

Case Presentation 13

Subcutaneous Panniculitis-like T cell Lymphoma

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Case Report

The patient was a 28-year-old female who had a 5-year history of tender erythematous plaques involving her thigh and upper arms, which followed a waxing waning course (Figure 1). Prior biopsies were interpreted as being compatible with lupus profundus. However, more recently the plaques became larger and the patient also developed constitutional symptoms of fever, fatigue and night sweats. A skin biopsy was performed and showed a necrotizing lymphomatoid panniculitis. The necrotic areas were characterized by extensive fibrin deposition with a supervening thrombogenic vasculopathy along with marked apoptosis. In viable areas there was significant hyperplasia of plasma cells along with supervening fibrosis and patchy well differentiated lymphocytic infiltrates permeating the interstitial spaces. From a cytomorphologic perspective the lymphocytes were predominantly small with mild nuclear contour irregularity. The adipocyte membranes were largely preserved although focally there was some disruption with a few lymphocytes permeating the adipocyte membrane (Figure 2, 3).

Immunohistochemical stains were conducted and highlighted the infiltration of the fat lobule including within the areas of necrosis by CD2 positive T-cells. A CD5 preparation showed a 30% reduction in staining (Figure 4) compared to CD2. A similar reduction was observed with CD7 (Figure 5). Minimal staining was noted with CD62L with 90% reduction. A CD3 preparation mirrored the CD7 stain. A CD4 preparation showed positivity of macrophages; there was a subset of lymphocytes with staining although overall there was a greater extent of positivity noted for CD8 including lymphocytes that may lie within the interior of the adipocyte, defining the concept of adipocyte rimming. There was also extensive immunoreactivity for Beta F1 (Figure 6). A CD56 preparation was negative.

Discussion

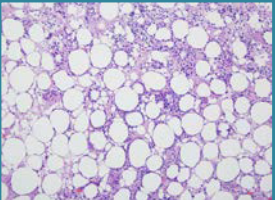
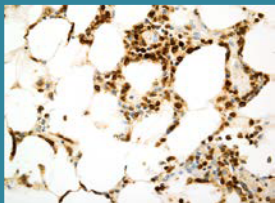
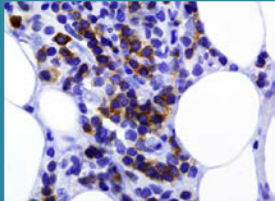
In our case, the findings were those of subcutaneous panniculitis-like T cell lymphoma associated with extensive necrosis attributable to both enhanced apoptosis as well as ischemia due to a thrombogenic vasculopathy. The lymphocytes were cytomorphologically mildly to moderately atypical. The extent of infiltration along with the degree of necrosis did not support a diagnosis of ALLP. Given the extent of granular necrosis within the fat lobule attributable to actual cellular necrosis of the infiltrate along with the pattern of adipocyte membrane disruption and the phenotypic profile including a dominance of CD8 lymphocytes showing cytotoxic properties with a reduction of CD7, CD5, and CD62L, the concern was one of subcutaneous panniculitis-like T cell lymphoma.

Subcutaneous panniculitis-like T cell lymphoma (SPTCL) is a primary form of cutaneous T cell lymphoma which shows dominant localization within the fat and is unique among the hematologic dyscrasias because of its almost exclusive involvement of the subcutaneous fat with little tendency toward extracutaneous dissemination; it has a predilection for adults in the third to fourth decades of life. This condition exhibits many striking overlapping features with lupus profundus. According to the WHO-EORTC classification of lymphoma the neoplastic cells of subcutaneous panniculitis like T cell lymphoma are of the Alpha beta subset (1-4).

The differential diagnosis in this case is one of atypical lymphocytic lobular panniculitis (ALLP), a distinct form of panniculitic T cell dyscrasia which was first recognized in 2004 (5). Patients usually have a clinical course characterized by waxing and waning bruise-like plaques unassociated with constitutional symptoms and without clinical features of collagen vascular diseases. This entity showed histologic, phenotypic and molecular features continuum with subcutaneous panniculitis-like T cell lymphoma although not equate to SPTCL. SPTCL and ALLP have many clinical similarities; however spontaneous regression is usually seen in ALLP in contrast to cases of SPTCL which show persistent and progressive plaques.

