A unique case of subcutaneous panniculitis-like T-cell lymphoma presenting as an abscess following an arthropod bite

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Abstract

Subcutaneous panniculitis-like T-cell lymphoma (SPTCL) is a rare form of low-grade cutaneous lymphoma that usually presents with multifocal non-tender subcutaneous nodules over the trunk and extremities. We present an exceptional case of SPTCL masquerading as a solitary abscess which developed following an antecedent arthropod bite. Unique histological features encountered include foci of neutrophilic aggregation and admixed eosinophils within the neoplastic lymphomatous subcuticular infiltrate. As SPTCL rarely presents as an abscess, the authors wish to highlight this diagnostic pitfall and suggest excluding SPTCL as a cause of pseudo-pyoderma in patients who are afebrile with a discordant inflammatory marker profile. In addition, this condition should be suspected in non-diabetic patients who experience a rapid clinical course with suppuration and demonstrate a poor response to appropriate antibiotics. As such, we recommend sending tissue for histopathological examination for patients with atypical presentations.

Keywords: abscess, arthropod bite, cellulitis, lymphoma, malignancy, panniculitis

Introduction

Subcutaneous panniculitis-like T-cell lymphoma (SPTCL) is a rare form of cutaneous lymphoma involving infiltration of cytotoxic T cells localized to the subcutaneous tissue with infrequent lymph node involvement. Resembling a panniculitis, it commonly presents as multiple non-tender subcutaneous nodules localized on the trunk and limbs [1-3]. Herein, we present an unusual patient with SPTCL presenting as an abscess.

Case Synopsis

A 39-year-old man, with no significant past medical history was referred to our center in 2018 for a right posterior thigh wound after an antecedent mosquito bite. The wound had initially started a week prior as a pruritic erythematous swelling. After two days, it ulcerated and discharged purulent material. He sought medical attention and was started on a course of oral cephalexin and topical mupirocin 2% ointment. As there was no improvement after four days and the antibiotic was switched to clindamycin.

Of note, the patient reported a similar episode over the right leg in 2016 whereby an ulcer developed following an unspecified arthropod bite. This resolved over two weeks with mild scarring following topical antibiotic treatment. Otherwise, past medical history and drug history were non-contributory.

On examination, he was afebrile and hemodynamically stable. Over the right thigh there was a large, fluctuant, erythematous, warm and tender plaque with central necrotic eschar (**Figure 1**). Separately, over the postero-medial aspect of the left knee, there were non-tender palpable purpuric plaques with well-circumscribed ovoid areas of

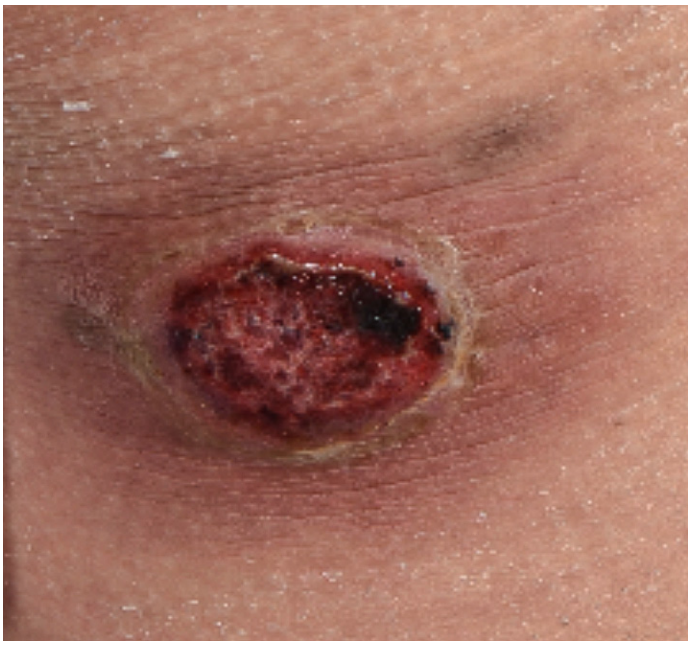

Figure 1. *A 2.5cm×2.0cm eschar overlying the center of a tender, erythematous, indurated, dermal/subcutaneous plaque on the right posterior thigh.*

