Figure 3 Sebaceous gland carcinoma of the upper right eyelid (haematoxylin and eosin, $\times 150$). Inset: Histology of the masses in the right upper and lower eyelids showed cells with vacuoles containing lipid, compatible with sebaceous gland carcinoma (oil red O, $\times 490$).

However even if a multicentric sebaceous gland carcinoma could be excluded in our patient, this entity does probably exist.^{1,2} There are currently no explanations available for multicentric malignant cell growth. Only recently we became aware of a new concept for malignant cell growth.¹² Genes may generate a determined number of cell divisions with subsequent inevita-

ble death. If the death gene is defective, the cells will never stop growing. One defective death gene could be responsible for more than one cell line and thus explain multicentric malignant growth. Manipulation of inactive death gene might play a role in future research projects aiming at more effective treatment for cancer.

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Therapeutic ptosis with botulinum toxin in epikeratoplasty

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We present six cases in a consecutive series of patients undergoing epikeratoplasty, in whom a therapeutic ptosis induced with botulinum toxin was given at the time of surgery. All patients achieved primary re-epithelialisation of their lyophilised grafts within 8 days or less, and no case of secondary epithelial breakdown was observed, nor any significant complication from the botulinum toxin. In patients with keratoconus and eye rubbing, epikeratoplasty may be the preferred method of surgical treatment because it does not compromise the integrity of the globe. An additional advantage of the procedure is that it is not associated with graft rejection problems,¹ which is particularly important for patients with mental handicap, Down's

syndrome, and those who have poor compliance with treatment or follow up. However, graft failure in epikeratoplasty can occur through primary failure of re-epithelialisation of lyophilised graft tissue, or secondary epithelial breakdown.² If epithelial defects are persistent, the lyophilised graft will suffer from stromal melting, and so the standard postoperative management includes close follow up, frequent application of topical ointment, and the use of bandage contact lenses, patching, etc. In patients with poor compliance, therapeutic ptosis induced by botulinum toxin could be a useful adjunct in the management of epikeratoplasty grafts, as it has been shown to be an effective treatment of epithelial defects in disease states.³

Table 1 Patient details

Case number	Ophthalmic diagnoses	Indication for therapeutic ptosis at time of epikeratoplasty surgery	Pre-ptosis graft cover achieved by	Age (years)	Time to full graft re-epithelialisation (days)	Follow up time (months)	Preop unaided acuity	Postop unaided acuity	Comments
1	Keratoconus, mature cataract	Down's syndrome, severe mental retardation, eye rubbing	Suture	28	≤7	32	NA	Fixes	Epikeratoplasty combined with cataract extraction and lens implant. Botulinum injection repeated at 5 weeks
2	Keratoconus, mature cataract	Down's syndrome, severe mental retardation, eye rubbing	Suture	29	≤7	12	NA	? NPL	Other eye of case 1. Epikeratoplasty combined with cataract extraction and lens implant. Found to have inoperable total retinal detachment
3	Keratoconus	Down's syndrome, severe mental retardation	CL	28	≤7	8	NA	Fixes	Previous acute hydrops in other eye
4	Keratoconus	Severe mental retardation, eye rubbing	CL	40	≤7	7	NA	NA	Previous acute hydrops in other eye
5	Keratoconus, Leber's congenital amaurosis	Blind, away at college, difficult to follow up	CL	18	≤8	5	PL	PL	Previous acute hydrops. Epikeratoplasty carried out as a tectonic procedure
6	Keratoconus, vernal catarrh	Lives abroad, attending school, difficult to follow up	Suture	10	3	3	4/60	6/18, N8	Awaiting epikeratoplasty surgery to other eye

CL=bandage contact lens; PL=perception of light; NPL=no perception of light; NA=not assessable.

Figure 1A Case 6: preoperatively, showing irregular keratoscopic mires from advanced keratoconus, and bulbar conjunctival congestion from vernal catarrh (visual acuity 4/60).

Figure 1B Case 6: 3 months after epikeratoplasty, showing improvement of the corneal contour and good recovery from the botulinum toxin induced ptosis (visual acuity 6/18 and N8 unaided).

Case reports

A series of six cases of keratoconus managed by epikeratoplasty combined with botulinum toxin induced ptosis is summarised in Table 1, and illustrated in Figure 1.

All the patients were treated with lyophilised lenticules (Keratec Eye Bank, London) prepared from desiccated corneal tissue lathed at room temperature.⁴ The lenticules were plano powered and 9 mm in diameter, sutured into an 8.5 mm bed with multiple interrupted 11/0 mersilene.

