Merkel cell carcinoma of the eyelid in association with chronic lymphocytic leukaemia

Merkel cell carcinoma (MCC) is a rare skin neoplasm. Tang and Toker first described MCC in 1978 and since then 19 cases in association with chronic lymphocytic leukaemia (CLL) have been reported. To the best of our knowledge, involvement of the eyelid by MCC has never been reported in the literature in association with CLL.

Case report

An 84 year old white man was referred with an 8 week history of a painless lump on his right upper eyelid (Fig 1A). He was complaining of visual obscuration secondary to a mechanical ptosis. Ophthalmic history was unremarkable. General examination did not reveal any abnormalities.

General medical history revealed that the patient had been diagnosed with CLL 11 months previously and was being treated with pulsed chlorambucil. His condition was considered to be stable by his oncologist. At the time he had a white cell count of 15.7 × 10⁹/l.

An 8 week history of a painless lump on his eyelid in association with chronic lymphocytic leukaemia (CLL) have been reported. To the best of our knowledge, involvement of the eyelid by MCC has never been reported in the literature in association with CLL.

Comment

The recent surveillance, epidemiology, and end results (SEER) programme³ in the United States has estimated the incidence of MCC at 0.23/100 000. MCC is very rare below the age of 50 and is more common on sun exposed sites. It is an aggressive tumour with 12–45% being lymph node positive at presentation. This increases to 55–79% during the course of the disease. The 5 year survival has been reported at 30–64%.⁴⁵ Involvement of the eyelid occurs in only 0.8% of MCC, and has not been reported in the literature in association with CLL.

Secondary tumours are common in B cell neoplasia with the relative risk of non-melanotic skin cancer being 4.7 in men and 2.4 in women.⁶ The frequency and aggressiveness of MCC and other skin neoplasms increases with immunosuppression, organ transplantation, as well as B cell neoplasia. The precise reason for such an association is not fully understood. Quaglino et al suggested that a depressed immunological system as well as exogenous oncogenic factors may, in various degrees, contribute to the development of neoplastic processes at different sites.⁷

The treatment is wide local excision with or without adjuvant therapy consisting of block dissection of lymph nodes or radiotherapy. Adjuvant therapy reduces local recurrence and regional failure from 39% and 46% to 26% and 22% respectively. Most patients die from causes directly related to the disease.⁸ Potentially there is an increased risk of all skin tumours including MCC in patients suffering from CLL and this diagnosis should be considered when evaluating an eyelid lesion in such patients. In a patient with reduced immunity it would be best practice to send all surgical specimens for histology even if a simple chalazion is thought to be responsible for the lid lesion.

References


Steatocystoma simplex of the caruncle

The caruncle has a non-keratinised epithelial lining similar to the conjunctival epithelium. However, unlike the conjunctiva, the caruncle contains skin elements such as hair follicles, sebaceous glands, sweat glands, and accessory...

Figure 1 [A] Merkel cell tumour involving most of the upper lid causing mechanical ptosis and visual obscuration. Biopsy site is seen laterally. [B] Merkel cell tumour after treatment with radiotherapy.

Figure 2 [A] Haematoxylin and eosin stain Merkel cell tumour. [B] Immunostaining with CAM5.2 showing characteristic para-nuclear accentuation.
plex (SS) of the caruncle.

Lesions are described on the forehead, nose, scalp, neck, axillae, chest, upper limbs, back, legs, and even intraorally. To our knowledge though, steatocystoma has not previously been reported in the caruncle. 

Thirty two cases of SS are reported in the literature, divided evenly between men and women and ranging in age from 15 to 70 years. 

Clinical and histological features in SS are usually identical to those seen in the individual lesions of SM. Lesions are described as asymptomatic, flesh coloured or yellow, intracutaneous, well circumscribed, soft, mobile, and non-tender. On incision they are found to contain an oily substance composed of sebum.

However, it is important to confirm the solitary nature of a steatocystoma. SM can be familial and autosomal dominantly inherited (steatocystoma multiplex congenita). Several familial cases have been linked to pachyonychia congenita and ectodermal dysplasia through a mutation in keratin 17. It has been associated with hypothyroidism, hypohidrosis, hypotrichosis and hypertrophic lichen planus, ichthyosis, and kollonychia. SM may be progressive with inflamed cysts, rupturing, and healing with scar tissue.

Steatocystoma is histologically characterised by a cystic structure with sebaceous glands within the cyst wall and epithelium that displays an eosinophilic cuticle. It is possible to make a diagnosis of steatocystoma if the characteristic hyaline luminal cuticle is present, even in the absence of sebaceous elements.

The differential diagnosis included sebaceous gland hyperplasia, sebaceous gland adenoma, and lipogranuloma. Clinically they are also characterised by a yellow, nodular appearance. Rarely, sebaceous gland carcinoma of the caruncle may occur. Along with hidrocystoma and eruptive vellus hair cyst they can usually be excluded histologically. Oncocytoma are asymptomatic, slowly progressive, solid or cystic masses but usually described as reddish blue/nec.

Most treatment regimens for steatocystoma reflect the multiplicity and widespread extent of lesions of SM. Oral isotretinoin has been used to reduce associated inflammation. Cryosurgery, carbon dioxide laser, and incision with removal of the cyst wall have been employed. We felt the best way to manage this solitary lesion arising in the caruncle was by simple excision with removal of the cyst wall intact, thereby reducing the risk of recurrence. We were able to confirm the unique nature of this lesion and rule out malignancy.

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References


Preliminary results with posterior lamellar keratoplasty for endothelial failure

We describe the technique and the results of the three cases where we performed a posterior lamellar keratoplasty.

