Bevacizumab suppresses choroidal neovascularisation caused by pathological myopia

Bevacizumab (Avastin, Genentech) is a recombinant humanised, full length, anti-VEGF monoclonal antibody that binds all isoforms of VEGF-A. It has been shown to prolong survival of patients with advanced colon cancer when combined with 5-fluorouracil. In this report, we describe the effect of bevacizumab in two patients with choroidal neovascularisation (CNV) secondary to pathological myopia, which was refractory to other treatment.

Case reports

Patient 1
AM is a 36 year old white man who was diagnosed with subfoveal CNV caused by pathological myopia (right eye = −11.50 D, left eye = −11.30 D) in his left eye in September 2002 for which he received three photodynamic therapy (PDT) treatments. He developed subfoveal CNV in his right eye in June 2003 and received one PDT treatment combined with an intravitreous injection of 4 mg of triamcinolone acetonide. In May 2004, he presented with recurrent subfoveal CNV in his right eye and refused PDT. Off-label use of bevacizumab was discussed and after informed consent, the patient decided to proceed.

Just before treatment in July 2004, best corrected visual acuity (VA) was 20/40 in the right eye and 20/25 in the left eye. There was a ring of hyperpigmentation centred on the fovea with a surrounding ring of subretinal blood and substantial subretinal fluid in the right eye (fig 1A). An optical coherence tomography (OCT) scan through the centre of the fovea confirmed the presence of extensive subretinal fluid (fig 1B, asterisks) with subretinal tissue in the centre of the fovea (arrowheads). An OCT map showed severe thickening and subretinal fluid throughout the centre of the macula (foveal thickness 510 µm, macular volume 9.29 mm³). In the left eye, there were pigmentary changes and no subretinal blood or fluid (foveal thickness, 201 µm). In the right eye, the early phase of a fluorescein angiography (FA) scan showed a central area of hyperfluorescence surrounded by blocked fluorescence from subretinal blood (fig 2A). Central fluorescence increased in the mid phase (fig 2B) and in the late phase the area of hyperfluorescence was larger with indistinct borders indicating leakage of dye into surrounding tissue (fig 2C).

The patient received an intravenous infusion of 5 mg/kg of bevacizumab, which he tolerated well. He noted subjective improvement in vision in both eyes within 7 days and 2 weeks after the infusion, VA was 20/20 in both eyes and biomicroscopy showed less subretinal fluid (fig 1C), confirmed by OCT (fig 1D, asterisk). Compared to the pre-infusion OCT, the retinal thickness map showed substantial improvement with a decrease in foveal thickness (330 µm from 510 µm) and macular volume (6.89 mm³ from 9.29 mm³). In the early phase of a FA in the right eye (fig 2D), the hyperfluorescent area was reduced compared to a corresponding frame of the baseline FA (fig 2A). The intensity of hyperfluorescence increased between the early and mid phase (fig 2E) and there was evidence of dye leakage from the CNV during the late phase (fig 2F). The patient received second and third infusions of 5 mg/kg of bevacizumab without any difficulty. Six weeks after the first infusion and just before the fourth infusion, VA was 20/20 in each eye and biomicroscopy showed no identifiable subretinal fluid in the right eye and resorption of almost all of the subretinal blood (fig 1E). OCT confirmed that there was no subretinal fluid (fig 1F) and the retinal thickness map showed further improvement compared to the map after the first infusion. Foveal thickness measured 244 µm and macular volume was 5.80 mm³. Early phase of the FA showed further reduction in the area of hyperfluorescence (fig 2G) compared to a corresponding frame of the FA done after the first infusion (fig 2D). There was only a mild increase in brightness of the hyperfluorescent area in the mid phase of the FA.

Figure 1 Fundus appearance and optical coherence tomogram of patient 1 at baseline and after starting infusions of bevacizumab.

