References

1 Lindén C, Alm A. Prostaglandin analogues in the treatment of glaucoma. *Drugs Aging* 1999; **14**: 387–398.
2 Hedner J, Everts B, Mollers CS. Latanoprost and respiratory function in asthmatic patients. *Arch Ophthalmol* 1999; **117**: 1305–1309.
3 Lai J, Jin H, Yang R, Winer J, Li W, Yen R *et al*. Prostagladin $F_{2\alpha}$ induces cardiac myocyte hypertrophy *in vitro* and cardiac growth *in vivo*. *Am J Physiol* 1996; **271**: 2197–2208.
4 Rao TS, Seth SD, Nayar U, Manchanda SC. The vagal involvement in the antiarrhythmic and arrhythmogenic effects of prostaglandin F2 alpha on ouabain-induced cardiac arrhythmias in cats. *Life Sci* 1987; **41**: 2363–2372.
5 Shigematsu S, Niwa H, Saikawa T. Vasospastic angina induced by prostaglandin F2 alpha. *Br Heart J* 1993; **69**: 364–365.
6 Besson JM. The neurobiology of pain. *Lancet* 1999; **353**: 1610–1615.
7 Minami T, Bakoshi S, Nakano H, Mine O, Muratani T, Mori H *et al*. The effects of capsaicin cream on prostaglandin-induced allodynia. *Anesth Analg* 2001; **93**: 419–423.
8 Wall PD, Melzack R. *Textbook of Pain*, 4th edn. Churchill Livingstone: New York NY, 1984.

MS Rajan, P Syam and C Liu

Sussex Eye Hospital
Eastern Road
Brighton BN2 5BF, UK

Correspondence: C Liu
Tel: + 44 1273 606 126 ext 7652
Fax: +44 1273 693 674
E-mail: CSCLiu@aol.com

Sir,

Cutaneous latanoprost in the treatment of alopecia areata

Eye (2003) **17,** 444–446. doi:10.1038/sj.eye.6700354

Alopecia areata is thought to be mediated by an autoimmune reaction against the hair follicle or melanocytes.[1] We report a case of a patient who developed alopecia areata and had successful regrowth of her eyelashes after cutaneous treatment with latanoprost.

Case report

An 11-year-old girl was referred to the ophthalmology department with a history of bilateral loss of eyelashes. An incident had occurred $2\frac{1}{2}$ years previously in which she had had an exacerbation of her asthma secondary to a viral illness. During her illness, it was noted by her GP that her eyelashes had fallen out bilaterally, from the upper and lower lids. There was no loss of hair from the scalp/eyebrows or pitting of her nails. She recovered well and a follow-up was arranged with the dermatology department.

During her review, several treatments were tried (eg lid hygiene/massage), but there was no change in the amount and position of lashes present (serial photography at each three-monthly visit). There was no history of any lash growth between appointments. She was on no systemic medication. There was no past or present history or family history of any psychiatric disorders. There was no, history of any obsessive–compulsive behaviour, and interview of the child by herself did not reveal any clinical features suggestive of depression or anxiety[2] or, on direct questioning, to suggest trichotillomania.

Initial slit-lamp examination revealed bilateral loss of eyelashes with no evidence of erosions, crusts, or hair follicle haemorrhage (Figure 1). There was no evidence of inflammatory lid disease or eyelid tumour. Intraocular pressure (IOP) was 10 mmHg in both eyes, and she had light blue irides. She was otherwise systemically well.

Both mother and child were keen on some form of treatment. After a detailed discussion, she was prescribed latanoprost to be used cutaneously, once a day, to all eyelids, to be applied by a dressed orange stick. Serial photography was done. Minimal lash growth was noted on all four lids 4 weeks after application. There was no change in IOP or iris colour. A further 8-week appointment showed pronounced lash growth of all four lids (Figure 2). There was no change in IOP or iris colour. Her treatment was altered to once a week cutaneous use. Follow-up for 6 months has shown maintenance of the number of eyelashes with no alteration in IOP or iris colour. Both mother and child are pleased with the result.