Case reports

The following surgical technique was performed in all cases. The donor posterior button was obtained from an entire fresh globe. We made sure that intraocular pressure was adequate by injecting BSS (balanced salt solution, Alcon) into the vitreous. With a Moria ONE microkeratome, an anterior cap of 250 µm was cut and lifted. A Barron trephine 7 mm in diameter was used to obtain the posterior button, covered afterwards with viscoelastic to protect it and to avoid desiccation.

With our microkeratome an 8.5 mm in diameter, nasal hinge and 250 µm flap was obtained. The trephination was made with a 7 mm Barron trephine and completed with corneal scissors, under viscoelastic protection.

After the intraocular injection of acetylocline the posterior donor button was placed on the recipient eye under viscoelastic protection. Six 10-0 Nylon interrupted sutures were used to secure and close the wound. Immediately after, the flap was put back and fixed with six interrupted 10-0 Nylon sutures and the knots were buried. The viscoelastic anterior chamber was exchanged with BSS using an automatic pressure controlled irrigation-aspiration system.

Case 1

This was a 36 year old woman with Fuchs’ endothelial dystrophy. Preoperative BSCVA was 0.4 in the right eye and 0.6 in the left. Slit lamp examination showed diffuse corneal oedema clearly affecting the anterior layers of the cornea. Endothelial cell count (ECC) was below 900 cells/mm in both eyes. Surgery was performed on the right eye (Fig 1A). The follow up was done for 12 months (Fig 1B).

Case 2

Case 2 was a 57 year old man with Fuchs’ endothelial dystrophy. Preoperative BSCVA was 0.1 in the right eye and 0.06 in the left. Slit lamp examination showed diffuse stromal corneal oedema in the left surgical eye. ECCs were difficult to perform because of the light
myopia in both eyes (right eye −4.00, left eye −9.00). There was a history of subretinal macular neovascularisation and cataract extraction in his left, surgical, eye, with an ECC of 990 cell/mm. Preoperative BSCVA was 0.5 in the right eye and 0.2 in the left. The follow up was done during 14 months (Fig 1D).

Examinations in all cases were at day 1, 1 week, 3, 6, 9, and 12 months. All Nylon sutures were removed before the 6 month control. All surgeries were technically uneventful. The immediate and late postoperative controls showed transparency of the cornea and no signs of rejection. In case 1 at the time of removing the superior suture (3 months postoperatively) a separation between the anterior cap and the edge of the corneal recipient eye was observed (because of the stromal flap oedema) and two interrupted 10–0 Nylon suture were placed for 3 more months.

Uncorrected and BSCVA did not improve in all cases in spite of corneal transparency (Table 1). We observed a significant increase in astigmatism in all cases during the follow up and also after the suture removal, but it was not the main cause of reduced vision (Table 2). We checked vision changes with refraction over rigid gas permeable lenses but the results were lower than expected.

### Table 1 Best corrected visual acuity before and after the endokeratoplasty

<table>
<thead>
<tr>
<th>Preoperative</th>
<th>2 Weeks</th>
<th>3 Months</th>
<th>6 Months</th>
<th>9 Months</th>
<th>12 Months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case 1</td>
<td>0.5</td>
<td>Counting fingers to 1 metre</td>
<td>0.1</td>
<td>0.1</td>
<td>0.32</td>
</tr>
<tr>
<td>Case 2</td>
<td>0.63</td>
<td>Counting fingers 0.5 metre</td>
<td>0.3</td>
<td>Counting fingers 0.5 metre</td>
<td>0.3</td>
</tr>
<tr>
<td>Case 3</td>
<td>Counting fingers 0.5 metre</td>
<td>0.5</td>
<td>Movements of hands 0.5 metre</td>
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<td></td>
</tr>
</tbody>
</table>

### Table 2 Astigmatism before and after of endokeratoplasty

<table>
<thead>
<tr>
<th>Preoperative</th>
<th>2 weeks</th>
<th>3 Months</th>
<th>6 Months</th>
<th>9 Months</th>
<th>12 Months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case 1</td>
<td>−0.75</td>
<td>−7.00</td>
<td>−7.50</td>
<td>−8.50</td>
<td>−9.50</td>
</tr>
<tr>
<td>Case 2</td>
<td>−2.00</td>
<td>−3.00</td>
<td>−4.00</td>
<td>−5.00</td>
<td>−6.50</td>
</tr>
<tr>
<td>Case 3</td>
<td>−0.5</td>
<td>−3.00</td>
<td>−4.00</td>
<td>−4.00</td>
<td>−3.50</td>
</tr>
</tbody>
</table>
Persistent accommodative spasm after severe head trauma

Spasm of accommodation is the sudden development of a considerable degree of myopia which disappears after cycloplegia, usually functional in origin.1 Bohlmann and France2 reported a patient with persistent spasm of accommodation 9 years after head trauma and suggested that a possible lesion in the upper brainstem might be responsible for the dysfunction. We report two similar cases in which magnetic resonance imaging (MRI) failed to show abnormalities in the mid-brain and revealed cerebellar and supratentorial traumatic lesions.

Case reports

Case 1

A 34 year old female patient came to the refractive surgery service for correction of myopia and astigmatism. She had been comatose for 45 days after suffering severe head injury at the age of 24, and 3 months later noticed difficulties in her distant vision and was prescribed corrective lenses.