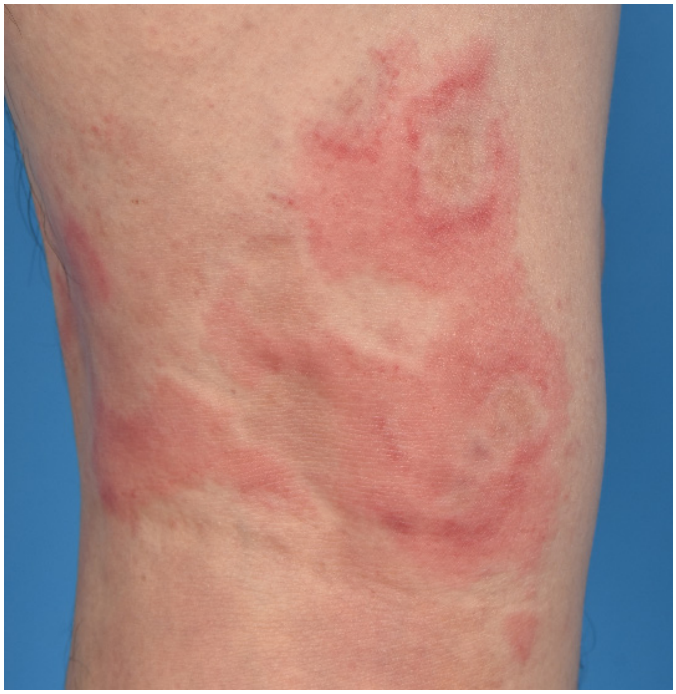

Figure 2. *Non-tender palpable purpuric plaques on the postero-medial aspect of the left knee.*

clearing (**Figure 2**). With the working diagnosis of an infectious panniculitis and abscess with secondary cutaneous small vessel vasculitis, he was admitted for further workup and commenced on intravenous amoxicillin-clavulanic acid.

Apart from the slightly raised erythrocyte sedimentation rate (27mm/hr, reference <19 mm/hr) and C-reactive protein (8.8mg/L, reference 0.0-5.0mg/L), the rest of the initial investigations, including a full blood count, liver function tests, anti-nuclear antibody level, and human immunodeficiency virus (HIV) serology, were unremarkable. X-ray of the right femur did not show any osteomyelitis.

The patient underwent an incision and drainage (I&D) of his right thigh abscess by a surgeon. Intra-operatively, purulent material was removed and healthy underlying fascia was visualized following I&D. Although not routinely performed during I&D of abscesses in our center, tissue samples were taken for histological evaluation on the request of the dermatologist. A skin biopsy of the purpuric plaques over the left popliteal fossa was examined histologically including direct immunofluorescence to exclude concomitant vasculitis.

Sections of tissue from the I&D of the right posterior thigh abscess showed a lobular panniculitis within fibroadipose tissue, without accompanying dermis or epidermis. There was an infiltrate of cells consisting of lymphocytes, plasma cells, histiocytes, occasional eosinophils, and small aggregates of neutrophils (**Figure 3**). There was a population of atypical lymphoid cells with medium-sized to large irregular, hyperchromatic nuclei, variably prominent

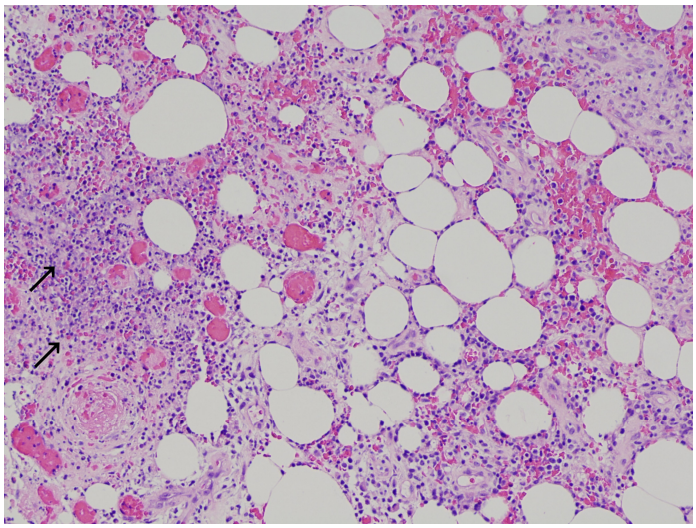

Figure 3. *The subcutaneous fat was infiltrated with lymphocytes, plasma cells, histiocytes, occasional eosinophils and small aggregates of neutrophils (arrowed). H&E, 100×.*

