Subcutaneous Panniculitis-Like T Cell Lymphoma Mimicking Early-Onset Nodular Panniculitis

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Patient: Male, 24
Final Diagnosis: Subcutaneous panniculitis-like T-cell lymphoma
Symptoms: Fever • skin nodules
Medication: —
Clinical Procedure: Skin biopsy • PET-CT
Specialty: Hematology

Objective: Rare disease
Background: Subcutaneous panniculitis-like T cell lymphoma is a very uncommon subtype of cutaneous T cell lymphoma. The manifestations of this rare disease are atypical at onset, and may mimic some rheumatic or dermatologic diseases, which causes the delay of diagnosis and treatment.

Case Report: We report a 24-year-old man suffering from intermittent fever and skin nodules on the left anterior chest wall, who was initially misdiagnosed with nodular panniculitis and finally diagnosed with subcutaneous panniculitis-like T cell lymphoma through repeat examination of biopsy of the skin nodule. Positron emission tomography revealed extracutaneous adipose tissue involvement. Subsequently, hemophagocytic syndrome occurred while under a conventional dose of glucocorticoid, but remission was induced by treatment with cyclosporine A and high doses of dexamethasone.

Conclusions: In order to avoid the delay diagnosis and inappropriate treatment of subcutaneous panniculitis-like T cell lymphoma, in addition to a thorough physical examination, PET-CT and disease-specific pathologic, immunophenotypic, and T cell receptor tests of the skin biopsy should be performed. Extracutaneous involvement, especially hemophagocytic syndrome, indicated worse prognosis. Even so, cyclosporine A plus high-dose corticosteroid could be an option of treatment.

MeSH Keywords: Cyclosporine • Lymphohistiocytosis, Hemophagocytic • Lymphoma, T-Cell, Cutaneous • Panniculitis, Nodular Nonsuppurative

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Background

Subcutaneous panniculitis-like T cell lymphoma (SPTCL) belongs to a new subset of peripheral T cell lymphoma characterized by infiltration of neoplastic cytotoxic T cells into subcutaneous tissue [1]. The diagnosis of SPTCL depends on the pathologic examination of skin biopsies, but the manifestations of SPTCL are varied and mimic autoimmune disorders. Some SPTCL patients were initially misdiagnosed with erythema nodosum, nodular panniculitis, lupus erythematosus profundus, systemic vasculitis, dermatomyositis, or pyoderma gangrenosum [2]. The unsustainable therapeutic effect of antirheumatic treatment led to reconsideration of the diagnosis. Systemic chemotherapy with CHOP (Cyclophosphamide, Hydroxydaunorubicin, Oncovin and Prednisone/Prednisolone) or other anthracycline-based regimen achieved complete or partial remission; however, failure of treatment due to disease progression or infectious complications also occur [3]. In this article, we report the case of a SPTCL patient with extracutaneous adipose tissue involvement and hemophagocytic syndrome (HPS), who was initially misdiagnosed with nodular panniculitis.

Case Report

A 24-year-old man was admitted to the hospital due to intermittent fever and skin nodules in the left anterior chest wall beginning 2 weeks before. He complained of night sweats and poor appetite. Relief could not be achieved through antibiotic treatment. He was a nonsmoker and had no special family history. After physical examination, subcutaneous painless nodules were found in the lower neck, back, abdominal wall, and left anterior chest wall (2×3 cm). The nodules were normal skin color, were not tender, and were without peripheral edema. He had moderate splenomegaly, but no lymphadenopathy. Laboratory tests showed complete blood cell counts were normal. Lactate dehydrogenase (LDH) was elevated (825 U/L, normal range 135–225 U/L). Elevated liver function tests were normal. Lactate dehydrogenase (LDH) was elevated (825 U/L, normal range 4–40 U/L), and gamma-glutamyl transpeptidase (GGT 159 U/L, normal range 15–60 U/L). The CT scan confirmed edema of subcutaneous soft tissue and adipose tissue involvement and hemophagocytic syndrome (HPS), who was initially misdiagnosed with nodular panniculitis.

