Case 12
A 43-year-old Thai female from Chonburi

Chief complaint: A 3 month history of multiple painful subcutaneous nodules and plaques on trunk and extremities


Fig.12.1

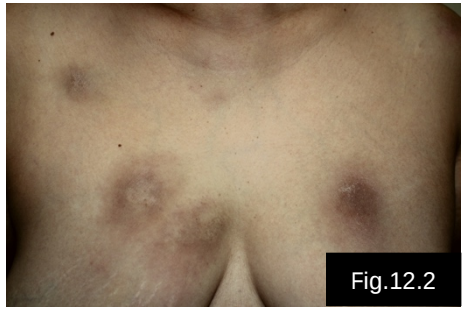
Fig.12.2

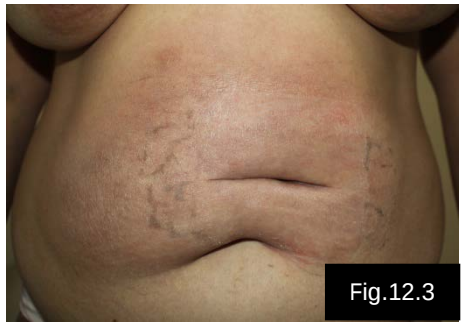
Fig.12.3

Present illness:
The patient presented with a painful subcutaneous nodule firstly developed on abdomen. The nodule gradually enlarged into plaque formation. One month later, multiple nodules were developed on her chest and extremities. Her face became persistent swelling. She also had low-graded fever but no significant weight loss nor night sweat. She denied any small joint tenderness, hair loss or photosensitivity. No previous treatment had been given.

Past history: She had no underlying disease

Family history: There was no family history of cancer or similar lesion

Physical examination:
- Vital signs: T 37.9°c, BP 105/70 mmHg, PR 103/min, RR 20/min
- HEENT: Bilateral periorbital swelling, no oral lesion
- Lymph node: No cervical, supraclavicular, axillary, inguinal lymphadenopathy
- Heart: Regular, normal S_1S_2, no murmur
- Lungs: Normal breath sound, no adventitious sound
- Abdomen: No hepatosplenomegaly

Dermatological examination:
- Ill-defined edematous erythematous to skin-colored plaques on both periorbital area
- Large ill-defined painful indurated erythematous plaque on abdomen
- Multiple discrete painful erythematous to brownish subcutaneous nodules on chest and extremities (Fig.12.1-12.3)

Histopathology (S18-041181, Left arm):

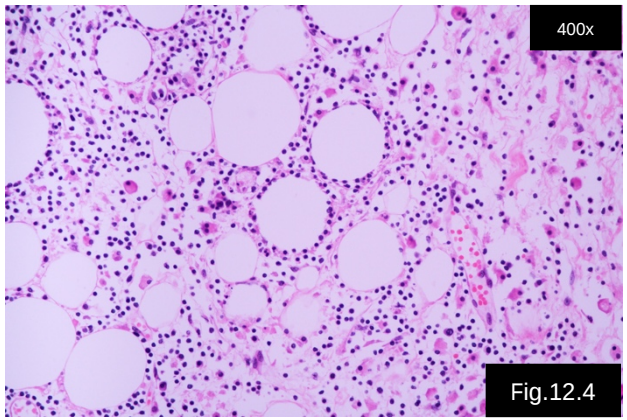

Fig.12.4

- Lobular panniculitis with small to medium-sized atypical lymphocytes with adipocyte rimming and beanbag cells
- Infiltrate of reactive small lymphocytes and plasma cells in the dermis and subcutaneous tissue (Fig.12.4)

Immunohistochemistry:

- Positive: CD3, CD8, granzyme B, βF1, Ki-67 (70%) for atypical lymphocytes
- Negative: CD20, CD4, CD30, CD56
- Negative for EBV in situ hybridization

Laboratory investigations:

- CBC: Hb 10.8 g/dL, Hct 33.4%, Plt 329,000/mm^3
  WBC 4,760/mm^3 (N 61%, L 33%, M6%)
- LDH: 862 U/L (125-220 U/L)
- AST/ALT: 107/74 U/L
- BUN/Cr 10/0.62 mg/dL
- ANA: 1:80 (fine speckled)
- Bone marrow biopsy: No lymphoma involvement

