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Unusual Presentation of Primary Extra Nodal Diffuse Large B Cell Lymphoma

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Abstract Diffuse Large B Cell Lymphoma (DLBCL) is the most frequently occurring type of Non-Hodgkin Lymphoma (NHL). Primary extra nodal Diffuse Large B Cell Lymphoma (PE-DLBCL) originating in the bone, specifically the thoracic spine, is rare. We describe the case of a 69-year-old male who presented to our facility with back pain and acute bilateral lower extremity paraplegia as Primary extra nodal Diffuse Large B Cell Lymphoma.

Keywords: *R-CHOP chemotherapy, Primary Extra nodal Diffuse Large B-cell Lymphoma (PE-DLBCL), Non-Hodgkin Lymphoma (NHL), Diffuse Large B Cell Lymphoma (DLBCL), Extra nodal Diffuse Large B-cell Lymphoma*

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1. Introduction

Diffuse Large B Cell Lymphoma (DLBCL) represents about 30% to 40% of Non-Hodgkin Lymphoma (NHL) cases [1]. Majority of DLBCL cases are nodal in origin with less than 40% emerging from extra-nodal locations [2]. Primary extra-nodal Diffuse Large B Cell Lymphoma (PE-DLBCL) are frequently found in the gastrointestinal tract and less commonly seen in the bone, thyroid, adrenal gland, skin, breast, testis, female genital system, pancreas, and central nervous system (CNS) [3]. We report a case of PE-DLBCL originating at the level of thoracic vertebrae three to eight with an unusual presentation of back pain and acute onset of bilateral lower extremity paraplegia.

2. Case Presentation

A 69-year-old Caucasian Male with a past medical history of Hypertension, Hyperlipidemia, Obstructive sleep apnea, and Prostate cancer in remission presented to the ED for worsening back pain and acute onset of bilateral lower extremity paraplegia. Patient attributed the back pain to lifting heavy objects. Prior to this visit, the patient was seen at another facility for back pain radiating to the epigastric area, and chest. His symptoms progressively worsened with difficulty urinating and constipation. Vital signs were within normal limits. Physical exam was remarkable for being non ambulatory with zero out of five strength in proximal legs, iliopsoas, and quadriceps. Slight diminished rectal tone noted. Patient was still able to wiggle his toes bilaterally with right greater than left side along with slight dorsiflexion and plantar flexion.

CT Angio Chest, Abdomen, Pelvis showed no evidence of aortic dilation, dissection, or lymphadenopathy. MRI Thoracic and Lumbar spine done revealed lesion replacing the entirety of normal marrow signal within the sixth thoracic vertebral body and posterior elements, with associated epidural tumor at the level of thoracic vertebrae three to eight, causing severe spinal stenosis and cord compression at the fifth to sixth thoracic vertebrae level with mild hyperintense signal at the second thoracic vertebrae, likely representing edema as seen in figure one. No evidence of a pathological compression fracture noted in imaging.

The patient had an emergent surgical laminectomy and tumor resection along with spinal cord decompression done. Four specimens: 1.2 cm epidural thoracic tumor, 2.0 cm T6 vertebral body tumor specimen, 2.5 cm T6 vertebral body tumor specimen, and 2.5 cm thoracic epidural tumor were all sent for further analysis. Frozen section specimen demonstrated that the tumor comprised of mitotically active large atypical lymphoid cells with moderate nuclear pleomorphism. Additionally, background tangible body macrophages were present along with associated areas of necrosis. Subsequent testing confirmed a high-grade Diffuse B Cell Lymphoma of germinal center type. Flow cytometry was limited by cell degeneration but remarkable for positive expression of CD20, CD45, Bcl6, and Ki67 estimated at greater than 80%. The sample was negative for the expression of CD3, CD5, CD10, CD30, CD30, cyclin D1, MUM1, and Bcl2. These findings supported the diagnosis of Large B cell lymphoma with a high proliferation rate.

CSF analysis was negative for malignant cells. Bone marrow biopsy indicated normocellular marrow (50%)

with no morphologic or flow cytometric evidence of malignant lymphoma. MRI Brain was unremarkable. Patient was given four mg IV Decadron every six hours for five days followed by tapering prednisone for seven days. Chemotherapy was planned, the first cycle of R-CHOP chemotherapy with Intrathecal Methotrexate was given in the hospital. During the hospital stay, motor strength on bilateral lower extremities improved with four out of five strength on the right, four out of five strength on the left, along with mild persistent sensory deficits in both lower extremities. Following patient's emergent surgery, his in-patient stay was complicated by an acute pulmonary embolism in his right upper and right lower lobe. At the time, the patient was not a candidate for anticoagulation due to his recent surgery and got an infrarenal IVC filter placed by interventional radiology. Plan to continue R- CHOP for a total of six cycles and physical therapy was recommended at discharge.

