



A Rare and Aggressive, Subcutaneous Panniculitis-like T-cell Cutaneous Lymphoma

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ABSTRACT

Subcutaneous panniculitis-like T-cell lymphoma (SPTCL) is a distinct variant of cutaneous T-cell lymphoma, characterized by primary involvement of the subcutaneous tissue in a manner imitating panniculitis. It accounts for less than one percent of all Non Hodgkin lymphoma. A 39 year old male presented with multiple erythematous subcutaneous nodules over upper, lower limbs and trunk for 6 months, few of which gradually increased in size with central ulceration. Histopathology of lesion was suggestive of cutaneous lymphoma. Immunohistochemistry confirmed the diagnosis of subcutaneous panniculitis like T cell lymphoma

Key Words- Subcutaneous, panniculitis, T-cell lymphoma.

Introduction

Subcutaneous panniculitis-like T-cell lymphoma (SPTCL) is a distinctive cutaneous lymphoma characterized by infiltration of the subcutaneous tissue by neoplastic cytotoxic T cells, imitating panniculitis. It was first described in 1991 by Gonzalez et al, they presented 8 cases of T-cell lymphoma primarily localized to the subcutaneous tissue without evident lymph node involvement. ⁽¹⁾ The incidence of SPTCL is less than 1% of the Non-Hodgkin lymphomas. ⁽²⁾

SPTCL usually affects young adults with a median age of 36 years (range 9–79 years), with 19% of patients being 20 years or younger with female preponderance, with a ratio of 1:2. ⁽³⁾ The clinical course of SPTCL may be either protracted with occasional spontaneous regression of lesions, or

rapidly progressive and deadly, despite the use of aggressive chemotherapy.

Case Report

A 39 year aged male presented to dermatology outdoor department with the chief complaints of multiple; red raised painless, non-itchy, non-oozy lesions all over body predominantly on limbs for 6 months duration. Lesions started over right leg followed by progressive involvement of left leg, subsequently involved upper limbs and trunk in a period of 2-3 months. Few lesions over legs resolved spontaneously over a period of 4-6 weeks. Lesions over right leg and right arm gradually increased in size to form large tumorous painful swellings with central ulceration (figure) and blood stained pus discharge over a period of 2-3

months. Patient did not complain any lesion over oral and genital mucosa. Apart from decreased appetite and weight loss for past few months otherwise he was asymptomatic.

Cutaneous examination of both upper and lower limbs including both hands, feet and lower abdomen revealed multiple, discrete, ill to well defined, erythematous to violaceous, rubbery, succulent papulo-nodular and tumorous lesions of size varying from approximately 1×1 to 15×15 cm. Few lesions had central ulceration with oozing of serosanguinous fluid and overlying brownish black adherent crust. Over the back, subcutaneous nodular lesions were interspersed with multiple, discrete, erythematous to brown patches and hypo-pigmented macular lesions of size approximately 1×1 to 2×3 cm. The hair, nails, mucous membranes and other systemic examination perceived no abnormality.



Figure 1: Ill to well defined, erythematous to violaceous, rubbery, succulent papulo-nodular lesion over forearm (initial lesion).



Figure 2: Well to ill defined, erythematous to violaceous nodule and tumorous swellings lesions with ulceration & blackish adherent crusting over axilla and upper arm.



Figure 3: Tumorous swellings lesions with ulceration and blackish adherent crusting over forearm.



Figure 4: Subsequent increased tumours growth with crusting and intense edema over axilla and upper arm.



Figure 5: Ulcerated tumours growth over right ankle joint and lower limb.



Figure 6: Papular and subcutaneous nodular lesions over the abdomen.



Figure 7: Healed subcutaneous nodular lesions were interspersed with multiple, discrete, erythematous to brown and hypo-pigmented patches over back.



Figure 8: Spontaneous healing of few lesions over lower limb with atrophy and scarring.

Patient was pale and had multiple non-tender, firm and non-matted lymph node enlargements in both inguinal region of 1x1 cm to 2 x 2.5 cm approximately.

Complete haemogram revealed Hb -9.7gm%, TLC- 5.17mm/mm³, DLC- P 86%, L 06%, M 07%, E 01%, platelets-298m/mm³. Peripheral smear revealed mild normocytic, normochromic anaemia with neutrophilic leucocytosis, ESR-35mm in 1st hour, Complete biochemistry was normal, except serum LDH levels which was raised to 907 U/L (<257 U/L), ANA by Hep2 method was positive -2+ (1:160 titre), homogenous pattern, 24 hour urinary protein was 388mg/24hour, pus culture revealed E. Coli infection sensitive to doxycycline and imipenem. ELISA for HIV was non-reactive, Chest X-ray revealed no abnormality. Ultrasonography of abdomen and pelvis was normal and no abnormality was detected on CT Abdomen. Tissue PCR for mycobacterium tuberculosis was negative. Bone marrow biopsy did not found any malignant invasion.

