Serpiginous choroidopathy presenting as choroidal neovascularisation

Serpiginous choroidopathy is an insidious, relentlessly progressive, idiopathic inflammatory disease affecting the retinal pigment epithelium and inner choroid. Choroidal neovascularisation (CNV) is a well-recognised late complication of serpiginous choroidopathy in 10–25% of affected patients. In all previously reported cases CNV was recognised at the time of or after the diagnosis of serpiginous choroidopathy was established. We report a patient presenting with CNV who subsequently developed clinical findings characteristic of serpiginous choroidopathy.

Case report

A 31 year old man presented with decreased vision in his right eye in July 1997. Examination revealed acuities of 20/40 right eye and 20/20 left eye with normal anterior segments. The right fundus showed subretinal fluid and haemorrhage adjacent to the disc (Fig 1A). The left eye showed an irregularity superior to the optic disc (Fig 1B). The vitreous and fundi were otherwise normal bilaterally. Fluorescein angiography (Fig 2A, B) revealed peripapillary choroidal neovascular membranes in both eyes that were treated with argon laser photocoagulation. In April 1998 and February 1999 the left eye required photocoagulation for recurrent peripapillary CNV. Evaluation for floaters in February 2000 revealed 1+ vitreous cells and new lesions in the left eye.

Examination at the National Eye Institute in April 2000 revealed acuities of 20/40 right eye and 20/16 left eye with normal anterior segments. The vitreous contained trace cells without haze bilaterally. The right fundus showed a large peripapillary chorioretinal scar. The left fundus revealed a chorioretinal scar superior to the disc and two yellow, irregularly circumscribed, deep macular lesions (Fig 3A, B). The retinal vessels and discs were normal and no subretinal fluid, haemorrhage, or macular oedema was noted in either eye.

Fluorescein angiography revealed early hypofluorescence and late hyperfluorescence corresponding to the macular lesions in the left eye (Fig 3C, D) with no evidence of CNV in either eye. Laboratory studies were non-diagnostic. A diagnosis of serpiginous choroidopathy was made based on the clinical and fluorescein characteristics of the macular lesions in the left eye.

Comment

CNV in serpiginous choroidopathy is associated with a poor visual prognosis. In a small study CNV was reported to develop within 16 months of the serpiginous diagnosis. In a larger retrospective study of 53 serpiginous patients active CNV was found in three patients at the time of initial diagnosis and in three others within 2–17 months. Our patient differs from those previously reported in that he was diagnosed and treated for idiopathic CNV before the recognition of clinical findings.
diagnostic of serpiginous choroidopathy. Other causes of posterior uveitis associated with CNV and choriotinal lesions similar to those seen in our patient include acute posterior multifocal placoid placoid epitheliopathy (APMPE), presumed ocular histoplasmosis syndrome (POHS), sarcoidosis, multifocal choroiditis, birdshot chorioretinopathy, and toxoplasmosis. As with most cases of serpiginous choroidopathy, the CNV in these entities typically occurs late in the disease course.

The exact pathogenesis of idiopathic CNV is unknown. CNV in eyes with uveitis, however, is believed to develop in direct response to the intraocular inflammation which may alter the balance between vascular growth factors, such as vascular endothelial growth factor (VEGF), and inhibitors. In the early stages of development active serpiginous lesions and CNV may appear as poorly defined subretinal lesions difficult to differentiate by ophthal-moscopy. Typically with fluorescein angiography classic CNV and serpiginous lesions are early distinguished as the former shows early hyperfluorescence while the latter characteristically shows early blockage. Occult CNV, which may show subtle or less pronounced early hyperfluorescence with late leakage, however, may be more difficult to distinguish from an early serpiginous lesion.

This case illustrates that serpiginous choroidopathy may present with CNV. In contrast to idiopathic CNV, optimal treatment of CNV in patients with uveitis may require immunosuppressive treatment that addresses the underlying ocular inflammation with or without adjunctive laser therapy. Further investigation is needed to better define the role of emerging therapies for CNV such as photodynamic therapy which may offer promise for the treatment of CNV in uveitis patients.

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References
1 Kuo IC, Cunningham ET Jr, Ocular neovascularization in patients with uveitis. Int Ophthalmol Clin 2000;40:111–26.
2 Jampol LM, Orth D, Daily Mj, et al. Subretinal neovascularization with geographic serpiginous choroiditis. Am J Ophthalmol 1979;88:683–9.
3 Erkiklo H, Laatikainen L. Subretinal and disc neovascularization in serpiginous choroiditis. Br J Ophthalmol 1982;66:326–31.
4 Blumenkrantz MS, Gass JD, Clarkson JG. Alterschichtige Chorioiditis. Arch Ophthalmol 1982, 100:1773–5.
5 Erkiklo H, Laatikainen L. A follow up study of serpiginous choroiditis. Acta Ophthalmol 1981;59:707–18.
6 Dees C, Arnold JJ, Forrester JV, et al. Immunosuppressive treatment of choroidal neovascularization associated with endogenous posterior uveitis. Arch Ophthalmol 1998;116:1456–61.
7 Fardet L, Costa RA, Mascioli C, et al. Photodynamic therapy with verteporfin for subfoveal choroidal neovascularization in Vogt-Koyanagi-Harada syndrome. Am J Ophthalmol 2002, 134:137–9.

Optic neuritis in anti-GQ1b positive recurrent Miller Fisher syndrome

Only five cases of optic nerve involvement in Miller Fisher syndrome (MFS) have been documented in the literature. This report further confirms that optic neuritis may be seen in anti-GQ1b positive MFS.

Case report
This 23 year old woman presented with acute blury vision, diplopia, and pain with eye movement. Her visual acuity was 20/20 right eye and 20/200 left eye with left relative afferent pupillary defect (RAPD). She had left red colour desaturation. Her visual field on tangent screen revealed an enlarged left blind spot and a left upper quadrant temporal peripheral field constriction. She had bilateral sixth nerve palsies, nystagmus in all gaxes, and left optic disc oedema. After 1 week her visual acuity improved to 20/20 in both eyes, but her left disc remained oedematous. She developed left lower limb gait ataxia to such a degree that she was unable to walk. Dysmetria and dysdiadochokinesia were more marked in her left upper extremity. She had very wide left upper extremity weakness, absent lower extremity deep tendon reflexes, and bilateral Babinski’s. She also had tingling in her hands and feet and decreased with sensory reflexes. Her mental status was normal throughout her illness. She was not taking any drugs. A magnetic resonance image (MRI) of the brain and entire spine and MR venogram were all normal. Her cerebrospinal fluid (CSF) opening pressure was 190 mm H2O. Her CSF protein was elevated at 70 mg/dl, but CSF glucose and cell count were normal; CSF VDRL, Gram stain, routine bacterial, viral, and fungal cultures were normal. The optic disc oedema was readily distinguished as the former shows early hyperfluorescence while the latter characteristically shows early blockage.

In the early stages of a recurrent Miller Fisher syndrome presenting as optic neuritis, the patient may present with a full recovery in this patient. Therefore, the elevated titres of anti-GQ1b antibody (212 EIA U (normal = 100) Athena Diagnostics, Wores- ter, MA, USA) was elevated again. She underwent plasmapheresis with full recovery in about 6 months.

Comment
In addition to the classic triad of ophthalmoplegia, ataxia, and areflexia, optic nerve involvement presenting as optic neuritis may be a feature of anti-GQ1b positive recurrent MFS. Only five cases of optic nerve involvement in MFS have been documented in the literature.2 In the two previously reported cases of visual impairment in MFS, visual evoked potentials were either absent6 or suggestive of pre-chiasmal and post-chiasmal visual pathway dysfunction.2 Demyelinating optic neuritis in patients with MFS have been documented in the literature recently.3-5 In the two previously reported cases, anti-GQ1b gangliosides are known to be present in the human optic nerve and anti-GQ1b antibodies can cross the blood-brain barrier, the optic disc oedema in this patient could represent a compromised optic disc due to optic neuritis in patients with MFS.6 MFS may be immunologically differentiated from GBS by the presence of anti-GQ1b and anti-GM1 antibodies. Although both anti-GD1a IgG and anti-GM1 IgG are associated with GBS, anti-GM1 IgG is present in patients with typical MFS who have limb weakness,7 as in this patient. As further evidence linking this antibody to MFS,7 the decrease in anti-GQ1b antibody levels after plasmapheresis correlated with the clinical recovery in this patient. Therefore, the elevated titres of anti-GQ1b and anti-GM1 antibodies, along with the clinical triad of ophthalmoplegia, ataxia, and areflexia in this patient also support the diagnosis of MFS, and not GBS.

In rare cases, MFS has been known to recur. This patient presented with a relapse of similar clinical features and neurological symptoms from her initial episode. In the study done by Chida et al.,9 patients with recurrent MFS appeared to have similar HLA typing characteristics as the non-recurring ones. Both types of HLA-DR2 and Cw3 alleles, but the frequency of HLA-DR2 was slightly higher in the patients with recurrent MFS.7 Therefore, this patient’s HLA-DR2-positive status may have been a risk factor for her recurrence of MFS.

This case report emphasises that optic neuritis may be a central nervous system feature that should be recognised as part of the Miller Fisher syndrome. The presence of both anti-GQ1b IgG and anti-GM1 IgG in this patient provides immunological evidence supportive
of typical MFS. The delayed P100 latency in her VEP also provides electrophysiological evidence that the optic nerve is affected in anti-GQ1b antibody positive MFS. Furthermore, this is the first documented case known to the author of optic neuritis in the recurrent subtype of MFS which is associated with a higher frequency of the HLA-DR2 allele.

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References
1 Fisher M. An unusual variant of acute idiopathic polymyelitis (syndrome of ophthalmoplegia, ataxia and areflexia). N Engl J Med 1956;252:57–65.
2 Ouhabi H, Bourassa A, Roumi A, et al. [Bilateral optic neuritis and ponto-mesencephalic involvement shown by MRI in Miller-Fisher syndrome] J [In French] Rev Neurol (Paris) 1996;154:780–2.
3 Toshniwal P. Demyelinating optic neuropathy with Miller Fisher syndrome. The case for overlap syndromes with central and peripheral demyelination. J Neurol 1987;234:353–8.
4 Carvalho AA, Galvao MD, Rocha MG, et al. Miller Fisher syndrome and optic neuritis: case report. Arq Neuropsiquiatr 2000;58:1115–7.
5 Colding-Jørgensen E, Vissing J. Visual impairment in anti-GQ1b positive Miller Fisher syndrome. Acta Neurol Scand 2001;103:259–60.
6 Sanaki Y, Takubo H, Arai T, et al. Atypical Fisher syndrome with optic nerve involvement. No To Shinkei 2001;53:571–3.
7 Yoshino H, Maeda Y, King M, et al. Sulfated glycosphingolipids and gangliosides in the optic nerve of humans. Neurology 1993;43:408–11.
8 Chida K, Nomura H, Konno H, et al. Serum IgG antibody to ganglioside GQ1b is a possible marker of Miller Fisher syndrome. Neurology 1994;44:35:234–7.
9 Kornberg AJ, Pestronk A, Biess K, et al. The clinical correlates of high-titer IgG anti-GM1 antibodies. Ann Neurol 1994;35:139–43.
10 Chida K, Nomura H, Konno H, et al. Recurrent Miller Fisher syndrome: clinical and laboratory features and HLA antigens. J Neurol Sci 1999;165:139–43.

Ocular myasthenia gravis and inflammatory bowel disease: a case report and literature review

Myasthenia gravis has been reported to be associated with both ulcerative colitis (UC) and Crohn’s disease (CD). The link between inflammatory bowel disease (IBD) and myasthenia gravis (MG) is thought to be related to the production of autoantibodies. Myasthenia gravis is also associated with other autoimmune diseases including alopecia, lichen planus, vitiligo, and systemic lupus erythematosus.

Similarly, IBD frequently presents with other autoimmune disorders. One study demonstrated a 9.4% prevalence of autoimmune disorders in patients with UC including sclerosing cholangitis, thyroid disorders, vitiligo, insulin dependent diabetes mellitus, thyroid disease, pernicious anaemia, scleroderma, and seropositive rheumatoid arthritis. Despite the association between MG and other autoimmune disorders, there are relatively few reports of ocular findings as the presenting sign of MG in patients with IBD.

Case report
A 21 year old African-American male, with a medical history of biopsy proved ulcerative colitis diagnosed in 1995, focal segmental glomerular sclerosis determined by renal biopsy in 1995, and primary sclerosing cholangitis determined by liver biopsy in 2000 presented to the neuro-ophthalmology service with complaints of binocular diplopia and ptosis of the left upper eyelid. Both the diplopia and the ptosis were better in the morning and worsened during the course of the day. His ulcerative colitis had been in remission for the past 5 years without medication.

Best corrected visual acuity was 20/25 in each eye. The external examination revealed ptosis of the left upper eyelid that worsened in sustained upgaze. He had limited extraocular motility in all fields of gaze (Fig 1). The remainder of the neuro-ophthalmic examination was normal and he had no difficulty with speech or swallowing.

Laboratory evaluation revealed a positive acetylcholine receptor antibody and normal thyroid function studies. There was no evidence of a thymic mass on magnetic resonance imaging of the chest.

The patient returned to the emergency room 1 week later with difficulty swallowing and shortness of breath. He was hospitalised for plasmapheresis and upon discharge treated with immun, prednison, and mestion. One month later his ptosis resolved and his extraocular motility was normal.

Comment
Autoimmune disorders, including MG, occur more frequently in UC than in CD. It is not clear how many other cases of IBD manifested with ocular presentations as the initial finding of MG as in our case report. Our literature review revealed only one other purely ocular presentation of myasthenia associated with ulcerative colitis; however, details of the ocular examination were not included.

Another report, of a 21 year old woman with a 3 year history of Crohn’s disease, documented diplopia and unilateral ptosis as the initial findings of MG. She was found to have acetylcholine receptor antibodies and her ocular findings improved with pyridostigmine.

Because of the relatively few reports of ocular myasthenia in patients with IBD we reviewed the English literature and found four additional reports of MG in patients with IBD. Based on these four reports and the three (including the present report) with ocular MG in patients with IBD (Table 1), the mean duration of IBD before the diagnosis of MG was 10 years.

Autoimmune dysregulation is the central defect in both MG and IBD. Both IBD and MG may be associated with an elevated carcinoembryonic antigen (CEA) and decreased peripheral lymphocyte counts that subsequently normalise following thymectomy. Some studies have shown abnormal thymic involution and the presence of an abnormal ratio of T suppressor to T helper cells in both MG and UC, while others have noted a decline in suppressor T cells and an increase in

Table 1 Previous reports of myasthenia gravis occurring in patients with inflammatory bowel disease

| Reference | Age (years) | Sex | IBD | Duration of IBD before diagnosis of MG (years) | AChR antibody reactivity |
|-----------|-------------|-----|-----|----------------------------------------------|-------------------------|
| Miller 1971| 35          | Male| UC  | 13                                           | Unknown                 |
| Tan 1974  | 38          | Male| UC  | 12                                           | Unknown                 |
| Martin et al, 1994 | 63 | Male | CD  | 15                                           | Positive                |
| Gowen-Rousseau et al, 1993 | 27 | Female | UC  | 10                                           | Positive                |
| Finnie et al, 1994 | 21 | Female | CD  | 3                                            | Positive                |
| Lossos et al, 1995 | 11 | Male | CD  | 9                                            | Unknown                 |
| Present report | 21 | Male | UC  | 7                                            | Positive                |

IBD = inflammatory bowel disease, MG = myasthenia gravis, AChR = acetylcholine receptor, UC = ulcerative colitis, CD = Crohn’s disease.

Figure 1 External photograph shows ptosis of the left upper eyelid, restriction of all extraocular movements of the left eye, and an elevation and adduction deficit of the right eye.

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immature helper T cells suggesting migration without normal maturation.\(^2\) The immunological link between MG and IBD is highlighted by two reports of patients undergoing surgical treatment. One report of a patient with both MG and CD documented improvement in perineal and perianal disease following proctectomy for severe uncontrolled MG.\(^3\) Another patient with both MG and UC demonstrated regression of the myasthenia following proctectomy.\(^4\)

Although the simultaneous occurrence of these two autoimmune disorders is uncommon, it is important to understand that ocular findings may be the initial manifestation of MG in patients with IBD. The authors have no proprietary interest in any contents of this manuscript.

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References
1 Martin RW, Shah A. Myasthenia gravis coexistent with Crohn’s disease. J Clin Gastroenterol 1991;13:112–13.
2 Souadjian JV, Enriquez P, Silverstein MN, et al. The spectrum of disease associated with thymoma. Coincidence or syndrome? Arch Intern Med 1974;134:374–9.
3 Finnie IA, Shields R, Sutton R, et al. Crohn’s disease and myasthenia gravis: a possible role for thymectomy. Gut 1994;35:278–9.
4 Tan RS. Ulcerative colitis, myasthenia gravis, atypical lichen planus, alopecia areata, vitiligo. Proc R Soc Med 1974;67:195–6.
5 Miller TN. Myasthenia gravis, ulcerative colitis and lichen planus. Proc R Soc Med 1971;64:806.
6 Papastesas AE, Kim U, Genkins G, et al. The association of carcinoembryonic antigen and peripheral lymphocytes. Surgery 1974;78:343–48.
7 Aso S, Yoshida T, Watanabe M, et al. Characterization of thymus cells in hyperplastic thymuses in patients with myasthenia gravis and ulcerative colitis with monoclonal antibodies. J Clin Lab Immunol 1984;13:137–9.
8 Gower-Rousseau C, Reumaux D, Bellard M, et al. Remission of myasthenia gravis after proctocolectomy in a patient with ulcerative colitis. Am J Gastroenterol 1993;88:1136–8.
9 Lossos A, River Y, Eilam A, et al. Neurologic aspects of inflammatory bowel disease. Neurology 1995;45(Pt 1):416–21.

