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Clinical History:
This is a previously healthy 72 year-old male who presented with a three-month history of rapidly enlarging and ulcerating lesions located on the right nasal sidewall, scalp vertex and left upper extremity. No constitutional symptoms or lymphadenopathy were associated with these cutaneous lesions. HIV testing was negative and there was no evidence of immunosuppression. CT scan of head and neck showed an ill-defined enhancing soft tissue mass confined to the right face and right nasal sidewall without erosive changes of the underlying nasal and frontal bones. Imaging studies showed no significant lymphadenopathy or systemic involvement. The staging bone marrow biopsy was negative. After the diagnosis was rendered, the patient was treated with CHOP regimen with good response. Follow up visits showed marked improvement with significant reduction of the mass size.

Biopsy Fixation Details:
10% buffered formalin

Description of Clinical Image if Any:
Figure 1: The patient presented with a large ulcerated nodule, measuring 6.0 x 4.0 cm, located on the right nasal sidewall.
Figure 2: An additional ulcerated nodule with indurated borders, measuring 2 cm in diameter, located in the left upper extremity.

Details of Microscopic Findings:
The nasal biopsy shows a diffuse proliferation of lymphocytes with marked epidermotropism. The proliferation consists of monomorphic population small- to medium-sized pleomorphic cells. No angiocentricity or angiodestruction is appreciated (Figure 3).

H&E sections of the scalp biopsy shows diffuse mixed lymphoid infiltration in the dermis with minimal epidermo- or folliculotropism. The proliferation consists of polymorphic population of small to medium-sized cells with occasional large cells, mixed with small lymphocytes, histiocytes, as well as, granulomas with giant cells, especially close to hair follicles. Formation of lymphoid follicles is also present (Figure 6-7)

Immunophenotyping by Immunohistochemistry and/ or Flow Cytometry:
Nasal biopsy (outside material, review of photomicrographs): Epidermotropic and dermal infiltrates are predominantly CD8+/TIA-1+ cytotoxic T cells that are positive for CD3, CD7, and are negative for CD4, CD30, CD56, Granzyme B, and CD20. (Figure 4 and 5)

Scalp biopsy: The epidermotropic and folliculotropic infiltrates are highlighted by immunohistochemical stains and consist of a predominance of CD8+/TIA-1+ T cells with aberrant loss of CD2 and CD5. CD7 appeared preserved. CD4+ cells are also occasionally present within epidermis and more frequent within the follicular epithelium, but show dendritic appearing staining, likely Langerhans cells which are increased as highlighted by CD1a. The neoplastic cells were also TCR-B positive. The dermal infiltrate is composed of mixture of CD4+ and CD8+/TIA-

1+ T cells. CD20 highlights lymphoid follicles and scattered small to medium-sized, as well as occasionally large B cells. CD163 labeled increased histiocytes. Ki67 shows high proliferative index of lymphoid follicles and approximately 30-50% of dermal infiltrate. PD1, CXCL13, Granzyme B, CD30, and CD56 are negative. EBV is negative by LMP-1 immunohistochemistry and by EBER *In Situ* hybridization. (Figure 8-10)

Special Stains:
none performed.

Cytogenetics:
none performed.

Molecular Analysis:
none performed.

Interesting Feature(s) of Submitted Case:
Three cutaneous nodules without plaque formation, as the sole manifestation of disease without clinical history of mycosis fungoides (MF).

Biopsies from different sites show different histological features and varying degree of epidermotropism and folliculotropism.

The nasal biopsy shows features of primary cutaneous aggressive epidermotropic CD8+ cytotoxic T-cell lymphoma (CAECCTL). The findings could also be consistent with MF, but is essentially excluded due to history and clinical presentation.

The scalp biopsy shows minimal epidermotropism with histopathological features that could be consistent with cutaneous small-medium pleomorphic T-cell lymphoma (CSMPTL).

Although CD8+ phenotype of CSMPTL has been reported, CAECCTL should be distinguished, since they represent two different entities with different clinical presentation and behavior.

The case is diagnostically challenging and it also emphasizes an importance of reviewing all available material, and using multidisciplinary correlation.

Proposed Diagnosis:
Cutaneous CD8 positive cytotoxic T-cell lymphoma, with overlap features between cutaneous aggressive epidermotropic CD8 positive cytotoxic T cell lymphoma and small/medium size pleomorphic T cell lymphoma (CD8 phenotype).

Panel Diagnosis:
Primary cutaneous CD8+ aggressive epidermotropic cytotoxic T-cell lymphoma.

Comments: