Not all swellings are lymph nodes! A case of subcutaneous panniculitis-like T-cell lymphoma

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SUMMARY

Subcutaneous Panniculitis-like T-cell Lymphoma (SPTL) is a rare cutaneous neoplasm of mature cytotoxic T cells, first described in 1991 by Gonzalez et al.[1] The incidence of SPTL in Asian countries ranges from 2.3% to 3%. In Malaysia, only 5 cases were reported from 2001 to 2004 in Hospital Kuala Lumpur, Malaysia.[2] SPTL typically presents as skin-coloured or erythematous subcutaneous nodules, most often on the extremities and trunk, but it can also involve the face, back and neck. Diagnosis of SPTL is made based on correlation of clinical findings and subcutaneous tissue biopsy along with immunohistochemical staining patterns.

CASE PRESENTATION

A 23-year- old man presented in 2015 with multiple swellings over the right axillary and left cervical region, associated with fever, malaise, weight loss, jaundice and oedema of extremities. An impression of cervical and axillary lymphadenopathy, to rule out lymphoma was made clinically. Excisional biopsies were first obtained in 2015 from the right axillary and left cervical swellings. The results showed lobules of adipocytes separated by fibrous tissues, without evidence of malignancy or granuloma. Lymph node tissue was not present in these biopsies. Immunohistochemistry staining was not performed on the biopsies samples. This patient subsequently defaulted follow up.

Over the course of 2 years, the patient's general condition worsened and the swellings became more progressive and widespread which necessitated a hospital admission for further investigation and treatment.

Clinical examination revealed jaundice, pallor, ecchymoses over the trunk, hepatomegaly and ascites. Cutaneous examination revealed multiple erythematous indurated subcutaneous nodules over bilateral forearm (Figure 1) and left thigh.

Significant laboratory investigations findings include pancytopenia (Hb 7 - 9g/dL, leukocyte count 1.3-1.6 X 10^9/L, platelet count 50 -70 X 10^3/nL), transaminitis (ALT 48 -131 U/L), isolated prolonged APTT (49.2 -64.9 sec), increase level of LDH (818 U/L), serum ferritin (9223ng/ml) and C-Reactive protein (146 mg/ml). Autoantibody profiles, infective screens for Hepatitis B, Hepatitis C and retroviral disease were negative. Bone marrow studies showed haemophagocytosis, in which the erythrocytes, granulocytes and lymphocytes were engulfed by macrophages.

Repeat skin biopsies from the right forearm and left thigh were obtained during this admission. Both biopsies showed unremarkable epidermis and dermis. The subcutaneous adipose tissue was infiltrated by mild, moderate to numerous atypical lymphoid cells involving the interstitium as well as surrounding the adipocytes (Figure 2). The cells are expressing CD2+, CD3+, CD4-, CD8+, CD7+, TIA+, Perforin+ and TCR Alpha/Beta+.

A diagnosis of Subcutaneous Panniculitis-like T-cell Lymphoma (SPTL) was made and this patient was subsequently referred to hematology department at Ampang Hospital for definitive treatment.

In Ampang Hospital, he was initially started on subcutaneous pegylated interferon. However, patient developed herpes zoster after a single dose of interferon. He was subsequently given oral cyclosporine after recovery from herpes zoster and the treatment with oral cyclosporine was planned for 2 years. His swellings reduced with cyclosporine.

DISCUSSION

SPTL is defined as a distinct type of T cell lymphoma with an aggressive clinical behavior according to WHO classification. Prognostic models used for other types of non-Hodgkin lymphoma have limited applicability to patients with SPTL. Most SPTL patients fall into the low risk category when assessed with either the International Prognostic Index (IPI) or the Prognostic Index for T-cell lymphomas (PIT) as these prognostic tools do not include the adverse prognostic effect of HLH (HaemophagocyticLymphohistiocytosis).[3]

SPTL is subdivided into two entities, SPTL with an alpha/beta T-cell phenotype (SPTL-AB) and SPTL with a gamma delta T-cell phenotype (SPTL-GD).