Magnetic resonance imaging findings in malignant melanoma of the lacrimal sac

A case of primary malignant melanoma of the lacrimal sac is presented. This is the first report of the preoperative magnetic resonance imaging (MRI) findings of malignant melanoma of the lacrimal sac.

Case report

A 54 year old Chinese woman was referred to an ophthalmologist complaining of a 6 month history of left sided bloody tears and epistaxis. She had a firm, non-tender left medial canthal swelling, and syringing revealed left nasolacrimal duct (NLD) obstruction. Ocular and periorbital examination was otherwise normal. A dacryocystogram (DCG) demonstrated a filling defect in the lacrimal sac with NLD obstruction.

An ENT opinion was sought, and nasal examination revealed left sided septal deviation, with no obvious cause for the epistaxis. Computed tomography (CT) of the head and orbits demonstrated a left lacrimal sac lesion extending into the NLD with proximal dilation of the duct and no apparent bone erosion (Fig 1A) MRI confirmed the presence of a lacrimal sac lesion with intermediate signal intensity on T1 and T2 weighted images (Fig 2A, B) The lesion enhanced with intravenous gadolinium.

An incisional biopsy of the lacrimal sac (Fig 1B) under frozen section control, and paraffin sections, confirmed malignant melanoma.

A full medical review, including MRI of the chest and abdomen, and liver function tests, excluded tumour elsewhere. However, abdominal MRI and ultrasound revealed a co-incidental polycystic liver.

Three weeks after biopsy, a wide local excision including the medial upper and lower eyelids, dacryocystectomy and medial maxillectomy was performed. A tumour, confined to the sac, and invasion through the medial wall of the upper NLD, into the lateral wall of the nose, and apposing nasal septal mucosa, was seen peroperatively and confirmed histologically.

She underwent postoperative adjuvant radiotherapy (55 grays) and to date, 4 months later, remains well.

Comment

Malignant melanoma of the lacrimal sac is rare accounting for 5% of lacrimal sac tumours.\(^1\) It has an unfavourable prognosis compared with other causes of lacrimal sac tumour, and is considered more aggressive than cutaneous malignant melanoma.\(^2\) Response to treatment is generally poor, with up to 80% of cases recurring within 2 years.

Radiological features of lacrimal sac tumours include filling defects on DCG and mass lesions on CT.\(^3\) However, to the authors’ knowledge, this is the first report of the MRI findings of malignant melanoma of the lacrimal sac. Owing to the paramagnetic properties of melanin, malignant melanoma appears hyperintense on T1 weighted imaging, and hypointense on T2 weighted imaging.\(^4\) A study of six mucosal melanomas of the head and neck found that on T1, five lesions were hyperintense and one was iso-intense.\(^5\) On T2, five were of mixed intensity and one was iso-intense. They concluded that hyperintensity on T1 of mucosal melanomas was characteristic but not universal.

The majority of malignant lacrimal sac tumours are epithelial in origin.\(^6\) Imaging features suggesting malignancy include invasion of bone, rapid growth, and irregular margins with skin fixation. On MRI, the majority of epithelial tumours have intermediate signal intensity on T1 and high T2 signal intensity. High tumour cellularity is associated with intermediate to low T2 signal intensity.\(^7\)

High signal intensity on T1 is not specific for malignant melanoma. Subacute haemorrhage caused by the presence of methaemoglobin is more likely and although melanoma may undergo intratumoral haemorrhage, other tumours with a tendency to bleed include small cell lung carcinoma, choriocarcinoma, and renal cell carcinoma metastases. Less likely causes include fat containing tumours (lipoma, dermoid, and teratoma)
reducing MRI fat suppression methods, paramagnetic material (manganese, iron, and copper), and very high (non-paramagnetic) intratumoral protein concentration.

MRI has been reported as a useful investigative tool in the assessment of lacrimal disease owing to its ability to delineate soft tissues. Intravenous and intracanalicular gadolinium adds useful information on lesion enhancement and lacrimal apparatus structure and function. The predictive value of MRI for lacrimal sac melanoma, however, appears to be variable. Hyperintensity on T1 relies on the paramagnetic properties of melanin, the presence of which is variable in an melanotic melanoma. This is supported by our case, where only moderate T1 hyperintensity with contrast enhancement was demonstrated.

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References
1. Owens RM, Wax MK, Kostik D, et al. Melanoma and melanocytoma of the lacrimal sac. Otolaryngol Head Neck Surg 1995;113:634–40.
2. Pejer JJ, Stefanyszyn M, Hidayat AA. Nonneoplastic tumors of the lacrimal sac. Ophthal Plast Reconstr Surg 1994;10:169–84.
3. Kim SH, Han MH, Park SW, et al. Radiologic-pathologic correlation of unusual lingual masses. Part II: Benign and malignant tumors. Korean J Radiol 2001;4:22–52.
4. Yoshioka M, Kamada T, Kanda T, et al. MRI of mucosal malignant melanoma of the head and neck. J Comput Assist Tomogr 1998;22:492–7.
5. Stark DD, Bradley WD. Magnetic resonance imaging. 3rd ed. St Louis: Mosby, 1999.
6. Atlas SW. Magnetic resonance imaging of the brain and spine. 3rd ed. Philadelphia: Lippincott Williams and Wilkins, 2002.
7. Goldberg RA, Heinz GW, Chu L. Gadolinium magnetic resonance imaging of the orbit. Am J Ophthalmol 1993;115:738–41.

Photodynamic therapy for recurrent myopic choroidal neovascularisation after limited macular translocation surgery

Limited macular translocation (LMT) is one of the treatment options for subfoveal choroidal neovascularisation (CNV) resulting from pathological myopia. The fundamental surgical principle involves the transposition of the foveal neurosensory retina to a new site with more healthy underlying retinal pigment epithelium. Direct laser photoagulation is usually employed as an adjunct measure in eradicating the original CNV after the surgery. It has been observed that geometrically sizeable translocation is a prerequisite for a long term surgical success. The degree of translocation is, however, not often predictable and any ineffective displacement may render the subsequent laser photoagulation extremely difficult or even impossible to perform. As a result, the recurrent or persistent CNV intruding the newly relocated fovea may jeopardise the final visual outcomes. Photodynamic therapy (PDT) may be considered a viable adjunct treatment option in such circumstance.

Case report
A 41 year old woman with pathological myopia of −11.0 dioptres in both eyes presented with a subfoveal CNV and subretinal haemorrhage in her right eye in July 2000. The best corrected visual acuity (BCVA) was 5/200 in the right eye and 20/30 in her left eye. LMT with superotemporal 6 mm scleral imbrication was performed in July 2000. The operation was uneventful and an inferior displacement of the fovea by 600 µm was achieved. The CNV however, was still located in the vicinity of the juxtafoveal area and therefore laser photoagulation, bearing the potential risk of late creeping scar, was not suggested. At the 4 months postoperative visit, her left BCVA was 20/200 and the original CNV became more fibrotic with minimal leakage upon fluorescein angiogram. Nevertheless, she came back at 5 months with a return of metamorphopsia and a drop in her right vision from 20/200 to 10/200. Dilated fundus examination showed a tiny patch of submacular haemorrhage in direct continuity with the old fibrotic scar (Fig 1A). Fluorescein angiogram of the early phase demonstrated a fresh recurrent CNV budding out from the original CNV, extending to the centre of the foveal avascular zone (Fig 1B). Moderate fluorescence leakage could be seen in the late phase (Fig 1C). Treatment comprised revision macular translocation surgery, submacular surgery, photodynamic therapy, and observation had been thoroughly discussed with the patient. In view of minimal invasiveness and comparatively better preservation of surrounding neurosensory retinal tissue, PDT was adopted in treating the CNV recurrence. PDT with verteporfin infusion and laser delivery was performed in accordance with the standard protocol. After the treatment, the blood clot in the fovea was gradually resolved and the vision improved to 20/200 at 3 months of follow up. Complete regression of the recurrent CNV at the fovea without angiographic leakage was documented over the follow up angiogram at 3 months and subsequently (Fig 1D). The vision remained stable at 20/200 in the latest visit at 24 months after the PDT.

Comment
It has been shown that significant visual improvement may be achieved by LMT for the treatment of subfoveal CNV associated with age related macular degeneration (AMD) or pathological myopia. However, the surgical techniques are demanding and the potential complications are not unusual. One of the late postoperative visually important complications is recurrence of the CNV and this is partially caused by an ineffective translocation of the fovea or a large lesion size of CNV. The incidence of persistent or recurrent CNV after limited LMT has been reported to be 40% and 35% respectively in age related macular translocation and being 21% and 14% respectively in pathological myopia. Not many treatment options are available once the fovea is involved. Viable surgical options including repeated LMT, full 360 degree retinotomy MT, or submacular surgery may be considered but the surgical risk may be inadvertently higher in the redensation of the neurosensory retina. PDT induces a selective thrombosis of the abnormal CNV and has been proved to be an effective treatment in preventing a significant loss of vision in patients with CNV secondary to AMD or pathological myopia.