Dynamic refraction revealed in the right eye −3.75 sph −1.50 cyl × 5 and in the left eye −3.50 sph −1.00 cyl × 170. Visual acuity was 20/25 in each eye with this correction. Pupils were equal in size and measured 5 mm in normal room light, with normal reactions. Cycloplegic refraction after instillation of two drops of 1% tropicamide revealed −1.25 sph −1.50 cyl × 5 right eye and −0.75 sph −1.25 cyl × 165 left eye, obtaining 20/20 in each eye. She had attention and memory deficits, left cerebellar ataxia, left pyramidal syndrome, and speech difficulties due to vocal cord paresis. The MRI scan showed multiple lesions in the periventricular and subcortical white matter involving the left temporal lobe (Fig 1) and in the frontal and parieto-occipital regions bilaterally on FLAIR sequences. High signal intensities were observed in the cerebellar vermis as well as in the dorsal pons (Fig 1). No abnormalities was observed in the mid-brain. Images with 3 mm thickness T2 weighted spin echo sequences also did not reveal abnormalities in the cerebellar vermis and the authors suggested that a possible supratentorial traumatic lesions.

Case 2

A 24 year old male patient had blurred distant vision soon after he recovered from head injury including a 2 months period in a coma. He had not worn glasses in the past.

On examination visual acuity was 20/200 both eyes without correction and 20/25 with −3.00 sph in each eye. Pupils measured 4 mm each with normal reactions. The rest of the ophthalmic examination was normal. Cycloplegic refraction, after instillation of two drops of 1% cyclopentolate and one drop of 1% tropicamide, revealed 20/20 vision both eyes (+0.25 sph in each eye). He had recent memory and gait deficits. MRI scan revealed a heterogeneous area, hypointense on T1 and hyperintense on T2 weighted images, affecting the left temporal lobe, compatible with gliotic reaction. There were no abnormalities in the dorsal mid-brain.

The patient was prescribed 1% atropine every 12 hours, which he took for 6 months with normal distance vision but he complained of difficulties reading and photophobia. Atropine was discontinued and blurred distant vision recurred. He then took atropine every other day for 2.5 years associated with reading glasses. When it was discontinued however, accommodative spasm again recurred and −1.30 sph correction in both eyes was prescribed.

Comment

In our patients, a relation of accommodative spasm and the head trauma seems well established because it appeared soon after they have recovered from severe head injury, persisted for several years despite the prolonged use of cycloplegic drops, and the patients were not trying to obtain any benefit by complaining of blurred vision. The supranuclear control of accommodation is poorly understood. In cats, neurons that discharge in temporal correlation with accommodation were found in the lateral suprasylvian area.5 Electrical stimulation on ipsilateral interpositus nuclei and on contralateral interpositus and fastigial nuclei in the cerebellum are known to induce accommodation.6 These nuclei are connected to parasympathetic oculomotor neurons in the mid-brain.7 Very little accommodative dysfunction resulting from central lesions has been reported in humans. Ohtsuka et al8 studied a patient with left middle cerebral artery occlusion who had reduced accommodative responses and markedly lowered accommodation velocity. Their patient had low density lesions on computed tomograph (CT) scan involving the left temporal lobe, near the sylvian fissure. Kawasaki et al9 reported a patient with normal accommodation amplitude but increased accommodation and relaxation times. Their patient recovered normal accommodation 10 days after removal of a large subtentorial arachnoid cyst and the authors suggested that the cerebellum might have a role in the organisation of the human central control system of accommodation.

Bohlmann and France described a patient with persistent spasm of accommodation after head trauma.10 CT scan revealed a skull base fracture without intracranial abnormalities and the authors suggested that a possible

References


Figure 1 Case 1. Magnetic resonance imaging FLAIR sequences (TR 8000, TE 150, TI 2300 ms) magnetic resonance imaging scan [6 mm thickness] showing white matter lesion in the temporal lobe (black arrows), in the dorsal pons (small white arrow), and in the cerebellar vermis (large white arrow). Cerebellar atrophy is indicated by enlarged folia.

Figure 2 Case 1. T2 weighted (TR 3570, TE 120 ms) spin echo sequences, 3 mm thickness, with normal findings in the mid-brain.
Extramedullary plasmacytoma of the eyelid

A 74 year old man presented with a foreign body sensation in the right eye superimposed on a slowly growing enlarging lump in the right eyelid. He had no history of recurrent infections, bleeding, weight loss, or night sweats. His only other symptom was chronic backache secondary to osteoarthritis. Past medical history included cataract extraction from the right eye 4 years previously and excision of a basal cell carcinoma from the right pinna 5 years previously. Examination revealed a large firm lesion in the right upper eyelid with no palpable lymph nodes. The clinical diagnosis was of a chalazion.

The lesion was removed surgically and histopathology (Fig 1) revealed an incompletely excised extramedullary plasmacytoma with a high proliferative index and amyloid change. Immunocytochemistry was positive for IgG kappa light chains. Further investigations including full blood count, liver function tests including lactate dehydrogenase (LDH), protein electrophoresis, skeletal survey, and bone marrow aspiration were normal with no evidence of multiple myeloma.

The whole of the upper eyelid was treated with radiotherapy using a customised lead cutout with internal shielding of the eye (Fig 2); 120 kVx rays were used giving a dose of 30 Gy in 10 fractions over 2 weeks. On follow up (at 2 years) there has been no evidence of local recurrence or the development of myeloma, and lacrimation in the eye appears normal.

Comment

Solitary plasmacytomas are rare tumours. They are classified as either solitary plasmacytomas of bone (SPPB) or extramedullary plasmacytomas (EMP) of soft tissue. The majority of EMPs (about 80%) involve the upper air passages of the head and are usually related to upper lateral suprasyllavian area in cats. J Neurophysiol 1984;52:879–91.

