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This educational series of case presentations is presented by the Weill Cornell Comprehensive Dermatopathology Service.

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 170 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.

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Case References

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CASE PRESENTATION 2

Case Presentation 2:

Subcutaneous Panniculitis-like T Cell Lymphoma Arising in a Background of Atypical Lymphocytic Lobular Panniculitis

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Excellence in Academic and Diagnostic Dermatopathology

CASE PRESENTATION 2

Subcutaneous Panniculitis-like T Cell Lymphoma Arising in a Background of Atypical Lymphocytic Lobular Panniculitis

Write up: Cynthia M. Magro, MD; Jochen Schaefer, MD; Molly Dyrsen, MD

Case contributor: Noah Heffler, MD, Weill Cornell Medical College

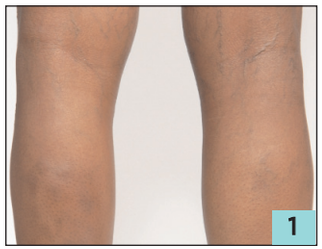
Case History

A 56-year-old African American woman developed progressive indurated plaques of the distal lower extremities in the fall of 2006. Her past medical history was unremarkable. Despite seeing 5 different specialists she remained a diagnostic conundrum. She first noted the lesions along the pretibial surface in October 2006 which then changed to a more posterior location overlying the left calf. Shortly thereafter she developed indurated, hyperpigmented plaques on the right calf and bilateral swelling of the legs (figure 1). She was referred to Dr. Hefler who performed a biopsy in an attempt to elucidate the nature of the eruption.

The specimen was sent to Weill Cornell Comprehensive Dermatology Service for analysis. The biopsy demonstrated a moderately dense lymphocytic infiltrate localized to the interstitial spaces of the fat lobule. There was mild lymphoid atypia. Foci of fat necrosis were noted. Immunophenotypic studies revealed that the lymphocytes were predominantly of the α-β-CD8 subtype and expressed cytotoxic proteins as manifested by fairly extensive granzyme positivity. A significant diminution in the pan-T-cell marker profile was present including CD3, CD7 and CD62L. Multiplex PCR analysis revealed a polyclonal result for the T-cell receptor gamma chain; no monoclonal rearrangements were observed.

Based on the patient's short clinical history in regards to lesional duration and her apparent state of well-being with no constitutional symptoms or peripheral blood abnormalities, a diagnosis of atypical lymphocytic lobular panniculitis was made.

Over the ensuing months however the lesions progressed and new lesions developed. A rebiopsy was performed.



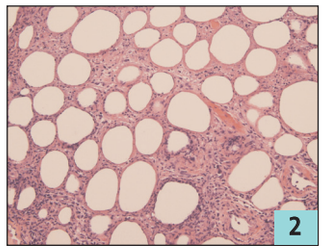
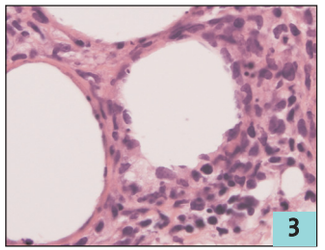


Figure 1: The patient developed indurated hyperpigmented plaques over the pretibial and posterior distal lower extremities. Figure 2: The biopsy shows permeation of the interstitial spaces of the fat by lymphocytes with attendant fat necrosis.



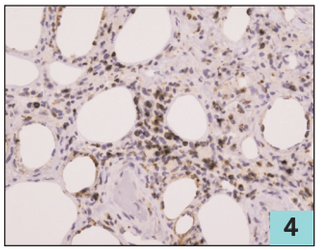
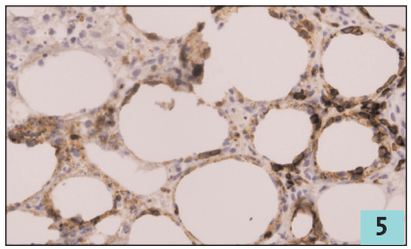


Figure 3: There is characteristic internal rimming of the adipocytes by lymphocytes. Figure 4: The cells manifest extensive cytotoxic protein expression as revealed by prominent granular staining for granzyme.