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Its clinical indications and applications are expanding. Its minimal invasiveness and clinical efficacy make it a safer and visually desirable supplementary treatment in recurrent CNV after LMT. In our patient, the complete closure of CNV was achieved with concomitant vision improvement after a single session of PDT without evidence of recurrence for 24 months.

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References
1. Tano Y. Pathologic myopia: where are we now? Am J Ophthalmol 2002;134:645–60.
2. Lewis M, Kaiser PK, Lewis S, et al. Macular translocation for subfoveal choroidal neovascularization in age-related macular degeneration: a prospective study. Am J Ophthalmol 1999;129:135–46.
3. Fujii GT, Humayun MS, Pieramici DJ, et al. Initial experience of inferior limited macular translocation for subfoveal choroidal neovascularization resulting from causes other than age-related macular degeneration. Am J Ophthalmol 2001;131:90–100.
4. Fujii GT, Humayun MS, Pieramici DJ, et al. Inferior limited macular translocation for subfoveal choroidal neovascularization secondary to age-related macular degeneration: 1-year visual outcome and recurrence report. Am J Ophthalmol 2002;134:69–74.
5. Hamelin N, Glacet-Bernard A, Brindeau C, et al. Surgical treatment of subfoveal neovascularization in myopic macular translocation vs surgical removal. Am J Ophthalmol 2002;133:530–6.
6. Treatment of Age-Related Macular Degeneration with Photodynamic Therapy (TAP) Study Group. Photodynamic therapy of subfoveal choroidal neovascularization in age-related macular degeneration with verteporfin: two-year results of 2 randomized clinical trials—TAP Report 2. Arch Ophthalmol 2001;119:206–207.
7. Sickenberg M, Schmidt-Erfurth U, Miller JW, et al. A preliminary study of photodynamic therapy using verteporfin for choroidal neovascularization in pathologic myopia, ocular histoplasmosis syndrome, angiod streaks, and idiopathic causes. Arch Ophthalmol 2000;118:372–36.

Acquired Glanzmann’s thrombasthenia causing prolonged bleeding following phacoemulsification

Phacoemulsification under topical anaesthesia had received 60 units of blood transfusion over a period of 1 year. Interestingly, she had appendicectomy and multiple dental extractions elsewhere many years previously without any significant bleeding. She has not been on any anticoagulant agents or antiplatelet. There was no family history of bleeding disorders.

A defect in the platelet function was suspected, as her coagulation screen including the platelet count was normal. Platelet aggregation tests showed no aggregation against any agonists other than ristocetin, which is dependent on platelet glycoprotein Ib. The patient showed normal normal platelet glycoprotein antigens IbIIa and Ib. The patient’s serum showed presence of inhibitory antibody against glycoprotein IbIIa. This led to a diagnosis of acquired Glanzmann’s syndrome, an extremely rare condition of autoimmune thrombasthenia. No underlying malignant, autoimmune, or lymphoproliferative disorder had been identified as a cause for this patient’s acquired Glanzmann’s thrombasthenia.

Comment

The patient described uncontrollable bleeding for 36 hours following a procedure, which is generally considered safe and can be performed with a bleeding disorder. She developed bleeding from the conjunctival site where the surgeon grasped the conjunctiva during certain stages of the procedure. One would usually not expect any significant bleeding from this site; however, in a patient with compromised haemostasis the bleeding may be prolonged. Although the bleeding was no more than a gentle ooze at any point in time it was persistent enough for 36 hours before the topical haemostatic material Surgicel had been put to use. The consequences of an intraocular bleed may have seriously threatened her sight.

We are not aware of any reports of the use of Surgicel in ophthalmic surgery. All reports of its use are in other fields of surgery. This material is supposed to swell up with blood and form a gelatinous mass that aids in the formation of clot. It acts as a haemostatic adjunct. The exact mode of its action in this patient with antiplatelet antibodies is unclear. Our experience shows that oxidised regenerated cellulose (Surgicel) may have a role in ophthalmic surgery especially in lacrimal and orbital surgery, when faced with bleeding that is difficult to stop. Various cautionary tales associated with use of Surgicel have been reported.

Our report suggests that in the presence of a severe bleeding disorder, clear corneal phacoemulsification under topical anaesthesia may not be totally safe. When performing such a procedure in a patient with known bleeding disorder it may be safe to take all the necessary precautions in consultation with a haematologist to avoid a serious bleed that may be sight and life threatening. There may be a role for haemostatic agents like Surgicel.
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References

1. George JN, Caen JP, Norden AD. Glanzmann’s thrombasthenia: the spectrum of clinical disease. Blood 1990;75:1383–85.

2. Greaves M, Pickering C, Porter NR, et al. Acquired Glanzmann’s thrombasthenia. Blood 1983;61:209.

3. Saatci AO, Kuvaki B, Oner FH, et al. Bilateral massive choroidal hemor rhage secondary to Glanzmann’s syndrome. Ophthalmic Surg Lasers 2002;33:148–51.

4. Aidonopoulos AP, Papavramidis ST, Gioutzamantis GD, et al. A simple and safe method for preservation of the injured spleen. Injury 1993;24:300–2.

5. Davidson RR, Burnett S, Javed MS, et al. Experimental study of a novel fibrin sealant for achieving haemostasis following partial hepatectomy. Br J Surg 2000;87:790–5.

6. Kothbauer K, Jallo GI, Siffert J, et al. Foreign body reaction to hemostatic materials mimicking recurrent brain tumor. Report of three cases. J Neurosurg 2001;95:503–6.

7. Young ST, Paulson EK, McCann RL, et al. Appearance of oxidized cellulose (Surgicel) on postoperative CT scans: similarity to postoperative abscess. Am J Roentgenol 1993;160:275–7.

8. Buckley SC, Brouse JC. A foreign body reaction to Surgical mimicking an abscess or tumour recurrence. Br J Neurosurg 1995;9:561–3.

Propionibacterium acnes endophthalmitis diagnosed by microdissection and PCR

Although Propionibacterium acnes, a Gram positive anaerobic bacillus, is the most commonly identified cause of delayed onset postoperative endophthalmitis, routine vitreous cultures are frequently inadequate for its diagnosis. This case describes the utility of the histopathological technique of microdissection and polymerase chain reaction (PCR) for the diagnosis of delayed postoperative endophthalmitis.

Case report

A 78 year old man with a history of vitreous floaters, a coronary bypass, and aortic valve replacement underwent an uncomplicated cataract extraction with intraocular lens (IOL) implantation in the right eye. Three months later, he developed increasing floaters in the right eye and was diagnosed with vitritis unresponsive to corticosteroid treatment. Examination revealed acuities of 20/25 in the right eye and 20/20 in the left with normal intraocular pressures. The right eye was significant for no anterior chamber cells or flare, dilated iris vessels, an IOL without deposits, 3+ vitreous cells with trace haze, and peripheral pigmented degeneration. The left eye was normal with the exception of trace vitreous cells and a choroidal naevus. A diagnostic vitrectomy was performed in the right eye. A portion of the vitreous specimen was cultured for fungi, aerobic and anaerobic bacteria, and the remainder was processed for cytopathological examination. All cultures for micro-organisms were negative.

The vitreous supernatant and unstained cytology slides were sent to the National Eye Institute for further evaluation. Viteal analysis for interleukin 2 (IL-2), IL-4, IL-6, IL-10, IFN-γ, and TNF-α using ELISA (Endogen, Woburn, MA, USA) revealed undetectable cytokine levels. The vitreous slides were stained with Giemsa, Gram, and immunohistochemical stains for T cells, B cells, and macrophages. Cytopathological examination showed clusters of macrophages admixed with CD4+ and CD8+ T cells and B cells (Fig 1A). Gram positive bacilli were seen in the cytoplasm of a few macrophages (Fig 1B). The engulfed bacilli were microdissected under a microscope with a 30 gauge needle and submitted for PCR.1 Nestled PCR with P. acnes specific oligodeoxynucleotide primers complementary to regions of 16S rDNA was used.2 The primers were Pa1, AAG GCC CTG CTT TTG TGG; Pa2, TCC ATC CGG AAC CGC CGA A; and rPa3, ACT CAC GCT TCG TCA CAG. Nested-PCR analysis revealed P. acnes (Fig 2). A diagnosis of delayed postoperative endophthalmitis was made.

Comment

The most common causes of vitritis in elderly patients are acquired or postoperative infections, sarcoidosis, and intraocular malignancies masquerading as uveitis.3 An early diagnostic procedure is indicated if postoperative endophthalmitis is suspected. In this case, although the chronic inflammation and intracytoplasmic Gram positive bacilli in a few macrophages suggested an infectious process, the negative cultures precluded the diagnosis of an infectious endophthalmitis. To further investigate the possibility of a bacterial infection nested PCR was performed on the microdissected bacilli.3 Molecular analysis verified the presence of P. acnes and a diagnosis of delayed postoperative endophthalmitis was confirmed.