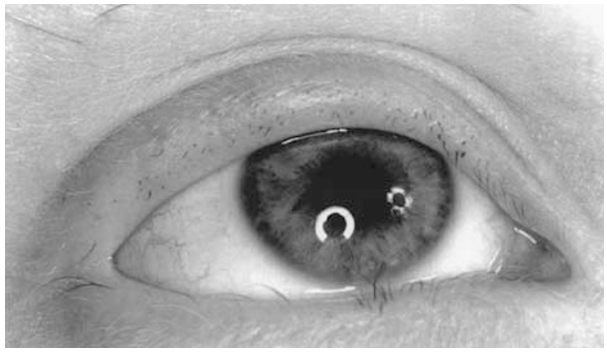

Figure 1 Right eye at initial presentation to the eye department. No change had been noted in lashes for $2\frac{1}{2}$ years.

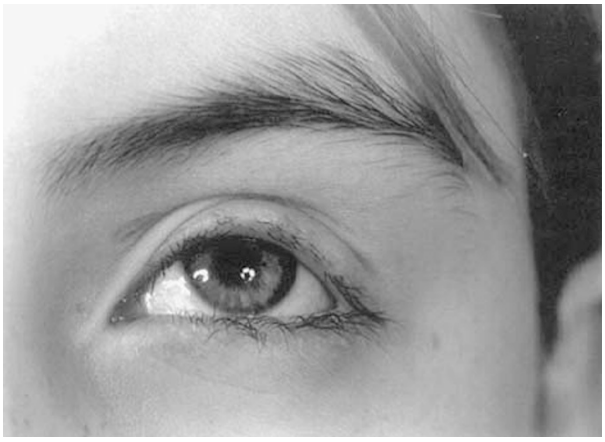

Figure 2 Left eye 3 months after initiation of treatment.

Comment

Alopecia areata is a condition on unknown aetiology with a possible ill-defined genetic factor. The condition may appear at any age, but is more common between the second or third decade affecting both sexes equally. An association with vitiligo, Down's syndrome, and organ-specific autoantibodies may be found. A lymphocytic infiltrate is present around the hair follicle, suggesting a T-cell-mediated autoimmune reaction. Pitting of the fingernails may also be seen. The hair follicles are stimulated into apoptotic degenerating (catagen) or resting (telogen) phase. Follicles can re-enter anagen but are prevented from progressing beyond an early stage before prematurely returning to telogen. The follicles probably undergo repeated truncated cycles until disease activity subsides. Frequently, the autoimmune reaction abates spontaneously and the hair follicle may re-enter a normal cycle or anagen. This is deemed less likely with prolongation of the disease in the telogen phase as in our case,[1] or in atopic patients who have a poorer prognosis for spontaneous regrowth. However, the potential for follicular function is retained even after decades of inactivity.[1]

The predominant differential diagnosis is trichotillomania; diagnostic exclusion can be difficult and may require lid biopsy.[3] However, unlike reports in the literature there were no episodes of spontaneous eyelash regrowth throughout the follow-up,[4,5] past/present history of any psychiatric disorder,[3] or direct admission of trichotillomania.[3] It would also be unusual to see both upper and lower eyelashes involved in a case of trichotillomania.