Solitary plasmacytomas are rare tumours. They are classified as either solitary plasmacytomas of bone (SPPB) or extramedullary plasmacytomas (EMP) of soft tissue. The majority of EMPs (about 80%) involve the upper air passages of the head and are usually related to upper lateral suprasyllavian area in cats. J Neurophysiol 1984;52:879–91.

There is a relation between solitary plasmacytomas and subsequent development of multiple myeloma. About 44–69% of patients with a solitary bone plasmacytoma will develop multiple myeloma within a median survival of 5–7 years. Although EMPs recur in a median of 50% of cases, this is usually in bone but unlike multiple myeloma it remains circumscribed within the bone with no predilection for the axial skeleton. However, progression to myeloma does occur though at a lower rate than for SPPB. Alexiou et al reported a rate of progression to myeloma for both upper aerodigestive tract and non-aerodigestive tract extramedullary soft tissue plasmacytomas of 16.1% and 14.6% respectively. As no predictors of progression have been identified patients probably need indefinite follow up.

Eye abnormalities such as cysts of the ciliary body and vascular lesions have been described in multiple myeloma but primary plasmacytomas involving the eye is rare. Nine-teen cases affecting the orbit have been described in the literature but this is only the fourth case of a primary plasmacytoma arising from the eyelid that has been reported. Most of the earlier reports of the plasmacytomas arising in the eye are not true plasmacytomas and are in fact granulomas due to chronic inflammation.

References


Figure 1 Photomicrograph showing infiltration of the conjunctiva by the neoplastic plasma cells with strong immunocytochemical staining for immunoglobulin IgG (>355).

Figure 2 Whole of upper eyelid treated by radiotherapy using a customised lead cutout with internal shielding of the eye.

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A 71 year old white woman was referred by her optician after attending for routine glasses update. On questioning she did complain of a “slight blurring of vision” gradually for many years. She had a history included oesophagitis and hiatus hernia and cervical spondylosis. Her unaided visual acuity was 6/12 right eye improving to 6/9 with pinhole, and 6/18 left eye improving to 6/12 with pinhole. She had bilateral nuclear cataracts and both fundi revealed numerous pale elevated lesions clustered around the superotemporal and inferotemporal arcades (Fig 2A).

Haematological investigations and chest x-ray were unremarkable. Ultrasound scanning revealed that these were areas of calcification with high reflectivity (Fig 2B).

Case 3
A 71 year old man attended routinely for review 2 weeks after cataract extraction. He had no past medical history and vision was 6/9 right eye and 6/6 left eye. He was noted to have a small optic disc haemorrhage coincidentally and therefore dilated fundal examination was performed. He had bilateral pale yellow elevated lesions along the superotemporal arcades and also nasally in both fundi. Again electrolytes were investigated and were within the normal range.

Comment
Sclerochoroidal calcification has been described in the literature as an uncommon condition found usually in older white patients.1 Patients have been unnecessarily investigated in the past and even treated for tumours unnecessarily.2 Calcification can be dystrophic or metastatic but in these idiopathic cases it is the former. The calcification is believed to be deposited at the sites of insertions of the oblique extraocular muscles in a similar way that Cogan scleral plaques are calcification at the insertions of the horizontal recti muscles.3 Reports have been made of sclerochoroidal calcification associated with Bartter syndrome,4 Gitelman syndrome,5 hyperparathyroidism, and hypomagnesaemia.6 It is important to exclude any electrolyte abnormality when a patient presents with this condition, but prolonged investigations are unnecessary. Autofluorescence and ultrasound appearances are very useful to diagnose this condition. Patients rarely develop visual disturbance with sclerochoroidal calcification, but infrequent follow up is advised as cases of associated choroidal neovascular membranes and serous detachments with the lesions have been documented.7

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References

Stereotactic irradiation of biopsy proved optic nerve sheath meningioma

The role of conventional external beam radiotherapy in the management of optic nerve sheath meningiomas (ONSM) has been controversial because of limited radiation sensitivity of these tumours and radiation damage to surrounding tissues. Recently, in a study of 64 patients with ONSM managed with observation, surgery, radiotherapy, or surgery and radiotherapy, Turbin and colleagues found that patients treated by (conventional) radiotherapy alone demonstrated the best long term visual outcome, and suggested fractionated external beam radiation (5000–5500 cGy) as the initial treatment in selected cases, when preservation of visual function is a reasonable goal.

The collateral damage secondary to conventional radiotherapy may be minimised by better focusing and shaping of the radiation beams, as in stereotactic radiotherapy (SRT). We report on a woman whom we treated with fractionated SRT for a biopsy proved, large ONSM.

In April 2000 a 41 year old woman was referred with a 1 month history of proptosis of her left eye (Fig 1, top left). She had been treated for a presumed orbital "pseudotumour" with oral prednisone (initial dose 90 mg/day) without effect.

At referral, she had no history of diplopia or retrobulbar pain. On examination, the visual acuity (VA) was 1.25 (unaided) of the right eye and 0.8+ (cc S+2) of the left eye. The intraocular pressure was 18 and 21 mm Hg in the right eye and left eye, respectively. There was a left relative afferent pupillary defect (RAPD). The motility of the left eye was slightly restricted in upgaze. The left eye showed mild periocular swelling and conjunctival chemosis. There was 5 mm of left upper lid retraction secondary to left upper lid ptosis. Bottom left. Orbital MRI scan (T1 weighted with fat suppression and gadolinium contrast enhancement) at presentation. Bottom right. Six months after radiotherapy. A decrease of both tumour size and proptosis is clearly visible.

