Primary Non-Hodgkin’s Lymphomas Presenting with Extradural Spinal Cord Compression as the Initial Manifestation

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Abstract

Objectives Spinal cord compression is a rare presentation of non-Hodgkin’s lymphoma (NHL), occurring in 0.1% to 10.2% of patients. Primary spinal extradural NHL, i.e. occurring in the absence of any detectable extraspinal lymphoproliferative disorder, has a potentially favourable outcome if diagnosed and treated early. The authors describe two patients with a clinical picture of acute spinal cord compression as the first presentation of NHL.

Methods The patients were 48-year-old female and 27-year-old female. Both presented with back pain followed by acute paraparesis and voiding difficulty. One patient was diabetic. Plain radiographs of the spine were not specific. Thoracic spine magnetic resonance imaging (MRI) revealed evidence of extradural soft tissue mass extending multiple vertebral segments.

Results The patients underwent emergency laminectomy for decompression and tissue diagnosis. Histological and immunohistochemical study revealed B-cell lymphoma, intermediate grade in both patients. Postoperative staging did not reveal any additional lesions other than extradural manifestation of the malignant lymphoma. Surgery with additional chemotherapy and radiotherapy allowed the clinical improvement of both patients.

Conclusion The authors report two patients with a clinical picture of acute spinal cord compression as the first presentation of NHL, and stress that primary spinal epidural NHL should be a diagnostic consideration in the patient without prior history of malignancy who presents with a prodrome of back pain followed by a rapid neurological deterioration.

Key Words Primary non-Hodgkin’s lymphoma - Extradural space - Spinal cord compression.
The authors describe two patients with a clinical picture of acute spinal cord compression as the first presenting feature of NHL.

**Patients and Methods**

Two patients were referred to our institution for acute paraparesis. They were 48-year-old female (case 1) and 27-year-old female (case 2). Case 1 was diabetic and had a prodromal period of regional back pain for 3 weeks prior to the onset of myelopathy, followed by voiding difficulty. Neurological examination revealed weakness of both lower extremities (Grade II), decreased knee and ankle jerks, and diminished light touch and pain sensation below T8 dermatome. Babinski sign was equivocally positive on both sides. Case 2 also had back pain for 2 weeks prior to the development of paraparesis, and exhibited a typical syndrome of acute cord compression that included urinary retention. Neurological examination revealed paraparesis of Grade I, absent knee and ankle jerks, and diminished light touch sensation below T9 dermatome level. Babinski sign was positive on right.

In the laboratory data, case 1 had moderate leukocytosis and slightly increased erythrocyte sedimentation rate (ESR). Random blood sugar level was 329mg/dL and hemoglobin A1C (reference range 4-6% of total hemoglobin) was 8.2% of total hemoglobin. Case 2 had normal complete blood counts and cell morphology. No patients were immunocompromised or found to be infected with the human immunodeficiency virus.

Plain radiographs of the spine showed absence of bony involvement in both patients. Emergency thoracic spine
magnetic resonance imaging (MRI) revealed evidence of an enhancing epidural mass extending from T5 to T8 in case 1 (Fig. 1), and an abnormal low signal in T9 vertebral body and spinous process with an extradural mass extending from T7 to T11 (Fig. 2), respectively.

**Results**

The patients underwent emergency laminectomy for decompression of the spinal cord and tissue diagnosis. In both patients, grayish tumor mass was located in the posterior epidural space, and markedly compressing the thecal sac. The tumors were soft in consistency and removed as much as possible, but some of tumor extending through the neural foramen to paravertebral area was remained in case 2.

Histological studies revealed proliferation and infiltration of large lymphoid cells in both patients and immunohistochemical stain demonstrated positive for CD79a (B cell antigen) in both patients (Fig. 3). Those findings were consistent with diffuse large cell lymphoma of B-cell origin and intermediate grade according to the International Working Formulation. Systemic investigations for occult disease, including haematology and biochemistry, chest radiograph, computed tomography (CT) of the abdomen and pelvis, iliac crest bone marrow biopsy and peripheral blood examination, did not reveal anything other than the disease strictly limited to the extradural space.

![Fig. 2. Case 2. Primary spinal epidural lymphoma with paraspinal and vertebral involvement. A] Preoperative sagittal T1WI of thoracic spine MRI showing abnormal low signal in T9 vertebral body and spinous process with an extradural mass, extending from T7 to T11. B & D] Preoperative Gadolinium-enhanced sagittal & axial T1WI demonstrating the moderate enhancement of the mass lesion (arrow) and T9 vertebra. The axial image shows enhancing epidural mass in the left posterolateral portion of the spinal canal with paravertebral soft tissue mass in the left side of the T9 vertebra. The spinal cord is markedly compressed and displaced to antero-laterally. C & E] Postoperative Gadolinium-enhanced sagittal & axial T1WI show fully decompressed spinal cord and remnant paravertebral mass in the left side of the T9 vertebra.](image-url)
Stage IE.

