The histology at 6 weeks was not diagnostic of pyoderma gangrenosum; this biopsy was, however, performed on a healing lesion. From the second biopsy a diagnosis of lymphomatoid papulosis was made (Figs 3 and 4). High dose tetracycline, 1 g twice daily, seemed initially to reduce the number of recurrences and allow recurrent lesions to resolve more quickly. After 4 months, tetracycline lost any apparent effectiveness and low dose methotrexate, 2.5 mg weekly was introduced, with some benefit.

COMMENT

The ulcer of pyoderma gangrenosum is unusually shallow and solitary, non-tender, and resolves over 5–6 weeks to leave a small white scar. In Panayi's review of 21 cases involved the eyelids. Positive cultures for Staphylococcus aureus are usually obtained. All other investigations, including syphilis serology, are negative.

Lymphomatoid papulosis was first described by Macleay as a chronic, recurrent, self-healing papulonodular or papulosquamous eruption, 'histologically malignant but clinically benign'2. The lesions regress spontaneously over several weeks, but recur every few months. Investigations are essentially normal.3

Ten per cent of patients with lymphomatoid papulosis may develop a cutaneous or systemic lymphoma, including mycosis fungoides, Hodgkin's disease, lymphoepithelial lymphoma, large cell lymphoma, and lethal midline granuloma.4 There are no predictive markers for this progression. The presence of atypical cells against a setting of follicular mucinosis has until now been routinely associated with a cutaneous T cell lymphoma. So far the patient has exhibited self-healing necrotic lesions only. Whether the presence of follicular mucinosis in this situation will turn out to be a poor prognostic sign remains to be seen.

The treatment of these patients is unsatisfactory. Steroids and antibiotics are ineffective. Complete, but often transient, remissions have been achieved with electron beam therapy, combination chemotherapy, PUVA, and methotrexate.5 Long term follow-up is mandatory.

Although four cases of follicular lymphomatoid papulosis have been reported,6,7 to our knowledge this is the first report of follicular mucinosis in lymphomatoid papulosis and the first report of bilateral symmetrical eyelid involvement as the presenting feature of this condition.

Figure 3 The biopsy shows the edge of a necrotic lesion with a moderately dense superficial and deep mononuclear infiltrate present interstitially and within pilosebaceous structures. (Haematoxylin and eosin, magnification ×10.) Although present perivascularly the infiltrate is particularly targeted on pilosebaceous structures involved follicles showing partial or complete destruction. Many of the cells invading the follicles are large, atypical, and contain hyperchromatic nuclei. Several of the partially disrupted follicles contain cystic spaces which stain positive for mucin.

Staphylococcus aureus was isolated from the preauricular lesion only. Mycobacterial and viral cultures, and syphilis serology were negative. A full blood count was normal, and random blood glucose was 3.6 mmol/l.

A diagnosis of pyoderma gangrenosum was made, and flucloxacillin continued for a further 2 weeks.

The lesions healed in 4 weeks, leaving flat, mildly atrophic scars. Six weeks after the initial presentation, four further papulonecrotic lesions appeared; in the left preauricular region, on the right side of the neck, and on both medial canthi. These were biopsied. At 4, 9, and 11 months after presentation, there were recurrences of self-healing multiple necrotic papules. A further biopsy was performed at 4 months.

Human papillomavirus DNA detected in case of inverted squamous papilloma of the lacrimal sac

EDITOR.—We present the first known report in which an inverted squamous papilloma of the lacrimal sac was associated with human papillomavirus (HPV). While squamous papillomas of the nasal cavity and paranasal sinuses are not uncommon, an inverted squamous papilloma that originates in the epithelium of the lacrimal sac is rare. Inverted papillomas of the lacrimal sac often reveal areas of invasive acanthosis of surface epithelium into the underlying stroma and show foci of carcinoma or foci that develop into carcinoma.1 We present a young patient with inverted squamous papilloma of the lacrimal sac in whom we identified HPV antigen and DNA within the dysplastic lesion.

CASE REPORT

A 26-year-old Japanese woman who had noticed 15 months earlier a painless swelling of the left lower eyelid that gradually increased in size was admitted to our clinic. She presented with a medial canthal mass associated with epiphora and discharge. Magnetic resonance imaging (MRI) revealed a lobular tumour that totally filled the lumen of the left lacrimal sac (Fig 1). On 9 July 1993, the tumour was resected under general anaesthesia. The solid tumour found within the lacrimal sac appeared to be continuous with the nasal cavity, presenting its total removal from the bony tract of the nasolacrimal duct. Postoperative MRI examination 2 months later showed no residual tumour within the nasolacrimal duct. Macroscopically, the tumour showed a lobular pattern and was surrounded totally by the...
Figure 1 TI weighted magnetic resonance image shows a lobular tumour within the lacrimal sac.

Figure 2 Histological examination reveals an inverted squamous papilloma that originated from the wall of the lacrimal sac. (Haematoxylin and eosin staining x13.)

Figure 3 Micrograph of tumour cells. There is mitotic activity and koliocytosis, especially near the surface of the tumour. (Haematoxylin and eosin staining x86.)

Figure 4 Micrograph of tumour cells. Cells near the surface of the tumour are positive for anti-HPV antibody immunohistochemical staining (x86).

Figure 5 Micrograph of tumour cells (x45). The nuclei of the tumour cells near the surface are positive for a wide spectrum HPV fluorescein-labelled DNA in situ hybridisation probe.

lumen of the lacrimal sac. Histologically, we observed an inverted squamous cell papilloma with dysplastic change, marked mitotic activity, and koliocytosis in the cells near the tumour surface (Figs 2, 3). The superficial epithelial tumour cells were positive for anti-HPV antibody (Dako Corporation, USA) including types 6, 11, 16, 18, 30, 31, 33, 35, 45, 51, and 52 HPV (Fig. 5). Cells were negative for a type 6/11 probe. Fluorescein staining of the nuclei of tumour cells was stronger in the superficial epithelial cells than the deeper cells. Follow-up at 10 months showed no clinical or radiological evidence of any recurrence.

COMMENT

Primary tumours of the lacrimal sac are rare. Most of them are benign, including adenomas and papillomas. The latter may be exophytic or inverted. Inverted papilloma can be readily transformed into carcinoma, even in a young adult. Anderson et al recently reported a 36-year-old patient with transitional cell carcinoma arising from an inverted papilloma.

In our case, epithelial dysplasia that displayed cytoplasmic clearing along with nuclear pyknosis and koliocytosis suggested HPV infection as an aetiology, since koliocytosis in squamous papilloma is commonly found in lesions associated with HPV. Based on the histopathological findings in this case, we conducted an immunohistochemical and molecular biological investigation of HPV in the lesion, which revealed HPV DNA. Previous studies have shown that ocular conjunctival squamous papilloma may be related to HPV types 6 and 11, and, squamous dysplasia or carcinoma to HPV type 16.

HPV antigens and DNA types 16, 18, 31, 33, and 35 have been identified within squamous dysplastic changes or carcinomas affecting the female reproductive tract. Such findings suggest an oncogenic potential of HPV infection. In the present case, HPV was, thus, probably responsible for squamous papilloma with dysplastic changes of the lacrimal sac. The mode of transmission of HPV to the epithelium of the lacrimal sac is unknown, but it could occur during passage of a fetus through the infected birth canal.

Ophthalmologists should be alert to the possibility of HPV infection, especially in a young adult with lacrimal sac papilloma, as this disorder may have oncogenic potential.

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