Case of Panniculitis like T-cell Lymphoma

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Citation

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Abstract

Published widely as an author or co-author of more than 100 studies, Dr. Foss serves on the editorial board for the journal Clinical Lymphoma, and is a reviewer for the New England Journal of Medicine, Journal of Clinical Oncology, Blood, Journal of American Academy of Dermatology and Cancer. Dr. Foss has been a member of numerous professional societies, including the American Medical Association, the American College of Physicians, the American Society of Clinical Oncology, and the American Association for Cancer Research.

Dr. Foss received her bachelor's degree from Dartmouth University and her medical degree from the University of Massachusetts Medical School. She completed her internship and residency at Brigham and Women's Hospital in Boston, Massachusetts.

INITIAL PRESENTATION

A 39 year old man presented with the sudden onset of a 10 centimeter mass in the left thigh which was slightly tender to palpation. He was initially treated with a course of oral antibiotics without improvement. As the original mass began to slowly regress over the next several months, the patient noted the appearance of several additional subcutaneous nodules in the bilateral lower extremities. The nodules persisted and slowly enlarged in size. He was otherwise healthy with no weight loss, fevers, chills, or other symptoms, and he continued to work full time.

STAGING WORK-UP – CONSIDERATIONS FOR THE DERM/ONC FROM THE REFERRING PHYSICIAN

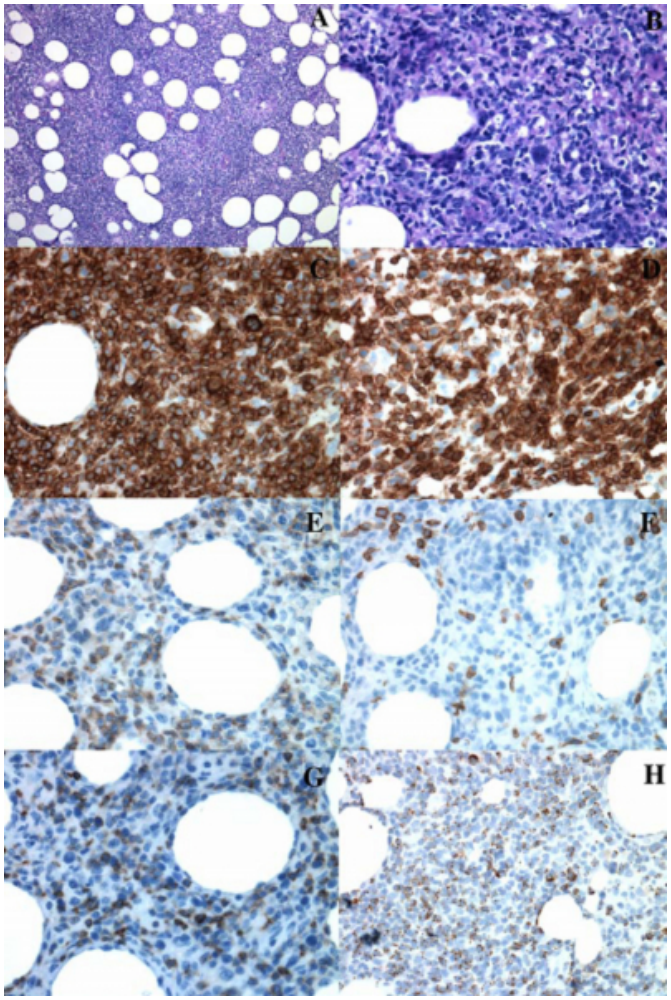
Although he presented to his primary care physician for evaluation, he was referred to the CTCL clinic at Yale for further evaluation and staging by a multi-disciplinary team. His past medical history was significant for a 10 year history of idiopathic thrombocytopenia and mild splenomegaly felt to be a complication of previous mononucleosis.

HISTOLOGY

Excisional biopsy of one of these nodules revealed an atypical lymphoid infiltrate with a panniculitic distribution that focally extended into the deep dermis. The infiltrate was composed of variably-sized lymphocytes ranging from small to large that also show significant cytological atypia (Figure 1).

Figure 1

Figure 1: (A) Dense lymphoid infiltrate in the panniculus (H&E staining; original magnification, X 40). (B) Atypical, variably-sized lymphocytes with focal rimming of adipocytes (H&E staining; original magnification, X 400). The neoplastic cells strongly express CD2 (C), CD3 (D), and TIA-1 (H). An admixture of CD4-positive and CD8-positive small reactive lymphocytes was noted, but the atypical lymphocytes were negative for CD4 (E), CD8 (F), and CD5 (G).