Latanoprost, an analogue of prostaglandin (PG) $F_{2\alpha}$, is a prodrug. However, it is rapidly activated to latanoprost acid (the active form) in the cornea before entering the anterior chamber.[6] The activation involves hydrolysis of its ester moiety, but no further metabolism is undertaken within the eye. Only 1% of the drug applied topically penetrates the eye, the rest being absorbed systemically.[6] Latanoprost-induced hypertrichosis was first documented by Johnstone[7] with an average increase of 19.5% in eyelash length. However, drug-induced hypertrichosis has been seen in association with diazoxide, phenytoin, minoxidil, streptomycin, corticosteroids, pencillamine, psoralens, cyclosporin, and alpha-interferon. The mechanism of the lash growth in most cases is unclear, but eyelash follicles do express FP receptors that are target receptors for latanoprost.[8] PG $F_{2\alpha}$ has been known to stimulate the initiation of DNA synthesis in resting cells and also to act as a mitogen.[9] It also evokes gene expression and prevention of apoptosis[10] as well as stimulating cell receptors linked to phosphorylase C that trigger activation of protein kinases that are known to play key roles in cell growth.

In a series of 317 patients, Demitsu *et al*[11] showed latanoprost-induced hypertrichosis in 77%. The same authors showed, in a dye distribution test, that the areas of hypertrichosis were analogous to the areas of skin discoloration. The evidence implies that cutaneous absorption may cause hypertrichosis. Since the active drug is formed in the cornea, hypertrichosis must be caused by the prodrug. Our case illustrates this theory, but also shows that the use of cutaneous cf. guttate[12] application of latanoprost can stimulate hair follicle activation from telogen/catagen into anagen with minimal other ocular side effects.

References

1 Messnger A, Simpson N. Alopecia areata. In: Dawber R (ed). *Diseases of the Hair and Scalp*, 3rd ed. Blackwell Sciences Ltd: Oxford, England, 1997; pp 338–369.
2 Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatr Scand* 1983; **67**: 361–370.
3 Mawn LA, Jordan DR. Trichotillomania. *Ophthalmology* 1997; **104**: 2175–2178.
4 Patil BB, Dowd TC. Trichotillomania. *Br J Ophthalmol* 2001; **85**: 1386–1387.
5 Smith JR. Trichotillomania: ophthalmic presentation. *Aust NZ J Ophthalmol* 1995; **23**(1): 59–61.
6 Stjernschantz J, Selen G, Sjoquist B, Resul B. Preclinical pharmacology of latanoprost, a phenyl-substituted $PGF_{2\alpha}$ analogue. *Adv Prostaglandin Thromboxane Leuko Res* 1995; **23**: 513–518.
7 Johnstone M. Hypertrichosis and increased pigmentation of eyelashes and adjacent hair in the region of the ipsilateral eyelids of patients treated with unilateral topical latanoprost. *Am J Ophthalmol* 1997; **124**(4): 544–547.
8 Strober BE, Potash S. Eyelash hypertrichosis in a patient treated with topical Latanoprost. *Cutis* 2001; **67**(2): 109–110.
9 Fagot D, Buquet-Fagot C, Mester J. Mitogenic signalling by prostaglandins in chemically transformed mouse fibroblasts: comparison with phorbol esters and insulin. *Endocrinology* 1993; **132**: 1729–1734.

10 Darnell J, Lodish H, Baltimore D. Cell to cell signalling: hormones and receptors. In: Darnel J, Lodish H, Baltimore D (eds). *Molecular Cell Biology*. WH Freeman and Company: New York, 1990; pp 738–743.
11 Demitsu T, Manabe M, Harima N, Sugiyama T, Yoneda K, Yamada N. Hypertrichosis induced by latanoprost. *J Am Acad Dermatol* 2001; **44**(4): 721–723.
12 Mansberger SL, Cioffi GA. Eyelash formation secondary to latanoprost treatment in a patient with alopecia. *Arch Ophthalmol* 2000; **118**: 718–719.

