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Langerhans Cell Histiocytosis Presenting as a Nodulo-Ulcerative Eyelid Lesion

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Abstract: **The authors describe a 23-year-old man with unilateral upper eyelid swelling that evolved into a multinodular lesion with central necrosis, mimicking a neoplasm. Biopsy showed a lympho-histiocytic, eosinophil-rich proliferation with positivity for Langerhans cell markers CD1a and S-100 and histiocytic marker CD68. A literature review disclosed 11 documented cases of Langerhans cell histiocytosis of the eyelid with variable clinical presentations. This rare eyelid lesion, nearly always solitary, has no clinically distinctive characteristics and requires biopsy for diagnosis. Langerhans cell histiocytosis (LCH), formerly histiocytosis X, comprises a group of rare disorders characterized by the proliferation of specialized bone marrow-derived Langerhans cells intermingled with mature eosinophils. Proliferations may be multifocal (disseminated) or unifocal (solitary). Ophthalmic lesions are usually unifocal and tend to be located in the orbital region. Isolated eyelid foci are rare and present with variable patterns that preclude clinical diagnosis. In this report, the authors describe a case of multinodular, ulcerative involvement of the eyelid skin that mimicked a basal cell carcinoma. This study was conducted in compliance with the rules and regulations of the Health Insurance Portability and Accountability Act.**

REPORT OF A CASE

A healthy 23-year-old man complained of worsening swelling of the left upper eyelid over 1 month. He took oral doxycycline for back acne. There was no relevant family medical history. Initial examination showed mild diffuse inflammation of the eyelid and an ill-defined 2-cm nodular area with central ulceration and crusting. Clinical diagnoses included ruptured dermoid cyst and cellulitis with underlying abscess. As these conditions are clinically indistinguishable, oral antibiotics were prescribed. An exploratory incision for possible drainage was performed, disclosing a poorly circumscribed, infiltrative, and rubbery mass. The subcutaneous portion of the lesion was debulked.

Histopathology showed an angiolymphoid proliferation with conspicuous eosinophilic infiltration admixed with larger histiocytes and dendritic cells. Immunohistochemical stains highlighted the dendritic cells with CD1a and S100 and the histiocytes with CD68 (Fig. 1).

Oral prednisone was prescribed for 1 week, attaining resolution of the eyelid swelling. A discrete, firm, multinodular cutaneous mass in the lateral third of the eyelid remained (Fig. 2). Subsequent

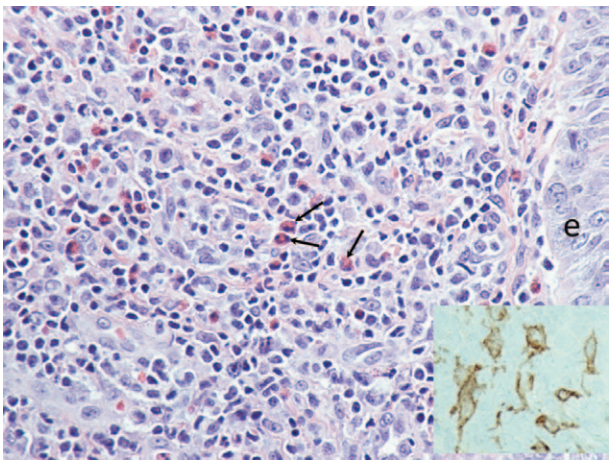

FIG. 1. Cellular admixture deep to epithelium (e) contains eosinophils (*arrows*) amidst lympho-histiocytic infiltrate (hematoxylin-eosin, original magnification, ×200). *Inset* CD1a immunostain highlighting Langerhans cells (immunoperoxidase reaction, diaminobenzidine chromogen, ×400).