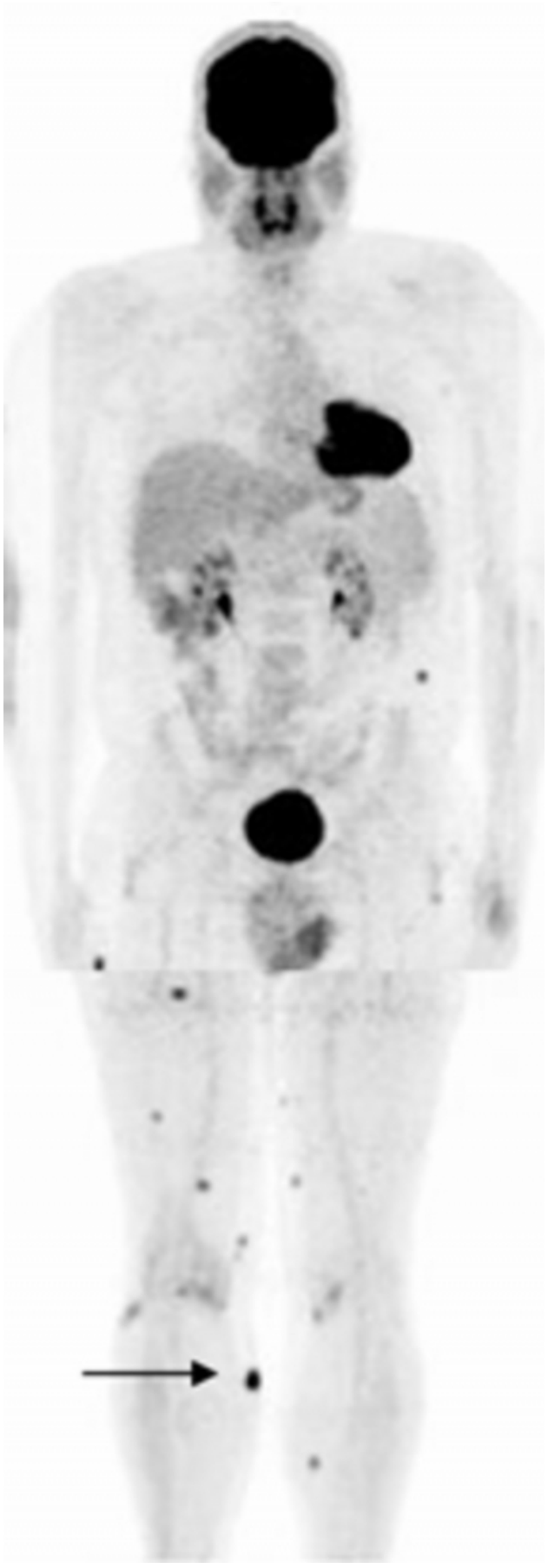


The atypical cells were T-cells positive for CD3, TIA-1, subpopulation positive for granzyme B and were negative for CD4, CD8 and beta-F1. Additionally, clonal rearrangement by PCR analysis for the T cell receptor gamma gene was positive. The absence of staining for CD4, CD8, and beta-F1 in conjunction with the expression of cytotoxic markers and a positive clonal T cell receptor gamma gene rearrangement supported the diagnosis of / cutaneous T-cell lymphoma.

On further evaluation, the white blood cell count was 3.9 x 1000/ul (4.0-10.0), the hematocrit was 44.3 and the platelets were mildly reduced at 145 x 1000/ul (150-350). Differential showed 63% neutrophils, 30% lymphocytes and 7% monocytes. Serum chemistries, liver function tests and LDH were within normal limits. Peripheral blood flow cytometry showed a normal lymphoid immunophenotye with no unusual phenotypic T cells. Bone marrow biopsy was negative for involvement by lymphoma. PET/CT demonstrated multiple FDG-avid subcutaneous nodules on the lower extremities and a single focus in the left abdomen (see figure 2). The scan demonstrated no nodal or visceral involvement.

Figure 2

Figure 2: CT PET scan at diagnosis, demonstrating multiple FDG-avid subcutaneous nodules in the lower extremities and one on the trunk.