After surgery we observed the patient for 9 months. During this period her left (corrected) VA deteriorated to 0.2 and her left visual field showed progression of her scotomas. This prompted us to treat her with fractionated SRT in March 2001. The radiation, delivered with a 6 MV linear accelerator (Varian), was given 5 days a week at 1.8 Gy per fraction, with a cumulative dose of 54 Gy. Treatment planning was based on orbital MRI scans. A non-invasive stereotactic frame was fixed with an external coordinate system (one isocentre). Treatment was delivered with a 6M V linear accelerator (Varian), was given 5 days a week at 1.8 Gy per fraction, with a cumulative dose of 54 Gy. Treatment planning was based on orbital MRI scans. A non-invasive stereotactic frame was fixed with an external coordinate system (one isocentre). Target and surrounding tissues at risk were defined as volume of interest on contrast media enhanced T1 weighted MRIs and transferred to CT by the stereotactic localisation technique using a three dimensional planning system (X Plan, Radionics). Portals were optimised using a beam's eye view technique. Five irregularly shaped non-coplanar beams (arses) per treatment were used. Beam shaping was done with a mini-multileaf collimator (Radionics). No early complications of the radiation treatment were noted. At 6 months after SRT, the (corrected) VA of her left eye had recovered to 0.8, while no RAPD was observed.

Her pericellular swelling had markedly diminished (Fig 1, top right). Compared to previous measurements, the protrusion of the left eye had diminished by 4 mm. Funduscopy, however, showed mild pallor of the left optic nerve head. Visual field testing showed unchanged loss of the left visual field compared to pretreatment values, with a higher false positive threshold. VEP measurements showed improved amplitudes, but prolonged latency compared to previous examination. Orthoptic examination showed ductions similar to those before treatment. Post-treatment MRI revealed a markedly decreased tumour size and a decrease of exophthalmos (Fig 1, bottom right). Colour Doppler ultrasonography showed a decrease in tumour size with markedly diminished vascularisation (Fig 2, top right). At the last follow up visit, 16 months after treatment, her left VA and visual fields were stable.

Comment
As in the recent report on a presumed ONSM by Moyer et al, fractionated SRT in our biopsy-confirmed case gave a remarkable visual recovery without detectable side effects. Both the size and the blood flow of the tumour regressed within the first 6 months, leading to reduced exophthalmos and pericellular swelling. The effect of restored cosmesis was important to this young woman whose main complaint was her unilateral exophthalmos.

Since our follow up is limited to 16 months, no conclusions with regard to long term outcome can be made. More cases of SRT for ONSM need to be studied over a longer period of time to assess the efficacy of this treatment.

Acknowledgements
This study was presented in part at the 1996th Annual Meeting of the Dutch Society of Ophthalmologists, Groningen, the Netherlands, March 2002. The SWOO foundation is kindly acknowledged for financial support.

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References

Severe interferon associated retinopathy
Interferon alfa is used in various human malignancies for its antitumour activity. One of its ocular side effects is retinopathy. Interferon associated retinopathy is generally mild and resolves completely. We describe a severe retinopathy in a hypertensive patient treated with interferon for multiple myeloma.

Case report
A 56 year old man presented with a 3 week history of deterioration and distortion of right vision. Visual acuities (VA) were 6/60 right and 1/60 left. Funduscoppy revealed bilateral extensive peripapillary cotton wool spots, retinal thickening, optic disc hyperaemia, and blot haemorrhages. Arteriolar changes were minimal.

He was anaemic (Hb 10.6 gdl/l) and slightly thrombocytopenic (platelets 93 × 10^9/l). Plasma viscosity was 1.59 (normal 1.5–1.7). Renal function was normal at presentation.

He underwent peripheral blood stem cell transplant for multiple myeloma 8 months previously after having melphalan 110 mg/m^2 and total body irradiation (including the head) in a total dose of 1200 cGy given in six fractions over 3 days. He then had interferon alfa therapy for 4 months, initially 3 mega international units three times a week, later reduced to twice a week. It was stopped immediately after visual deterioration.

Five years previously, he had macular laser treatment following left inferotemporal branch retinal vein occlusion. On discharge 1 year later, VAs were right 6/5, left 6/36.

He was a known hypertensive, taking lisinopril, but control was poor around the time his VA began to deteriorate, with readings up to 150/100 mm Hg. He was not diabetic. His melanoma was stable. Cytomegalovirus (CMV) antigen checked by polymerase chain reaction (PCR) and pre-transplant HIV status were negative.

One week after presentation at the eye clinic, VAs dropped to right 2/60, left finger counting and did not improve after a course of intravenous methylprednisolone (1 g/day for 3 days). He was registered blind.

A further 5 weeks later, bilateral cotton wool spots and haemorrhages were more numerous and both foveas showed gross thickening with exudates (Fig 1). Fundus fluorescein angiography revealed retinal ischaemia with capillary non-perfusion, pruning, and tortuosity of vessels, vessel wall staining, and leakage (Fig 2).

Five months later preproliferative retinopathy was noted and subsequent proliferative changes were treated with bilateral panretinal laser photoagulation. At 9 months, VAs were 1/60 right and left.

Comment
In a review article on interferon retinopathy, initial interferon alfa doses ranged from 3–9 mega units three to six times per week for several weeks. In a prospective randomised placebo controlled trial of interferon alfa therapy for macular degeneration, retinopathy was noted with increasing frequency in the highest dose group (5% of the patients taking 6 mega units three times a week). The interferon doses in our patient were at the lower level of these regimens.

