Langerhans’ cell Histiocytosis of the Eyelid: a rare case report

Histiocitose de células de Langerhans palpebral: relato de caso raro

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ABSTRACT
The Langerhans’ Cell Histiocytosis (LCH) is a group of disorders caused by clonal proliferation and accumulation of these cells in various organs, such as skin, hematopoietic or lymphoid tissues, lungs, liver, hypothalamus and bones. The eyelid presentation is extremely rare. Here, we report a case of a skin-limited upper eyelid LCH. The 35-year-old woman presented solid crusted nodule on the left upper eyelid margin, causing the misdirection of some of the adjacent eyelashes with progressive growth for 1 year. Excisional biopsy was performed, and histological analysis revealed histiocytes with eosinophilic cytoplasm, immunohistochemical positivity for S-100, laminin and CD1a, which showed LCH. Though rare, the skin-limited LCH should be included in the differential diagnoses of tumoral lesions of the eyelid.

Keywords: Histiocytosis; Eyelid, Langerhans Cells.

RESUMEN
A histiocitose de células de Langerhans (LCH) abrange um grupo de desordens caracterizadas pela proliferação clonal e acúmulo dessas células em vários órgãos como pele, tecidos hematopoiéticos ou linfóides, pulmões, figado, hipotálamo e ossos. A apresentação de lesão palpebral é extremamente rara. Aqui, relatamos um caso de LCH de pápebra superior limitada à pele. Uma paciente de 35 anos apresentou um nóculo sólido com crosta na margem da pápèbra superior esquerda, causando mal direcionamento de alguns dos cílios adjacentes com crescimento progressivo durante um ano. Biópsia excisional foi realizada e a análise histológica revelou histiócitos com citoplasma eosinofílico, positividade imunoistoquímica para S-100, laminina e CD1a, revelando LCH. Embora rara, a LCH limitada à pele deve ser incluída nos diagnósticos diferenciais de lesões tumorais palpebrais.

Palavras-chave: Histiocitose; Pálpebras; Células de Langerhans.

RESUMO
A histiocitose de células de Langerhans (HCL) abrange um grupo de desordens caracterizados pela proliferação clonal e acúmulo de dichas células en varios órganos, como piel, tejidos hematopoyético o linfóide, pulmones, hígado, hipotálamo y huesos. La presentación de lesión palpebral es extremadamente rara. Aquí, relatamos un caso de HCL de párpado superior limitada a la piel. Una paciente de 35 años presentó un nódulo sólido con crosta en el margen del párpado superior izquierdo, causando mal direccionamiento de algunas de las pestañas adyacentes con crecimiento progresivo durante un año. Se ha realizado la biopsia excisional y el análisis histológico ha indicado histiocitos con citoplasma eosinófilo, positividad inmunohistoquímica para S-100, laminina y CD1a, indicando HCL. Aunque rara, la HCL limitada a la piel debe incluirse en los diagnósticos diferenciales de lesiones tumorales palpebrales.

Palavras Clave: Histiociotose; Párpados; Células de Langerhans.

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Histiocytosis are macrophages and dendritic cells proliferative lesions and can cause a wide range of systemic disorders. Langerhans cells are an immature type of dendritic cells typically present in skin and mucosa that play an important role in immune responses. The Langerhans’ Cell Histiocytosis (LCH), also called Histiocytosis X, is a group of disorders caused by clonal proliferation and accumulation of these cells in various organs, such as skin, hematopoietic or lymphoid tissues, lungs, liver, hypothalamus and bones. Typically described in children, its course ranges from benign spontaneous involution to systemic failure. The eyelid presentation has rarely been reported, few of them in adults. We present herein a case of this uncommon eyelid margin diagnose.

**CASE REPORT**

Female, 35 years old, presented solid crusted nodule on the left upper eyelid margin (Figure 1), causing the misdirection of some of the adjacent eyelashes. The lesion had been growing for 1 year. The patient denied other similar lesions along the body and, except for hypothyroidism, she did not report any personal or familial antecedents of interest. BCVA 20/20 in both eyes. Other ophthalmic examination results were within normal ranges. Excisional biopsy was performed. The anatomopathological analysis revealed histiocytes with eosinophilic cytoplasm, immunohistochemical stains for S-100, laminin and, more remarkably, positivity to CD1a (Figure 2). Given those findings, the diagnosis of LCH was made.