CLINICAL EVIDENCE AND MANAGEMENT ISSUES

In summary, this patient who was otherwise healthy presented with subcutaneous panniculitis-like T-cell lymphoma. SPTCL was initially included as a provisional entity in the Revised European-American Lymphoma classification, followed by the European Organization for Research and Treatment of Cancer classification as a primary cutaneous lymphoma, and subsequently as a distinct entity by the World Health Organization classification. It is known that patients diagnosed with SPTCL usually respond poorly to therapy, and the tumor progresses aggressively. Data from recent studies in a series of cases of SPTCL by the European Organization for Research and Treatment of Cancer Cutaneous Lymphoma Group have further identified SPTCL as a heterogeneous disease entity, which comprises an subtype (SPTCL-AB) and a subtype (SPTCL-GD). The latter has recently been included in the entity of "cutaneous T-cell lymphoma" by the World Health Organization, Pathology and Genetics of Skin Tumors.

TEACHING POINTS

The clinical, histopathologic, and immunophenotypic data, treatment, and prognosis, appear different in the 2 subtypes of SPTCL The subtype often involves the subcutaneous tissue whereas the subtype involves the dermis and shows epidermotropism. Expression of CD56 is variably present on the but not the subtype.

It is becoming increasingly apparent that while cases of the / T-cell phenotype of SPTCL generally present with and follow a clinically indolent behavior, the / variant is a typically more aggressive disease, is often resistant to multi-agent chemotherapies.5-10 Appropriate staging for patients with panniculitis-like T-cell lymphoma include imaging studies to evaluate for visceral disease as well as bone marrow biopsy.

TREATMENT GUIDELINES AND SAFETY ISSUES

Based on the inferior outcomes with / panniculitis-like T-cell lymphoma, the recommendation was that Mr B receive systemic therapy. Because he had limited stage disease with no visceral involvement and felt otherwise well, he was reluctant to undergo aggressive therapy with CHOP, so he was offered therapy with single agent denileukin diftitoxin 18mcg/kg for three days every 21 days. He experienced mild flu-like symptoms following the initial treatment that resolved within seven days. His CBC remained stable but he did experience a mild transaminitis following his first cycle of therapy which resolved spontaneously. Clinically, the patient's nodules had resolved by the end of the second cycle, with only a few scattered remaining areas of skin thickening on the lower extremities. Follow-up PET/CT scan demonstrated no significant FDG uptake in the subcutaneous lesions in the left abdomen and lower extremities, with the exception of faint residual activity in a lesion in the right upper calf.

Fourteen months later, restaging PET scan again demonstrated recurrent nodules in the lower extremities (subcutaneous nodules in the right anterior thigh/inguinal region superiorly (SUVm 3.9) and inferiorly in the same region (SUVm 10.8), posteromedial right leg at the level of the knee joint (SUVm 4), and right medial lower leg (SUVm 1).At this point he was placed on bexarotene 300 mg (4 capsules) per day along with denileukin diftitox. Repeat scans demonstrated resolution of FDG-avid disease for 12 months, after which he again developed FDG avid skin nodules (uptake at right inguinal (SUVm=13.3, right gluteus (SUVm=9.7), and left knee medially (SUVm=5.7).

MORE MULTIDISCIPLINARY TEAM AND MANAGEMENT ISSUES

Restaging studies demonstrated no visceral involvement. At this point it was determined that he had progressed after combination treatment with denileukin diftitox and bexarotene. Because of the poor outcomes reported in patients with pannicultis like T-cell lymphoma, an aggressive strategy was again discussed with the patient. He and his siblings underwent HLA typing and his brother was found to be an HLA-identical match. Despite the few new skin nodules, he felt well and continued to work full-time. Staging studies including flow cytometry of his peripheral blood and bone marrow biopsy demonstrated no extracutaneous disease. It was recommended that he consider systemic chemotherapy followed by a stem cell transplant, but he refused this option and asked for alternative therapy. He was then started on Interferon alfa at a dose of 10 million units subcutaneously twice a week. He experienced constitutional symptoms in the form of

fevers and chills over the first month of therapy. Restaging CT PET scan after four months demonstrated no adenopathy and no FDG avid disease. He remains in remission on Interferon therapy for one year.

CONCLUSIONS

Given the overall poor prognosis of the / panniculitis like

T-cell lymphomas and the propensity for development of the hematophagocytic syndrome, the recommendation was made that this patient consider undergoing a stem cell transplant after his next recurrence.

References

Author Information

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