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THE HIDDEN LYMPHOMA: A CASE OF SUBCUTANEOUS PANNICULITIS-LIKE T-CELL LYMPHOMA MISDIAGNOSED AS TUBERCULOSIS

Oncology

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ABSTRACT

Subcutaneous panniculitis-like T-cell lymphoma (SPTCL) is a rare and often misdiagnosed form of non-Hodgkin lymphoma that primarily involves the subcutaneous fat, mimicking benign conditions such as panniculitis or tuberculosis. We report the case of a 36-year-old female initially misdiagnosed with tuberculosis and treated with anti-tubercular therapy. Persistent symptoms and the development of new nodules prompted further evaluation. A PET-CT and excision biopsy, followed by histopathological and immunohistochemical analysis, confirmed the diagnosis of SPTCL, characterized by CD3+, CD8+, TCR αβ+ atypical lymphoid cells. The patient was treated with six cycles of chemotherapy, including CHOP and etoposide, with good clinical and radiologic response. This case underscores the importance of considering SPTCL in the differential diagnosis of persistent subcutaneous nodules and highlights the critical role of biopsy and immunophenotyping in achieving timely diagnosis and appropriate management.

KEYWORDS

SPTCL, Misdiagnosis, Subcutaneous nodules, Biopsy, Tuberculosis mimic

INRODUCTION

The presence of malignant T-cells in the subcutaneous adipose tissue is the feature of the rare non-Hodgkin lymphoma, the subcutaneous panniculitis-like T-cell lymphoma (SPTCL). In that sense, SPTCL is generally associated with ulcerations, plaques, or nodules, which are normally found on the trunk and extremities. In clinical practice, SPTCL is frequently confused with panniculitis [1,2].

The extremely rare subtype known as SPTCL is very rare and it might contribute to less than 1% of all non-Hodgkin lymphomas. Due to its rarity, its incidence is difficult to estimate but is estimated to infect about 0.9 per 1,000,000 people per annum [3]. It is inclined to occur in young adult patients with a mild female preponderance [1,4].

The scarcity of SPTCL partly accounts for the high number of misdiagnosed cases that are experienced in this condition. Generally, it is misdiagnosed as benign conditions (erythema nodosum) and infectious conditions (tuberculosis). The clinical presentation with tender erythematous nodules with systemic symptoms such as fever, weight loss is too much like tuberculosis in its endemic countries. This clinical overlap characteristic is, in most cases, the cause of the first wrong diagnosis and therapy [5].

However, a significant level of clinical suspicion is required for the diagnosis of SPTCL, which is verified by immunophenotyping and histological analysis. A biopsy of the tissue usually reveals an infiltration of atypical T-cells along with a lobular panniculitis pattern. Thus, immunohistochemical labelling confirms the T-cell origin and shows that neoplastic cells include T-cell markers, including CD8, CD3, and T-cell receptor (TCR) αβ. Additionally, the cytotoxic nature of these cells is indicated by the production of cytotoxic granule-associated proteins as TIA-1, perforin, and granzyme B. Notably, SPTCL cells are distinct from other T-cell lymphomas in that they do not express CD4, CD56, or TCR γδ. High proliferative activity is indicated by an increased Ki-67 proliferation index. To further distinguish SPTCL cells from anaplastic large cell lymphoma (ALCL), they typically test negative for CD30 and CD15 [1,3,5].

A patient was diagnosed as a case of tuberculosis and referred to the tuberculosis department. In the current patient, the initial misdiagnosis was in the form of tuberculosis, as the patient had subcutaneous nodules with systemic symptoms, which resulted in delayed appropriate treatment. This was further confirmed when a thorough histopathological and immunohistochemical evaluation of the lesion was done [4,6].

Case :

History

A 36y/o female from Tumkur, Karnataka, presented with a right neck swelling in April 2023, which gradually increased in size. She also experienced high-grade fevers primarily in the evenings, accompanied by sweating. She was prescribed medication by a physician but saw no improvement. After two months, she visited a clinic where a fine-needle aspiration cytology (FNAC) of the cervical swelling was performed. The FNAC suggested granulomatous inflammation, and she was referred to a tertiary general hospital in Bangalore.

