Primary Cutaneous CD30-Positive T-cell Lymphoma of the Eyelids

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Abstract

A case of a cutaneous CD30-positive pleomorphic T-cell lymphoma primarily involving both the upper and lower left eyelids of a 50-year-old man is reported. A firm, partly ulcerated mass was the initial and only clinical sign. Histopathologic examination of a shave biopsy revealed atypical neoplastic cells in close relation with epidermal appendages, suggesting epithelial derivation of the lesion.

Nevertheless, the results of the immunohistochemical testing disclosed diffuse reactivity for T-cells and CD30 positivity in more than 70% of neoplastic cells, thus supporting the diagnosis of a CD30-positive lymphoma, T-cell phenotype. The diagnosis of this entity is particularly challenging, especially at such a site, since primary ocular adnexal non-Hodgkin lymphomas are virtually of B-cell type. The differential diagnosis and a review of the relevant literature are presented.

INTRODUCTION

Most of ocular adnexa lymphomas bear a close relationship to MALT lymphoma and are low-grade B-cell tumors deriving from the marginal zone B-cell. High-grade lymphomas of the ocular adnexa are distinctly uncommon. T-cell origin in primary lymphomatous lesions of the eyelid is indeed rare₁. CD30 represents a differentiation antigen whose expression is associated with activation of lymphoid cells; its immunohistochemical staining with the recent antibody of choice in diagnostic pathology (ie, monoclonal antibody Ber-H2) usually results in specific, circumferential membranous and paranuclear dot-like positivity.

CD30-positive primary cutaneous anaplastic or pleomorphic large cell lymphoma (C-ALCL) belongs to the spectrum of CD30-positive T-cell lymphoproliferative disorders, originating from transformed or activated CD30-positive Tlymphocytes. Some of these lesions have ambiguous clinical and histological features and are referred as borderline lesions₁.

CASE REPORT

A 59-year-old man was admitted to the hospital for evaluation of a severe erythematous swelling of both the upper and lower left eyelids and the cheek, which had been rapidly enlarged for the last 2-3 weeks. Medical and family histories were unremarkable.

In the clinical examination, there was a large (1.8X1.5X0.7 cm), raised, firm, nodular mass located mainly in the lower left eyelid, with extensive ulceration and hemorrhage. It was surrounded by severe edema. Visual acuity was unaffected and bulbar movements were not significantly restricted; the eye did not appear to be infiltrated by the mass. Physical examination did not reveal any peripheral lymphadenopathy or hepatosplenomegaly. Before the final diagnosis was made, material from the ulcerated area was cultured and fungi of Candida Albicans type was found. According to this, the patient went under amphoterikine.

Biopsies from both eyelids were taken. Hematoxylin and eosin sections showed partly necrotic and ulcerated, severely inflammed skin specimens. In the dermis, there was a diffuse infiltration of solid sheets of atypical cells, displaying foci of angiocentric growth pattern (Figure 1). The cells were large, pleomorphic, with hyperchromatic nuclei, while atypical mitotic figures were frequent. Some foci of keratinization, perineural distribution and sebaceous differentiation (Figure 1) were suggested. The above features were indicative of a neoplasm deriving from the sebaceous glands.

Figure 1

Figure 1: Diffuse infiltration of malignant cells around blood vessel and adnexal structures. Remnans of sebaceous glands giving the erroneous impression of sebaceous differentiation of neoplastic cells (Haematoxylin-Eosin, X100)



Immunohistochemically, the neoplastic cells, however, were negative for markers of epithelial origin [pancytokeratin and epithelial membrane antigen (EMA)] as well as for the melanoma antigen HMB-45. Some tumour cells showed a weak positivity to S-100 protein, while almost all reacted positively for common leucocyte antigen (CLA). Additional immunohistochemistry was performed and the lymphoid cells showed negative B-cell immunophenotype [L26 (-), I light chain (-)]. They reacted positively for T-cell markers [CD45RO (UCHL₁) and CD3], CD30 [ki-1, clone Ber-H₂, positivity in clusters of more than 70% of tumour cells in total] (Figure 2), but they were negative for anaplastic lymphoma kinase (ALK) and natural killer cell marker CD56.