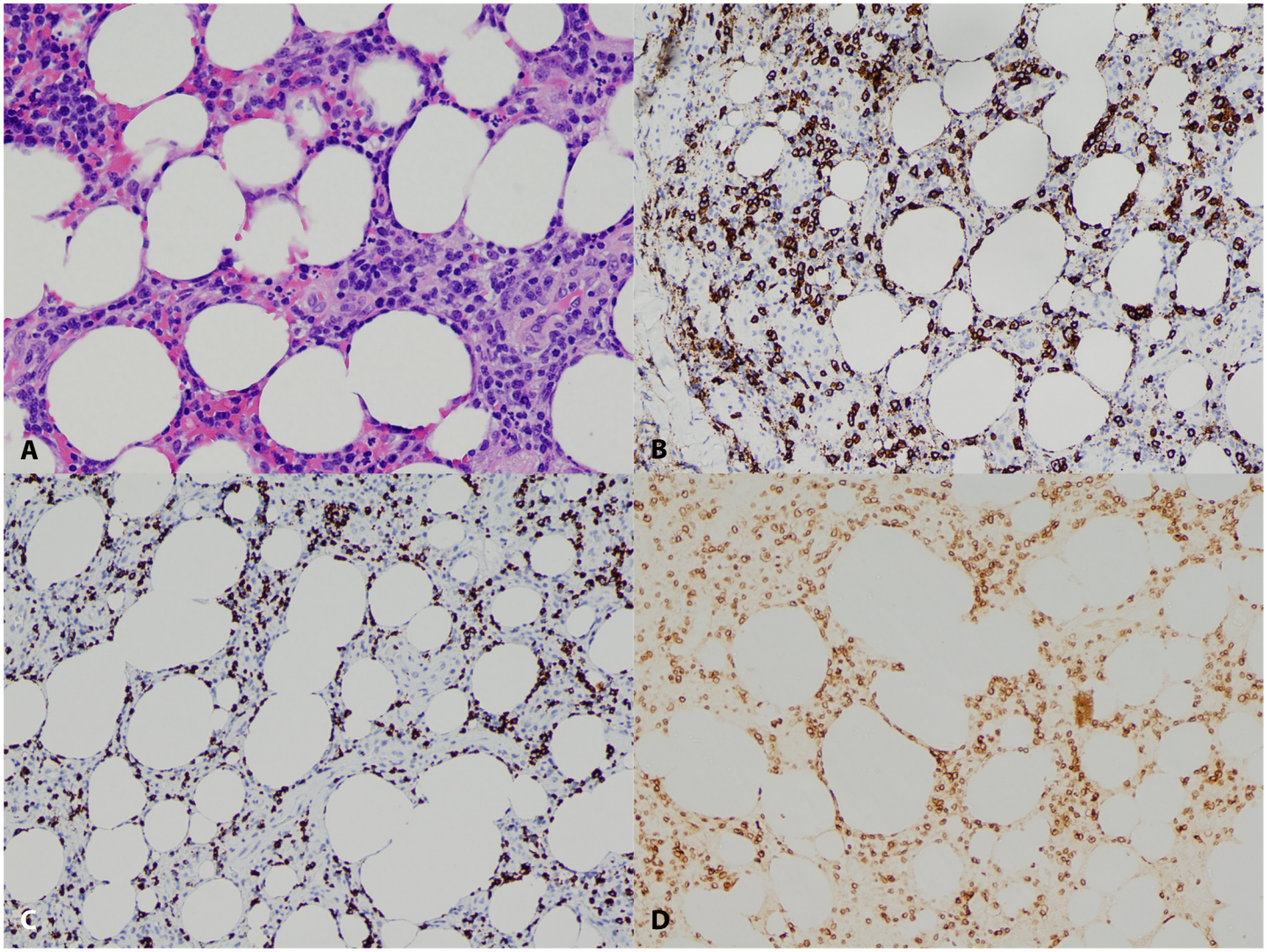

Figure 4. ***A)*** *Atypical medium-to-large sized lymphoid cells with irregular hyperchromatic nuclei were seen rimming adipocytes. Scattered eosinophils and neutrophils can be seen in the surrounding infiltrate. H&E, 200×.* ***B)*** *The atypical lymphoid cells rimming the adipocytes stained CD8+, 200×.* ***C)*** *The atypical lymphoid cells rimming the adipocytes stained TIA+, 200×.* ***D)*** *The atypical T cells were mostly βF1+, 200×.*