Postoperative MRI showed fully decompressed spinal cord and minimal enhancing lesion in both cases (Fig. 1, 2). They recovered from the paraparesis and achieved bladder control. Additional chemotherapy and radiotherapy were given by the consulting oncology team. They are now being followed up for 10 and 8 months, respectively.

**Discussion**

Since first being described by Welch and Ginsburg, lymphoma occupying the extradural space has emerged as an important cause of spinal cord compression. Extraneural presentations account for 15 to 30% of all lymphoma cases. Of these, the spinal extradural involvement represents only 0.8 to 2.8%. Cord compression, one of the most common neurological syndromes seen in lymphoma, may occur in up to 7% of all lymphomas. Extraneural presentations of lymphoma have been described in all age groups, including childhood, but tend to cluster in the fifth to sixth decades.

Spinal cord compression occurs during the course of NHL in from 0.1% to 10.2% of patients. In Korea, the incidence of cord compression as a presenting feature among patients with NHL has not been reported yet. Such involvement tends to develop late in the course of established disease, when dissemination has occurred. Cord compression as the initial presenting feature of lymphoma is relatively uncommon. The propensity for NHL to involve and present in the extradural space, compared with Hodgkin’s Disease (HD), has been recognized for many years. Perry, et al. reported a marked preponderance of male patients among their cases, but somewhat lower figures in other series argue that NHL in extradural space is predominantly a male disease. Epidural extension from adjacent vertebral and paravertebral lesions is a common growth pattern in spinal lymphoma. However, haematogeneous involvement of the epidural space is possible. The symptoms are those to be expected with any epidural tumor, and as with other causes of malignant extradural compression, back pain tends to precede the onset of myelopathy by a variable period of time. Less commonly, NHL may arise subdurally or within the spinal cord, and the disease may take on the behaviour of primary cerebral lymphoma, recurring within the central nervous system.

The tumor has a tendency to spread over several vertebrae and has a definite predilection for the thoracic spine followed by the lumbar, cervical and lumbosacral levels. The location of lymphoma in our cases was the thoracic segment, in agreement with other reports. Mullins, et al. suggested that patients with lesions involving segments T5-T8 have a less-favourable outcome because there are fewer radicular arteries to the spinal cord and because this region may be more susceptible to ischemic injury secondary to epidural compression. The site of the tumor within the epidural space has not well been described in previous reports. In the study of Lyons, et al., the tumor was posterior to the spinal cord in seven of eight cases. The lymphoma may also be located laterally. In our cases, the tumors were posterolateral to the spinal cord in both cases.

In the literature, the most common histological grade is...
intermediate, followed by low1-39 high-grade lesions are infrequently reported1. Both of our cases were intermediate grade.

Plain radiographs of the spine are of little help compared to those of patients with metastatic carcinoma causing extradural cord compression. The only sign on plain films, bony destruction, is seen in up to 30-42% of patients19. Thus, the lack of bony involvement on plain films or computed tomography (CT) scan often provides an important clue to diagnosis. Botterell, et al. emphasized that extradural compression of the spinal cord in the presence of normal radiographs should suggest a process such as lymphoma9. Both of our cases also had no radiographic evidence of bony abnormalities.

Lymphomas have characteristic appearance on MRI, and most lymphomas give lower signal than fat and slightly higher signal than that of muscle on T1-weighted image (T1WI), with a homogeneous appearance, and are isointense with or give lower signal than fat and higher signal than muscle on T2-weighted image (T2WI)19. Contrast-enhanced T1WI affords good detection and delineation of epidural lymphoma, paravertebral extension, vertebral involvement and thereby of the full extent of the lesion, and are helpful for demonstrating the sites of spinal cord compression on unenhanced T1WI. NHL can be confused with epidural infiltration by carcinoma, myeloma or sarcomas39.

Spinal epidural hematoma or spinal subdural hematoma must be considered in differential diagnosis when the epidural mass gives high signal on both T1WI and T2WI19. In diabetics, epidural abscess must be also considered in differential diagnosis and they are usually fusiform, centered on and contiguous with the diseased disc and adja-cent vertebral bodies, and often show lower signal than normal disc. Lymphoid malignancies are isointense with marrow on T2WI. As most metastatic carcinomas and sarcomas give higher signal than fat on T2WI it may be possible to distinguish these pathologies19. Lyons, et al. stressed that primary spinal epidural NHL should be a diagnostic consideration in the older patient with a syndrome of spinal cord compression manifested by a prodrome of back pain, followed by a rapid neurological deterioration, no prior history of cancer, normal plain spine radiographs, and neuroimaging consistent with an extradural compressive lesion49.