Morphologically, ALLP shares with SPTCL infiltration of the panniculus by small- to intermediate sized atypical lymphocytes of the interstitium of the reticular dermis. However, unlike SPTCL, the density of infiltration in ALLP is significantly less and the lymphoid atypia is not sufficient for the diagnosis of lymphoma. The angiodestructive changes, significant luminal thrombosis and extensive fat necrosis that are encountered in SPTCL are not seen in ALLP. (5-7)

The other condition morphologically resembling subcutaneous panniculitis-like T cell lymphoma is lupus profundus. Patients typically present with a several year history of plaques and nodules located over the anterior thighs and upper arms, which follow a waxing and waning course. Useful discriminating light microscopic features include atrophying interface dermatitis, plasmacellular infiltration, germinal center formation, a positive lupus band test and the absence of red cell phagocytosis. A deletion of CD5 or CD7 and clonality can be seen in lupus profundus (8, 9).



In both lupus profundus and SPTCL there is an unusual predilection to involve the thigh and proximal arms and as well there is a female preponderance. It is not surprising that many patients with subcutaneous panniculitis-like T cell lymphoma are initially diagnosed with lupus profundus. The most important clues to distinguish subcutaneous panniculitis like T cell lymphoma from lupus profundus include erythrocyte phagocytosis and the absence of destructive atrophying interface dermatitis with hyperkeratosis; dermal mucin deposition is not a discriminating feature as this phenomenon can be observed in both disorders (10).

Both local and systemic macrophage activation are a cardinal manifestation of subcutaneous panniculitis-like T cell lymphoma. The basis of the hemophagocytosis is the production of a phagocytosis-inducing factor by neoplastic T lymphocytes. While some patients with subcutaneous panniculitis-like T cell lymphoma present very acutely other patients report a waxing and waning course of several years before being diagnosed with subcutaneous panniculitis-like T cell lymphoma (11).

Immunophenotypically primary subcutaneous panniculitis-like T cell lymphoma frequently express a CD3+CD8+ phenotype along with cytotoxic proteins such as granzyme B, T cell intracellular antigen 1 (TIA) and perforin. The cells frequently manifest a deletion of CD5 and CD7 with variable diminution in CD3 expression. The mature counterpart is a cytotoxic CD8 T-cell. The prominent tissue necrosis probably results from the cytotoxic properties of the tumor cells (2, 3).

Patients with subcutaneous panniculitis-like T cell lymphoma untreated will die while those treated can achieve remission. Those who die succumb to hemophagocytic syndrome (HPS), initially or after several years rather than one related to extracutaneous dissemination. Due to the inherent cytopenia associated with HPS, the terminal event is typically one of bacterial or fungal sepsis. Dissemination to lymph nodes is uncommon and usually occurs late in the disease course. While the natural history is indeed aggressive most patients respond to combination chemotherapy (3).

Case References

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Figure Legend



Figure 1: The patient presents with indurated plaques on the thigh..

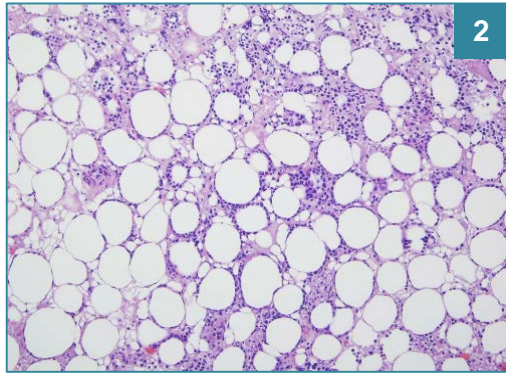


Figure 2: There is a striking lymphocytic infiltrates permeating the interstitial spaces of the subcutaneous fat. Concomitant vascular thrombosis and interstitial fibrin deposition is also noted. The morphology is that of a necrotizing lymphomatoid lobular panniculitis.

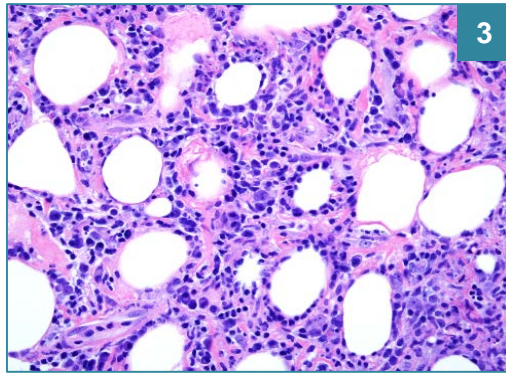


Figure 3: Higher magnification reveals a dominant small cell populace. The lymphocytes are hyperchromatic and exhibit nuclear contour irregularity. A characteristic features is one so called adipo-cyte rimming which represents internalization of the neoplastic lymphocytes to lie in apposition to the inner aspect of the cytoplasmic membrane of the adipocyte.