Figure 2 Fluorescein angiography of patient 1 at baseline and after starting infusions of bevacizumab.
Macular volume was 5.91 mm$^3$. There was a laser scar inferonasal to the fovea (fig 3C, arrow). OCT in the right eye showed reduced hyperfluorescence compared to the baseline examination, but persistent macular thickening (fig 3D) confirmed by OCT, which showed a foveal thickness of 304 μm and a macular volume of 7.37 mm$^3$. In the right eye, there was mild subretinal fluid and a few flecks of subretinal blood temporal to the laser scar. OCT in the right eye showed reduced retinal thinning and minimal subretinal fluid with foveal thickness of 249 μm and a macular volume of 5.78 mm$^3$ (fig 3F). In the left eye, early phase of a FA (fig 4A), but substantially less fluorescence during the mid (fig 4E) and late (fig 4F) phases than the corresponding phases of the baseline FA, indicating less filling of the CNV with dye. There was still substantial leakage of dye into surrounding tissue in the late phase (fig 4F). The patient returned 2 months after the fourth infusion noting subjective visual improvement that had allowed her to resume many activities that she had previously stopped. VA was 20/64 in the right eye and 20/200 in the left eye. Biomicroscopy in the left eye showed reduced subretinal blood compared to the baseline examination, but persistent macular thickening (fig 3D) confirmed by OCT, which showed a foveal thickness of 304 μm and a macular volume of 7.37 mm$^3$. In the right eye, there was mild subretinal fluid and a few flecks of subretinal blood temporal to the laser scar. OCT in the right eye showed reduced retinal thinning and minimal subretinal fluid with foveal thickness of 249 μm and a macular volume of 5.78 mm$^3$ (fig 3F). In the left eye, early phase of a FA (fig 4A), but substantially less fluorescence during the mid (fig 4E) and late (fig 4F) phases than the corresponding phases of the baseline FA, indicating less filling of the CNV with dye. There was still substantial leakage of dye into surrounding tissue in the late phase (fig 4F). The patient returned 2 months after the fourth infusion noting subjective visual improvement that had allowed her to resume many activities that she had previously stopped. VA was 20/64 in the right eye and 20/200 in the left eye. Contact lens biomicroscopy in the left eye showed no identifiable subretinal blood or fluid, and macular thickness appeared reduced (fig 5G). This was confirmed by OCT (fig 3H; foveal thickness 253 μm, macular volume 6.40 mm$^3$). In the right eye, there was no identifiable subretinal blood or fluid and OCT showed no changes from the scan at week 6. FA in the left eye showed reduced hyperfluorescence compared to previous FAs at all phases, early (fig 4G), mid (fig 4H), and late (fig 4I), and no leakage.

**Comment**

In two patients, intravenous infusions of bevacizumab resulted in reduced fluorescein angiographic evidence of leakage from CNV and decreased retinal thickening and subretinal fluid. This anatomical evidence of...
improvement was accompanied by visual improvement in two of the three eyes in which there was active subfoveal CNV at baseline. The one eye that did not show objective evidence of visual improvement had prominent subretinal fibrosis and a central area of retinal atrophy at baseline. Although spontaneous improvement cannot be ruled out, the discrepancy in the outcome of these two patients suggests that antagonism of VEGF with bevacizumab provided benefit. No ocular or systemic side effects were observed.

Recent studies have suggested that VEGF may be an important stimulus for neovascular age related macular degeneration (AMD). Despite differences in pathogenesis among the disease processes, the effect of bevacizumab in the two patients reported here suggests that VEGF may be an important stimulus for CNV in pathological myopia as well as AMD. While uncontrolled observations in two patients do not justify widespread use of bevacizumab in patients with CNV, additional studies are warranted. A controlled clinical trial is needed to determine if bevacizumab is safe and effective in patients with subfoveal CNV caused by pathological myopia and, if so, to determine the appropriate frequency of administration.