JS Mehta[1,2], J Raman[1], N Gupta[1] and D Thoung[1]

[1]Broomfield Hospital
Mid-Essex Healthcare
Chelmsford, UK

[2]Moorfields Eye Hospital
City Road, London ECIV 2PD, UK

Correspondence: JS Mehta
9 Sandringham Court, King & Queen Wharf
Rotherhithe Street, London SE16 5SQ, UK
Tel: 07980 691 396
Fax: 08701 316 622
E-mail: jodmehta@hotmail.com

Sir,

Corneal adherent leukoma associated with measles

Eye (2003) **17,** 446–447. doi:10.1038/sj.eye.6700353

Measles is an endemic disease that may cause epidemic outbreaks in the rural areas of developing countries, although it is rarely seen in developed countries. It may cause severe corneal pathologies such as adherent leukoma, corneal ulceration, perforation, and may even lead to phthisis bulbi.[1,2]

Case report

Two patients aged 51 and 57 years, respectively, were found to have adherent leukoma. The patients' histories revealed measles infection affecting their eyes in childhood, which coincides with the epidemic outbreak in Turkey at the first half of this century. However, they could not be accurately treated due to low socioeconomic status of their families. Both the cases had pupil distortion and adherent leukoma located at the 6 o' clock position (Figures 1 and 2). Visual acuities of the patients were 7/10 and 8/10, respectively, and ocular examination was otherwise normal. The systemic and laboratory findings revealed no abnormalities except positive antirubeola IgG antibodies in both patients.

Comment

Superficial punctate lesions at the bulba conjunctiva and corneal side of the limbus can be seen to be synchronous with the body rash of measles. It commonly resolves without symptoms or sequalae in well-fed and vaccinated children. However, these lesions can progress into the central cornea, and exposure ulcerations at the 6 o'clock position may result with perforation or leukomas in children with protein energy malnutrition and vitamin A deficiency. Bacterial or herpetic superinfections may develop secondary to exposure ulcerations, which tends to be bilateral.[1–5] Our patients most probably had malnutrition due to low socioeconomic status in their childhood, and corneal exposure ulceration after measles infection progressed into adherent leukoma.

The four main mechanisms by which measles may cause corneal ulceration are sudden decompensation of subclinical vitamin A deficiency and xerophthalmia, the use of traditional eye medicines, infection with herpes

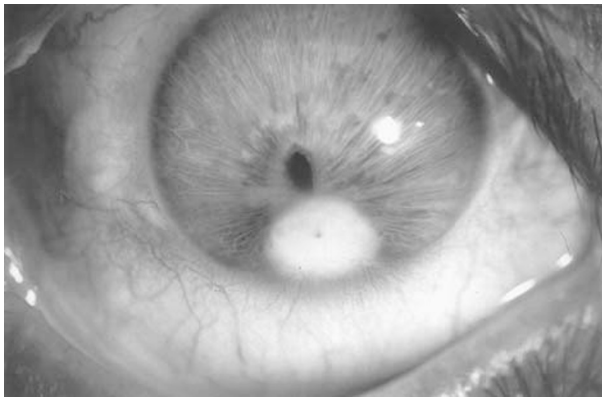

Figure 1 Anterior segment photograph of the first patient showing the adherent leukoma located at the 6 o'clock position secondary to measles infection.

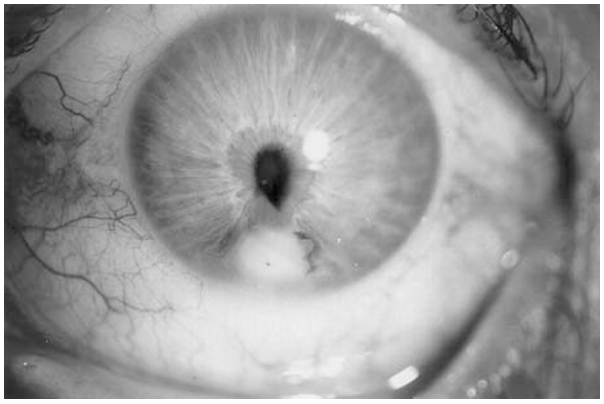

Figure 2 Anterior segment photograph of the other patient showing similar clinical presentation and location of adherent leukoma secondary to measles infection.