The ptosis was obtained by making up 500 units of botulinum toxin A with 2.5 ml of saline (Porton International) and injecting 0.1 ml (20 units) into the levator palpebrae superioris muscle at the beginning of surgery. Kirkness *et al*³ used 62.5 pg of toxin (equivalent to 3 units) to induce ptosis, but had a higher rate of failure and repeat injections.

In three of the cases a 6/0 prolene tarsorrhaphy suture tied over a bolster was used to close the eyelids temporarily while the onset of the ptosis was awaited – usually 1–3 days. In the other three patients a collagen bandage lens was used as an alternative to give cover during this period, but was not retained in the uncooperative patients (cases 3 and 4).

Comment

The exact time to complete re-epithelialisation was not known in cases 1–4, since they were all discharged following surgery and returned after 7 days for examination under anaesthesia. Case 5 was similarly discharged following surgery and reviewed as an outpatient on day 8. However, case 6 was managed as an inpatient, and examination of the graft surface by manually assisted opening of the eyelids at the medial canthus showed full re-epithelialisation on day 3, at which time the tarsorrhaphy suture was removed. The ptosis persisted in all cases for a minimum of 6 weeks, and during this period the epithelium stabilised on the graft and there were no instances of secondary epithelial breakdown.

In cases 1–4 it was difficult to measure the visual function due to the patients' mental retardation and/or behavioural disturbance. Case 6 gives an indication of the degree of unaided visual improvement that can be expected in epikeratoplasty for keratoconus.⁵ Where there is significant corneal scarring deep lamellar keratoplasty with lyophilised tissue can be used,⁶ and this latter technique could perhaps also benefit from botulinum toxin induced ptosis as part of the early postoperative management.

In conclusion, our case reports suggest that therapeutic botulinum toxin ptosis is a useful adjunct in the management of patients undergoing epikeratoplasty with freeze dried tissue since it promotes stabilisation of the epithelium on the graft.

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Exotropia as a sign of myasthenia gravis in dysthyroid ophthalmopathy

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The association between thyroid disorders and myasthenia gravis (MG) has long been recognised. The occurrence of Graves' disease is reported in 3–10% of myasthenic patients.¹ In contrast, MG occurs in considerably less than 1% of dysthyroid patients.² When a full blown thyroid ophthalmopathy, systemic myopathy, or both are present, additional muscle weakness caused by the onset of MG may be difficult to detect by examination alone. We present four patients with dysthyroid orbital disease who developed exotropia and variable ptosis caused by MG. Subsequent review of the records of 91 patients with dysthyroid orbitopathy, none of whom had MG when evaluated, revealed no additional cases with exotropia.

Case reports (Tables 1, 2)

Four patients with typical signs of dysthyroid orbitopathy had the new onset of diplopia. All

four patients were being treated with methimazole (Tapazole) or propylthiouracil or had been treated for hyperthyroidism. In each patient, the examination of the visual sensory system, pupils, anterior segment, intraocular pressure, and fundus was normal. Varying degrees of ocular motility limitation resulted from both the thyroid disease and MG. In primary gaze, an exotropia from 5 to 45 dioptres was measured in all four patients. Ptosis associated with proptosis and lid oedema in addition to MG occurred in all four patients. An edrophonium test was positive in three patients; the test was deferred in the fourth because of unstable arrhythmias. The serum acetylcholine receptor antibody assay was negative in all four patients. Three patients had marked improvement after treatment with oral prednisone, started at 60 mg/kg per day and tapered over 4–6 weeks. The fourth patient had a positive skin test for tuberculosis which precluded corticosteroid therapy. Computed tomography (CT) of the orbits, performed in two patients, showed bilateral enlargement of inferior and medial rectus. CT of the chest in all four patients showed no thymoma.

Comment

Clinical differentiation between MG and dysthyroid orbitopathy is usually not difficult. Although the extraocular muscles are frequently

Table 1 Ocular motility evaluation

Case	Age/sex	Ptosis (R/L)	Proptosis (mm R/L)	Edrophonium response	Ocular deviation Primary gaze (D)
1	60/F	Mild R	3 L	Infraduction R/L Ptosis	XT 45, LHT 2
2	60/F	Moderate L	5 R/L	Not performed	XT 5, RHT 20
3	28/F	Mild R	–	Infraduction R/L Horizontal gaze R/L Ptosis	XT 30
4	48/M	Mild R/L	4 R/L	Horizontal gaze R/L Ptosis	XT 40