Q D Nguyen, S Shah, S Talipinar, D V Do, E V Anden, P A Campochiaro
Department of Ophthalmology, Johns Hopkins University School of Medicine, 600 North Wolfe Street, Baltimore, MD, USA
Correspondence to: Peter A Campochiaro, MD, Maumenee 719, Wilmer Eye Institute, Johns Hopkins University School of Medicine, 600 North Wolfe Street, Baltimore, MD 21287-9277, USA; pcmcp@jhmi.edu

doi: 10.1136/bjo.2005.066431

 Accepted for publication 14 January 2005

References


Methods

One hundred consecutive patients using topical medication to lower intraocular pressure attending a UK teaching hospital’s glaucoma service clinics were asked which drops they were using and how often they put them in. Each patient was only entered into the study once. If any deviation from the drop regime described in their notes was identified then further questioning was used to identify the cause of that discrepancy.

Results

In total, 30 of the 100 patients were not using the antiglaucoma medication as described in their notes. Eighteen cases were caused by ophthalmologists either changing a regime without informing the general practitioner or not giving clear instructions to the patient. Examples include transcription errors by the ophthalmologist when dictating the letter to the general practitioner (four cases), patients stopping treatments because of side effects without contacting clinic (four cases), patients stopping their antiglaucoma drops after a cataract surgery (three cases), and ambiguity between Xalatan and Xalacom (one case). Patient error can be attributed to nine cases. Examples include patient using drops less frequently than prescribed (three cases), patient using drops in the wrong eye or one eye only (two cases), patients changing the dose frequency of their own accord (one case), and using drops too frequently (one case). The other three cases were the result of ‘‘unravelable’’ nursing home staff (two cases), and failure to prescribe eye drops on admission to a general medical ward.

Comment

Ophthalmologists communicating poorly with patients or with general practitioners caused nearly one in five patients to use the wrong regime. The responsibility for ensuring that all communication between the ophthalmologist and patients or general practitioners is intelligible and unambiguous lies with the ophthalmologist.

One frequent cause of non-compliance is newly diagnosed patients thinking that the initially prescribed bottle is the full course of treatment, and ceasing treatment when this bottle expires. This is a well recognised phenomenon on the literature on persistency with topical ocular hypotensive treatment. We were alarmed that 30% of the sample were using an incorrect drop regime. Involuntary non-compliance merits further research and poses a considerable threat to the control of patients’ disease. Furthermore, failure to identify compliance as the cause of a patient’s apparent lack of response to treatment may result in prescription of more toxic medication, and increasingly complex drop regimes, which can lead to further compliance problems.

A J Buller, B Connell, A F Spencer
Manchester Royal Eye Hospital, Manchester, UK
Correspondence to: A J Buller, Manchester Royal Eye Hospital, Oxford Road, Manchester M13 9WH, UK; alexbuller@mac.com

doi: 10.1136/bjo.2005.066175

Accepted for publication 9 January 2005

Safety of phacoemulsification in a patient with an implanted deep brain neurostimulation device

A 69 year old woman with nuclear sclerotic cataracts was examined. She was awaiting neurosurgery for treatment of drug refractory titubation (head tremor). Before cataract surgery, she underwent successful neurosurgery. The implanted Medtronic deep brain stimulation device rendered her asymptomatic of tremors. At the cataract preoperative clinic she showed the device identification card that stated “ultrasound diathermy … anywhere on your body … can result in severe injury or death.” Following confirmation from Medtronic that it was safe to proceed, the patient had an uneventful left phacoemulsification performed under general anaesthesia with the neurostimulator turned “off.” Seven months later she underwent a similar successful right phacoemulsification.

Comment

Deep brain neurostimulation of the thalamus is the treatment of choice for drug refractory essential tremor. Indications for its use are widening and include use in multiple sclerosis, advanced Parkinson’s disease, and movement disorders such as dystonia. Deep brain neurostimulator has three implanted components. The electrodes are implanted into the subthalamic nucleus or the globus pallidus interna, then an insulated lead is placed subcutaneously from the burr hole to a sealed neurostimulator device beneath the clavicle. The neurostimulator electrical stimulation pulses can be adjusted from external devices.

