8. Edelstein C, Shields JA, Shields CL, De Potter P, Eagle RC, Turtel L, Hagstrom N. Non-African Burkitt lymphoma presenting with oral thrush and an orbital mass in a child. Arch Ophthalmol 1998;124:859–61.

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Sir,

Watery eye: a new side-effect of isotretinoin therapy

Isotretinoin (13-*cis*-retinoic acid), a synthetic vitamin A analogue, is commonly used in the treatment of severe acne. It is associated with a number of adverse reactions, and its teratogenicity is well known. Common ocular side-effects include blepharitis, conjunctivitis, dry eyes, contact lens intolerance, and corneal opacitieis.[1] We report a case of epiphora due to lacrimal punctal occlusion association with isotretinoin therapy; as far as we are aware, this side-effect has never been described before.

Case report

A 19-year-old Caucasian man presented with a 2 month history of watery right eye. He had no previous ophthalmic problems. He had been commenced on isotretinoin 4 months previously for severe acne, and was on no other medications. The course of treatment was for 12 months.

Examination revealed an occlusion of the right superior lacrimal punctum (Fig. 1), while the lower punctum was open (Fig. 2). The nasolacrimal duct was

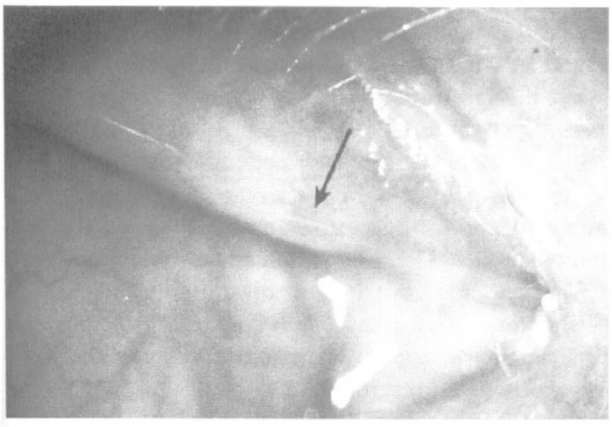

Fig. 1. *Occluded right superior lacrimal punctum (arrow).*

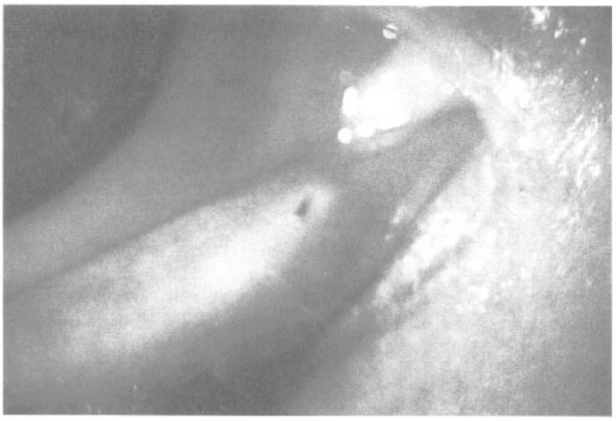

Fig. 2. *Normal inferior punctum.*

patent to syringing. Meibomian glands appeared normal in both eyes. Schirmer's test showed no reduction in tear production. His skin was noted to be very dry, with significant scaling.

In consultation with his dermatologist, the isotretinoin treatment was suspended. The lacrimal punctum remained occluded 6 months after stopping the medication, and his epiphora was only marginally improved. We suggested opening the punctum and intubating the canaliculi with silicone tubing. However, the patient declined further intervention at this stage.

Comment

Although its exact mechanism of action is not known, isotretinoin works in the treatment of acne by reducing sebaceous gland size and sebum production in the skin.[2] It has a similar effect on the Meibomian glands of the eyelids.[3] This is thought to account for the commonly observed ocular side-effects of dry eyes and blepharoconjunctivitis.

This case was unusual because the patient developed a unilateral watery eye instead. An occluded lacrimal punctum accounted for his symptoms. The mechanism by which this had occurred is uncertain. Isotretinoin has been used in the treatment of certain keratinising dermatoses,[4] and *in vitro* studies have demonstrated that isotretinoin can modify epithelial differentiation by modulating keratin expression.[5] It is therefore possible that punctal occlusion resulted from increased keratinisation of the lacrimal canaliculus. Further evidence to support this came from histological studies in acne patients treated with isotretinoin, showing that pilosebaceous units in the skin were sometimes replaced by an epidermal-like cord.[2]

Unlike other ocular side-effects of isotretinoin, most of which are reversible upon cessation of therapy,[1] lacrimal punctal occlusion appears to be irreversible in this case. It remains speculative as to whether early recognition of the problem and discontinuation of treatment might have resulted in spontaneous re-opening of the punctum. Dermatologists and ophthalmologists should be aware that such a complication can occur with isotretinoin.

None of the authors had any commercial interest in the findings presented.