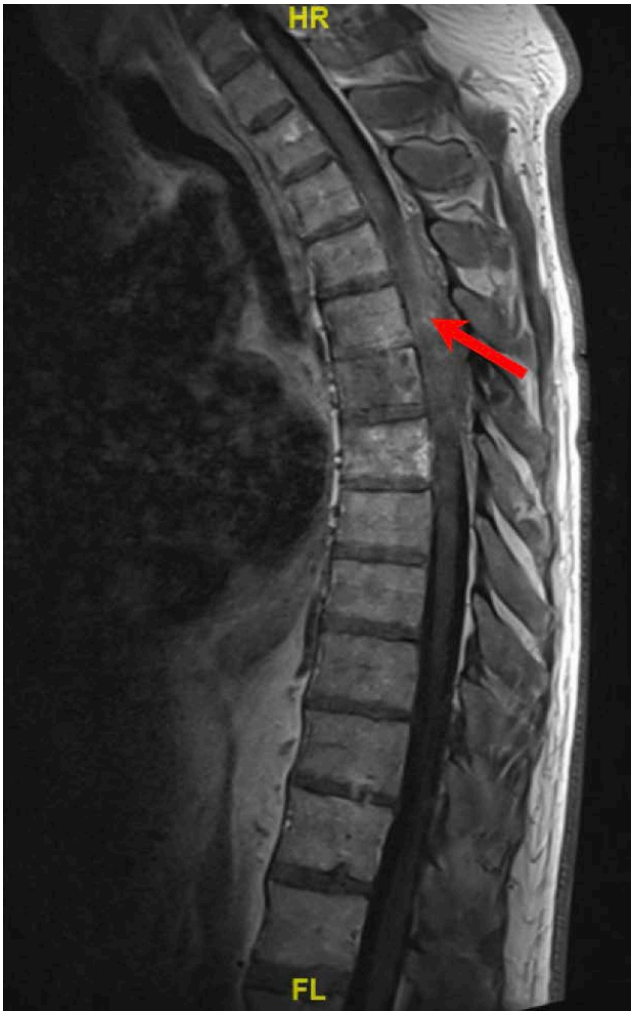

Figure 1. MR imaging of the vertebrae with arrow indicating tumor at the level of thoracic vertebrae three to eight.

3. Discussion

Diffuse Large B Cell Lymphoma can be divided into two major subclasses based on the cell of origin [1,4]. These two subclasses are known to be Germinal Center B-cell like Diffuse Large B Cell Lymphoma (GCB DLBCL) and Activated B-cell like Diffuse Large B Cell Lymphoma (ABC DLBCL) [1,4]. GCB DLBCL has been shown to have a better prognostic outcome in comparison to ABC DLBCL [1]. The patient in our case presentation was confirmed to have a high-grade Diffuse B Cell Lymphoma of germinal center type (GCB DLBCL) along with extra nodal involvement in the thoracic vertebrae.

Malignant lymphoma of bone represents 7% of bone tumors and 5% of extra nodal lymphoma. This can signify secondary hematologic disease or primary extra nodal disease. Bone lymphoma is typically a result of NHL with the most frequently occurring type being Diffuse Large Cell Lymphoma. Primary extra nodal malignancy of the bone typically involves the axial skeleton for example the spine and pelvis [5].

The pathophysiology behind primary extra nodal NHL with thoracic involvement is not entirely clear. The lymphoma is known to originate from paraspinal soft tissues for example epidural lymphoid tissue that then makes its way into the epidural space through the vertebral foramen without producing bony destruction [6,7]. This mechanism of invasion has been found to be specific to spinal lymphomas as other tumors associated with cord invasion have vertebral bone destruction [7].

A case series study performed by Chang et al. in patients with DLBCL associated spinal cord compression showed positive progression from presenting neurological deficit after surgical decompression along with a possible survival benefit following chemotherapy [8]. Our patient is very likely to have a better outcome with the surgical decompression and chemotherapy administration post-surgery.

Standard of care for Diffuse Large B Cell Lymphoma is six cycles of R-CHOP-21 therapy [9]. This therapy entails a regimen of rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone every 21 days [9]. R-CHOP therapy has been shown to be curative in 90% of patients with early stage DLBCL and 60% of patients with advanced stage DLBCL [10].

There are currently deviations present in R-CHOP therapy administration such as R-CHOP-14 versus R-CHOP-21 [11]. A clinical trial comparing R-CHOP-14 regimen versus R-CHOP-21 regimen in untreated DLBCL patients indicated no remarkable difference in overall survival between the two treatment groups [11,12]. A randomized phase 3 trial comparing R-CHOP-14 with R-CHOP-21 in elderly DLBCL patients showed no difference in therapeutic efficacy between the two regimens as well as the presence of similar side effect profiles noted except for increased requirement for red blood cell and platelet transfusion in the R-CHOP-14 therapeutic group [13].

Another clinical trial comparing the efficacy of R-CHOP-14 versus R-CHOP-21 of untreated DLBCL in the Asian population showed similar outcomes in disease free survival for both therapeutic groups [14]. A systematic review and meta-analysis study of R-CHOP-14 versus R-CHOP-21 in aggressive or advanced B cell lymphoma indicated no remarkable difference in therapeutic response and toxic side effects for both regimens [15]. Affected patients with GCB DLBCL undergoing standard R-CHOP regimen have a five-year survival rate [16].

4. Conclusion

Primary extra nodal Diffuse Large B Cell Lymphoma (PE-DLBCL) originating in the bone, specifically the thoracic spine, is a rare condition. Our case illustrates an individual with this condition, specifically the germinal center B cell type upon tissue biopsy. Our patient had an unusual presentation of acute onset bilateral lower extremity paraplegia with an initial zero out of five strength in proximal legs and worsening back pain that was triggered after lifting a heavy object. The mechanism of thoracic involvement in primary extra nodal NHL is not entirely clear. The lymphoma involvement is known to originate from paraspinal soft tissues that makes its way into the epidural space through the vertebral foramen without producing bony destruction [6,7]. Standard of care for Diffuse Large B Cell Lymphoma is six cycles of R-CHOP-21 therapy entailing a regimen of rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone every 21 days with a five-year survival rate [16].

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