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A Wolf In T-Cell Clothing: Unveiling the Diagnostic Masquerade of T Cell / Histiocyte Rich Large B Cell Lymphoma

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ABSTRACT

T cell/histiocyte-rich large B cell lymphoma (THRLBCL) is an uncommon and aggressive form of non-Hodgkin lymphoma (NHL) characterized by sparse neoplastic B cells within a predominant reactive T-cell background. A female patient aged 53 years presented with generalized constitutional symptoms accompanied by laboratory findings of cytopenias and elevated serum calcium levels. FDG PET-CT revealed widespread lymphadenopathy, skeletal involvement, and dural uptake. Bone marrow biopsy showed diffuse and sinusoidal infiltration by monomorphic lymphoid cells without fibrosis. Immunohistochemistry demonstrated scattered CD20+ B cells, abundant CD3+ T cells, co-expression of CD15 and BCL2, and the absence of CD30 and ALK, confirming THRLBCL with marrow involvement. This case highlights the diagnostic challenge posed by THRLBCL and emphasizes the critical role of integrated clinical, imaging, histopathologic, and immunophenotypic assessment for accurate diagnosis and management.

Keywords: *T cell/histiocyte-rich large B cell lymphoma (THRLBCL), Bone marrow infiltration, Immunohistochemistry*

1. INTRODUCTION

T-cell/histiocyte-rich large B-cell lymphoma (THRLBCL) represents an uncommon and clinically aggressive variant of NHL, marked by scarce neoplastic B-cells dispersed within a background dominated by reactive T-cells. Unlike other subtypes of NHL, THRLBCL can pose significant diagnostic challenges due to its morphological overlap with other lymphoid malignancies, especially in cases with extensive extranodal involvement. Bone marrow infiltration, while recognized, is an uncommon presentation and requires high diagnostic suspicion. Accurate diagnosis depends on a combination of clinical evaluation, imaging, histopathological examination, and immunohistochemistry. Identification of bone marrow involvement is crucial for proper staging and guiding treatment decisions.

2. CASE REPORT

A female patient aged 53 years with longstanding diabetes, hypertension, and chronic kidney disease was evaluated for complaints of giddiness, anorexia, and notable weight reduction. Laboratory investigations revealed severe normocytic, normochromic anemia (Hb: 7.1 g/dL), leucopenia, and neutrophilic predominance. Liver function tests were within normal

limits. Vitamin D3 was adequate (48.7 ng/mL), but parathyroid hormone was markedly reduced (5.7 pg/mL), and serum calcium was elevated (12 mg/dL), indicating hypercalcemia.

Serum protein electrophoresis showed hypoalbuminemia and hypoproteinemia, suggesting systemic involvement.

Whole-body FDG PET-CT demonstrated metabolically active generalized lymphadenopathy, hypodense splenic lesions, low-grade nodular thickening of the adrenal gland, and patchy dural metabolic activity. Increased FDG uptake was seen in the axial and proximal appendicular skeleton, as well as in soft tissue around the dorsal and lumbar spine, with focal involvement of cranial bones— findings strongly suggestive of a lymphoproliferative disorder (Fig.1).