FNAC of the lesion revealed intermediate to large sized lymphoid cells having round to irregular nuclei with coarse granular chromatin with conspicuous to moderate eosinophilic cytoplasm giving the impression of cutaneous lymphoma.

Cutaneous histopathology revealed keratinized squamous epithelium with mild hyperkeratosis; dermis had diffuse interstitial infiltrate of medium to large sized lymphoid cells showing round to oval nuclei, vesicular chromatin, conspicuous nucleoli, scanty cytoplasm, increased mitotic activity and occasional lymphoid cells with nuclear cleavage and scanty cytoplasm infiltrating blood vessels, nerves and sweat glands. Atypical lymphoid cells infiltrating subcutaneous tissue and deep dermis there was rimming of adipose tissue and adnexal structures by atypical lymphoid cells.

Immunohistochemistry revealed CD3+, CD5+, CD7-, CD4-, CD56-, CD20-, CD30, KI-1 - and

Ki 67 antigen-80-90%. These findings were suggestive of high grade T cell NHL favoring-Sub cutaneous panniculitis like T-cell lymphoma.

Patient was started on chemotherapy (CHOP) in the oncology department of our institution. After getting to know the final diagnosis and prognosis, patient left against medical advice he collapsed after two days at his home.

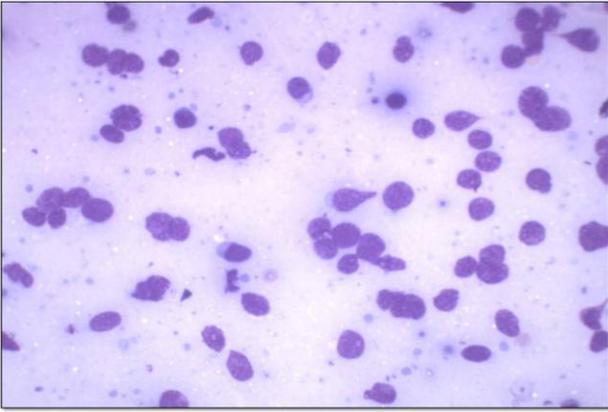


Figure 9 (FNAC): dispersed population of atypical cells with a background of numerous lymphoglandular bodies

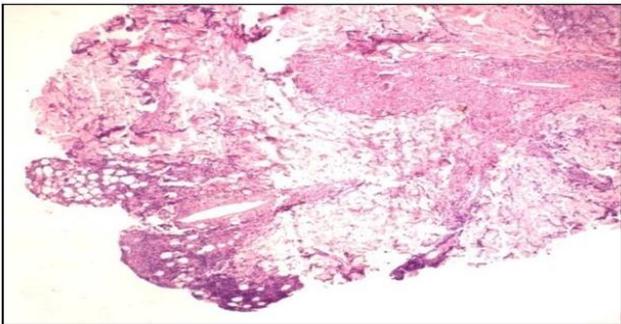
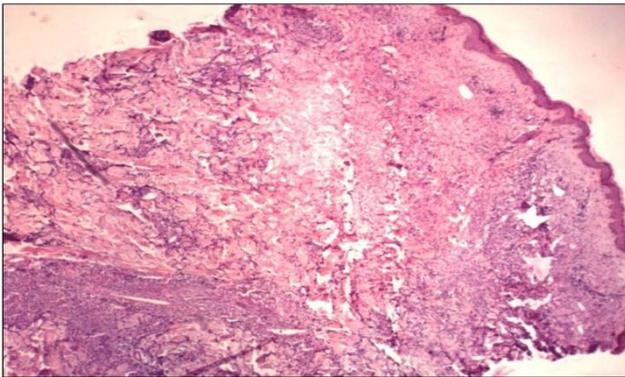


Figure 10, 11 : Atypical lymphoid cells infiltrating deep dermis and subcutaneous tissue.

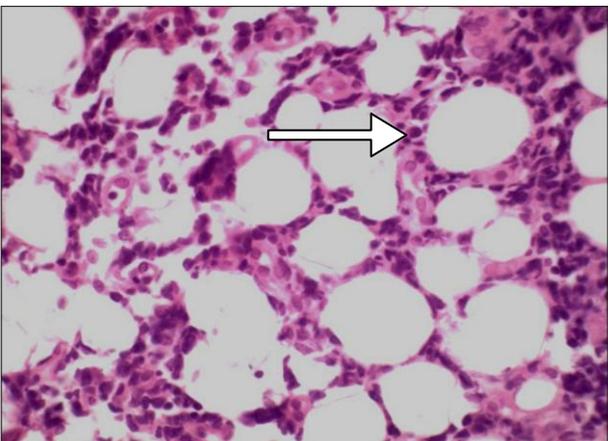


Figure 13: Rimming by atypical lymphoid cells around adnexal structures.