curvature of the stomach (SUVmax 7.1), shown in Figure 1. Three needle aspiration examinations for the subcutaneous nodule revealed lymphocytes, histocytes, macrophages, and adipocytes, without neoplastic cells. The histological findings of skin biopsy from the left anterior chest wall showed adipocytes “rimmed” by atypical (neoplastic) lymphoid cells. The abnormal lymphocytes were positive for CD2, CD3, CD7, CD8, TIA1, and granzyme B, but negative for CD4, CD56, CD20, and CD79a. Some atypical lymphoid cells were CD5-positive. The Ki67 labeling index in these neoplastic cells was about 50% (Figure 2). In situ hybridization excluded the involvement of latent Epstein-Barr virus infection in atypical lymphoid cells. Immunohistochemical staining of TCRβ was positive for atypical lymphoid cells, while TCRγ was negative. Multiplex polymerase chain reactions of TCRβ and TCRγ were performed, but unfortunately both of them were negative. The patient was misdiagnosed with nodular panniculitis initially because of the results of needle aspiration examination and histologic lobular panniculitis without immunohistochemical staining, and received glucocorticosterone treatment (10 mg dexamethasone intravenously daily, later tapered to prednisone 40 mg orally daily). The fever could be controlled initially and the subcutaneous nodules disappeared and could not be palpated anymore, but the high fever returned after 2 weeks of stability. After infection was excluded through blood culture, cerebrospinal fluid tests, and tests for antibodies against HBV, HCV, HIV, syphilis, CMV, and EBV in serum, the dosage of dexamethasone was increased to 20 mg daily intravenously. However, after several days his thrombocytes decreased unexpectedly as 2×10^9/L, the bone marrow cytomorphologic examination detected phagocytic histiocytes, which phagocytosed platelets and both mature and naive erythrocytes. Extremely elevated ferritin (49508.0 μg/L, normal range 30–400 μg/L) was found. Due to the dramatic deterioration of the patient’s condition without further detection of skin lesions, review of the skin biopsy was performed by an experienced pathologist, and immunohistochemical staining was done. Along with a potentially fatal decrease of fibrinogen, HPS was confirmed secondarily to SPCTL. The patient then received dexamethasone 40 mg daily intravenously combined with cyclosporine A (CsA) 250 mg daily. Two weeks later, his temperature and thrombocytes returned to normal, along with the same type of platelet transfusion. Remission has lasted 5 months, and follow-up visits are expected.

Discussion

Rheumatologists or dermatologists should be vigilant that SPTCL may resemble some rheumatologic or dermatological diseases characterized by inflammation involving the skin or subcutaneous tissue. Cutaneous T cell lymphoma (CTCL) and other reactive conditions should also be considered during...
differential diagnosis, because atypical T cells could be found in these circumstances. This case taught us a lesson – that diagnosis of SPTCL depends not only on the clinical manifestations, but also on the pattern of disease-specific pathologic, immunophenotypic, and T cell receptor tests. In the latest edition of the World Health Organization classification of lymphoid neoplasms [1], SPTCL is defined as a CD8+ cytotoxic T cell lymphoma expressing αβ T cell receptor, normally having indolent clinical behavior with excellent prognosis. However, some patients suffer from HPS, which results in fatal outcomes. HPS occurred in the process of SPTCL in our patient, which indicated a worse prognosis.

CT scans can easily show the location, number, distribution, size, and morphological characteristics of lesions, as well as the shapes, margins, and depths of the lesions. However, FDG-PET is a useful and sensitive examination to detect all the lesions, including the ones palpated on physical examination and abnormal FDG uptake in the involved sites following treatment. The SUV is elevated in the subcutaneous lesions; for instance, an analysis of 8 cases reported that maximum SUVs on initial PET varied from 1.2 to 4.7, decreasing after treatment [4]. PET provides valuable insights in detecting lesions in SPTCL and may be useful in monitoring response to treatment. Since the failure of repeat biopsies is a common occurrence in patients with SPTCL [2], use of PET scans in initial diagnosis may help to differentiate SPTCL from misleading clinical and histopathologic manifestations. The use of FDG-PET in the initial diagnosis of SPTCL was recently suggested due to the reduction of SPTCL-associated morbidity and the elimination of physical and psychological burdens associated with unnecessary repeat biopsies [5], which had occurred in this case.

Besides the common extracutaneous involvement of SPCTL, such as lymphadenopathy, splenomegaly, and hepatomegaly, PET imaging helped us to find more extracutaneous lesions. We reviewed the literature and found that in a summary of 8 patients diagnosed with SPTCL, only 1 patient showed involvement

Figure 1. FDG-PET (A) images show hypermetabolism in multiple subcutaneous nodular lesions in upper extremities, right trunk, and breast. Multiple patchy foci of F-18 FDG uptake were found in adipose tissue of fat pad of pericardium, peritoneum, retroperitoneal, pelvic cavity, right axilla and bilateral inguinal regions. Fused PET/CT demonstrated the largest nodular lesion, located in the left upper anterior chest wall (B), and increased uptake of F-18 FDG was detected in the adipose tissue near the lesser curvature (C).
of the iliac lymph nodes. According to the author, lymph node involvement is uncommon [4]. Rodriguez et al. reported a case in which abdominal FDG uptake involved the subcutaneous tissues throughout the body and axillary lymph nodes without any visceral involvement [6]. In a case of low-grade nodal active disease in the right and left inguinal lymph nodes, abnormal FDG uptake was detected in an intra-abdominal visceral fat lesion [7]. In another case, increased FDG uptake in an area of fat stranding in the perirenal fat was detected in the coronal PET, axial PET, CT, and fused PET/CT images [8]. Additionally, the involvement of the bone marrow in SPTCL was reported by the indications of PET findings and bone marrow biopsy [9,10]. Breast involvement [11] was also described by morphological (CT and MRI) and functional (FDG-PET) imaging findings. Our case revealed elevated FDG uptake by the diffuse visceral adipose tissues beside the subcutaneous tissues. Therefore, although extracutaneous involvement is rare, the possibility of its occurrence should not be overlooked.