Severity of retinopathy was found to be related to the presence of the following risk factors: large initial dosages, long duration of treatment, and systemic diseases like diabetes mellitus or hypertension. Early onset of retinopathy was also a good indicator of severity.
and fundal examination up to 8 weeks from start of treatment was advocated for those at risk. Significant visual impairment attributed to interferon therapy was associated with macular oedema in a hypoaabuminemic but non-hypertensive, non-diabetic patient; and in two other cases in a case series report, one of whom had poor control of blood pressure and the other an occasional mildly elevated blood glucose level. All three patients had resolution of the lesions by 2 months and subsequently made good visual recoveries, unlike in our case.

In another case series report, two out of seven patients on high dose interferon alfa-2b suffered permanent visual loss after developing macular oedema. Both patients were hypertensive and one had radiation treatment to the brain. The latter later developed proliferative retinopathy as well. Deposition of immune complexes in the retinal vasculature has been postulated as a pathogenetic mechanism for the retinopathy. Interferon alfa was also found to induce leukocyte capillary trapping in rat retinal microcirculation.

Radiation may have contributed to the development of the clinical picture although its use in the treatment of myeloma is frequently not of a high dose and side effects have not been widely recognised in the past. Low doses to the eye similar to that used in our patient have been associated with retinopathy after treatment of age related macular degeneration. Retinal oedema is an indicator of severity in interferon associated retinopathy. Early detection of it, especially in hypertensives and diabetics, may help avoid progression to permanent visual loss.

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Figure 1 Fundus photograph of the left optic disc shows diffuse swelling and increased surface vascularity. Additionally, a more focal elevation at the inferotemporal quadrant gives a nodule-like appearance to the disc swelling). The irregular white spot at the lower left corner of the figure is a photographic artefact.

Mass lesions of the posterior segment associated with Bartonella henselae

Bartonella (previously Rochalimaea) henselae is the infectious agent causing cat scratch disease, a self limited regional lymphadenopathy associated with flu-like symptoms. In approximately 10% of cases, extranodal dissemination of the organism results in a variety of intraocular inflammatory lesions. We report a patient with a Bartonella henselae infection in whom the only physical manifestation was multiple, mass-like lesions in the eye which resembled ocular metastases.

Case report

A 12 year old boy developed daily headaches and blurred vision. Four weeks later, he noted a central grey spot in his left eye. Visual acuity was 20/20 in his right eye and 20/400 left eye. Goldmann perimetry of the left eye revealed a dense central scotoma with steep margins nasally and moderate constriction of the temporal periphery. An afferent papillary defect was present on the left side. Slit lamp examination was normal in both eyes. Funduscopy of the left eye showed nodular optic disc swelling with peripapillary subretinal elevation (Fig 1). A large creamy-coloured mass (approximately one and one half disc diameter) without exudates or haemorrhages was present in the macula. Several smaller but similar, elevated lesions of the choroid were detected in the periphery as well as an inferior serous retinal detachment. There was no evidence of ocular inflammation. An orbital ultrasound showed the macular lesion to be a solid mass without associated subretinal fluid (Fig 2).

Complete blood count, electrolytes, and glucose were normal. A sedimentation rate was marginal at 18 mm/hour (normal less than 15 mm/hour). Antinuclear antibodies were elevated at 1:320, speckled pattern. Rheumatoid factor was negative. Evaluation for various infectious aetiologies was negative, including Bartonella serologies (IgM and IgG). A systemic evaluation of a primary tumour causing possible ocular metastases was negative. The patient was empirically treated with doxycycline 100 mg twice daily for 10 days. The macular mass and choroidal lesions resolved in 4 weeks. Shortly thereafter, the disc swelling resolved. Because a diagnosis remained lacking, serologies were repeated 1 month later and revealed a marked rise of Bartonella titres, confirming Bartonella infection (B henselae IgM = 24, normal less than 16, and B henselae IgG = 1024, normal less than 256). Final visual acuity was 20/70 left eye due to residual peripapillairy and macular gliosis.

Comment

The range of oculocutaneous findings associated with B henselae continues to expand. The classic follicular conjunctivitis described with lymphadenopathy and fever (Parinaud’s ocular glandular syndrome) is due to direct inoculation of the conjunctiva. Neuroretinitis, a syndrome of acute visual loss and with optic disc swelling and macular star, was the first established intraocular complication from disseminated Bartonella. Since then, other reported intraocular findings include inflammatory chorioretinal white spots, papillitis, serous detachment, vitritis, uveitis, vasculitis, retinal vaso-occlusive disease, and vitreous haemorrhage. A mass lesion at the optic nerve head has been noted in several instances. A solitary macular lesion without other ocular inflammatory findings has also been reported. Such lesions in the posterior pole have been presumed to represent a mass focus of Bartonella inflammation.

We report a patient with a circumscribed, elevated lesion in the macula as well as other mass-like lesions at the optic nerve head and in the choroid. These lesions occurred in the absence of systemic or ocular inflammation, and clinically resembled ocular metastases. This case highlights the importance of recognizing the wide spectrum of ocular bartonellosis. Furthermore, clinicians are reminded that cat exposure is not essential for contracting the bacteria and, therefore, Bartonella titres should be obtained whenever there is a clinical index of suspicion, regardless of cat exposure.

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References


Optic neuritis with marked distension of the optic nerve sheath due to local fluid congestion

Distension of the subarachnoid space of the optic nerve is not a common feature of optic neuritis. We describe a patient with optic neuritis with swelling of the optic nerve head of the right eye. On magnetic resonance imaging (MRI) there was marked distension of the optic nerve sheath due to an increase of fluid in the subarachnoid space. The location of the lesion in the optic nerve and concurrent inflammatory changes of the arachnoid trabecula and septae may have had a role in the pathophysiology of this condition.