In September, she was started on anti-tubercular therapy (ATT). During treatment, the right cervical swelling subsided, but new swellings appeared in her right breast and left forearm. The patient developed drug-induced liver injury, leading to frequent interruptions of ATT. Despite three months of treatment, her swellings increased in size, and her general condition worsened. After that, she was sent to a cancer clinic in Bangalore, where a PET-CT scan showed several subcutaneous fat strands that could be indicative of cutaneous lymphoma. An excision biopsy of the left cervical and upper limb lymph nodes showed fibroadipose tissue with focal lymphoid aggregates mixed with histiocytes.

Subsequently, the patient visited our hospital. A review of the biopsy specimen confirmed the diagnosis of SPTCL.

The patient does not have a family history of cancer, diabetes, hypertension, cancer, or tuberculosis. The patient appeared to be moderately nourished and built upon general inspection. Upon local examination, a 4x5 cm area in the upper outer quadrant of the right

breast showed skin alterations, including redness, thickness, tenderness, and elevated temperature. Additionally, multiple hyperpigmented, firm, subcutaneous nodules were noted over both forearms and the left proximal thigh, with the largest measuring approximately 2x3 cm. These nodules were firm, slightly mobile, and tender on palpation as shown in **Figure 1**.

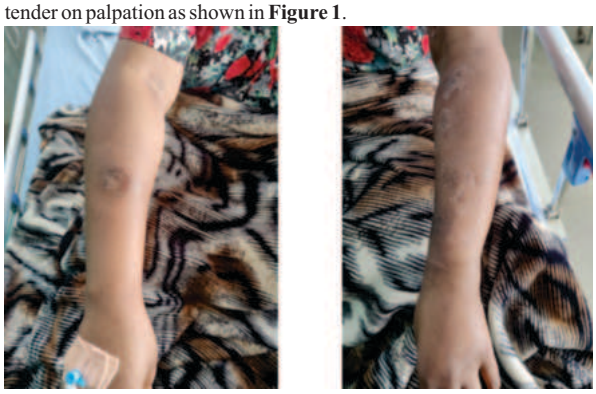

Figure 1: Multiple hyperpigmented, firm, subcutaneous nodules over the forearms, with overlying skin changes including dryness and scaling

Investigations

The patient presented with mild normocytic normochromic anaemia (Hb: 10.3 g/dL). Blood results revealed leukopenia with a total leukocyte count of 3530/µL, which included neutropenia (2120/µL) and lymphopenia (1030/µL), as well as mild thrombocytopenia (platelets: 1.43 lakh/µL). The peripheral smear revealed a normal differential count, a decreased total leukocyte and platelet count, and normocytic normochromic red blood cells. Liver function tests revealed mild hyperbilirubinemia (total bilirubin: 1.4 mg/dL) and hypoalbuminemia (2.6 g/dL). Iron tests showed high serum ferritin levels (2200.12 ng/mL). However, the indicators for hemophagocytic lymphohistiocytosis (HLH) were negative. The findings of infection screening for viral indicators, Montoux, and IGRA were all negative. The cardiac evaluation's ECG and 2D echocardiography results fell within normal limits.

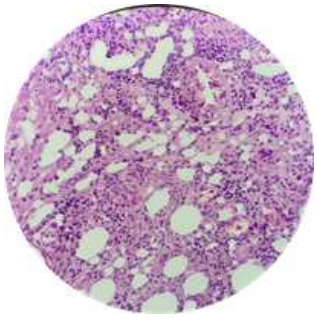

Figure 2: Skin biopsy shows epidermis and dermis. Subcutaneous tissue infiltrated by atypical lymphoid cells, which are small-sized with irregular nuclear membranes, few lobulated, having dispersed nuclear chromatin, and scant cytoplasm. Rimming of lymphoid cells around adipocytes admixed with histiocytes and plasma cells is observed.

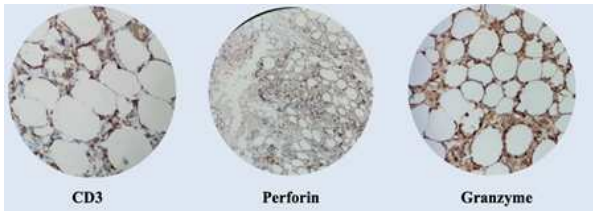

Figure 3: Displays immunohistochemistry (IHC) staining from a biopsy specimen, showing positive cytoplasmic staining for **CD3, Perforin,** and **Granzyme** in lymphoid cells within adipose tissue.