There are two recorded fatalities in patients with implanted deep brain neurostimulation device.

www.bjophthalmol.com

Figure 1 Implanted deep brain neurostimulation device.
devices who had received short wave diathermy. Heat energy released directly to the body from an external source can be conducted via the insulated lead of an implanted neurostimulation device, raising the temperature at the electrode. Ultrasound diathermy transfers heat directly to the body. Where short wave diathermy results in an induced electrical current,\(^1\) one study calculated a potential rise of 9.76°C at the deep brain neurostimulator electrode when short wave diathermy was used.\(^2\) For phacoemulsification to be safe in patients with deep brain neurostimulators, it must not produce significant heat or generate an electric current.

The phacoemulsification hand piece uses the piezoelectric effect to drive the phacoemulsification needle tip in a linear jackhammer-like movement, physically cutting the lens.\(^3\) Acoustic cavitation results from an explosive collapse of vacuoles formed in fluid around the swiftly moving phacoemulsification needle tip.\(^4\) A study showed a maximum temperature rise of 3.5°C in the anterior chamber during routine phacoemulsification.\(^5\) The risk of this generated heat spreading to the implanted electrodes must be low. The phacoemulsification tip does not generate an oscillating magnetic field that might induce an electrical current. Theoretically, this should render ultrasound phacoemulsification safe in the presence of implanted deep brain neurostimulators.

With expanding technology, there will naturally be situations with the potential for interactions between equipment from different specialties. Consent should include the possibility of heat conduction to the implanted neurostimulation device. The use of local anaesthesia may allow early detection of discomfort or neurological sequelae. The surgeon should make use of all techniques to reduce the heat generated during phacoemulsification. Medtronic advise turning the neurostimulator off and not placing any cables over the patient’s chest and neck (R Coffey, 3 February 2005, personal communication). There are various neurostimulators, including cortical devices, that may have increased sensitivity to localised temperature increases. Heat formation at the phacoemulsification needle tip has been analysed; however, further research on the extent of heat dissipation is required.

**References**


**Vertical deviation exacerbated by convergence and accommodation**

We report a patient with hypertropia causing diplopia exacerbated by convergence and accommodation.

**Case report**

A 36 year old man presented with 8 year history of worsening intermittent double vision. Visual acuities were 6/5 in each eye. For near there was manifest left hypertropia and left hyperphoria at distance (fig 1A, table 1). Extraocular movements were full with no overactions. No significant difference in vertical deviation in different gaze positions or cycloversion was found, the deviation increased on head tilt to the left (table 2). There was no dissociated vertical deviation.\(^7\)

The angle of deviation varied between 2 and 7 prism dioptries at distance and 24 and 45 prism dioptries at near on repeated examinations. Stereovision was 55 seconds of arc when deviation was prism corrected. The A/C ratio was normal using gradient method. The vertical fusion range was 13 prism dioptries at distance (9 prism dioptries base-down and 4 prism dioptries base-up).

The vertical deviation increased on accommodation with concave lenses and the deviation decreased with 10 dioptre base-in prisms at near (table 1). Eye movement recordings are shown in figure 1C. Pupil reactions and fundoscopy were unremarkable. Thyroid functions, thyroid peroxidase and acetylcholine receptor antibodies were normal. Tension test was negative. Orbicularis oculi muscle single fibre electromyogram was unremarkable. Neurological examination and magnetic resonance imaging of the brain and orbits were normal.

**Comment**

Klein-Scharff and Komerrell\(^8\) first reported three patients with hypotropia and two with...
In our patient it is unclear whether the abnormality was congenital and decompensation of hyperphoria increased symptoms, or whether it was acquired. Increased vertical fusion range argues for a longstanding squint. The history of most patients in the literature was similar, with slow increase of diplopia and vertical deviation at near over several years. In several patients, combined amblyopia or other strabismus forms—such as dissociated vertical deviation—argue for an early onset of the eye motility problem. Interestingly, one patient seemed to have developed the vertical deviation in combination with convergence after trauma. It is possible that the aberrant re-innervation can be either congenital or acquired. It would be interesting to investigate systematically the influence on near and distance fixation in patients with vertical squint.