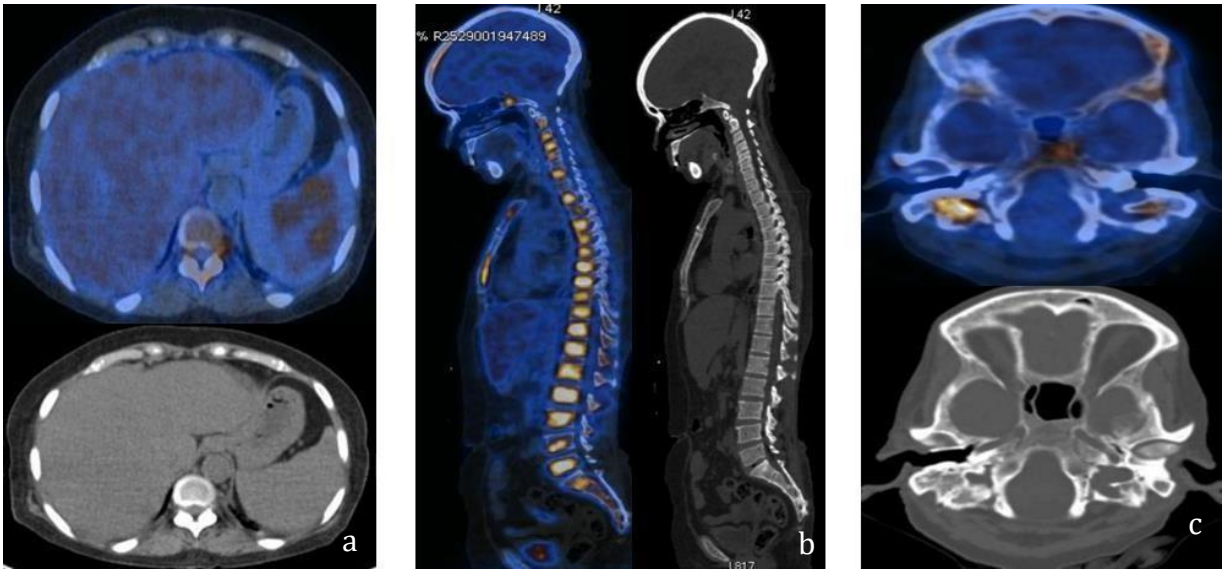

Fig.1: a.) Metabolically active, ill-defined hypodense lesions in the spleen, b.) Diffuse, intensely increased FDG uptake is seen in the axial and proximal appendicular bone marrow with no corresponding lytic/sclerotic lesions, c.) Patchy heterogeneously increased metabolic activity along the dura in bilateral frontal and parietal convexities.

Bone marrow aspiration was aparticulate and diluted with peripheral blood. Bone marrow biopsy showed marrow spaces infiltrated by small monomorphic cells exhibiting rounded nuclei with densely packed chromatin in diffuse and sinusoidal patterns, with occasional megakaryocytes and scattered histiocytes. Histochemical staining techniques, including Masson Trichrome and Van Gieson, were used to assess fibrosis and were negative for collagen fibrosis, helping to exclude myelofibrosis or other marrow fibrosis-related pathologies (Fig.2).

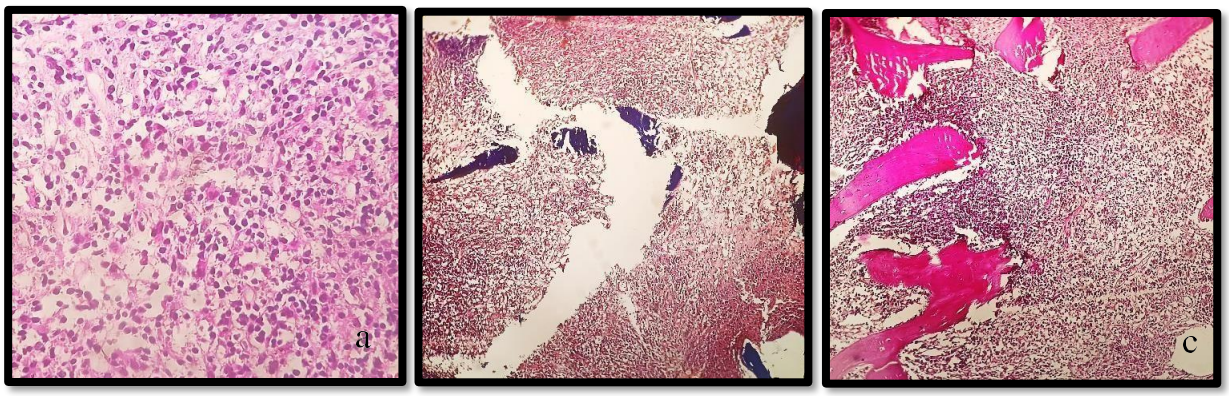

Fig.2: a.) Monomorphic cells exhibiting rounded nuclei with densely packed chromatin(400x), b.) Masson Trichrome shows negative for collagen fibrosis(40x), c.) Van Gieson shows negative for collagen fibrosis(40x)

Immunohistochemistry provided critical diagnostic insight. CD45 showed strong positivity in the atypical lymphoid cells, confirming their hematopoietic origin. CD3 positivity in background cells highlighted a predominant T-cell component.

CD20 was positive in a minority of large abnormal lymphoid cells, pointing towards a sparse neoplastic B-cell population seen in THRLBCL(Fig.3). CD15, typically related to classical Hodgkin lymphoma, showed diffuse positivity, which can also be seen in THRLBCL and supports its diagnosis when correlated with other markers. Strong BCL2 expression further confirmed the presence of neoplastic B-cells with anti-apoptotic activity. CD10 positivity was mild, supporting a B-cell lineage (Fig. 4). The absence of immunohistochemical expression for CD30, along with ALK, effectively excluded classical Hodgkin lymphoma (CHL) and anaplastic large cell lymphoma (ALCL), respectively (Fig. 5).