Figure 2

Figure 2: CD30-immunoreactive neoplastic cells invading the epidermis (Immunoperoxidase stain, X400)



All these features were compatible with non-Hodgkin lymphoma of large, pleomorphic, CD30-positive T-cells, possibly of primary cutaneous type, with angiocentric growth pattern and epitheliotropism, which was the final diagnosis. A bone marrow aspiration biopsy and a CT-scan followed and failed to show any other tumourous lesion, thus confirming the primary origin of the lesion.

The patient went under radiotherapy, as further excision would result in a severe deformity of the eyelids with functional problems, and the clinical improving was impressive.

DISCUSSION

When the ki-1 antibody was first described in 1982, it was believed to be specific for Reed-Sternberg cells of Hodgkin lymphoma. However, in the last two decades, studies have shown that there are more ki-1 positive benign or malignant lesions, including primary cutaneous CD30-positive T-cell lymphoproliferative disorders_{2,33}. The latter account for approximately 20-25% of T-cell lymphomas primarily arising in the skin_{1>4>5}. Most lymphomas primarily involving the eyelid are of B-cell origin. With regard to T-cell lymphomas, mycosis fungoides represents the most common (secondary) manifestation of T-cell lymphomas in the ocular adnexa. Only a few cases of primary cutaneous anaplastic CD30-positive T-cell lymphoma, located in the eyelid, have been reported in the literature_{67>8}.

The most interesting differential diagnostic problem in the present case was the exclusion of a carcinoma arising from the sebaceous glands. Histologically, the impression of focal keratinization and sebaceous differentiation of neoplastic cells (Figure 1), made us really concerned and could lead, without the help of immunohistochemistry, up to an incorrect diagnosis and therapy. In contrast to the generally favourable outcome of patients with primary cutaneous-type lymphoma, patients with sebaceous gland carcinoma are characterized by a very poor prognosis and therefore require aggressive therapy. On the basis of the lymphoid immunophenotype of the lesion and with a careful subsequent evaluation of the morphological features, the erroneous impression of focal epithelial differentiation of the neoplastic cells was due to the lymphoma's epidermotropic invasive growth pattern, which, however, is referred as a rare feature of this type of lymphoma₁; to the best of our knowledge, epidermotropism of lymphomatous cells has not been reported in any T-cell lymphoma of the eyelid.

As far as primary cutaneous lymphoid lesions are concerned, differential diagnosis should be made between CD30(+) large cell lymphoma and lymphomatoid papulosis. In the present case, the clinical, morphological and histological features, i.e. the increased number and the clustering growth pattern of CD30(+) cells, were diagnostic for lymphoma_{1,5}.

Furthermore, the distinction of the primary cutaneous anaplastic CD30-positive T-cell lymphoma from systemic anaplastic large cell lymphoma (ALCL) with cutaneous involvement and secondary high-grade lymphomas with CD30 expression is very important clinically; a thorough examination for their exclusion had been required so that appropriate treatment was given.

Studies have shown that primary CD30-positive cutaneous T-cell lymphomas frequently exhibit a cytotoxic T-cell phenotype, expressing cytotoxic proteins, such as perforin and granzyme B. This finding suggests a strong correlation between expression of the CD30 molecule and cytotoxic mediators_{9,10}. In addition, in primary cutaneous CD30positive T-cell lymphoproliferative disorders, anaplastic lymphoma kinase (ALK) gene products are not detectable or are only rarely detected_{11,12}. In the present case, the lymphomatous cells were negative for ALK gene products. Primary cutaneous CD30-positive T-cell lymphoproliferative disorders have also been analyzed for the presence of Epstein-Barr virus with negative results₁₁₂₁₃₁₄.

Although the prognosis of the primary cutaneous CD30positive anaplastic T-cell lymphoma is favorable with a 5year survival rate of approximately $90\%_{15}$, a continued clinical follow-up for local recurrence or extracutaneous dissemination is always required.

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