Histopathological analysis of skin and lymph node samples revealed features of a lymphoproliferative illness. The skin biopsy showed that the subcutaneous tissue had been invaded by unusually small-sized lymphoid cells with uneven nuclear outlines, some of which had lobulated nuclei, scattered chromatin, and little cytoplasm. A characteristic rimming of these atypical lymphoid cells was observed around adipocytes, together with admixed histiocytes and plasma cells (**Figure 2**). A biopsy of the lymph nodes in the right axilla showed partial effacement of the nodal architecture and occasional aberrant lymphoid cells.

Immunohistochemistry was used to confirm the diagnosis of a T-cell lymphoproliferative disease (IHC). The atypical lymphoid cells tested positive for CD3, CD8, CD7, CD5 (patchy), Granzyme B (patchy), and Perforin (patchy), all of which are consistent with the cytotoxic T-cell phenotype (**Figure 3**). The cells' negative TdT, CD30, and CD20 findings ruled out B-cell and immature lymphoid neoplasms. A high proliferation index was indicated by the 70% of cells that were Ki-67 positive. The entire immunomorphological profile was consistent with SPTCL, according to the results of the upper limb skin biopsy. No indications of infiltration were found in the bone marrow study.

Imaging results further confirmed the diagnosis. The breast ultrasound showed extensive right breast subcutaneous edema and bilateral axillary lymphadenopathy. PET-CT revealed FDG-avid skin thickening in multiple regions, including the right breast, left neck, presternal region, bilateral upper limbs, and both thighs, with a high SUV max of 12.3. Bilateral axillary lymphadenopathy (SUV max 8.1), modest bone marrow uptake (SUV 4.2), and diffuse splenic uptake (SUV 3.4) were also noted. In line with SPTCL, which involves the skin and lymph nodes but excludes the bone marrow, these findings suggest metabolically active cutaneous lymphoma. Bone marrow study shows not involved by lymphoma.

Treatment History :

The patient received three cycles of CHOP chemotherapy. Post-treatment, there was mild FDG uptake in the subcutaneous skin thickening involving the medial aspect of the forearm, with the disappearance of the rest of the lesions. Following this, the patient received an additional three cycles of CHOP with Etoposide. Reassessment PET CT showed a complete metabolic response.

DISCUSSION

The case report of a 36-year-old woman who had systemic symptoms and subcutaneous nodules was first misdiagnosed as tuberculosis, a typical problem observed in individuals with comparable clinical presentations [1,7]. PET-CT and immunohistochemistry were used for accurate diagnosis, and this indicates the importance of these methods in differentiating SPTCL from other diseases [7, 8]. Immunosuppressive therapies were used in addition to CHOP chemotherapy (cyclophosphamide, doxorubicin, vincristine, and prednisolone), which meets multi-agent chemotherapy regimens reported in other studies [9,10]. Regarding the protected optimism for this patient, the prognosis for the SPTCL-AB subtype without hemophagocytic syndrome (HPS) is good overall, with 5-year overall survival rates being more than 80% [1,11]. As it was documented in the recent systematic review [7], this case highlights the necessity of potent diagnostic instruments and care for high clinical suspicion to deliver timely and enough care to the patients suffering from SPTCL.

CONCLUSION

This case illuminates the position of the SPTCL in the differential diagnosis of subcutaneous nodular lesions and, particularly, of those patients who do not respond to the traditional infection therapies, including the tuberculosis. Better care and outcome require correct diagnosis that has to be confirmed by immunohistochemistry and histology.

SPTCL is an unusual case of non-Hodgkin lymphoma characterised by infiltration of cytotoxic T-cells into subcutaneous fat. Clinically, it can be confused with benign infection or panniculitis, which is commonly misdiagnosed. The youths, especially women, have a high incidence of painful nodules that are likely to be systemically associated.

Diagnosis is established by biopsy, presence of lobular panniculitis with atypical CD8+, CD3+, and TCR αβ+ cells that are positive for granzyme B and perforin; this is a diagnosis that should be a high index of suspicion. The corticosteroid and chemotherapy treatments can lead to a dramatic clinical improvement, making knowledge and early detection important.

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