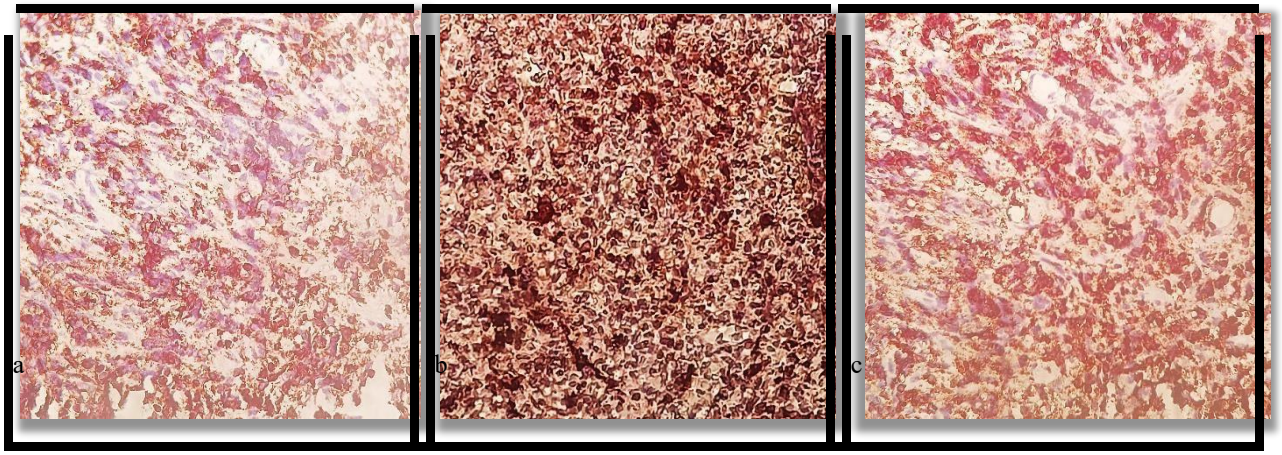

Fig.3: a.) IHC CD45: Strong cytoplasmic positivity in atypical (lymphoid)cells(400x), b.) IHC CD20: Positive in large cells with histiocytic morphology(400x), c.) IHC CD3: Strong cytoplasmic positivity in background atypical (lymphoid) cells(400x)

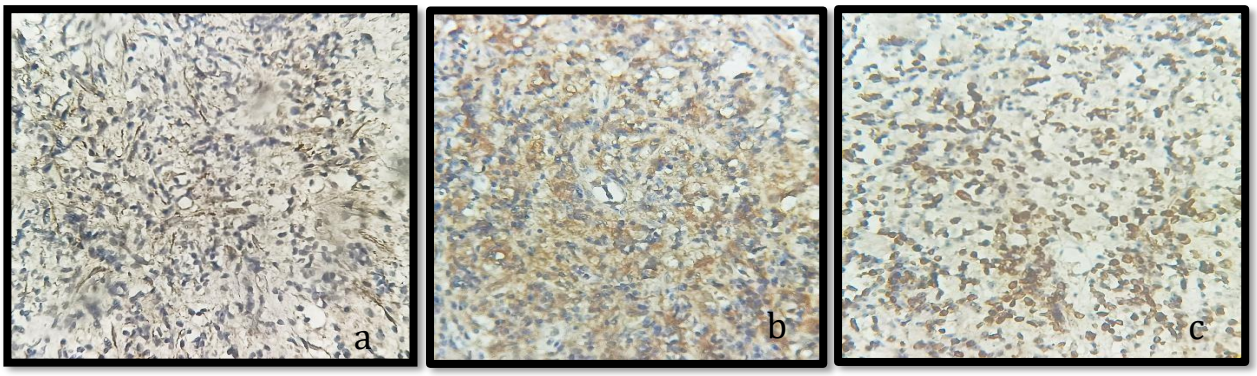

Fig.4: a.) IHC CD10: Diffuse mild membranous positivity in atypical lymphoid cells(400X), b.) IHC CD15: Diffuse strong membranous and cytoplasmic positivity in atypical lymphoid cells(400X), c.) IHC BCL2: Diffuse strong nuclear and cytoplasmic staining in atypical lymphoid cells(400X)