nucleoli, increased mitotic activity, and high nuclear cytoplasmic ratios. Some of the atypical lymphoid cells were seen rimming fat cells (**Figure 4A**). The atypical lymphoid cells were shown to be CD3+, CD2+, and CD7+, with partial loss of CD2, 3, 5, and 7. The atypical T cells were CD8+ (**Figure 4B**) and CD56-. They expressed TIA1 (**Figure 4C**) and granzyme B in keeping with a cytotoxic profile. A few scattered CD30+ cells and a small proportion of reactive CD20+ B-cells were seen within the infiltrate. The atypical lymphoid T cells rimming the adipocytes had a proliferation Ki67 index of up to 50%. The atypical T cells stained mostly βF1+ (**Figure 4D**), with only a few scattered T cells being positive for TCRγ. In situ hybridization for EBV-encoded RNA (EBER-ISH) was negative. Review of the H&E-stained slides showed no established features of hemophagocytosis. The immunophenotypic profile of the atypical lymphocytes was diagnostic of SPTCL and excluded a diagnosis of lupus panniculitis.

The punch biopsy from the left popliteal fossa showed an intact epidermis. There was prominent red cell extravasation around superficial vessels with a superficial perivascular infiltrate of lymphocytes and neutrophils. Although there was no overt fibrinoid necrosis of vessels seen, the presence of neutrophils in the perivascular infiltrate in addition to the extravasated red cells were compatible with

early features of small vessel vasculitis where fibrinoid necrosis of vessels may not be fully established.

Correlating the overall morphologic, immunophenotypic, and molecular genetic findings, a diagnosis of SPTCL with reactive cutaneous small vessel vasculitis was made.

Over the five days of his inpatient stay, the patient remained afebrile and the purpuric plaques over the left popliteal fossa completely resolved with topical clobetasol propionate 0.05% cream. Tissue bacterial culture obtained from the right posterior thigh intraoperatively returned sterile. The patient received a week's duration of amoxicillin-clavulanic acid.

In view of the diagnosis of SPTCL, the patient was sent for an outpatient computed tomography of the neck, thorax, abdomen and pelvis which was unremarkable. Close follow-up over the past five years has not shown any recurrence; no further treatment was required following healing by secondary intention post-I&D.

Case Discussion

Based on the WHO-EORTC classification, SPTCL is a diagnosis reserved for cases with the α/β T-cell phenotype that are CD4-, CD8+, and CD56- [1-3]. It is a rare form of cutaneous lymphoma with good prognosis, generally affecting young adults [4]. A distinction should be made from cases of cutaneous γ/δ T-cell lymphoma involving the subcutaneous compartment as these are conversely associated with rapid clinical deterioration and poorer prognosis. Although both entities may exhibit expression of granzyme B, TIA-1 and perforin, the latter are usually CD4-, CD8-, and CD56+ [1-3].

Subcutaneous panniculitis-like T-cell lymphoma commonly presents as multiple non-tender subcutaneous nodules which are localized on the trunk and limbs [1-3]. In addition to our case, various benign-looking, non-characteristic histological appearances have been encountered in SPTCL, including that of lipomembraneous panniculitis [5]. Other unusual clinical presentations include eyelid swelling with visual disturbances [6] and cranial nerve involvement. More severe cases develop hemophagocytic syndrome (HPS) which usually leads to multiorgan failure and death [7-9].

The initial presentation of SPTCL can mimic pyoderma and patients can present with features such as fever, erythema, and tender swelling. However, these persist despite courses of antibiotics with bacterial cultures returning sterile [2,10]. To the best of our knowledge, aside from the case reported herein, there are two other reports exemplifying how pseudo-pyoderma may be a pitfall in the diagnosis of SPTCL. Following a clinical diagnosis of lower limb bacterial cellulitis that responded poorly despite appropriate antibiotics, Mody et al. reported an unexpected diagnosis of SPTCL from pathological evaluation of lesional tissue obtained following I&D and fasciotomy [2]. Another case reported by Lewis et al also documented a patient presenting with tender, erythematous, subcutaneous nodules over bilateral thighs and fever. The patient underwent I&D for these presumptive abscesses and tissue biopsy yielded the diagnosis of SPTCL [11]. However, a unique feature of our case was the report of an antecedent arthropod bite followed by the clinical presentation of an abscess. The salient findings of these cases are summarized and juxtaposed against ours in **Table 1**.

