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Primary Bone Lymphoma: case report and literature review

Fariña AM[1], França MVS[2], Farias J[2], Segura M[3], Piazera FZ[4]

[1]Academics of the Faculty of Medicine of the University of Brasilia, Asa Norte, Brasília

[2] Clinical Oncologists at the Cancer Treatment Center of Brasília, Asa Norte, Brasília

[3] Pathologist of the Lamina Laboratory, Asa Sul, Brasília

[4]Adjunct Professor of Hematology of the Faculty of Medicine, Asa Norte, Brasília

Abstract: ***Primary non-Hodgkin's lymphoma of bone (PLB) represents 5% of extranodal lymphoma manifestations and 7% of all bone lymphomas and is considered a rare clinical condition. Its manifestation is predominant in long bones, such as femur and pelvis (50%), and less frequently can affect the vertebral column (1,7%), with or without lymph node dissemination. In this case, we report a 55-year-old male patient with primary diffuse large B-cell non-Hodgkin's lymphoma (DLBCL), affecting the vertebral body of L4, with marked reduction of the vertebral canal and neuroforamina***

Keywords: primary bone lymphoma, diffuse large B-cell non-Hodgkin's lymphoma**.**

1. Introduction

Primary non-Hodgkin's lymphoma of bone (PLB) represents 5% of extranodal lymphoma manifestations and 7% of all bone lymphomas [1]. PLB is thought to arise from paraspinal lymphoid tissue and subsequently invade the spinal column. Its manifestation can occur at any age, but it becomes more prevalent in individuals in its adult phase, with the primary involvement of the vertebral column being a rare form of extranodal lymphoma, representing 1.7% of the sites of bone manifestation [2-3].

2. Case report

We report a 55-year-old male patient with complaints of low back pain associated with paresthesia in the lower limbs bilateral that occurred during the last X? months.

As initial management, treatment with analgesic Tonsilax was indicated, with a good response to pain, but persistence of paresthesia. Treatment with Prednisone was started, resulting in improved sensitivity. Magnetic resonance imaging (MRI) of the dorsal spine was performed, weighted on T1 and T2, showing signs of a specific process in the vertebral body of L4, leading to a marked reduction of the vertebral canal and neuroforamina (Figure 1).

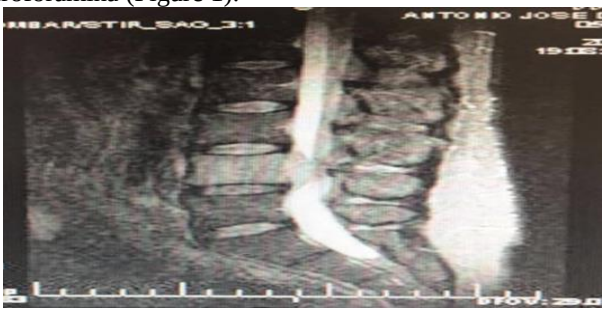

Figure 1. MRI in lumbar spine with presence of signal hyperintensity evidencing specific process signals in L4 vertebral body.

Patient PET-scan revealed a lesion invading the medullary canal at the L4 level, associated with two pelvic hypermetabolic lymph nodes (Figure 2,3), suggesting neoplastic involvement.

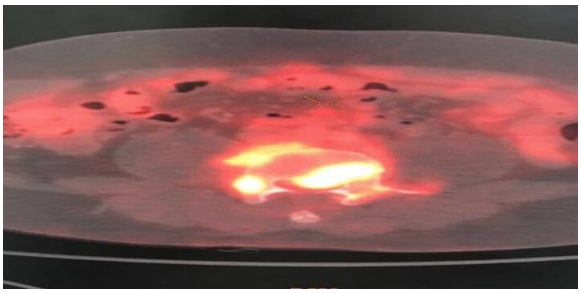

Figure 2: PET-scan showing lesion invading medullary canal in L4.

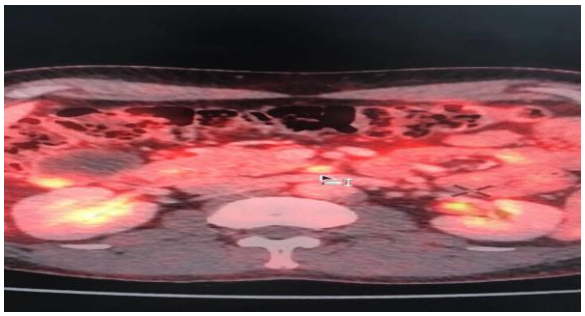

Figure 3: PET-scan showing pelvic hypermetabolic lymph nodes.