Vitreous cultures are positive in less than 50% of postoperative endophthalmitis cases. In a study of 23 patients with delayed onset endophthalmitis aqueous culture and microscopy were diagnostic in 0% of cases, vitreous culture was positive in 24% and PCR from the aqueous and vitreous yielded a positive diagnosis in 84% and 92%, respectively.4 Treatment of P. acnes endophthalmitis includes intravitreal vancomycin plus consideration of pars plana vitrectomy with or without capsulotomy with or without IOL removal. Although aggressive surgical intervention eradicates the infection similar visual outcomes are reported with more limited surgical treatment.

In our case the intracytoplasmic bacteria in the macrophages were the only evidence of a bacterial infection. To detect the presence of P. acnes we referenced the PCR method described by Hykin that used 150 µl of the vitreous for culture and 100 µl for PCR.5 Using the technique of microdissection and PCR with a similar volume of vitreous we additionally performed cytology and cytokine analysis which are helpful in the diagnosis of other causes of vitritis.6

This case further illustrates the benefits of molecular analysis for the diagnosis of culture...
negative delayed onset endophthalmitis. It also describes for the first time microdissection and PCR for the evaluation of endophthalmitis. Advantages of this technique are that it allows for a more comprehensive pathological examination on a limited specimen and provides the option of having the molecular studies being performed elsewhere.

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References
1 Zhuang Z, Berheudeau P, Emmert-Buck MR, et al. A microdissection technique for archival DNA analysis of specific cell populations in lesions <1 mm in size. Am J Pathol 1995; 146: 935–9.
2 Hykin PG, Tabol K, McIntyre G, et al. The diagnosis of delayed post-operative endophthalmitis by polymerase chain reaction of bacterial DNA in vitreous samples. J Med Microbiol 1992;40:408–15.
3 Bertain AM, Davis JL. Uveitis following intraocular surgery. Ophthalmol Clin North Am 2002;15:357–64.
4 Lohmann CP, Pinch HJ, Reischl U. Improved detection of microorganisms by polymerase chain reaction in delayed endophthalmitis after cataract surgery. Ophthalmology 2000;107:1047–51; discussion 1051–2.
5 Aldave AJ, Stein JD, Deramo VA, et al. Treatments strategies for postoperative Proptosis due to naspharyngeal endophthalmitis. Ophthalmology 1999;106:2395–401.
6 Buggage RR, Whitcup SM, Nussenblatt RB, et al. Using interleukin 10 to distinguish primary intraocular lymphoma and uveitis. Invest Ophthalmol Vis Sci 1999;40:2462–3.

Figure 1 | (A) Conjunctival MALT lymphoma, nasal fornix of left eye. (B) Histological section of conjunctival mucosa demonstrating dense lymphoid infiltrate (haematoxylin and eosin, original magnification ×200).

Interferon treatment of childhood conjunctival lymphoma
Mucosa associated lymphoid tissue (MALT) lymphoma is the most common ocular adnexal neoplastic lesion. These neoplastic lesions have a more indolent course than non-MALT lymphomas, are usually found in the older age groups (50–70 years), are usually limited to localised (stage I) disease at presentation, and radiotherapy and chemotherapy have been the mainstay of treatment.1

Case report
A 15 year old male was referred by an ophthalmologist after an 8 month history of unusual painless follicles at both nasal fornices (Fig 1A). There were no visual symp- toms and, based on a working diagnosis of an atypical vernal reaction, topical steroid treatment had resulted in mild size reduction of the lesions. Incisional biopsy was performed after the lesions remained static for 3–4 months.

The patient’s visual acuity was 6/4 in both eyes and intraocular pressures measured 15 mm Hg in each eye. Slit lamp examination demonstrated small follicular deposits in both nasal fornices and nasal palpebral conjunc- tiva. The rest of the ocular examination was unremarkable. Review of systems was negative and the patient’s past medical history and family medical history did not reveal the presence of lymphoproliferative or autoimmune diseases. There were no findings suggestive of Sjögren’s syndrome and physical examination was normal.

The limited amount of biopsy tissue was divided for routine processing and flow cytometry; frozen tissue was therefore unavailable. Histologically a dense lymphoid infiltrate including benign appearing lymphoid follicles was identified (Fig 1B). Lymphoid follicles were surrounded by centrocytic-like cells and small lymphocytes, some of which infiltrated the conjunctival epithelium. Flow cytometry identified a monoclonal B cell population with a CD5−, CD20+, CD10 equivocal phenotype. The histopathological findings in isolation may have represented either an early marginal zone lymphoma or a benign B cell follicular hyperplasia. Absolute distinction on the small amount of tissue was not possible. However, in conjunction with the flow cytometric finding of a monoclonal B cell population, a diagnosis of low grade B cell lymphoma (probably of MALT type) could be made.

Systemic disease was excluded after the following investigations: lumbar puncture; bone marrow aspirate and trephine; CT chest, abdomen, pelvis and sinuses; gallium scan. The patient was subsequently treated with 10 intralusal injections of 10 x 10^6 IU of interferon alfa (IFN-α) over a 4 week period; no side effects were noted during this time. Complete resolution was achieved at 2 months, with no sign of recurrence after 18 months follow up.

Comment
Conjunctival lymphoma is mostly a disease of the elderly, with Shields et al reporting a mean age of diagnosis of 61 years.2 While not a common disease, Akpek et al suggest that its prevalence is higher than previously recognised, and that vigilance is required in patients with chronic ocular irritation and conjunctivitis who do not respond to conventional therapy.3 This is the youngest case of conjunctival lymphoma that we know of in the literature; hence conjunctival lymphoma should be considered in the differential diagnosis of atypical conjunctival lesions in younger patients.

Treatments outlined by Shields et al included radiotherapy (44%), complete excisional biopsy (36%), observation (9%), chemotherapy (6%), and cryotherapy (4%).1

Radiotherapy has been widely used with successful results,4 but ocular morbidity in the form of corneal ulcer, radiation induced cataract and ocular lubrication disorders have been reported.5 6 Intralosomal IFN-α is a relatively new therapy which has been shown to be both effective and safe in a small number of cases.5 7 8 Non-sight threatening ocular complications such as subconjunctival haemor- rhage and local chemotherapy have been reported, as well as minor transient systemic effects including headaches, nausea, fever, chills, and myalgia.9 Administration of intralosomal IFN-α is also a relatively simple and quick procedure. It shows great promise as a first line agent to treat conjunctival lymphoma, but long term follow up is needed.

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References
1 Blasi MA, Gherlinzoni F, Calvisi G, et al. Local chemotherapy with interferon-α for conjunctival mucosa-associated lymphoid tissue lymphoma. Ophthalmology 2001;108:559–62.
2 Shields CL, Shields JA, Carvalho C, et al. Conjunctival lymphoid tumours. Clinical analysis of 117 cases and relationship to systemic lymphoma. Ophthalmology 2001;108:979–84.
3 Akpek EK, Polcharoen W, Ferry JA, et al. Conjunctival lymphoma masquerading as chronic conjunctivitis. Ophthalmology 1999;106:757–60.
4 Heuring AH, Franke FE, Hütz WW. Conjunctival CD5+ MALT lymphoma. Br J Ophthalmol 2001;85:498–9.
5 Cahill MT, Moriarty PA, Kennedy SM. Conjunctival “MALToma” with systemic recurrence. Arch Ophthalmol 1998;116:97–9.
6 Scullia L, Manganello C, Turca S, et al. Bilateral non-Hodgkin lymphoma of the conjunctiva. Eye 1999;13:379–80.
7 Bessel EM, Henk JM, Whitelocke JF, et al. Ocular morbidity with radiotherapy of orbital and conjunctival lymphoma. Eye 1998;1:90–6.
8 Larcherrele RR, Rathee R, Kratky V, et al. Treatment of conjunctival mucosa-associated lymphoid tissue lymphoma with intralcellular injection of interferon alfa-2b. Arch Ophthalmol 2000;118:284–9.
9 Cellini M, Possati G, Puddu P, et al. Interferon alpha in the therapy of conjunctival lymphoma in an HIV+ patient. Eur J Ophthalmol 1996;6:473–7.

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Unilateral corneal anaesthesia and ulceration following squint surgery in a child with Pendred syndrome and bilateral sixth nerve palsy

We present a 4 year old child with Pendred syndrome and bilateral sixth nerve palsy. To our knowledge this association has not been previously reported. In addition, this patient developed unilateral corneal ulceration with associated corneal anaesthesia following squint surgery. We will discuss the pathophysiology of this unusual complication following squint surgery.

