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CASE REPORT

Primary Extradural Lymphoma with Marginal Zone Transformation- A Rare Presentation

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Abstract

Background: Primary spinal extradural non-Hodgkin lymphoma is rare, and marginal zone transformation is extremely uncommon. We report a rare case of primary spinal EMZL with marginal zone transformation, without systemic or CNS involvement. **Case Presentation:** We report a 38-year-old premenopausal female with type 1 diabetes who presented with 2 months of paraparesis and sensory loss below the umbilicus. MRI revealed patchy meningeal thickening from D1–L3, and PET-CT confirmed a localized thoracolumbar extradural lesion. Surgical D3–D6 laminoplasty with excision was performed. Histopathology and immunophenotyping confirmed follicular centre cell NHL with marginal zone transformation, with CD20, CD10, PAX5, CD23, BCL6 positivity and Ki-67 20% overall with a focal hotspot of 75%, indicating high-grade transformation. Differential diagnoses including mantle cell lymphoma, CLL/SLL, and pure follicular lymphoma were excluded. The patient received six cycles of modified R-GMALL chemotherapy with triple intrathecal therapy. Treatment was well tolerated, with only grade 2 neutropenia and grade 1 mucositis, and she achieved near-complete neurological recovery. Follow-up at 14 months demonstrated sustained neurological function and complete metabolic remission. **Conclusion:** This case highlights the importance of early recognition, intensive chemoimmunotherapy, and careful supportive care in rare transformed MZL, supported by emerging prognostic models incorporating systemic inflammation markers.

Keywords: Non-Hodgkin lymphoma- Marginal zone transformation- Extradural lymphoma

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Introduction

Primary spinal extradural non-Hodgkin lymphoma (NHL) is rare, accounting for approximately 1% of all localized NHLs, and may present with spinal cord compression in 0.1–3.3% of cases [1, 2]. The diagnosis is often challenging, as symptoms such as paraparesis, back pain, or sensory deficits are nonspecific and may mimic other spinal pathologies, which can lead to delayed recognition and treatment.

Marginal zone lymphoma (MZL) is a mature B-cell neoplasm arising from memory B lymphocytes in the marginal zone of secondary lymphoid follicles. While typically indolent, MZL can rarely undergo high-grade transformation, which significantly alters prognosis and necessitates more intensive therapy. Extranodal MZL (EMZL) may arise in various anatomical sites, but primary spinal involvement is exceedingly uncommon, making early identification crucial to prevent irreversible neurological deficits [3, 4].

We report a rare case of primary spinal EMZL with marginal zone transformation, without systemic or CNS involvement, which was successfully managed with intensive chemoimmunotherapy, resulting in both neurological recovery and complete metabolic remission. This case underscores the importance of prompt diagnosis, surgical decompression when indicated, and tailored systemic therapy in rare transformed spinal NHLs.

Case Presentation

A 38-year-old premenopausal female with type 1 diabetes mellitus presented in our institute with a 2-month history of paraparesis with loss of sensation below the umbilicus. She was evaluated with magnetic resonance imaging (MRI) of the spine, which revealed patchy meningeal thickening from D1-L3 (Figure 1). She

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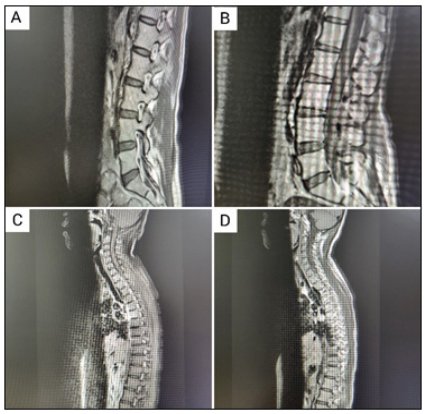

Figure 1. Sagittal T2-weighted MRI of the lumbosacral spine (A, B) and Sagittal Post-Contrast T1-weighted Magnetic resonance imaging (MRI) of the Whole Spine (C, D) showing patchy meningeal thickening from D1-L3

underwent D3-D6 laminoplasty with excision of the lesion for diagnosis and decompression.