Hematological malignancies such as chronic lymphocytic leukemia, mantle cell lymphoma, and small lymphocytic lymphoma have been associated with exaggerated or exuberant reactions to insect bites. However, patients will often misinterpret an erythematous papule or nodule as an insect bite. Although the exact pathophysiology is unclear, it is postulated to be a type IV delayed hypersensitivity reaction as cutaneous lesions are rich in both T cell and eosinophilic infiltration [12-14]. In the case of our patient, follow-up thus far has not revealed an occult systemic lymphoproliferative disease.

Hypersensitivity to mosquito bites (HMB) is also associated with Epstein-Barr Virus (EBV) infection. During the insect bite, immunogenic components in the saliva of the mosquito activates NK cells, which are immortalized by EBV infection, thereby resulting in a hypersensitivity reaction. Prolonged activated states of NK cells may in turn cause genetic damage

Table 1. *Characteristics and features of the three patients with subcutaneous panniculitis-like T-cell lymphoma presenting as an abscess.*

	Age (years)	Sex	Race	Location	Lesion morphology	Treatment	Follow -up
Our patient	39	Male	Chinese	Right posterior thigh	Large, fluctuant, erythematous, warm and tender dermal induration with central necrotic eschar	I&D, amoxicillin- clavulanic acid	No recurrence over 5 years
Mody et al. [2]	48	Male	Native American (Arizona)	Right thigh and left arm	Subcutaneous, tender, erythematous nodules	Multiple courses of antibiotics and steroids, I&D with fasciotomy, 7 cycles of CHOP-E (cyclophosphamide, hydroxydaunorubicin, oncovin, prednisone, etoposide phosphate) chemotherapy	Remission and no signs of systemic disease
Lewis et al. [11]	51	Female	Caucasian	Medial aspect of bilateral thighs	Subcutaneous, tender, erythematous nodules	Referred to a tertiary oncology center	No details

I&D, incision and drainage.

resulting in the development of hematological malignancies. However, some patients may already have lymphoma or leukemia prior to the manifestation of HMB [15]. Of note, the EBER-ISH was negative in our case.

It is worth noting that our patient had two separate episodes of swelling and ulceration both following a suspected arthropod bite. Whilst this might be a plausible novel presentation of SPTCL via such a hypersensitivity reaction, more research needs to be carried out to ascertain this association.

Although spontaneous remission can occur, this is uncommon [4]. Several treatment guidelines have been proposed including the European Society for Medical Oncology (ESMO), British Association of Dermatologists and U.K. Cutaneous Lymphoma Group, and Go et al [4, 16-19]. For localized or indolent lesions without HPS, radiotherapy, single-agent corticosteroids (e.g., prednisolone) or immunosuppressive agents (e.g., cyclosporine, cyclophosphamide, methotrexate) are recommended as first-line treatment options. In cases refractory to immunosuppressive therapy, with more aggressive disease or HPS, combination chemotherapy regimens such as CHOP therapy (consisting of cyclophosphamide, hydroxydaunorubicin, vincristine, and prednisolone), other high-dose chemotherapy, or hematopoietic stem cell transplant is recommended [4,16-19]. Overall, prognosis is good as the disease runs a relatively indolent clinical course. It has a 5-year overall survival (OS) rate of 82% [20,21].

Conclusion

Subcutaneous panniculitis-like T-cell lymphoma presenting as an abscess is rare. For patients with atypical presentations of abscesses such as afebrile state, rapid clinical course with suppuration, poor response to appropriate antibiotics, discordant inflammatory marker profiling, and sterile bacterial cultures, we recommend that it would be prudent to send a tissue biopsy so as not to miss a similar atypical presentation of SPTCL.

Potential conflicts of interest

The authors declare no conflicts of interest.