The pathology of SPTL-ABs was typically confined to the subcutis, had a CD4-, CD8+, CD56-, beta F1 + phenotype. SPTL-ABs was uncommonly associated with a haemophagocytic syndrome (HPS 17%) and had a favourable prognosis (5-year overall survival [OS]: 82%).[4] Patient with haemophagocytic syndrome associated with

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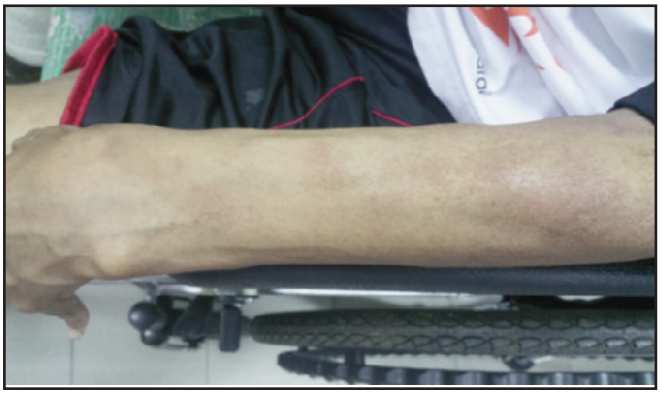

Fig. 1: Multiple Erythematous indurated Subcutaneous Nodules over patient's left forearm

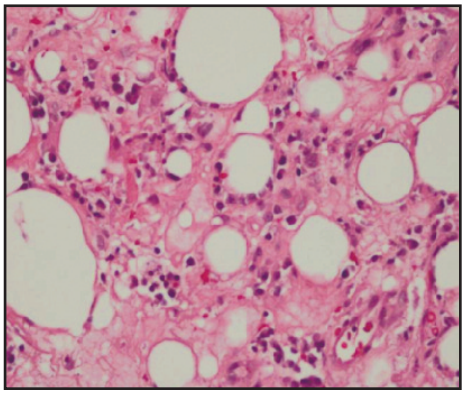

Fig. 2: Slide with H&E stain showed the subcutaneous adipose tissue is infiltrated by atypical lymphoid cells involving the interstitium as well as surrounding the adipocytes (X 40 magnification).

malignancy had been found to have very poor survival with median overall survival of only 40 days.[5] Hence, the presence of HPS at diagnosis of SPTL-AB is one of the most important prognostic factors that predict poor overall survival. In the case illustrated, patient has SPTL-AB with the presence of haemophagocytosis. This implies a significantly poorer prognosis.

In contrast to SPTL-ABs, SPTL-GDs showed epidermal and dermal involvement with or without ulceration. They are characterised by CD4-, CD8-, CD56+/- and beta F1- T-cell immunophenotype. This subtype of SPTL carries poor prognosis (5-year OS: 11%) irrespective of the presence of HPS.[4]

The initial diagnosis of SPTL may be delayed, due to its indolent nature, and similarity to inflammatory or infectious process.

There was a delay in the diagnosis for our patient, due to the lack of clinical suspicion. Panniculitis was not recognised in this patient, and was mistaken as lymph nodes due to the involvement of axillary and cervical region. Hence, cutaneous lymphoma was not listed as one of the differential diagnosis.

SPTL is characterised by the rimming of adipocytes by neoplastic T-cells showing a degree of atypia. It is a challenge to diagnose histopathologically because the cytology can mimic nonspecific panniculitis or lobar panniculitis. The diagnosis of SPTL can be easily missed if this possibility is not included in the differential diagnosis of patients with panniculitis. More often than not, repeated biopsies are required before the diagnosis made. This case highlights the importance of repeat biopsies and meticulous examinations of slides, as the previous biopsies were non-diagnostic. Immunohistochemical studies must be considered in cases with high suspicious of SPTL.

Due to rarity of disease, no standardised therapy for SPTL currently exists. In general, for local disease, local radiotherapy can be used as an effective treatment modality. For disease with a more generalised distribution, immunosuppressive agents such as prednisone and cyclosporine or systemic biologic agents, such as bexarotene and interferon, as well as low-dose chemotherapy such as methotrexate may be used.

CONCLUSION

Subcutaneous panniculitis-like T-cell lymphoma (SPTL) is a rare cutaneous T-cell lymphoma that resembles panniculitis. Clinicians should be aware of the clinical presentation of SPTL as it is an indolent disease. SPTL should be suspected in patients presented with recurrent unexplained fever and subcutaneous nodules. It is important to repeat biopsies in cases highly suspicious of SPTL when the previous biopsies were non-diagnostic, and immunohistochemical studies must be considered. The presence of haemophagocytosis indicates an aggressive disease and poorer prognosis.

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