Histopathology using Hematoxylin and eosin (H&E) staining demonstrated an aggregate of large lymphoid cells with small lymphocytes (Figure 2). Immunohistochemistry showed membrane positivity for CD20, CD10, PAX5, CD23, and BCL6 (Figure 3), with focal weak CD30 expression. IgD highlighted the mantle zone, and light-chain restriction analysis demonstrated κ predominance, supporting clonality. Foci of cells exhibited a high nuclear–cytoplasmic ratio and brisk mitosis, with an overall Ki-67 proliferation index of ~20% and a focal hotspot of 75%, indicating areas of high proliferative activity consistent with transformation to a higher-grade lymphoma. The diagnosis was follicular centre cell NHL with marginal zone transformation. The diagnosis of follicular centre cell NHL with marginal zone transformation was based on histology, immunophenotype, and proliferation index, with differential diagnoses excluded: mantle cell lymphoma (Cyclin D1−, CD5−), chronic lymphocytic leukemia/small lymphocytic lymphoma (CD5−, low CD23), and pure follicular lymphoma (excluded due to marginal zone areas and Ki-67 hotspots).

On further work-up with positron emission tomography–computed tomography (PET-CT) scan confirmed a localised extradural lesion in the thoracolumbar spinal canal with few mildly enlarged axillary, retroperitoneal and inguinal lymph nodes with low SUV uptake. Bone marrow biopsy revealed a lymphoid nodule with normocellular marrow, and cerebrospinal fluid (CSF) analysis showed protein of more than 3000 mg/dL.

Given the aggressive features, she received six cycles of modified R-GMALL chemotherapy over 12 weeks, administered every 2 weeks. Each cycle included rituximab, vincristine, high-dose methotrexate, ifosfamide, cytarabine, etoposide, and triple intrathecal therapy. During treatment, she developed grade 2 neutropenia after cycles 3 and 5, which was managed with G-CSF support, and mild grade 1 mucositis with nausea, which was controlled with antiemetics. Supportive measures included hydration with mesna, leucovorin rescue post-methotrexate, transfusions as needed, and close laboratory monitoring.

Neurological improvement was noted progressively after the third cycle, with near-complete recovery at the end of the sixth cycle. Follow-up at 14 months demonstrated sustained neurological function and complete metabolic remission on PET-CT, with no evidence of relapse.

Discussion

Primary extradural NHL is a rare entity, most commonly presenting in the fourth to fifth decade of life, with the thoracic spine being involved in approximately 69% of cases [5]. This predilection is attributed to the higher concentration of lymphatic drainage in this region. Notably, the involvement of vertebrae D5 and D8 is associated with poorer outcomes due to limited radicular artery supply, increasing susceptibility to ischemic injury [6]. Patients often present with a triad of lower limb weakness, localized back pain, and bladder dysfunction, [7] consistent with the paraparesis and sensory loss observed in this case.

Radiological imaging plays a crucial role in diagnosis. MRI revealed patchy meningeal thickening from D1 to L3, while PET-CT confirmed a localized extradural soft tissue mass in the thoracolumbar spinal canal. These findings are consistent with previous reports of iso/hypointense lesions on T1/T2-weighted images and homogeneous enhancement on post-contrast images, extending over multiple vertebrae [8-10]. However, plain spine radiographs are normal, whereas an MRI scan can predict the extranodal involvement.

Surgical intervention is often required for both diagnosis and decompression in cases of spinal cord compression without a known primary lesion [7]. In this instance, D3–D6 laminoplasty with excision of the lesion was performed. While some studies suggest no significant difference in outcomes between decompressive laminectomy with radiotherapy and radiotherapy alone,

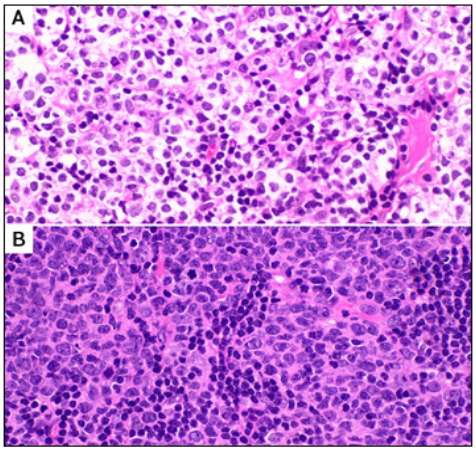

Figure 2. Hematoxylin and Eosin (H&E) (x 40)-staining of the Microscopy Section (A and B) Showing an Aggregate of Large Lymphoid Cells with Small Lymphocytes