References

1. Faunfelder FT, LaBraico JM, Meyer SM. Adverse ocular reactions possibly associated with isotretinoin. Am J Ophthalmol 1985;100:534–7.
2. Jones H, Blanc D, Cunliffe WJ. 13-*cis*-retinoic acid and acne. Lancet 1980;II:1048–9.
3. Mathers WD, Shields WJ, Sachdev MS, Petroll WM, Jester JV. Meibomian gland morphology and tear osmolarity: changes with Accutane therapy. Cornea 1991;10:286–90.
4. Peck GL, Yoder FW. Treatment of lamellar ichthyosis and other keratinising dermatoses with an oral synthetic retinoid. Lancet 1976;II:1172–4.
5. Zouboulis CC, Korge B, Akamatsu H, Xia L, Schiller S, Gollnick H, Orfanos CE. Effects of 13-*cis*-retinoic acid, all-*trans*-retinoic acid, and acitretin on the proliferation, lipid synthesis and keratin expression of cultured human sebocytes *in vitro*. J Invest Dermatol 1991;96:792–7.

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Sir,

Proteus syndrome: a variant with eye involvement

Proteus syndrome (PS) is a rare neurocutaneous syndrome wherein epidermal naevi are associated with disproportionate overgrowth phenomena, tumours, and occasionally vascular malformations and facial dysmorphism.[1]

We present a young girl with PS and outline the clinical features and differential diagnosis. Besides skin lesions, hemihypertrophy and hemimegalencephaly, she demonstrated eye changes, severe psychomotor retardation and resistant seizures. Association with ocular anomalies has not been reported previously.

Case report

A 15-month-old infant girl, born to consanguineous parents, presented with progressive left-sided hemihypertrophy and delayed development since birth. There was no history of similar illness in the family. Prominent features on examination were linear hyperpigmentation (more on the left side of the trunk and face) and somatic hemihypertrophy (left half of the body and face was larger than the right). The skin lesions were flat and soft, and had a distinct linear pattern (Fig. 1). The infant showed global delay in development

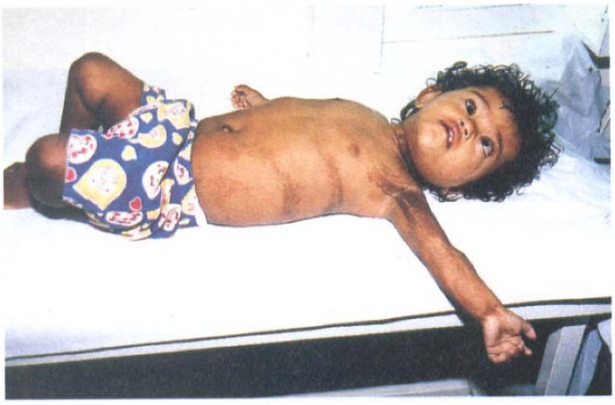

Fig. 1. *Photograph of an infant with Proteus syndrome showing the characteristic skin changes and left-sided hemihypertrophy.*

(development quotient 66%) and was hypotonic, but had no focal neurological deficit. The head circumference was 44 cm (< 3rd centile) and the left half of the skull was larger than the right.

Ocular abnormalities were observed; these were limited to the left side, with the left eyeball being larger than the right, resulting in a severe degree of myopic anisometropia and amblyopia. There was a conjunctival capillary haemangioma in the left eye. The cornea was large but clear and the intraocular pressure was normal. The left optic disc was large with an eccentric coloboma. A trial of spectacles with patching was instituted; this therapy was eventually terminated due to poor patient compliance and lack of any objective benefit.

Computed tomography of the brain revealed left hemimegalencephaly and a spinal radiograph demonstrated thoracic kyphoscoliosis. An ultrasound scan of the abdomen, echocardiography and electroencephalography were normal. Skin biopsy showed papillary hyperplasia of the epidermis, hyperkeratosis and acanthosis with elongation of rete ridges, thus confirming the clinical diagnosis of epidermal naevus.

Comment

Five well-defined syndromes have been described in association with epidermal naevi, namely Schimmelpenning (naevus sebaceous) syndrome, naevus comedonicus syndrome, pigmented hairy epidermal naevus syndrome, Proteus syndrome (PS) and CHILD syndrome.[2] These are distinguished by the type of skin lesions, the spectrum of associated anomalies and inheritance pattern.[3]

PS is characterised by the presence of soft, velvety, flat and non-organoid epidermal naevi, with histological features of hyperorthokeratosis, acanthosis and papillomatosis.[3,4] Connective tissue naevi when present are pathognomonic but are not obligatory for diagnosis.[5] The skin lesions are associated with partial gigantism of limbs, hemihypertrophy, asymmetrical macrocephaly or disproportionate overgrowth of viscera.[6] Hemimegalencephaly is a rare congenital brain anomaly due to a hamartomatous overgrowth and has been