Diagnosis: Subcutaneous panniculitis-like T-cell lymphoma (SPTL)

Treatment:

- Dexamethasone 40mg/day
- Chemotherapy (CHOP regimen)

Presenter: Pintusorn Kungvalpivat, MD
Consultant: Saneerat Porntharukcharoen, MD

Discussion

Subcutaneous panniculitis-like T-cell lymphoma (SPTL) is a rare subtype of non-Hodgkin lymphoma that preferentially involves subcutaneous tissue and mimics panniculitis. It was first described by Gonzales et al. in 1991,[1] as a distinctive cytotoxic T-cell lymphoma of subcutaneous tissue. Previously, it was classified into α/ß T-cell and ɣ/δ T-cell phenotype, differentiated on clinical course, prognosis, histopathological, immunophenotypic, and genotypic analysis.[2] However, in 2005, the World Health Organization-European Organization for Research and Treatment of Cancer (WHO-EORTC) classification for cutaneous lymphoma defined the term “SPTL” as CD8+ cytotoxic T-cell lymphoma with α/ß T-cell phenotype as a distinctive disorder, while cases with ɣ/δ T-cell phenotype were described as cutaneous ɣ/δ T-cell lymphoma.[3]

SPTL usually affects young adults and has female predominance.[4] From a recently published retrospective study of sixteen patients from our Ramathibodi hospital,[5] the median age of onset was 26 years with male-to-female ratio of 1:2.2. The duration of skin lesions before diagnosis ranged from 2 weeks to 4 years (median 1 year) similar to previous study.[4] Most of patients

presented with subcutaneous nodules and/or plaques, predominantly on lower extremities, trunk, upper extremities and head, respectively.[5] An uncommon presentation of periorbital and/or facial swelling had been increasingly reported,[6-8] similar to our patient, which had persistent periorbital swelling for 2 months. This emphasizes the heterogenous clinical manifestation of SPTL and should be considered in any atypical skin lesion involving subcutaneous fat.

Constitutional symptoms such as fever, malaise, night sweat and weight loss, had been recorded in most of the patients. Laboratory abnormalities such as anemia, leukopenia, thrombocytopenia, elevated liver function tests and elevated lactate dehydrogenase (LDH) can be presented.[9] From our retrospective study[5], hemophagocytic syndrome (HPS) was noted in 37.5% of patients. These patients showed hepatosplenomegaly, high serum ferritin and high LDH levels. Fortunately, our presented case had no such a complication.

Histopathology, along with immunophenotyping is a mandatory to make a diagnosis. The atypical lymphocytes mainly infiltrate in subcutaneous layer with a lobular pattern, and may show the rimming of individual fat cells by atypical lymphocytes.[5] Cytophagocytosis is commonly presented and there are usually mild or absent of septal panniculitis. The overlying epidermis and dermis are sometimes challenging with features of lupus erythematosus-like and might misinterpret as lupus panniculitis. Focal area of high Ki-67 index[10] and low expression of CD123[11] may help differentiate between those. In SPTL, the atypical lymphocytes express CD3, CD8, βF1 and cytotoxic proteins (granzyme B, TIA-1, perforin) and negatively stain for CD4, CD20, CD56 and T-cell receptor(TCR) gamma.[4, 5] Although TCR gene rearrangement studies show monoclonal rearrangement in most of the patients, polyclonal TCR gene rearrangement alone cannot exclude the possibility of SPTL.[5, 12]

SPTL has an indolent course, in contrast to γ/δ T-cell phenotype.[13] Five-year overall survival rate was 82%.[3] Initial treatment with systemic corticosteroids or immunosuppressive drugs (e.g. cyclosporine) are considered first-line treatment in patients without an associated HPS or systemic involvement.[12, 14] In case of SPTL associated with HPS, recurrent or refractory disease, chemotherapy followed by hematopoietic stem cell transplant is considered as curative option for eligible patients.[15] In our patient, further investigation showed no systemic involvement. However, due to poor clinical response to oral dexamethasone, the treatment was substituted with CHOP-regimen (consisting of cyclophosphamide, doxorubicin, vincristine, prednisolone) chemotherapy. After receiving chemotherapy, her clinical was subsided within 2 weeks and stable in condition since then.

