Case Report

Unifocal Langerhans Cell Histiocytosis Simulating a Limbal Papilloma

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Purpose: To report a rare presentation of unifocal Langerhans cell histiocytosis (LCH) simulating a limbal papilloma.
Case report: A 24-year-old man presented with a limbal mass in his left eye which had initially been suspected to be a papilloma based on clinical findings. The mass was excised and a histopathological diagnosis of "acute bullous inflammation with granulation tissue" was made. The lesion relapsed 10 months later which necessitated repeat resection along with corneoscleral patch grafting. Histopathological studies of the excised lesion led to a final diagnosis of LCH.
Conclusion: To the best of our knowledge, this is the second report of a rare presentation of LCH in the limbus which recurred after excision of the primary mass. The recurrent lesion was diagnosed based on histopathology and managed accordingly.

Keywords: Langerhans Cell Histiocytosis; Limbal Mass; Histopathology

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INTRODUCTION

Langerhans cell histiocytosis (LCH) is a relatively rare disorder characterized by monoclonal proliferation of histiocytes. The condition can be unifocal with involvement of a single organ, or multifocal presenting as disseminated disease. Unifocal involvement is the most common presentation of LCH and the bone is the most frequently affected tissue.[1] Ocular involvement can be observed in 1% to 20% of LCH cases.[2] The condition may primarily involve the orbit, eyelid, epibulbar conjunctiva, cornea, iris, vitreous, choroid and optic nerve, or secondarily infiltrate ocular tissues from surrounding structures.[3,4] Intraocular involvement by LCH has rarely been reported in Letterer-Siwe disease.[5] The orbit is usually involved with unifocal LCH, which has a distinct tendency for the superotemporal bone at the rim of the orbit.[6] The limbus can rarely be involved in unifocal LCH presenting clinically as an infiltrative solitary limbal nodule which may be misdiagnosed as amyloidosis, fibrous histiocytoma, lymphoma, and juvenile xanthogranuloma.[2,7]

The diagnosis of LCH is based on characteristic histopathological features. Electron microscopy may also assist the diagnosis by demonstrating intracytoplasmic inclusions named Birbeck granules.[1]

The natural course of untreated LCH varies from progressive and fatal systemic disease to localized self-limited lesions.[8] Local resection for unifocal involvement and systemic

chemotherapy for extensive multifocal lesions have been proposed as treatment modalities in LCH,[9] however spontaneous regression has been reported in some unifocal LCH cases.[1]

Herein, we report a case of unifocal LCH presenting as an unusual limbal lesion which recurred after primary excision.

CASE REPORT

A 24-year-old man was referred to our center for a recurrent and painless limbocorneal lesion in his left eye. The primary lesion had been removed 10 months earlier with a clinical impression of limbal papilloma at another eye care center. The histopathological diagnosis had been "acute bullous inflammation with granulation tissue" composed of scattered single- and multi-nucleated histiocytes.

Uncorrected visual acuity was 20/20 in the right eye and 20/80 in the involved left eye. On slit lamp biomicroscopy, there was an elevated vascular mass extending from the temporal limbus to the central cornea in the left eye. Intraocular pressure was within normal limits and fundus examination was unremarkable.

With a clinical diagnosis of a recurrent limbocorneal papillomatous/dermoid-like lesion, the patient underwent mass resection together with corneoscleral patch grafting and lateral tarsorrhaphy. The excised specimen was fixed in 10% formalin and sent for histopathology. Slit lamp photography was overlooked preoperatively since the lesion was thought to be a simple recurrent limbal papilloma.

After surgery the patient received topical betamethasone 0.1% and chloramphenicol 0.5% eye drops along with non-preserved lubrication four times a day for four weeks.

On gross histopathological examination, the excised mass was cream-colored and lobulated, measuring 14×8×4 mm. Light microscopy disclosed non-keratinized stratified squamous epithelium overlying a diffuse inflammatory background composed of nests and clusters of large histiocytes with indented and grooved nuclei intermixed with lymphocytes, plasma cells and eosinophils (Figures 1A and 1B). The

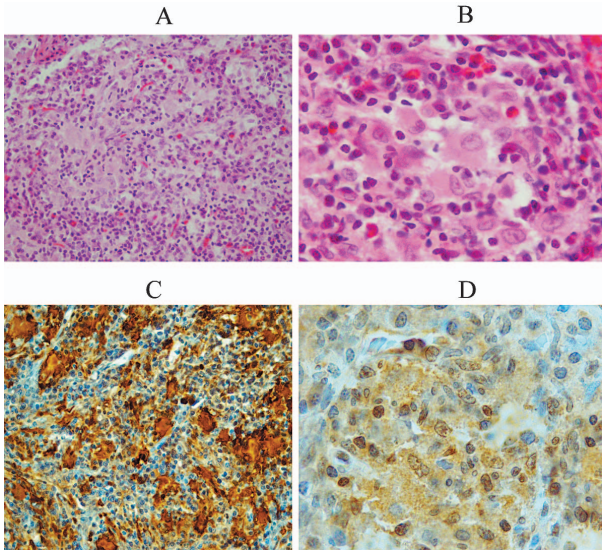

Figure 1. A and B; note the presence of large histiocytes with indented and grooved nuclei intermixed with lymphocytes, plasma cells and eosinophils [hematoxylin and eosin stain; magnification ×200 (A) and ×1000 (B)]. C; note strong immune reactivity of the histiocytic cell population for S-100 protein (magnification ×200). D; the histiocytes are immune reactive for CD1a (magnification ×1000).