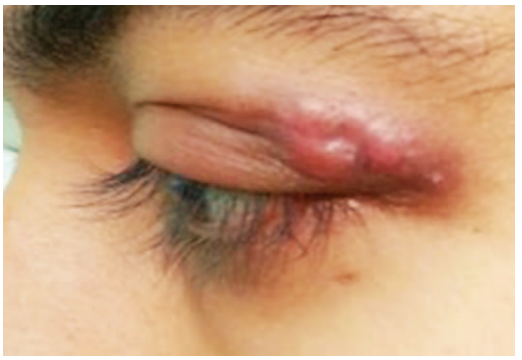

FIG. 2. Multiple cutaneous nodules surround a central ulceration.

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excision of the lesion was performed with intralesional steroid injection. Histopathology showed similar results. Oncologic evaluation, including orbital CT and positron emission tomography/CT scan, disclosed no orbital or systemic abnormalities. The eyelid lesion ultimately resolved with excellent cosmetic results.

DISCUSSION

In 1987, The Writing Group of the Histiocyte Society reintroduced the nomenclature and diagnostic criteria for Langerhans cell histiocytosis. Presumptive histopathologic diagnosis is facilitated by the presence of distinctive Langerhans cells with an inflammatory component composed of eosinophils, histiocytes, neutrophils, lymphocytes, and plasma cells. There is often an eosinophilic predominance in the accompanying granuloma.[1] Electron microscopy demonstrating Birbeck granules or documenting T-6 antigenic determinants further assists with definitive diagnosis. Immunohistochemistry has largely replaced diagnostic electronic microscopy by demonstrating positivity for CD1a, S-100, CD207 (langerin), and BRAF V600E (mutant oncogene).

Solitary extraocular sites of LCH have involved skin, mucous membranes, bone, lymph nodes, and spleen.[2] In the dermatologic literature, LCH has been linked with juvenile xanthogranuloma, a histologically distinct clonal disorder. Rare reports note conversion of cutaneous LCH to eyelid juvenile xanthogranuloma after chemotherapy, suggesting a role of the cytokine milieu in determining the lineage of cellular proliferation in these lesions.[3–5]

Ophthalmologists occasionally encounter LCH in orbital or periorbital regions, including the orbital soft tissues and bones. Among unusual sites are the corneal limbus, choroid, optic nerve, and lacrimal gland. Isolated eyelid lesions are rare and—to our knowledge—only 11 cases have been reported.[6–16] Systemic evaluation was unrevealing in all cases, although 1 report documented lymph node-positive LCH 7 days after excision of the primary lesion.[9]

Classically a disorder of children, 5 of 12 cases—including ours—appeared in adults.

Eight of 11 eyelid cases involved the conjunctiva, tarsus, and eyelid margin, suggesting chalazia, and only 4 were purely cutaneous without direct involvement of the tarsus or conjunctival mucosa. One case presented as preseptal cellulitis as did ours initially. Other cases were described as "cystic" or "seborrheic blepharitis." None showed several nodules surrounding central ulceration as in the current case, mimicking basal cell carcinoma and other malignancies.

It is apparent that no single clinical presentation is characteristic and that biopsy is required to establish the diagnosis.

Observation, surgical excision, intralesional or systemic corticosteroid, radiation therapy, intralesional or systemic interferon, and chemotherapy have been used to treat this disease spectrum.[6,8,17,18] Our patient responded well to surgical debulking with intralesional and systemic steroids (oral prednisone, 80 mg daily for 1 week) without recurrence at 6 months follow up.

Although most reports of ophthalmic LCH involve solitary foci, lesions in unusual ocular locations—as in the current case—merit oncologic investigation including PET/CT and orbital scans with attention to lung, liver, spleen, skin, and bones. Rationale for such studies includes a recently reported association of LCH with Erdheim-Chester disease linked to the BRAF V600E mutation.[19]

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Giant Ocular Horn Occurring in a 10-Year-Old Female

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Abstract: **Cutaneous horns uncommonly involve the periocular region. Involvement of the ocular surface is particularly rare. The authors present a patient who**

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