Case report

A 38 year old man was admitted with pain on eye movements and loss of vision in the right eye. Best corrected visual acuities measured 20/40 on the right and 20/20 on the left. The patient identified 16 out of 18 Ishihara plates with the right eye and 18/18 with the left eye. There was a relative afferent pupilary defect (RAPD) on the right. Funduscopy demonstrated a swollen optic disc on the right. The left optic disc was normal. Spontaneous venous pulsations (SVP) were detectable bilaterally. Laboratory examinations, including red and white blood counts, C reactive protein, sedimentation rate, serologies for syphilis, HIV, herpes, toxoplasmosis, Lyme disease and cytomegalovirus, as well as collagen vascular disorders and coagulopathies were all in normal range. The right visual field (Octopus program G2) demonstrated a wedge-shaped defect in the inferior nasal and temporal visual field pointing towards the macula. The left visual field was normal. Neurological examination was normal. MRI of the brain was normal but showed enhancement of the right optic nerve in the T1 weighted axial and coronal (not shown) with fat suppression demonstrating enhancement of the right optic nerve (arrow). CT demonstrated localised and isolated stasis of fluid in the right optic nerve subarachnoid space only. The reason for this fluid congestion causing a optic nerve sheath compartment syndrome could not be identified by neuroimaging. The site of inflammation of the optic nerve and local anatomical variations and alterations of the subarachnoid space—for example, the amount and number of trabecula and septae in the subarachnoid space, may have a crucial role in the pathophysiology of unilateral papilloldea.

Figure 1  [A] Enhanced axial T1 weighted MRI with fat suppression demonstrating enhancement of the right optic nerve (arrow). [B] Axial T2 weighted MRI shows hyperintensive fluid in the expanded subarachnoid space due to increase of total fluid (arrowhead). The hypointense optic nerve head protrudes into the posterior aspect of the globe (arrow). [C] Axial T2 weighted MRI 7 weeks later demonstrating normal optic nerves and subarachnoid spaces bilaterally.

Figure 2  Fundus photograph of the right eye demonstrating a prominent optic disc with blurred margins and nerve fibre obscurasion in the superior and temporal quadrant. Patton folds are observed extending to the macula. The veins appear engorged.

References


Corneal opacification following keratoplasty in the rat model

I read with great interest the excellent perspective by Plskova et al., in which they raise the issue of transient corneal opacification following corneal transplantation in the mouse model and argue that it might be due to a sufficient number of endothelial cells regaining function.

What the authors describe for the mouse model also occurs in the rat model. In fact,
most researchers on the rat model probably have this experience, but for some reason do not think it is very important and/or choose to ignore it. Apart from the article by Williams et al., there is—as far as I know—only one other article[7] who has explicitly mentioned this transient opacification. In their paper, Herbert et al. wrote “The grafts began clearing 4 weeks after surgery. . . and vessels in the graft vanished from 6 weeks post-surgery.” and “It has to be noted that after acute rejections most corneas regain some clarity by 7–8 weeks.” Transient corneal opacification also occurs in the rat model used (AO rats (strain RT1u)) served as recipients of corneas from PVG rats (strain RT1) and corneas were sutured with a single running suture). Allogeneic transplanted corneas showed no initial opacification immediately postoperatively; neither did the syngeneic controls. All allogeneic corneas “rejected” (or more precisely showed total opacification) around day 11–13 and those corneas, when followed long enough, all cleared. Opacification remained higher than 2 (meaning an increased corneal haze, but some anterior chamber structures still visible) at days 17–21 and became lower than 2 (slight haze) around days 21–32.

It would be exciting to know if the hypothesis put forward by Plsková et al would also apply to the rat model and to find out if this “clearing” of the opacification also occurs in other rat models than the ones mentioned. Plsková et al have raised a very important topic where a lot of uncertainty still exists, and which warrants further research.

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References

Surgery for glaucoma in the 21st century

The authors of the article “Surgery for glaucoma in the 21st century” should be commended for attempting to tackle this issue. Nevertheless, we do feel that their fundamental points and principal arguments merit reconsideration.

The authors state categorically that “This finding of a higher ‘failure’ rate based on intraocular pressure after ‘non-penetrating’ surgery compared with trabeculectomy has been found in the majority of randomized trials comparing the two procedures” and then go on to quote three references allegedly supporting this remark.

3 Chisletta D. Non-penetrating sclerectomy versus trabeculectomy in primary open angle glaucoma surgery. Eye 2001;15:197–201

When discussing the other two papers[3,4] it is of paramount importance to understand that given the long learning curve associated with deep sclerectomy, it is neither fair nor scientifically sound to compare a surgeon’s first 20 cases of trabeculectomy with his first 20 cases of deep sclerectomy. As an example, one group[3] reported 0% success rate in their first series of viscoanastomolysis patients and then presented their second series with a success rate of 15.6%. The same group also analysed the depth of their dissection of the deep sclera to find that they dissected too superficially in 48% of their cases and too deeply in 17%; meaning that the proper depth of dissection, which should be between 7 and 9 mm, was not always achieved in the majority of their cases. The authors also failed to cite published long-term results (SD 14 months) results for deep sclerectomy with collagen implant. The study provided a qualified success rate of 94.8% and the complete success rate, 61.9% after 60 months (survival analysis), with a mean IOP at end of follow up of 11.8 (SD 3) mm Hg. Although the study reports a randomized consecutive series of patients, it should be taken as a proper indication of results achieved by experienced surgeons.