Discussion

Subcutaneous panniculitis-like T-cell lymphoma (SPTCL) is an exceptional T-cell lymphoma recognized by the new World Health Organization (WHO)-European Organization for Research and Treatment of Cancer (EORTC) classification for cutaneous lymphomas.⁽⁴⁾ Patients present with multiple subcutaneous nodules or deep seated plaques, most commonly on the extremities, trunk, face, neck and back can be involved. The nodules are usually painless, but rarely can be painful. Ulceration of nodules in SPTCL is rare, only 6% of the cases may show ulceration at some stage of the clinical course.⁽³⁾ Multiple ulcerated lesions were a feature in the present case mimicking pyoderma gangrenosum. In the initial phases of illness, the subcutaneous nodules may regress spontaneously without treatment which was also eminent in our patient. Prodromal symptoms include fever, chills, weight loss, and myalgia can be present.⁽³⁾ More than 50% of patients have cytopenias; however, in most instances laboratory abnormalities are not severe.

It is pragmatic that clinical course of SPTCL is varied depending upon T-cell receptor (TCR) phenotype and immune-phenotypic characteristics of the tumor cells. Lymphomas that are TCR- $\alpha\beta$ phenotype are usually CD4-, CD8+, CD56- and has an indolent course. On the contrary, lymphomas that is TCR $\gamma\delta$ phenotype, usually CD4+, CD8-, CD56+ has a poorer prognosis, and are often grave due to an accompanying hemophagocytic syndrome.⁽⁵⁾ In our patient Immunohistochemistry was suggestive of $\alpha\beta$ type of SCPTL, which usually has a good prognosis but in our patient disease progressed aggressively leading to the mortality. This observation in the present case was striking. Currently, the medical community uses the SPTCL designation for patients with TCR $\alpha\beta$, whereas TCR $\gamma\delta$ is designated as cutaneous gamma/delta positive T-cell lymphoma (C $\gamma\delta$ -TCR).^(3,9)

The diagnosis of SPTCL is based on the combination of clinical presentation, pathologic examination of cutaneous/subcutaneous tissue, IHC staining pattern, and molecular analysis. Histological, dense lymphoid infiltrate of small or

medium to large-sized lymphocytes is present preferentially in the subcutaneous tissue, predominantly in lobular pattern. Septal pattern is uncommon and represents secondary spillage of neoplastic lymphocytes from the lobules. In most cases, dermal invasion is minimal, and it is rare to see neoplastic cells in superficial dermis or epidermis.⁽⁶⁾ This was an additional finding in the present case atypical lymphoid cells infiltrating deep dermis and subcutaneous tissue. Aggressiveness of this case can be explained due to this finding. Neoplastic cells may be found in deeper dermis and surrounding the sweat glands and hair follicles.⁽³⁾ The lymphocytes show slight atypical features, including hyperchromatic, angulated nuclei and indistinct cell borders. Admixed benign histiocytes, plasma cells, and neutrophils which may give a false appearance of a benign panniculitis.

Evaluation of the degree of cellular proliferation of malignant cells can be done by immunohistochemical techniques using Ki-67 antigen that is expressed in the G1, S, G2 phases of the cell cycle, the highest levels being found in the M phase. Its expression is associated with a high mitotic count and a high histology grade. When the Ki-67 index is higher than 20%, there is a shortened overall survival period and increased chance of development of metastasis.⁽⁷⁾ It was 80-90% in our patient indicating a poor prognosis.

The treatment of SPTCL is not standardized and may include systemic steroids, cyclosporine or multidrug chemotherapy. The response is variable but generally the prognosis is poor in the presence of constitutional symptoms, cytopenia, multiple sites involvement and associated hemophagocytic syndrome (HPS). The increased proportion of γ/δ subsets and expression of CD56 are more prevalent among patients who develop HPS and have progressive disease with a mortality rate of over 50%.⁽⁸⁾ Exclusive treatment with radiotherapy in cases of localized skin lesions is highly effective, with reported partial or full response rates of around 80%. CHOP-like therapies are the most commonly used initial types of chemotherapy, with overall complete or partial remission rates of 50%.⁽¹⁰⁾

The overall five-year survival rate for TCR $\alpha\beta$ exceeds 80%. The presence of HPS, however, significantly decreases survival rates; the five-year survival rates for TCR $\alpha\beta$ without HPS are around 90%, whereas if HPS is present the rate falls to less than 50%. Even without treatment, metastasis of TCR $\alpha\beta$ SPTCL is very rare. Metastasis is more common in $C\gamma\delta$ -TCL, and metastatic sites have included the lungs, liver, kidneys, CNS, and oral mucosa.

Conclusion

SPTCL is a distinct variant of a lymphoma derived from either α/β or γ/δ T cells. The former tends to follow a more indolent course while the latter is more aggressive with a poor clinical outcome. The prudent utilization of molecular techniques like TC rearrangement helps to predict which SPTCL requires more aggressive treatment from the outset. Delayed diagnosis can lead to worsening of symptoms and higher probability of morbidity and mortality.

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