**Figure 1.** The biomicroscopic aspect of the lesion: solid nodule with a crust on its inferior surface, on the upper left eyelid. Magnification: 10 ×.

**Figure 2.** The histological sections of the lesion. A) Hematoxylin-eosin showing eosinophilic cells in a lymphocytic background; B) Immunohistochemical positivity to CD1a. Magnification: 10 ×.
DISCUSSION

Histiocytes are cells of the reticuloendothelial system and include macrophages, dendritic cells and Langerhans cells (LC). The LC are usually characterised by the presence of Bierbeck granules, organelles supposedly involved in antigen internalization\(^4\). LC normally occur in body surface, such as epidermis, conjunctiva and corneal limbus. They are rare in healthy tarsal conjunctiva. However, LC are numerous in subconjunctival tissue and eyelid margin skin of patients with allergic conjunctivitis\(^5\).

Nodular lesions of the eyelid are among the most frequent abnormalities of the periorcular area. The base of the eyelashes is an usual spot for eccrine hydrocistoma, chalazion, sebaceous cyst, siringoma, xanthelasma, epidermal inclusion cyst and malignant tumors. Differential diagnosis is paramount for the correct treatment and follow-up and is made both clinically and histologically. The LCH however, is exceptionally located in this site. We were not able to find more than 6 case reports of the tumor in the eyelid, and only one in the upper [3,4,6-9].

The LCH was first described in 1893 by Alfred Hand Jr, who observed exophthalmia, hepatosplenomegaly, lymphadenopathy and diabetes insipidus. Throughout the twentieth century, other contributors shed light on the various aspects of the disease, although the nature of the physiopathology is yet to be unveiled\(^2\). As the pathogenesis is poorly understood, different origins for the disease have been postulated. Viral infection, immune dysfunction and malignancy have already been suggested as mechanisms for the development of the disease. Some association with thyroid disease have also been demonstrated\(^4\). Recently, the discovery of frequent oncogenic BRAF mutations in LCH supports its classification as neoplasm\(^10\).

The peak of incidence of LCH occurs between 1-4 years, however, it may present at all ages. With an estimated incidence of 4.0-5.4 cases per million children, its epidemiological data is difficult to attain due to the rarity of the disease\(^11\). In addition, LCH seems to be underdiagnosed as it can be symptomless or mistaken for other disorders\(^12\).

The LCH affects most frequently the osseous, pulmonary, mucocutaneous, thalamic and lymphatic tissues\(^13\). In the ophthalmic practice, the disorder involves more frequently in the orbit, accounting for less than 1% of the orbital tumefactions. The typical presentation is of a slowly growing upper palpebral swelling over a period of weeks to months. Acute presentation is rare, usually appearing due to inflammatory response to the lesion, and can be confused with periorbital cellulitis or dacryoadenitis. Proptosis, nerve palsies, papilledema and cavernous sinus syndrome can be found in orbital disease\(^14\). The occurrence of LHC in the lacrimal gland of the adult was reported\(^15\). The eyelid is rarely affected.

Histological examination reveals cells with abundant eosinophilic cytoplasm, and background eosinophils, lymphocytes, histiocytes and neutrophils present in variable quantities. The immunophenotype of LCH includes expression of CD1a, S100 protein and langerin (CD207). The differential diagnosis includes Langerhans cell sarcoma, other histiocytic lesions and lymphoma. The immunohistochemical and morphologic features described are generally enough to diagnose\(^16\).

The multisystem disease treatment is protocol based and dependent on a number of variables. Complete excision of the lesion may be curative for focal cutaneous disease. Steroids, nitrogen mustard of psoralen combined with ultraviolet A (PUVA) are second-line options. Radiation therapy is an option when the lesions are recurrent or progressive\(^4\). The lesions may progress to chronic or relapsing process with spontaneous remission or treatment. Skin-limited LCH has excellent overall prognosis\(^17\).

As this case report demonstrates, the LCH can be skin-limited and found in exceptional locations as the eyelid. Thus, it should be considered as a differential diagnose towards tumoral lesions of the eyelid.

REFERENCES

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