Case report

This patient presented when he was 6 months old with right congenital squint. He was diagnosed with Pendred syndrome (sensorineural hearing loss and thyroid dysfunction) by the paediatricians and the oto-laryngologists following abnormal thyroid function tests and a computed tomograph (CT) scan of the temporal bones showing Mondini malformations of both cochleae. At presentation his visual acuities were 6/60 right eye and 6/60 left eye using the Cardiff acuity cards. He had bilateral alternating esotropia with an inability to abduct either eye. There was no globe retraction or abnormal lid movements and a magnetic resonance imaging (MRI) scan had shown congenital absence of the auditory nerves but no other abnormality. A diagnosis of bilateral sixth nerve palsy was made. The squint was cosmetically poor and measured at 45 prism dioptres in the distance and near. He had low hypermetropia with no significant anisometropia. Funduscopy was normal. He was reviewed regularly in the paediatric eye clinic over the next 3 years during which time his visual acuities were within normal limits, the best recorded acuity being 6/9 right eye and 6/9 left eye using singles.

When he was 4 years old, he underwent bilateral superior rectus and inferior rectus lateral transpositions under general anaesthesia, which was uneventful with no immediate postoperative complications, and a cosmetic improvement achieved. The alternate position of the superior rectus before surgery is shown in Fig 1 with surrounding punctate epitheliopathy which surprisingly did not seem to cause him as much distress as expected. The left corneal sensation was definitely reduced compared to the right which appeared normal. Sensation was assessed clinically (an anaesthesiometer was not available), and was consistently reproducible by different ophthalmologists. There was no exophthalmos or any other sign of thyroid orbitopathy. The right eye remained asymptomatic. Empirical therapy with topical ofloxacin and lubricants was unhelpful. He proceeded to have glue tarsorrhaphy which transiently aided the healing of the corneal ulcer. However, the ulcer quickly recurred when the tarsorrhaphy reversed. He subsequently had left inferior lid shortening with a caudal sling to elevate the lower lid to protect the corneal epithelium. The ulcer resolved leaving an area of corneal scarring. He is being reviewed regularly in the eye clinic.

Comment

Pendred syndrome is an autosomal recessive disorder characterised by congenital deafness and thyroid goitre. The hearing loss is usually severe and is present at birth, and the goitre generally appears at puberty or later but may be present in early childhood with an associated euthyroid or hypothyroid state. The affected individuals are reported to be otherwise normal.

The pathophysiology of the corneal anaesthesia and ulceration in this patient is uncertain. In the absence of corneal anaesthesia, they include herpes simplex keratitis, postoperative anterior segment ischaemia, surgical trauma to the long posterior ciliary nerves or ciliary ganglion, congenital absence of sensation, and surgery reducing Bell’s phenomenon. The clinical course was not typical of herpes simplex and there was no previous history of corneal pathology. Postoperative anterior ischaemic syndrome was unlikely as only two recti muscles were operated on and no anterior uveitis was observed. To our knowledge there are no reported cases of corneal anaesthesia after squint surgery. There was no evidence of pre-existing involvement, which one may expect with trauma to the long posterior ciliary nerves or ciliary ganglion.

Congenital absence of corneal sensation was the most likely cause, especially in view of his unusual cranial nerve anomalies, and we believe he had pre-existing corneal anaesthesia before squint surgery despite the absence of any other fifth cranial nerve signs. Following the lateral transposition of the superior rectus his Bell’s phenomenon was noted to be absent thereby compromising his corneal protection. In addition, he was observed to have significant lagophthalmos while asleep. We believe that the combination of corneal anaesthesia, abolished Bell’s phenomenon, and lagophthalmos compromised his corneal integrity resulting in corneal ulceration.

This case highlights the importance of determining corneal sensation before transposition surgery on the superior rectus as Bell’s phenomenon may be abolished therefore compromising corneal protection. This is especially relevant in patients with unusual cranial neuropathy and lagophthalmos.

References

1 Pendred V. Deaf mutism and goitre. Lancet 1896;11:532.

2 Reardon W, Trembath RC. Pendred syndrome. J Med Genet 1996;33:1037–40.

3 Reardon W, Coffey R, Phelps PD, et al. Pendred syndrome—100 years of underascertainment? Q J Med 1997;90:443–7.

4 Fraser GR. Association of congenital deafness with thyroid goitre (Pendred’s syndrome) of study of 207 families. Ann Hum Genet 1965;28:201–49.

Gemella haemolyans acute postoperative endophthalmitis

Endophthalmitis is perhaps the most feared complication of cataract surgery, with a reported incidence between 0.01% and 0.13%. The most common organisms reported in previous studies are Gram positive staphylococci and streptococci. We report a case of severe endophthalmitis with an unusual Gram positive organism, after uncomplicated phacoemulsification, with foldable intraocular lens implantation.

Case report

A 66 year old white man underwent routine phacoemulsification cataract extraction with posterior chamber lens implantation (Acrylent, Modiphacos, Hydrotan HM60, Bausch & Lomb) to the right eye in January 2002. The left eye had previously undergone similar surgery in September 2001. He was generally in good health, and on no medication. There was a past medical history of sarcoidosis treated with oral prednisolone in 1970, which has since been in remission, and an episode of staphylococcal septicemia in 1987, without sequelae.

On the first postoperative day, visual acuity measured 6/9 unaided and ocular examination was unremarkable. That same afternoon the patient developed ocular pain, initially relieved by paracetamol (acetaminophen), which however, worsened during the night with progressive deterioration of vision. He presented to the ophthalmic emergency department the following morning with the aforementioned symptoms. Visual acuity was reduced to hand movements right eye and 6/9 left eye. Slit lamp examination revealed an oedematous cornea with Descemet’s folds. The anterior chamber was hazy, with 1 mm hypopyon and the intraocular pressure measured 38 mm Hg.

There was no red reflex. B-scan ultrasound examination showed extensive vitreous debris with attached retina. The left eye was pseudo-phakic with no abnormalities of note. A diagnosis of acute postoperative endophthalmitis was made. Anterior chamber and vitreous samples were obtained for aerobic and anaerobic culture/sensitivity and Gram staining. Intravitreal vancomycin 2 mg and amikacin 300 µg, each in 0.1 ml of balanced salt solution and subconjunctival ceftazidine 125 mg were administered. Oral ciprofloxacin 500 mg once daily, prednisolone 1 mg once a day, topical gentamicin hourly, ofloxacin hourly, and atropine 1% twice a day were commenced.

Preliminary Gram staining suggested a Gram positive coccus sensitive to ciprofloxacin—oral and topical antibiotics were therefore continued. Owing to difficulty in identifying the nature of the organism, the samples were sent to a regional reference laboratory, which identified Gemella haemolyans from both anterior chamber and vitreous aspirates. The organism was reported to be sensitive to gentamicin, ciprofloxacin, laevofloxacin, amoxicillin, clavulanate, chloramphenicol, and resistant to trimethoprin.

Figure 1 Inferior corneal ulcer before treatment.
The patient continued to make steady progress; 2 months later vision had improved to 6/9 unaided. The patient at that time was troubled by floaters secondary to considerable vision loss. It was reported to have active sarcoidosis on 21 July 2003.

Comment

Gemella haemolysans is an aerobic or facultative anaerobic, Gram positive coccus, a normal commensal of the oral cavity and upper respiratory tract of low virulence.1 Systemic infection may lead to septic shock, meningitis, arthritis, or pneumonia, all of which are rare. Identification is difficult. Though Gram positive, the cocci are easily decolourised and hence may appear Gram variable or even negative.

Initially Gemella was included under the genus Neisseria but is now classified as a separate genus within the family Streptococcaceae.1 No studies on susceptibility to antiseptics have been published, though there is no reason to believe that it may be resistant to povidone-iodine preparations. The organism is stable in vitro to penicillin, streptomycin, vancomycin, chloramphenicol, and tetracyclines.

A literature search revealed only one previously reported case of infection by Gemella haemolysans, with keratitis and consecutive endocarditis.1,2 Interestingly this patient was reported to have active sarcoidosis on systemic steroid therapy, whereas our patient had a past history of sarcoidosis. This possible association between sarcoidosis and infection by Gemella may be purely coincidental, as no such association has been reported with systemic infection.

Gemella haemolysans is difficult to identify, because of its close resemblance to viridans streptococci and Neisseria. As diagnostic technology improves, Gemella haemolysans endophthalmitis may be described more often in the future.

References

1. Aaberg TM Jr, Flynn HW Jr, Schlaifer J, et al. Nosocomial acute-onset postoperative survey, a ten-year review of incidence and outcomes. Ophthalmology 1998; 105: 1004–10.
2. Javitt JC, Virda S, Canner JK, et al. National outcomes of cataract extraction: endophthalmitis following inpatient surgery. Arch Ophthalmol 1991; 109: 1083–9.
3. Shroder KS, Band JD, Lauter CB, et al. The clinical spectrum of endophthalmitis, predisposing factors, and features influencing outcome. J Infect Dis 1990; 162: 810–20.
4. The Endophthalmitis Vitrectomy Study Group. Results of the endophthalmitis vitrectomy study, a randomised trial of immediate vitrectomy and of intravenous antibiotics for the treatment of postoperative bacterial endophthalmitis. Arch Ophthalmol 1995; 113: 1479–96.
5. Fresard A, Michael VP, Rueda X, et al. Gemella haemolysans endocarditis. Clin Infect Dis 1993; 16: 585–7.
6. Ritterband D, Shih M, Kressloff M, et al. Gemella haemolysans endocarditis and consecutive endophthalmitis. Am J Ophthalmol 2002; 133: 268–70.
7. Klipper-Britton K, Schleifer KH. Transfer of Streptococcus morbillorum to the Gemella genus, Gemella morbillorum comb nov. Int J Syst Bacteriol 1998; 38: 442–3.