The majority of patients had advanced disease at the time of diagnosis, and the existence of "primary" extradural lymphoma has been an ongoing controversy for decades9. Other than entering the extradural space from paraspinal tissue and bone, it has been suggested that tumor may arise de novo from extradurally located lymphoid rests59. Blakeslee and Rubinstein mentioned the presence of these rests39. The prolonged survival of Stage I E patients treated with only surgery and radiotherapy provides an argument against a systemic disease process secondarily seeding the spinal canal. In more recent series there has been a tendency to define as primary spinal epidural lymphoma all cases with spinal cord compression as the first sign of a latent disease, irrespective of the presence of other previously undetected neoplastic foci39. In our cases, case 2 had paraspinal and vertebral involvement, but case 1 did not.

The treatment of NHL is based on prognostic indicators such as histology, age and the extent of disease. Because of the known radiation sensitivity of lymphoma, extradural NHL has traditionally been treated by radiotherapy, either alone or followed by chemotherapy after initial decompressive surgery2410710. But, recent studies have suggested an improved survival and tumor control with surgery followed by combined chemotherapy and radiotherapy2.

Eeles, et al. reported that following decompressive surgery, chemotherapy would be the initial treatment of choice in most patients with intermediate and high grade NHL, followed by radiotherapy in localized presentations2. This would treat subclinical metastases and the timing of chemotheraphy, preceding radiotherapy would result in less normal tissue damage. Also, radiation therapy prior to chemotherapy may decrease bone marrow reserve, thus limiting the total amount of chemotherapy8. They also reported that no further improvement in mobility or sphincter control followed radiotherapy or chemotherapy and that the functional gain observed was due to the first intervention i.e. surgery48. Although radiotherapy and, rarely, chemotherapy alone have been used to treat patients with known lymphoma8, these modalities play no primary role when tissue diagnosis is required. Perry, et al. reported disproportionate numbers of relapses and deaths in their patients treated with either therapy alone9. Low-grade localized disease is a rare entity and, until further data are
obtained for this subgroup, aggressive treatment of all patients is indicated, with surgery for tissue diagnosis followed by both chemotherapy and radiotherapy. Unlike other extradural malignancies, in which up to 26% of patients will be worse after surgery\(^2\), evidence suggests that patients with lymphoma will improve or remain stable. The lack of bony involvement may contribute to this improved outcome, but this remains speculative\(^9\).

The overall mean survival of patients with all types of extradural tumor is known to be 8 to 9 months, with less than 10% of patients surviving more than 1 year\(^9\). The prognosis for patients with primary spinal epidural lymphoma are reportedly more favourable, with about 50% of patients surviving more than 3 years. Its occurrence in otherwise healthy patients, sensitivity to treatment, and favorable prognosis as compared with other malignant extradural tumors underscores the need to define this condition better\(^9\). The presence of epidural lymphoma does not adversely affect the overall prognosis of the disease\(^\) indeed, the prognosis of cord compression due to epidural lymphoma is far better as regards both functional recovery and survival than that of cord compression in metastatic carcinoma\(^1\).

**Conclusions**

Spinal epidural involvement is an uncommon initial presentation of NHL. The authors report two patients with a clinical picture of acute spinal cord compression as the first presentation of NHL, and stress that primary spinal epidural NHL should be a diagnostic consideration in the patient without prior history of malignancy who presents with a prodrome of local back pain followed by a rapid neurological deterioration.

Surgery to provide a tissue diagnosis, followed by combined chemotherapy and radiotherapy, should be performed for all cases in order to achieve good local response and long-term survival.

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References

초기 증상으로 척수 압박 증상을 보인 원발성 Non-Hodgkin 임파종

김세훈·임동준·조태형·박정율·정용구·이훈갑·이기찬·서중근

= 국문초록 =

초기 증상으로 척수 압박 증세를 보인 원발성 Non-Hodgkin 임파종은 0.1~10.2%로 드물게 나타나며, 이는 척수 압박 증세를 보인 원발성 Non-Hodgkin 임파종 중 6%를 차지한다. 초기 증상으로는 척수 압박 증세를 보이지 않으면서도 B-형 Non-Hodgkin 임파종으로 진단받기도 한다. 이러한 경우에는 치료를 받지 않으면서도 척수 압박 증세를 보이지 않는 Non-Hodgkin 임파종을 보이는 경우가 많다.

중심 단어: 척수 압박 증세, 원발성, Non-Hodgkin, 임파종.