 66% was achieved with intensive therapy using Radiotherapy (RT) and combination chemotherapy.⁴ In the presence of severe neurological deficit or if tissue diagnosis is needed, an innovative algorithm in which primary neurosurgical intervention is pursued. In case of clinical deterioration, primary chemoradiation can be attempted and surgical intervention can be performed. After primary surgical intervention, adjuvant chemoradiation should still be considered. A suggested regimen consists of six to eight cycles of CHOP or R-CHOP with radiation therapy at 40–55 Gy with 2 Gy per fraction.⁵ The chances for a favorable response to treatment are predicted by the International Prognostic Index (IPI) for diffuse large B-cell lymphoma in general.⁹

Primary spinal extradural NHL has poor prognosis for patients >50 years of age, with aggressive histological types and with paraplegia and bladder and bowel involvement. Long term survival is favorable in young patients with surgical decompression followed by chemotherapy and radiotherapy. The overall mean survival of patients is eight to nine months with less than 10% surviving one year.¹⁰

Conclusion

It is highly important that recognition of Primary NHL tumor be recognized as part of the differential diagnosis however atypical and uncommon in patients with lower back pain with neurologic deficits in the lower extremities. Since other conditions mimics compressive symptoms in the spinal cord, aside from doing a complete physical examination as well as comprehensive neurologic testing the role of imaging serves to facilitate management and treatment of the case. Although the atypical finding of NHL in the spinal cord is rare, this case will provide insight to the Physicians to maintain a high index of suspicion .

References

1. Vanneuville, B., Janssens, A., Lemmerling, M., De Vlam, K., Mielants, H. And Veys, E.M., 2000. Non-Hodgkin's lymphoma presenting with spinal involvement. *Annals of the rheumatic diseases*, 59(1), pp.12-14
2. Mally, R., Sharma, M., Khan, S. And Velho, V., 2011. Primary lumbo-sacral spinal epidural non-Hodgkin's lymphoma: a case report and review of literature. *Asian spine journal*, 5(3), pp.192-195.
3. Ansell, S.M. and Armitage, J., 2005, August. Non-Hodgkin lym-

phoma: diagnosis and treatment. In *Mayo Clinic Proceedings* (Vol. 80, No. 8, pp. 1087-1097). Elsevier.

4. Monnard, V., Sun, A., Epelbaum, R., Poortmans, P., Miller, R.C., Verschueren, T., Scandolaro, L., Villa, S., Majno, S.B., Ostermann, S. And Ozsahin, M., 2006. Primary spinal epidural lymphoma: patients' profile, outcome, and prognostic factors: a multicenter Rare Cancer Network study. *International Journal of Radiation Oncology* Biology* Physics*, 65(3), pp.817-823.
5. Moussaly, E., Nazha, B., Zaarour, M. And Atallah, J.P., 2015. Primary Non-Hodgkin's Lymphoma of the Spine: A Case Report and Literature Review. *World Journal of Oncology*, 6(5), pp.459-463
6. Cugati, G., Singh, M., Pande, A., Ramamurthi, R., Balasubramanyam, M., Sethi, S.K. and Singh, A.K., 2011. Primary spinal epidural lymphomas. *Journal of Craniovertebral Junction and Spine*, 2(1), p.3.
7. Wada N, Kohara M, Ikeda J, Hori Y, Fujita S, Okada M, Ogawa H, Sugiyama H, Fukuhara S, Kanamaru A, Hino M, Kanakura Y, Morii E, Aozasa K. Diffuse large B-cell lymphoma in the spinal epidural space: A study of the Osaka Lymphoma Study Group. *Pathol Res Pract*. 2010 Jul 15;206(7):439-44. doi: 10.1016/j.prp.2010.02.003. Epub 2010 Apr 15.
8. Peng X, Wan Y, Chen Y, Chen L, He A, Liao W, Shen J, Fu Q, Han S, Li F, Zou X. Primary non-Hodgkin's lymphoma of the spine with neurologic compression treated by radiotherapy and chemotherapy alone or combined with surgical decompression. *Oncol Rep*. 2009 May;21(5):1269-75.
9. Kasper, Hauser et al. *Harrison's Principle of Internal medicine* 19th edition, 2015. *Malignancies of lymphoid cells.*, (Vol 2, pp 695-710). McGraw-Hill Education.
10. Cho, H.J., Lee, J.B., Hur, J.W., Jin, S.W., Cho, T.H. and Park, J.Y., 2015. A rare case of malignant lymphoma occurred at spinal epidural space: a case report. *Korean Journal of Spine*, 12(3), pp.177-180.
11. Mkandawire, N., 2003. Case Report: Primary spinal cord epidural non-Hodgkin's Lymphoma as cause of paraplegia. *Malawi Medical Journal*, 15(2), pp.72-75.
12. Mak KS, Lee LK, MAK RH, Wang S, Pile-spellman J, Abraham JL, Prigerson HG, Balboni TA, 2011. Incidence and treatment in hospitalizations for malignant spinal cord compression in the United States, 1998-2006. *Int J Radiat Oncol Biol Phys*. 2011;80(3):824.