HPS is one of the most serious and frequently life-threatening complications of SPTCL. The prognosis of SPTCL is considered to be generally favorable; however, patients whose cases are complicated by HPS have a significantly worse survival rate [12]. HPS is characterized by fever, cytopenia, and pathologic findings of hemophagocytosis in bone marrow. The detailed mechanism of HPS associated with SPTCL remain unclear, but is thought to be related to cytokine and chemokine production by the malignant cells, perhaps in a setting of comprised cytolytic function. Only thrombocytopenia occurred in our patient, but the diagnosis of HPS was confirmed by fever, splenomegaly, abnormal liver function, decreased fibrinogen, elevated ferritin, and phagocytosis in bone marrow.

Based on the development of the SPTCL disease, decisions for treatment may be made in different ways. For patients who had a relatively indolent presentation, immunosuppressive agents such as prednisone, cyclophosphamide, or methotrexate are the initial treatment options; while for the patients with aggressive disease, combination chemotherapy regimens are most frequently used [3]. In addition, radiotherapy and stem cell transplantation were reported as options for treatment. CsA plus dexamethasone was administered in our case and induced the improvement of SPTCL. There were significant parallels with the report according to which CsA plus methylprednisolone treatment improved HPS with chemotherapy-resistant SPTCL, and induced complete remission after 3 months [13]. Because the time of first response to CsA was within 2 weeks in most cases, according to the review on CsA for SPTCL (as well as with our case), CsA was suggested as a candidate in the treatment strategy for SPTCL [13].

Conclusions

Some rheumatic or dermatologic diseases, such as nodular panniculitis in our case, may be initially misdiagnosed in the
early stage, but were finally diagnosed as SPTCL. To avoid delayed diagnosis and inappropriate treatment of SPTCL, PET and disease-specific pathologic, immunophenotypic, and T cell receptor tests of the skin lesions should performed in addition to a thorough physical examination. Extracutaneous involvement, especially HPS, indicates a worse prognosis. Even so, CsA plus high-dose corticosteroid could be a treatment option.

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Conflict of interest

No disclosure statement of any conflict of interest.

References:

1. Swerdlow S, Campo E, Harris NL et al., (eds.): WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues. Lyon: IARC Press, 2008
2. Yi L, Qin S, Wenjie Z et al: The presenting manifestations of subcutaneous panniculitis-like T-cell lymphoma and T-cell lymphoma and cutaneous gammadelta T-cell lymphoma may mimic those of rheumatic diseases: A report of 11 cases. Clin Rheumatol, 2013; 32: 1169–75
3. Go KS, 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: 1404–13
4. Kim JW, Chae EJ, Park YS et al: Radiological and clinical features of subcutaneous panniculitis-like T-cell lymphoma. J Comput Assist Tomogr, 2011; 35: 394–401
5. Bennani-Baiti B, Yadav S, Flynt L, Bennani-Baiti N: Value of positron emission tomography in diagnosing subcutaneous panniculitis-like T-cell lymphoma. J Clin Oncol, 2013; 33: 1216–17
6. Rodriguez VR, Joshi A, Peng F et al: Positron emission tomography in subcutaneous panniculitis-like T-cell lymphoma. Pediatr Blood Cancer, 2009; 52: 406–8
7. Mitsuhashi K, Momose M, Masuda A et al: Positron emission tomography revealed diffuse involvement of the lower legs and occult extracutaneous lesions in subcutaneous panniculitis-like T-cell lymphoma. Clin Nucl Med, 2013; 38: 209–11
8. Ravizzini G, Meirelles GS, Horwitz SM, Grewal RK: F-18 FDG uptake in subcutaneous panniculitis-like T-cell lymphoma. Clin Nucl Med, 2008; 33: 903–5
9. Huang CT, Yang WC, Lin SF: Positron-emission tomography findings indicating the involvement of the whole body skin in subcutaneous panniculitis-like T cell lymphoma. Ann Hematol, 2011; 90: 853–54
10. Brown NA, Ross CW, Gunderson JE et al: Subcutaneous panniculitis-like T-cell lymphoma with bone marrow involvement. Am J Clin Pathol, 2015; 143: 265–73
11. Schramm N, Pfluger T, Reiser MF, Berger F: Subcutaneous panniculitis-like T-cell lymphoma with breast involvement: functional and morphological imaging findings. Br J Radiol, 2010; 83: e90–94
12. 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: 838–45
13. Mizutani S, Kuroda J, Shimura Y et al: Cyclosporine A for chemotherapy-resistant subcutaneous panniculitis-like T cell lymphoma with hemophagocytic syndrome. Acta Haematol, 2011; 126: 8–12