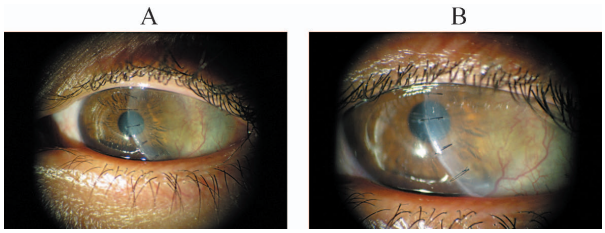

Figure 2. Note the absence of recurrence four months after tumor resection and limbocorneal patch graft with a satisfying cosmetic result.

histiocytes were strongly immune reactive for S-100 protein (Fig. 1C) and moderately for membrane based CD1a immune staining (Fig. 1D).

The histopathological features were characteristic of LCH with incomplete surgical excision. During follow-up and after four months, no signs indicative of recurrence were observed and the appearance was cosmetically acceptable (Figures 2A and 2B).

DISCUSSION

LCH results from proliferation of Langerhans cells normally present in the epidermis.[10] The

condition is characterized by a wide clinical spectrum varying from spontaneous regression to rapid progression, recurrence and long-lasting sequelae.[11] LCH encompasses three main clinical subtypes; unifocal LCH (eosinophilic granuloma), multifocal LCH (Hand-Schuller-Christian disease) and systemic LCH (Abt-Letterer-Siwe disease).[1] Younger patients with LCH, have a predisposition for multifocal involvement.[12]

The etiology of LCH remains unclear but immune dysregulation with different cytokines has been postulated.[1] The orbit is the most common site of involvement in the eye which often includes the orbital diploe.

Light microscopy reveals tumor cells as large histiocytes with grooved nuclei. Mononuclear histiocytes and multinucleated giant cells are intermixed with eosinophils, lymphocytes, plasma cells and neutrophil polymorphs.[10] Langerhans cells are immune reactive for S-100 protein and CD1a.[1] Electron microscopy demonstrates "tennis racket" shaped cytoplasmic inclusions named Birbeck granules in histiocytes which are the gold standard for a diagnosis of LCH.[1,12]

Treatment options for unifocal lesions include observation, partial or complete resection, combined resection and low dose radiation, and intralesional corticosteroids. Systemic chemotherapy may be indicated for extensive multifocal and systemic lesions.[1,9]

To the best of our knowledge, after the report by Saxena et al[2], our patient is the second case of unifocal limbal LCH presenting as a recurrent solitary vascularized nodule. Despite the presence of mono- and multi-nucleated histiocytes amongst the intrastromal inflammatory cell infiltrates on histopathological examination of the primary lesion, LCH was not diagnosed initially which might be due to the very rare presentation of this condition in the limbocorneal area.

Differential diagnoses for limbocorneal LCH include dermoid, amyloidosis, fibrous histiocytoma and juvenile xanthogranuloma.[2] In our case, a limbal papilloma was the initial clinical diagnosis which should be added to this list.

There is only a single case report of limbal LCH in which the patient remained asymptomatic for a while after complete excision of the primary lesion, but the tumor recurred 15 months afterwards.[2,7] Based on clinical and histopathological evaluations, the recurrent tumor partially responded to combination chemotherapy and the patient was clinically stable for 5.5 years.[7] In our case, recurrence developed 10 months after resection of the primary lesion for which repeat resection together with corneoscleral patch grafting were performed and the patient has been tumor-free up to 4 months.

Although Bakhshi et al[7] stated that surgery or radiotherapy for unifocal ocular involvement improves function or cosmesis, the functional and cosmetic outcomes of surgical intervention alone were also favorable in our patient. The other treatment option for limbal LCH is chemotherapy. Theoretically due to poor penetration of chemotherapeutic agents into the corneal side of the tumor, such treatment may be associated with a partial response.[7] Whether surgical therapy, in the form of resection of the recurrent lesion along with a limbocorneal patch grafting, is associated with a low risk of recurrence or not requires longer follow-up.

In summary, herein we report the second case of recurrent limbocorneal LCH which had missed correct diagnosis on initial histopathological studies. The recurrent lesion was managed surgically which included mass resection and a limbocorneal patch grafting, with satisfying cosmetic and functional results.

Conflicts of Interest

None.

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