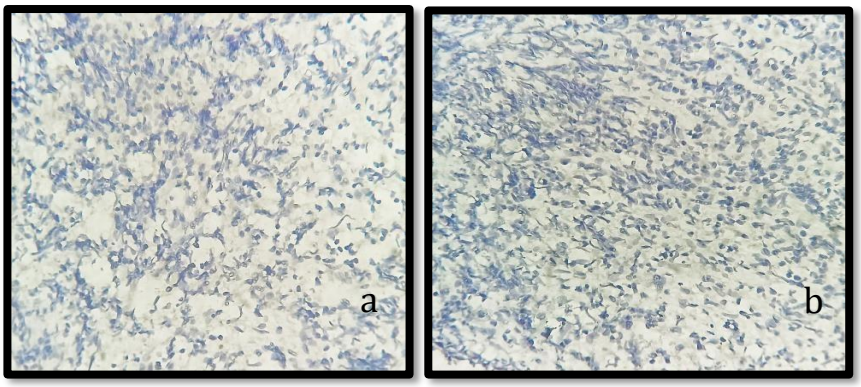

Fig.5: a.) IHC CD30: Negative in lymphoid cells, occasional large cells are positive(400X), b.) IHC Alk: Negative in lymphoid cells(400X)

Very few studies have reported cases of THRLBCL with bone marrow involvement, making this presentation particularly uncommon and diagnostically challenging. Taken together, the immunohistochemical profile, with scattered CD20+ B-cells within a CD3+ T-cell-rich background, co-expression of CD15 and BCL2, and absence of CD30 and ALK, along with the histologic and imaging findings, substantiated the diagnosis of THRLBCL with bone marrow infiltration. This rare presentation highlights the critical role of detailed morphological assessment and comprehensive immunophenotypic analysis in establishing an accurate diagnosis of uncommon lymphomas.

3. DISCUSSION

T cell/histiocyte-rich large B cell lymphoma (THRLBCL) is an uncommon, aggressive form of B-cell lymphoma with a distinct histological pattern, few neoplastic B-cells amidst a predominant reactive T-cell and histiocyte background [1]. This lymphoma subtype often mimics classical Hodgkin lymphoma and other lymphoid malignancies, making accurate diagnosis challenging [2]. In this case, the patient exhibited non-specific but concerning systemic symptoms, including giddiness, anorexia, and significant weight loss, clinical signs frequently observed in hematologic malignancies [3].

Hypercalcemia with suppressed parathyroid hormone (PTH) was a key metabolic clue. This PTH-independent hypercalcemia is often mediated by malignancy- related bone resorption [4]. PET-CT findings of generalized lymphadenopathy, skeletal and cranial bone involvement, and dural uptake pointed toward a high- grade lymphoproliferative disorder with systemic dissemination [5]. Histopathological analysis of the bone marrow showed diffuse and sinusoidal infiltration by small monomorphic lymphoid cells with condensed chromatin [6]. Fibrosis was absent, confirmed by negative Masson Trichrome and Van Gieson stains, ruling out primary myelofibrosis and other fibrotic marrow disorders [7].

Immunohistochemistry played a decisive role. CD45 positivity confirmed hematopoietic lineage, while the background CD3+ T-cell infiltrate supported the characteristically reactive pattern seen in THRLBCL. CD20 positivity was restricted to a minority of atypical large cells, indicating the sparse neoplastic B- cell population [8-10]. The co-expression of CD15 and BCL2 further supported the diagnosis. Although CD15 is traditionally associated with Hodgkin lymphoma, it is also found in T cell/histiocyte-rich large B cell lymphoma (THRLBCL), particularly when evaluated in conjunction with a broader panel of markers. BCL2 positivity reflects the anti-apoptotic potential of the neoplastic B- cells, reinforcing their malignant nature [11,12].

Mild CD10 positivity suggested a non-germinal center origin. At the same time, negative staining for CD30 and ALK effectively excluded CHL and ALCL, respectively, two critical differential diagnoses [13,14].

THRLBCL is primarily treated with rituximab-based immunochemotherapy, most commonly the R-CHOP regimen (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone), similar to standard treatment for DLBCL. Despite its aggressive nature, THRLBCL shows a relatively favorable prognosis with this approach, achieving a 5-year overall survival rate of around 66% [15].

In summary, this case illustrates the diagnostic complexity of THRLBCL and emphasizes the role of integrated diagnostic strategies, including imaging, bone marrow histopathology, and immunohistochemistry, in confirming this rare lymphoma.

4. CONCLUSION

This case of THRLBCL highlights the importance of comprehensive diagnostics in identifying rare lymphomas. Non-specific symptoms were clarified by detailed lab tests, FDG PET-CT, and bone marrow biopsy. Immunohistochemistry was crucial, showing sparse CD20+ B-cells amid a T-cell–rich background with CD15 and BCL2 co-expression. Combining imaging, morphology, and immunophenotyping enabled accurate differentiation from similar lymphomas, emphasizing a systematic approach in complex cases.

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