Reference:

1. Gonzalez CL, Medeiros LJ, Braziel RM , Jaffe ES. T-cell lymphoma involving subcutaneous tissue. A clinicopathologic entity commonly associated with hemophagocytic syndrome. Am J Surg Pathol 1991;15:17-27.
2. Salhany KE, Macon WR, Choi JK, Elenitsas R, Lessin SR, Felgar RE et al. Subcutaneous panniculitis-like T-cell lymphoma: clinicopathologic, immunophenotypic, and genotypic analysis of alpha/beta and gamma/delta subtypes. Am J Surg Pathol 1998;22:881-93.
3. Willemze R, Jaffe ES, Burg G, Cerroni L, Berti E, Swerdlow SH et al. WHO-EORTC classification for cutaneous lymphomas. Blood 2005;105:3768-85.
4. Willemze R, Jansen PM, Cerroni L, Berti E, Santucci M, Assaf C et al. Subcutaneous panniculitis-like T-cell lymphoma: definition,

classification, and prognostic factors: an EORTC Cutaneous Lymphoma Group Study of 83 cases. Blood 2008;111:838-45.
5. Rutnin S, Porntharukcharoen S , Boonsakan P. Clinicopathologic, immunophenotypic, and molecular analysis of subcutaneous panniculitis-like T-cell lymphoma: A retrospective study in a tertiary care center. J Cutan Pathol 2019;46:44-51.
6. Kosari F , Akbarzadeh Hosseini S. Local facial edema: a novel presentation of subcutaneous panniculitis-like T-cell lymphoma in a 30-year-old Iranian woman. Acta Med Iran 2014;52:950-3.
7. Bhojaraja MV, Kistampally PK, Udupa KS , Thomas J. Subcutaneous Panniculitis-Like T-Cell Lymphoma: A Rare Tumour. J Clin Diagn Res 2016;10:Od29-30.
8. Hashimoto R, Uchiyama M , Maeno T. Case report of subcutaneous panniculitis-like T-cell lymphoma complicated by eyelid swelling. BMC Ophthalmol 2016;16:117.
9. Ohtsuka M, Miura T , Yamamoto T. Clinical characteristics, differential diagnosis, and treatment outcome of subcutaneous panniculitis-like T-cell lymphoma: a literature review of published Japanese cases. Eur J Dermatol 2017;27:34-41.
10. LeBlanc RE, Tavallaee M, Kim YH , Kim J. Useful Parameters for Distinguishing Subcutaneous Panniculitis-like T-Cell Lymphoma From Lupus Erythematosus Panniculitis. Am J Surg Pathol 2016;40:745-54.
11. Chen SJT, Tse JY, Harms PW, Hristov AC , Chan MP. Utility of CD123 immunohistochemistry in differentiating lupus erythematosus from cutaneous T cell lymphoma. Histopathology 2019;74:908-16.
12. Lopez-Lerma I, Penate Y, Gallardo F, Marti RM, Mitxelena J, Bielsa I et al. Subcutaneous panniculitis-like T-cell lymphoma: Clinical features, therapeutic approach, and outcome in a case series of 16 patients. J Am Acad Dermatol 2018;79:892-8.
13. Bhatt VR, Giri S, Verma V, Manandhar S, Pathak R, Bociek RG et al. Survival of Subcutaneous Panniculitis-Like T-Cell Lymphoma and Peripheral T-Cell Lymphoma Not Otherwise Specified: A Propensity-Matched Analysis of the Surveillance, Epidemiology, and End Results Database. Clin Lymphoma Myeloma Leuk 2016;16:373-8.
14. Michonneau D, Petrella T, Ortonne N, Ingen-Housz-Oro S, Franck N, Barete S et al. Subcutaneous Panniculitis-like T-cell Lymphoma: Immunosuppressive Drugs Induce Better Response than Polychemotherapy. Acta Derm Venereol 2017;97:358-64.
15. Lin TA, Yang CF, Liu YC, Liu JH, Chiou TJ, Hsiao LT et al. Hematopoietic stem cell transplantation for subcutaneous panniculitis-like T-cell lymphoma: single center experience in an Asian population. Int J Hematol 2019;109:187-96.