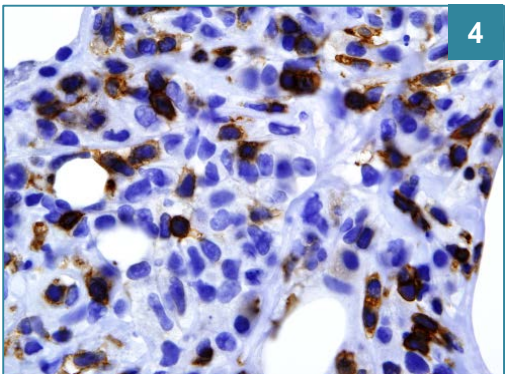
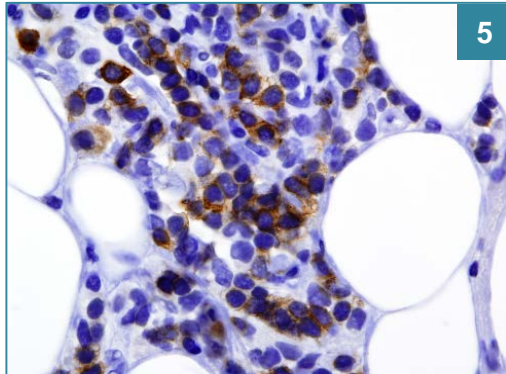


Figure 4: Phenotypically the T cells are abnormal by virtue of the reduction in the expression of CD5.



Figures 5: Phenotypically the T cells are abnormal by virtue of the reduction in the expression of CD7.

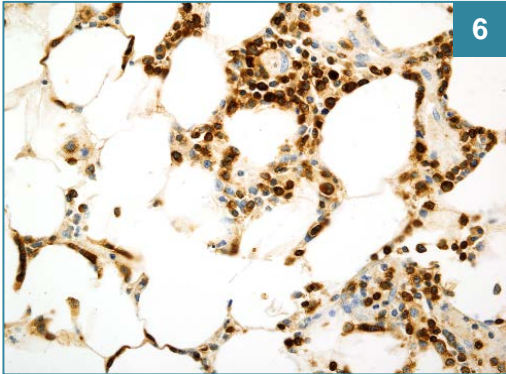


Figure 6: The neoplastic cell in this form of lymphoma is of the alpha beta subset as revealed by extensive immunoreactivity for Beta F1.

Under the direction of Dr. Cynthia M. Magro, the Weill Cornell Comprehensive Dermatopathology Service is a leading edge consultation service and CAP-accredited laboratory for dermatologists, plastic and general surgeons and other dermatopathologists. Dr. Magro is an internationally renowned dermatopathologist, educator and author. She is a Professor of Pathology and Laboratory Medicine at the Weill Cornell Medical College in Manhattan, and is board certified in anatomic pathology, dermatopathology and cytopathology. Dr. Magro is an expert in the diagnosis of complex inflammatory skin diseases. Her areas of expertise include cutaneous manifestations of auto-immune disease, systemic viral disease and vasculitis, atypical drug reactions, benign, atypical and overtly malignant lymphocytic infiltrates of the skin, and diagnostically difficult melanocytic proliferations. The award-winning author of *The Melanocytic Proliferation: A Comprehensive Textbook of Pigmented Lesions*, Dr. Magro has recently completed her second book, *The Cutaneous Lymphoid Proliferation, a comprehensive textbook on benign and malignant lymphocytic infiltrates*. She has co-authored over 250 peer reviewed papers and several textbook chapters. Dr. Magro frequently presents courses on inflammatory skin pathology and difficult melanocytic proliferations to the American Academy of Dermatology, the United States and Canadian Academy of Pathology, and the American Society of Clinical Pathology. Dr Magro has consistently been recognized in Who's Who in America®, Castle Connolly's renowned America's Top Doctors – New York Metro Area® edition and in the Super Doctors® list published in The New York Times Magazine.

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