The bone biopsy revealed Diffuse Large B-cell Non-Hodgkin's Lymphoma (DLBCL) variant of Germinal Center B-cell (GCB) (Figure 4). The immunohistochemistry (IHC) was compatible with grade 3B follicular lymphoma, with coexpression of CD10 and BCL-6, high Ki-67 proliferative index and partial BCL-2 immunoexpression, raising the possibility that DLBCL progressed from a follicular lymphoma [4]. The

histopathological markers are listed in table 1. Also other exams were requested, such as β2 microglobulins with value of 5.68 μg / ml^4, protein electrophoresis evidencing hypergammaglobulinemia and LDH dosage of 200 U / L.

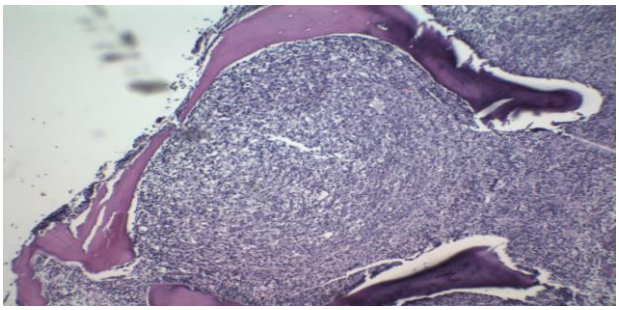

Figure 4: LDGCB variant of CGB bone biopsy.

Table 1. Antibody screening performed on biopsy

Antibodies	*Results*
AE1 / AE3 (AE1 / AE3)	*Negative*
BCL-2 (124)	*Positive in numerous cells*
BCL-6 (PG-B6p)	*Diffusely positive*
CD10 (56C6)	*Diffusely positive*
CD138 (MI15)	*Negative*
CD20 (pan B) (L26)	*Diffusely positive*
CD23 (DAK-CD23)	*Negative*
CD3 (pan T) (Polyclonal rabbit)	*Negative*
CD45 (LCA) (2B11 PD762)	*Diffusely positive*
CD5 (4C7)	*Negative*
Cyclin D1 (EP12)	*Negative*
Glycophorin A (JC159)	*Negative*
Ki-67 (MIB-1)	*Positive in about 80% of cells in germinal centers*
MPO (Polyclonal rabbit)	*Negative*
MUM 1 (MUM1p)	*Negative*
Protein S-100 (Polyclonal rabbit)	*Negative*

From the examinations and clinical presentation of the patient, we conclude that this is a high grade DLBCL in stage IV A, due to the involvement of bone tissue and absence of B symptoms [2]. The immunoexpression of BCL-6 and/or BCL-2 associated with a possible mutation in the MYC gene raises the possibility of Double Hit or Triple Hit Lymphoma (DHL/THL), respectively. As manner, we chose to start cyclophosphamide, doxorubicin, vincristine and prednisone combined with rituximab (R-CHOP) therapy in 4 cycles with complete response to therapy.

3. Discussions

PLB represents about 1% of all non-Hodgkin's lymphomas, one of the highest classified as DLBCL. Its manifestation is predominant in long bones with persistence of bone marrow, such as the tibia and hips, and in rare cases are manifested in the vertebral column, with few reports in the literature [3-5].

The recommended treatment consists of the combination of R-CHOP chemotherapy, which has shown positive results in patient survival. In cases where there is medullary compression due to involvement of the vertebral column, R-CHOP can be associated with radiotherapy [6].

The most common histological type of non-Hodgkin's lymphoma is B-cell lymphoma, which accounts for 80% to 90% of all cases, and 30% of these are DLBCL, which are divided into B cell (GCB) and activated B-cell type (ABC) lymphomas. Most LDGCBs have specific IHC markers, including CD20, PAX-5, CD10, BCL-2 and BCL-6 [5-7]. The mutation in the MYC gene is prominent in LDGCB and can be detected concomitantly with mutations in BCL-2 and/or BCL-6, which are classified as DHL or THL, characterized by aggressive clinical behavior, usually refractory to R-CHOP therapy [8].

In this case, we present a patient with PLB in the vertebral column, affecting the body of L4, resulting in medullary compression. Differential diagnoses for this lesion include lumbar disc herniation, non-specific infections, tuberculosis and therefore a CT-guided biopsy associated with an IHC was required for the diagnosis. We emphasize the determination of the invasive potential of the tumor through staging, serum LDH level, presence of extranodal disease and age of the patient [1-9]. This information may help a better therapeutic choice, estimate the tumor response and the patient's ability to tolerate indicated therapy. The analysis of serological parameters, such as β2 microglobulin levels, the search for specific gene mutations and the tumor cell proliferation indexes from certain specialties, allows a better understanding of the biological heterogeneity of PLB [10].

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Conflict of interests: the authors report no conflict of interest.