Does topical brimonidine tartrate help NAION?

There is no proved treatment for non-arteritic anterior ischaemic optic neuropathy (NAION). Topical brimonidine tartrate has been reported to have a neuroprotective benefit for retinal ganglion cells following experimental elevation of intraocular pressure and optic nerve injury in the rat, which is blocked with coadministration of the α2 antagonist, rauwolscine.3 Increased retinal ganglion cell survival has also been shown to occur following oral administration of brimonidine in monkeys with experimental glaucoma.4 These results were the basis of the recently aborted clinical trial of topical brimonidine purrute for acute NAION and our prospective study of 31 patients with NAION, who were evaluated within 3 weeks of the onset of visual loss and followed up for a minimum of 8 weeks. During 2001–2, we treated all (14) patients with brimonidine tartrate within 14 days (mean 3.5, SD 5.52) of the onset of visual loss. Five patients were treated after 1 day of symptoms. Three were taken four times a day in 11, three times a day in one, and twice a day in two patients. All (17) untreated patients were evaluated the year before and were matched to the treated group for age, sex, cardiovascular risk factors, previous aspirin use, and previous first eye NAION.

Snellen visual acuity and colour vision, using the Ishihara colour plates, were documented and expressed as a decimal equivalent (for acuity: 20/60 = 0.33 and light perception = 0.001; for colour vision: the number of correctly identified plates/the total number of isotypes). The visual fields (Humphrey or tangent perimetry) were analysed and detected as graded according to the following scale: 0 = normal, 1 = arcuate nerve fibre bundle defects, 2 = retinal perimetry defects (6 degrees), 3 = centrocaecal or altitudinal defects, 3 = altitudinal defect plus additional loss, 4 = no light perception. A third examiner, who was unaware of the dates of the visual fields and the patients' treatment status, also evaluated all visual fields and determined, in each patient, whether the field was better or worse than or equivalent to the other field. The intraocular pressure was measured before and after treatment on two patients. The pressure was 25 mm Hg in one patient in the untreated group and 24 mm Hg in one patient in the treated group.

Statistical analysis of the data involving comparisons of the treated and untreated groups at baseline and 8–12 weeks was performed using the two tailed t test. The Wilcoxon signed rank test was used to compare the individual vision performance from baseline to the 8–12 week examination. For visual acuity and colour vision, a positive rank indicated improvement and a negative rank indicated a worse visual outcome. For the visual field grade value was better for the treated group (p = 0.007). At the 8–12 week examination, the mean visual acuity was 0.29 (SD 0.30) for treated and 0.49 (SD 0.39) for untreated patients. The mean visual field grade value was 2.2 (SD 0.81) for treated and 1.6 (SD 0.70; p = 0.04) for untreated patients. The mean colour vision was 0.42 (SD 0.41) for treated and 0.55 (SD 0.46; p = 0.43) for untreated patients.

For the masked examiner’s evaluation, the mean baseline visual field (2.0, SD 0.91) was similar to the field (1.93, SD 0.96: p = 0.85) for controls. At the 8–12 week examination, the mean visual field grade was 2.15 (SD 0.99) for treated and 1.87 (SD 0.92; p = 0.43) for untreated patients. This examiner further found that the outcome visual fields for the treated group were improved in two patients, worsened in six patients (50%), and unchanged in four patients. The outcome visual fields for the control group were improved in five patients, worse in two patients (13%), and unchanged in eight patients.

The Wilcoxon signed rank analysis demonstrated that for visual acuity, two patients in the control group and 10 patients in the treated group had negative values or a worse outcome at 8–12 weeks (p = 0.007). For colour vision, one patient in the control group and eight patients in the treated group had negative values or a worse outcome (p = 0.013). For visual fields, one patient in the control group and four patients in the treated group showed positive values or a worse outcome at 8–12 weeks (p = 0.046).

The average time to start the drops was 3.5 days from the onset of visual loss in the patients who worsened. There was no correlation with a worse outcome and time to initiate therapy.

For all parameters of vision testing, there was a trend for worse visual performance at 8–12 weeks in the group treated with topical brimonidine. Although there was no significant difference for the colour vision outcome, this might reflect that the baseline colour vision value was better for the treated group. The outcome visual field grade was significantly worse in the treated group. The masked examiner’s visual field evaluations demonstrated that more treated patients worsened than in the untreated group. When the baseline and outcome of all visual parameters for each individual were compared, the treated group had a significantly worse outcome at 8–12 weeks.

Our results are not the first description of worse outcome in patients treated with α2 agonists for central nervous system ischaemic disease. Studies in animal models and clinical studies in humans suggest that α2 agonists, including α2 receptor agonists, may impede recovery following stroke. Clonidine administration caused recurrence of the neurological deficit in animals who had initially recovered. In a retrospective study, the level of motor recovery of stroke patients was worse in those treated with α2 agonists than in patients not receiving these agents.

Although in experimental optic nerve injury in animal models, brimonidine appears to offer neuroprotection, our results demonstrate that brimonidine tartrate, applied topically up to four times daily, does not appear to be a beneficial treatment for acute NAION. It
is possible earlier treatment might have been more effective, although patients who worsened received treatment sooner than those who did not worsen. Increased dosing frequency or using a different preparation of brimonidine might be more effective. Additionally, the number of subjects in the study was small and a negative trend could appear more profound.

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References
1. Woldemussie E, Ruiz G, Wijono M, et al. Neuroprotection of retinal ganglion cells by brimonidine in rats with laser-induced chronic ocular hypertension. Invest Ophthalmol Vis Sci 2001;42:2849–55.
2. Wheeler LA, Woldemussie E. Alpha-2 adrenergic receptor agonists are neuroprotective in experimental models of glaucoma. Eur J Ophthalmol 2001;11(suppl 2):330–5.
3. Yoles E, Wheeler LA, Schwartz M. Alpha-2 agonists are neuroprotective in a model of optic nerve degeneration. Invest Ophthalmol Vis Sci 1999;40:65–73.
4. Wheeler LA, Gill DW, Woldemussie E. Role of alpha-2 adrenergic receptors in neuroprotection and glaucoma. Surv Ophthalmol 2001;45(suppl 3):S290–4.
5. Fisher LD, Van Belle G. One- and two-sample inference. In: Biostatistics, a methodology. Berlin: the health sciences. Ch 5. New York: John Wiley, 1993:146–7.
6. Fisher LD, Van Belle G. Nonparametric, distribution-free and permutation models: robust procedures. In: Biostatistics, a methodology for the health sciences. Ch 8. New York: John Wiley, 1993:310–14.
7. Fisher LD, Van Belle G. Association and prediction: linear models with one predictor variable. In: Biostatistics, a methodology for the health sciences. Ch 9. New York: John Wiley, 1993:385–6.
8. Goldstein LB. Potential effects of common drugs on stroke recovery. Arch Neurol 1998;55:454–6.

Chronic eye movement induced pain and a possible role for its treatment with botulinum toxin

Chronic ocular pain may have many causes and can be a frustrating problem for both patient and doctor alike. We describe two patients who had similar symptoms and eye findings who had been unable to relieve their pain with conventional analgesia. We postulate a cause for their pain and describe our experience of a treatment strategy using a standard dose of botulinum toxin injection into an extraocular muscle.

Case 1

A 56 year old white woman presented with right sided facial weakness, nausea, and right sided ptosis. She had a 9 month course of oral steroids and despite this needed tramadol, paracetamol, and flurbiprofen to control her pain. Her symptoms and examination findings slowly stabilised until she was left with marked limitation of upgaze in her right eye. Her symptoms did not change over the next 3 years, at which point she was referred to our care. When she attempted to look up she described a juddering sensation and severe pain just above the eye. She rarely had pain at night but was still using regular oral buprenorphine for pain relief. Her pain was exacerbated by reading or looking at the computer and she complained of vertical diplopia.

On examination she had limitation of abduction and elevation of her right eye and prisms did not improve her symptoms. A tentative diagnosis of inflammatory spasm was made. She was treated with botulinum toxin injection to her right inferior rectus. Two weeks later there was much less tightness and discomfort in the orbit but she had diplopia in all positions of gaze and was forced to occlude her right eye. Three months later the pain was much improved compared to the pre-injection; she still found the diplopia intolerable and declined further treatment.