It should be considered that non-penetrating surgery is a broad genre of surgery, under which different surgeons perform fundamentally different procedures that include sinusotomy, ab externo trabeculectomy, deep sclerectomy with or without the use of an implant, viscoanastomolysis, performance of postoperative gonio-puncture, and the use of antimatobolites. The different techniques have in common, however, the element of non-perforation.

What is true is that this type of surgery is continuously evolving, so it is unlikely that a proper judgment can be made yet. At the risk of sounding dramatic, it is valid to say that editors like the one by Khaw et al seem to indirectly sign a death certificate of non-penetrating surgery. It is much more useful to encourage research in non-penetrating surgery, including multicentre randomised studies, to see if trabeculectomy will remain king.

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References

NOTICES
Role of optometry in Vision 2000

The latest issue of Community Eye Health (No 43) discusses the mobilisation of optometry to deal with uncorrected refractive error, which is now a major cause of functional blindness.

For further information please contact: Journal of Community Eye Health, International Centre for Eye Health, Institute of Ophthalmology, 11–43 Bath Street, London EC1V 9EY UK (tel: +44 (0)20 7608 6910; fax: +44 (0)20 7250 3207; email: eyeresource@ucl.ac.uk; web site: www.jche.co.uk). Annual subscription (4 issues) UK£25/US$40. Free to workers in developing countries.

International Centre for Eye Health

The International Centre for Eye Health has published a new edition of the Standard List of Medicines, Equipment, Instruments and Optical Supplies (2001) for eye care services in developing countries. It is compiled by the Task Force of the International Agency for the Prevention of Blindness. Further details: Sue Stevens, International Centre for Eye Health, 1–43 Bath Street, London EC1V 9EY UK (tel: +44 (0)20 7608 6910; email: eyeresource@ucl.ac.uk).

Second Sight

Second Sight, a UK based charity whose aims are to eliminate the backlog of cataract blind in India by the year 2020 and to establish strong links between Indian and British optometrists, is regularly sending volunteer surgeons to India. Details can be found at the charity web site (www.secondsight.org.uk) or by contacting Dr Lucy Matthen (lucymatthen@yahoo.com).

Specific Eye Conditions (SPECS)

Specific Eye Conditions (SPECS) is a not for profit organisational which acts as an umbrella organisation for support groups of any conditions or syndrome with an integral eye disorder. SPECS represents over fifty different organisations related to eye disorders ranging from conditions that are relatively common to very rare syndromes. We also include groups who offer support of a more general nature to visually impaired and blind people. Support groups meet regularly in the Boardroom at Moorfields Eye Hospital to offer support to each other, share experiences, and explore new ways of working together. The web site www.eyeconditions.org.uk acts as a portal giving direct access to support groups own sites. The SPECS web site is a valuable resource for professionals and may also be of interest to people with a visual impairment or who are blind. For further details about SPECS contact: Kay Parkinson, SPECS Development Officer (tel: +44 (0)1803 524238; email: k@eyeconditions.org.uk; web site: www.eyeconditions.org.uk).

The British Retinitis Pigmentosa Society

The British Retinitis Pigmentosa Society (BRPS) was formed in 1975 to bring together people with retinitis pigmentosa and their families. The principle aims of BRPS are to raise funds to support the programme of medical research into an eventual cure for this hereditary disease, and through the BRPS
16th Annual Meeting of German Ophthalmic Surgeons

The 16th Annual Meeting of German Ophthalmic Surgeons will be held 8–11 May 2003 in Nürnberg, Germany, Messezentrum. Organised by the Professional Association of German Ophthalmologists Ophthalmic Surgery Group the conference will cover cataract surgery, refractive surgery, glaucoma surgery, vitreoretinal surgery, corneal surgery, eye surgery in developing countries, and orbita, lacrimal and lid surgery. Further details: MCN Medizinische Congress organisation Nürnberg AG, Zerzebelshofstr 29, 90478 Nürnberg, Germany (tel: +49 911 3931621; fax: +49 911 3931620; email: doc@mcnag.info; web site: www.doc-nuernberg.de).

3rd British Oculoplastic Surgery Society Meeting

The 3rd British Oculoplastic Surgery Society Meeting will be held 18–19 May 2003 in Birmingham, UK. For further details please contact the Secretary of the British Oculoplastic Surgery Society Jane Olver (tel: +44 (0)121 424 5464; fax: +44 (0)121 424 4464; email: MartiDi@heartsol.wmids.nhs.uk; web site: www.bopss.org).

13th Meeting of the EASD Eye Complication Study Group

The 13th Meeting of the EASD Eye Complication Study Group will be held on the 23–25 May 2003, in Prague, Czech Republic. The scientific programme includes keynote lectures from Professor John H Fuller (UK) on The epidemiology of diabetic retinopathy; Dr P Martin van Hagen (The Netherlands) on Growth factors and diabetic retinopathy; Profesor Jerecic Pelikanova (Czech Republic) on Pathophysiology of diabetic microvascular complications; Dr Tomas Sosna (Czech Republic) on Risk and protective factors of diabetic retinopathy.

Three travel grants of €1000 each, sponsored by GlaxoSmithKline for young scientists (under 35 years at the time of the meeting). Applications should be made with the submission of abstracts. The deadline for abstracts is 14 February 2003. Further details: Ortopedické Centrum, s.r.o., Střeckovské nabrezi 51, 400 03 Usti nad Labem, Czech Republic (tel: +420 47 521 6588; fax: +420 47 533 40 77; email: ortcentrum-ul@voln.vy.cz; web site: www. ortopedick-centrum.cz).