The morphology was similar however there was enhanced lymphoid atypia and fat necrosis. The phenotypic profile was similar. On this occasion however molecular studies exhibited a clonal T cell population. A diagnosis was now made of subcutaneous panniculitis-like T cell lymphoma. Following this diagnosis the patient sought an outside opinion from an expert hematopathologist whereby a diagnosis of lupus profundus was made.

She was subsequently treated with plaquenil. A striking worsening of her eruption and the onset of massive proteinuria ensued. A kidney biopsy evaluated by the Cornell Renal Pathology team showed severe podocyte injury compatible with a rare form of kidney dysfunction designated as collapsing glomerulopathy. This unusual condition has been linked to macrophage activation whereby the podocytes acquire a macrophage phenotype and elicit products which damage supporting intraglomerular epithelial cells critical for maintaining the structural integrity of the glomerulus; there is a predilection for its occurrence in African American patients. Given the deterioration in her status based on plaquenil treatment and the development of a life threatening condition attributable to T cell driven macrophage activation it was agreed upon by the Cornell Hematology team that her eruption was best treated and categorized as panniculitis-like T cell lymphoma.

In this regard she has undergone therapy with cyclophosphamide, vincristine, adriomycin, and prednisone (CHOP). Her lesions have undergone regression, her renal function is improving and she is without any constitutional symptoms.



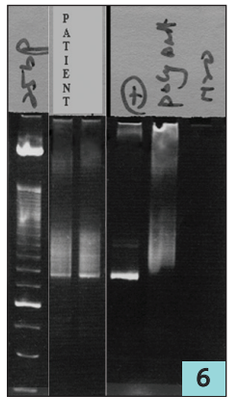


Figure 5: The cells are predominantly of the CD8 subset. Figure 6: Molecular studies revealed a clonal population of T cells.

Discussion

This case represents a classic form of cutaneous lymphoma falling under the designation of subcutaneous panniculitis-like T cell lymphoma. This unusual form of lymphoma may not be recognized initially either in a clinical or pathological context. Conversely even when recognized pathologically there may be varying opinions among pathologists in regards to diagnosis. The classic entity with which panniculitis-like T cell lymphoma may be confused is lupus profundus as was exemplified by this case. This lymphoma when composed of T cells of the alpha beta subset is considered a relatively indolent form of lymphoma based on the EORTC WHO classification. Those lymphomas composed of cells of the gamma delta subset follow an aggressive clinical course with a significant percentage of patients succumbing to hemophagocytic syndrome. Despite dominant localization to the fat they fall under the rubric of a cutaneous gamma delta T cell lymphoma and are not really considered under the EORTC WHO classification scheme as subcutaneous panniculitis-like T cell lymphoma. The latter term is now reserved exclusively for those malignant panniculitic infiltrates composed of T cells of the alpha beta subset. While the course of the alpha beta variant may be indolent patients still require systemic treatment. There is no role for topical treatment in this condition. There may be accompanying cytopenias and fevers. The cytopenias are attributable to phagocytosis of hematopoeitic elements by macrophages which in turn are activated by the neoplastic T cells. The clonal T cells apparently induce the production of macrophage activating factor. It is interesting to note that while this patient did not have any cytopenias she sustained significant adverse clinical sequelae of this macrophage activation phenomenon in the context of collapsing glomerulopathy. Panniculitis-like T cell lymphoma can be associated with mortality not due to multiorgan dissemination but related to cytokine release and more specifically macrophage driven cytopenia.

The precursor state in this patient was a distinctive form of panniculitis-like T cell dyscrasia designated as atypical lymphocytic lobular panniculitis. This particular dyscrasia likely represents the prelymphomatous waxing and waning phase that can be encountered in a significant percentage of patients with the alpha beta variant of panniculitis-like T cell lymphoma. The exact events leading to oncogenic transformation is unclear. This variant of cutaneous lymphoid dyscrasia shows T cell clonality and certain phenotypic alterations including losses of CD7, CD62L and CD5. The lack of systemic symptoms and a course of spontaneous resolution and or rapid resolution with steroid administration are among the clues pointing toward this diagnosis.

We have achieved success using ATRA therapy to treat this prelymphomatous subcutaneous T cell dyscrasia. Multi-agent chemotherapy however is still the most reasonable treatment option for those patients who have evolved into frank lymphoma.