Case 2

A 46 year old white man presented complaining of chronic constant ocular discomfort which followed strabismus surgery 8 years earlier for an A-pattern exotropia with diplopia on downgaze. The pain was worsened by prolonged television watching and prisms in his glasses did not help. Pain was much worse on upgaze and right gaze, which were limited. Oral non-steroidal anti-inflammatory agents (NSAIDs) did reduce the pain a little but only when taken in high doses (100 mg three times daily flurbiprofen).

On examination he had a right hyperphoria, with an A-pattern exotropia and an abnormal head posture for distance. He still had diplopia. Botulinum toxin was injected into his left medial rectus muscle, which resulted in a profound reduction in his symptoms, leaving him with a small exophoria. His diplopia resolved completely after 10 weeks. The “pressure sensation” and pain in the right eye recurred after about 6 months, this time with no diplopia. He had a further injection of toxin 8 months after the first which again significantly improved his pain but gave him diplopia for 3 weeks. He continues to take flurbiprofen 50 mg three times daily orally.

Comment

The pain demonstrated by these two patients is typically much worse in certain directions of gaze and particularly during prolonged gazing holding such as when reading or watching television. It had a clear precipitating event and the most remarkable feature is that it has persisted for over 2 years in each case without significant progression or regression. No active disease process could be found to account for the continued pain. The pain is severe and responds only to high doses of analgesics, particularly NSAIDs. None of our patients felt that their pain was satisfactorily controlled by their analgesics.

We believe that there may be a process of chronic low grade inflammation affecting the extraocular muscles in the tissues around them which is exacerbated by continued contraction and relaxation of the same muscles. Muscular spasm perhaps triggered by this inflammatory process may be the cause of the most severe pain and this could account for the exacerbations of pain in certain directions of gaze and on prolonged gaze holding activities. Ocular muscle ischaemia, perhaps caused by constricting scar tissue, remains a possibility but the onset of the pain is very fast making this less likely.

The pain relief seen in our patients may simply be the result of paralyzing an inflamed muscle but there is growing evidence for a separate antinociceptive effect of botulinum toxin.1 No direct peripheral cutaneous antinociceptive effect could be shown by Blersch et al2; however inhibition of release of substance P has been demonstrated in vitro and it can be hypothesised that botulinum toxin treatment may reduce the local release of nociceptive neuropeptides from either cholinergic neurons or from C or A delta fibres in vivo. The mechanisms by which botulinum toxin may relieve pain, including a possible analgesic effect of botulinum toxin metabolites, are reviewed by Goyer.3

There is a growing literature on the use of botulinum for painful conditions,4 particularly those in which muscle spasm plays a part. These include writer’s cramp,5 postoperative pain in spastic cerebral palsy,6 and perhaps more surprisingly migraine7 and painful tic convulsif.8 Many of the reported uses are single case studies and not all controlled trials have shown a positive effect of treatment.9

It is not possible to rule out a powerful placebo effect in our patients but, whatever the mechanism of action, their pain was vastly improved and botulinum toxin treatment is very safe in competent hands.

In the cases described above botulinum toxin served a dual purpose in that it had the potential to improve their ocular deviation for which it is well known and it also reduced the severe ocular discomfort. Unfortunately, the resulting diplopia limited its usefulness in one case but we feel that this treatment should be considered in this unusual group of patients who present a difficult management problem even to the most experienced ophthalmologists.

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References
1. Sheean G. Botulinum toxin for the treatment of musculoskeletal pain and spasm. Curr Pain Headache Rep 2002;6:460–9.
2. Blersch W, Schulte-Matthai WJ, Przywara S, et al. Botulinum toxin A and the cutaneous nociception in humans: a prospective, double-blind, placebo-controlled, randomized study. J Neurol Sci 2002;208:69–75.
3. Koiki K. Pharmacology and immunology of botulinum toxin serotypes. J Neurol 2001;248(Suppl 1):1–10.
4. Guyer BM. Mechanism of botulinum toxin in the relief of chronic pain. Curr Rev Pain 1999;3:427–31.
5. Joshi WH, Koiki K. Botulinum toxin: evidence-based medicine criteria in rare indications. J Neurol 2001;248(Suppl 1):39–44.
6. Turjanski N, Pirtosek Z, Quirk J, et al. Botulinum toxin in the treatment of writer’s cramp. Clin Neuropharmacol 1996;19:314–20.
7. Barwood S, Baillieu C, Boyd R, et al. Analgesic effects of botulinum toxin A: a randomized, placebo-controlled clinical trial. Dev Med Child Neurol 2000;42:116–21.
Femtosecond laser technology allows a new type of intrastromal lamellar keratoplasty with removal of a mid-stromal segment and preservation of an intact Bowman’s membrane. Considering the decreased amount of allogenic corneal tissue transplanted, and regarding the preservation of the original corneal surface, lamellar intrastromal femtosecond laser keratoplasty may be associated with a smaller rate of immunological graft reaction and with a lower postoperative corneal astigmatism in some eyes. Future clinical studies may show whether positional edges in the superficial flap increase its postoperative rotational stability.

Case report

Using a corneal contact lens and a femtosecond laser (20/10 Perfect Vision, AmTaufenfeld 21/1, D-69123 Heidelberg, Germany) with a wavelength of 1060 nm, a spot size of about 10 μm, and a laser pulse duration of several hundred femtoseconds, a pre-descentemal incision running parallel to the corneal surface was created in five postmortem eyes of slaughterhouse pigs. The diameter of the deep stromal incision was 7 mm. In a second step, a circular sagittal incision was performed starting from the peripheral edge of the already existing incision in the pre-descentemal level to the superficial layer of the corneal stroma. In continuation of the latter sagittal corneal flap was prepared with a diameter of 7 mm, a thickness of about 100 μm, a hinge, and three positional pikes. The pikes in the flap with the corresponding marked folds of the flap were formed to increase the rotational stability of the flap after repositioning. The height of the peaks was about 0.40 mm. After opening of the flap the intrastromal segment situated between the pre-descentemal incision and the incision in the superficial stromal level was removed and exchanged against a similar formed segment obtained from another (donor) pig eye. After that, the flap was reposioned.

For all eyes included in the study, the intrastromal corneal button and the superficial flap with the three positional pikes could be prepared without major difficulties. The corneal buttons could easily be repositioned into their original beds as well as into the recipient beds of other eyes in which the recipient corneas were created with the same diameter as the donor button. The time taken for preparation of the intrastromal corneal button and the corneal flap, and for the exchange of the corneal buttons was less than 10 minutes in all cases.

Comment

Femtosecond laser technology allows a new type of intrastromal lamellar keratoplasty.
We wish to apologise for an error in the extended report by Barry and König (Br J Ophthalmol 2003;87:909–16). On p 910 under the heading Orthoptic screening, point four of the bulleted list, line four should have read: “positive”: visual acuity 0.4 (10/25).

NOTICES

Helping the blind and visually impaired

The latest issue of Community Eye Health (No 45) discusses help for the blind, with an editorial by Sir John Wall of the Royal National Institute for the Blind on the rights of blind people. For further information please contact: Journal of Community Eye Health, International Resource Centre, International Centre for Eye Health, Department of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine, Keppel Street, London WC1E 7HT, UK (tel: +44 (0)20 7612 7964; email: Anita.Shah@lshtm.ac.uk; website: www.jche.ac.uk). Annual subscription (4 issues) UK£28/US$45. Free developing country applicants.

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 ophthalmologists, is regularly sending volunteer surgeons to India. Details can be found at the charity’s website (www.secondsight.org.uk) or by contacting Dr Lucy Mathen (lucymathen@yahoo.com).
5th International Symposium on Ocular Pharmacology and Therapeutics (ISOPT)

The 5th International Symposium on Ocular Pharmacology and Therapeutics (ISOPT) will take place 11–14 March 2004, in Monte Carlo, Monaco. Please visit our website for details of the scientific programme, registration, and accommodation. To receive a copy of the Call for Abstracts and registration brochure please submit your full mailing details to http://www.kenes.com/isopt/interest.htm.

Further details: ISOPT Secretariat (website: www.kenes.com/isopt).

XVth Meeting of the International Neuro-Ophthalmology Society

The XVth Meeting of the International Neuro-Ophthalmology Society will take place 18–22 July 2004, in Geneva, Switzerland.

Further details: Prof. A Safran, University Hospital Geneva, c/o SYMPORG SA, Geneva (fax: +41 22 839 8484; email: info@symorg.ch; website: www.symorg.ch).

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on 29–30 November 2003 and 1–4 December 2003 respectively, at the Razi Conference Center, Hemmat Hyw, Tehran, Iran. Further details: Scientific programme: Prof Ingrid Kreissig, University of Tuebingen, Schleichstr. 12, Breuningerbau, 72076 Tuebingen, Germany (tel: +49 7071 295209; email: ingrid.kreissig@med.uni-tuebingen.de). Local organisation: Dr Arman Masheykhi, Dr Siamak Moradian, Dept of Ophthalmology, Labbanfinejad Medical Center, Pasdaran Ave, Boostan 9, Tehran, 16666, Iran (fax: +98 21 254 9039; email: labbafi@hotmail.com).