References

1. Willemze R, Jaffe ES, Burg G, et al. WHO-EORTC classification for cutaneous lymphomas. *Blood*. 2005;105:3768-3785. [PMID: 15692063].
2. Mody A, Cherry D, Georgescu G, Koehler C, Gill V. A Rare Case of Subcutaneous Panniculitis-Like T Cell Lymphoma with Hemophagocytic Lymphohistiocytosis Mimicking Cellulitis. *Am J Case Rep*. 2021;22:e927142. [PMID: 33428607].
3. Willemze R, Jansen PM, Cerroni L, et al. Subcutaneous panniculitis-like T-cell lymphoma: definition, classification, and prognostic factors: an EORTC Cutaneous Lymphoma Group Study of 83 cases. *Blood*. 2008;111:838-845. [PMID: 17934071].
4. Go RS, Wester SM. Immunophenotypic and molecular features, clinical outcomes, treatments, and prognostic factors associated with subcutaneous panniculitis-like T-cell lymphoma: a systematic analysis of 156 patients reported in the literature. *Cancer*. 2004;101:1404-1413. [PMID: 15368328].
5. Weenig RH, Ng CS, Perniciaro C. Subcutaneous panniculitis-like T-cell lymphoma: an elusive case presenting as lipomembranous panniculitis and a review of 72 cases in the literature. *Am J Dermatopathol.* 2001;23:206-15. [PMID: 11391101].
6. Hashimoto R, Uchiyama M, Maeno T. Case report of subcutaneous panniculitis-like T-cell lymphoma complicated by eyelid swelling. *BMC Ophthalmol*. 2016;16:117. [PMID: 27440138].
7. Baxi KD, Rathod SP, Chaudhary RG, Jagati A. Subcutaneous panniculitis-like T-cell lymphoma. *Indian J Dermatol Venereol Leprol*. 2020;86:606. [PMID: 31975700].
8. Henter JI, Horne A, Aricó M, et al. HLH-2004: Diagnostic and therapeutic guidelines for hemophagocytic lymphohistiocytosis. *Pediatr Blood Cancer*. 2007;48:124-131. [PMID: 16937360].
9. Aricò M, Danesino C, Pende D, Moretta L. Pathogenesis of haemophagocytic lymphohistiocytosis. *Br J Haematol*. 2001;114:761-769. [PMID: 11564062].
10. Hill CR, Wang A, Elewski BE, Pavlidakey PG. Subcutaneous panniculitis-like T-Cell lymphoma: A mixed diagnostic approach to diagnosing a vague clinical picture. *SKIN*. 2019;3:90–97.
11. Lewis DJ, Falck BA, Kantrow SM, et al. Necrotizing granulomatous dermatitis and panniculitis masquerading as T cell lymphoma. *Skinmed*. 2019;17:406-408. [PMID: 31904333].
12. Davis MD, Perniciaro C, Dahl PR, et al. Exaggerated arthropod-bite lesions in patients with chronic lymphocytic leukemia: a clinical, histopathologic, and immunopathologic study of eight patients. *J Am Acad Dermatol*. 1998;39:27-35. [PMID: 9674394].
13. Dodiuk-Gad RP, Dann EJ, Bergman R. Insect bite-like reaction associated with mantle cell lymphoma: a report of two cases and review of the literature. *Int J Dermatol*. 2004;43:754-758. [PMID: 15485536].
14. Lachowiez C, White K, Spurgeon S. Exaggerated arthropod assault: Eosinophilic dermatosis in a patient with small lymphocytic lymphoma. *Clin Case Rep*. 2018;6:1893-1895. [PMID: 30214788].
15. Singh S, Mann BK. Insect bite reactions. *Indian J Dermatol Venereol Leprol*. 2013;79:151-164. [PMID: 23442453].
16. 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. [PMID: 28120776].
17. Sakurai E, Satoh T, Akiko YA, et al. Subcutaneous panniculitis-like T-cell lymphoma (SPTCL) with hemophagocytosis (HPS): successful treatment using high-dose chemotherapy (BFM-NHL & ALL-90) and autologous peripheral blood stem cell transplantation. *J Clin Exp Hematop*. 2013;53:135-140. [PMID: 23995110].
18. Willemze R, Hodak E, Zinzani PL, Specht L, Ladetto M. ESMO Guidelines Committee. Primary cutaneous lymphomas: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol*. 2018;29:30-40. [PMID: 29878045].
19. Gilson D, Whittaker SJ, Child FJ, et al. British Association of Dermatologists and U.K. Cutaneous Lymphoma Group guidelines for the management of primary cutaneous lymphomas 2018. *Br J Dermatol*. 2019;180:496-526. [PMID: 30561020].
20. Guenova E, Schanz S, Hoetzenecker W, et al. Systemic corticosteroids for subcutaneous panniculitis-like T-cell lymphoma. *Br J Dermatol*. 2014;171:891-894. [PMID: 24725144].
21. Dong P, Wang L, Zhu H, Li L. Relapsed subcutaneous panniculitis-like T cell lymphoma evaluated by FDG PET/CT: A clinical case report. *Medicine (Baltimore)*. 2018;97:e12980. [PMID: 30431571].