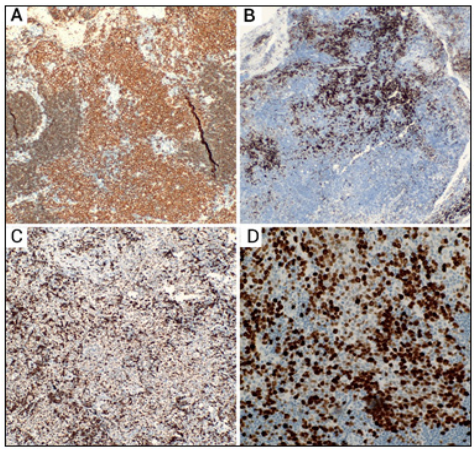

Figure 3. Immunohistochemistry (IHC) Section of A) CD10 (x 100) showing strong diffuse membranous staining of cells B) CD20 revealing nuclear positivity, C) BCL6 showing diffuse population of positive B-cells, D) Ki-67 positivity indicating a high proliferative index

early surgical intervention can provide tissue diagnosis and relieve neurological deficits [2, 11]

Histopathological examination revealed an aggregate of large lymphoid cells with small lymphocytes. Immunohistochemistry (IHC) demonstrated positivity for CD20, CD10, PAX5, CD23, and BCL6, confirming a diagnosis of NHL of follicular center cell type with marginal zone transformation. Differential diagnoses, including mantle cell lymphoma, chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL), and pure follicular lymphoma, were excluded based on IHC findings and morphological features.

High-grade transformation (HGT) in marginal zone lymphoma is rare but associated with a significantly poorer prognosis [12]. Patients with HGT have a 2-year overall survival (OS) rate of 57% and a 5-year OS rate of 65% [13]. Factors such as prolonged paraplegia, bladder and bowel involvement, and high Ki-67 labeling index correlate with adverse outcomes. Long-term survival is favourable for only young patients with surgical decompression followed by chemotherapy and radiotherapy, with the overall mean survival being 8-9 months, with less than 10% surviving one year. Also, it was noted that the CHOP regimen was given in previous cases [2, 8]. However, in this case, modified G-MALL protocol chemotherapy, comprised of a combination of Rituximab, Vincristine, Methotrexate, Ifosfamide, Cytarabine, Etoposide, and Triple Intrathecal therapy was given for better clinical outcomes.

Although marginal zone and follicular lymphomas are typically indolent and managed with R-CHOP or bendamustine-rituximab, the histopathology here demonstrated focal transformation with a hotspot Ki-67 of ~75%, brisk mitosis, and a germinal center B-cell phenotype. In such settings, standard regimens are associated with suboptimal outcomes [14, 15]. Hence, R-GMALL protocol was chosen because it is a short-intensive and address the aggressive biological component and potential CNS risk, offering superior disease control compared to conventional regimens [16].

Prognostic factors in primary spinal extradural NHL include histologic subtype, stage at presentation, proliferative index, neurological status at diagnosis, and response to systemic therapy. Patients presenting with aggressive histology (e.g., diffuse large B-cell or transformed indolent lymphomas), high Ki-67, or multifocal/systemic involvement generally have worse outcomes, while early diagnosis and preserved neurological function correlate with improved survival. Several studies of primary spinal epidural NHL report that prognosis is primarily determined by histological grade and systemic dissemination rather than local control, highlighting the need for systemic chemoimmunotherapy as the mainstay of treatment, with radiotherapy reserved for residual or bulky disease [17-19].

Moreover, recent studies support the integration of systemic inflammation markers and prognostic nomograms in NHL by incorporating monocyte count, platelet-to-lymphocyte ratio, and systemic immune-inflammation index to predict overall survival in DLBCL patients [20]. While these models were studied in DLBCL, they underscore the importance of objective markers in risk stratification, which could inform management in high-risk or transformed MZL. Procedural planning in NHL patients may also benefit from awareness of potential complications. A recent comparative study reported that lymphoma patients undergoing port catheter placement, particularly via left-sided or jugular access, had a higher risk of complications [21]. Such data emphasize the importance of careful device selection and monitoring during supportive care in intensive chemotherapy protocols like R-GMALL.

Given the rarity of MZL and rarity of HGT, it is unlikely that randomised and prospective studies will ever be conducted; thus, multi-institutional studies attempting to address gaps in the understanding of biology and treatment of high-risk/transformed patients with MZL [22]. This case underscores the importance of early identification and aggressive treatment in improving outcomes for patients with primary spinal extradural NHL.

In conclusion, primary extradural NHL is a rare entity that is commonly overlooked and misdiagnosed, resulting in delayed intervention. So, it should be investigated in the differential diagnosis of individuals who present with paraparesis with loss of sensation below the umbilicus. Plain spine radiographs are unremarkable, and an MRI scan shows an extradural lesion squeezing the cord in such circumstances. The surgical excision of the lesion for diagnosis, followed by chemotherapy and intrathecal therapy, should result in considerable neurological improvements.

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Originality Declaration for Figures

All figures included in this manuscript are original

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