**References**


**Tetracycline induced green conjunctival pigment deposits**

There have been no reports, to our knowledge, of a clinical presentation of ocular pigmentation secondary to the use of oral tetracycline only. Tetracycline hydrochloride is not a well recognised cause of ocular pigmentary changes, but has been reported to cause pigmentation of teeth and nails. Of all the tetracyclines, minocycline (a second generation drug) is most often associated with the adverse effect of pigmentation. There have been several case reports of minocycline induced scleral pigmentation. Ocular pigmentary changes reportedly caused by tetracycline have been noted in association with use of minocycline. Both patients in these case reports had had tetracycline/minocycline therapy for more than 10 years for acne vulgaris and had their deposition localised within the tarsal conjunctiva. It is believed that most of the cysts are found at the inferior border of the lower tarsus because of the frequency of pre-existing invaginations of conjunctival epithelium in

---

**Figure 1** Patient fixating at near with large left over right squint (A) and at distance with no manifest vertical deviation (B). Eye movement recordings of patient during near and distance fixation demonstrating a slow upward drifting of the left eye, which occurred simultaneously with the convergence movement (C).
brown-yellow tinge. There was no appreciable inflammatory reaction or giant cell reaction to the material. Pathology was consistent with that of previously described reports of tetracycline.

Comment

Tetracyclines of the first generation (tetracycline, oxytetracycline, and tetracycline chloride) are the most commonly prescribed oral antibiotics for acne. Tetracycline has also been shown to result in improvement of the ocular manifestations of rosacea. Both conditions are frequent; thus, the ophthalmologist will encounter many patients being treated with tetracycline. Tetracycline fluorescence has been detected in the conjunctiva of all patients who have taken tetracycline orally. Fluorescence was not generalised but was restricted to a thin film-like layer on the surface and to small areas in the surface layer of cells.

This is the first case report, to our knowledge, of clinically visible conjunctival bulbar deposits caused by the use of tetracycline without a history of minocycline use. Pigmentary changes may initially be noted by the ophthalmologist, as in our case report. It is important to recognise signs of tetracycline pigmentation as it is a commonly used medication, and cessation of the medication may help avoid further pigmentary changes.

Case report

A 48 year old healthy white asymptomatic man presented for evaluation of “green crystals” on the conjunctiva of both eyes (fig 1). The patient had noted the onset of this pigmentation over the previous several months. The patient was treated for acne vulgaris with tetracycline 500 mg a day for the past 2 1/2 years. He denied the use of any topical ophthalmic drops. He took Lotensin for the treatment of hypertension. Past medical history was otherwise unremarkable. On examination the patient was noted to have several dark green granular deposits on the temporal bulbar conjunctiva of both eyes. The granules appeared discrete, crystalline, and varied in size. Otherwise, the examination was unremarkable. Pigmentation was not noted in any other region.

Pathology

Pathology confirmed the presence of tetracycline. The specimen was positive for a non-polarisable foreign material in a submucosal and intraepithelial distribution (fig 2). This material was calcified and had a faint pigmentary deposits were only seen in the conjunctival cysts over the tarsal conjunctiva. Recently, there has been a case report of a patient with a 5 year history of minocycline use for rheumatoid arthritis who developed focal palpebral conjunctival pigment deposits. This patient did not have a reported use of tetracycline.

Our patient was taking only tetracycline without concomitant or previous minocycline use and had bulbar conjunctival lesions. Our patient had also been on tetracycline for 2 1/2 years.

Figure 1 Clinical photograph of the conjunctival pigmentary deposits.

Figure 2 Light microscopy of the pathology specimen of the conjunctival biopsy showing a non-polarisable foreign material in a submucosal and intraepithelial distribution.
underlying dry eye state. If tear deficiency and degree of astigmatism are extreme, desiccation of the corneal epithelium is possible, leading to non-healing defects and associated sequelae.

In cases where high or irregular astigmatism is associated with postoperative non-healing corneal defects, addressing the degree of corneal astigmatism may help restore physiological tear dynamics and resolution of the epithelial defect. Corneal sutures may themselves impede epithelial migration, but if this were the only explanation all grafts would be exposed to the same risk. Conversely, not all patients with high astigmatism (non-surgical) have epithelial defects. This would suggest that more than a single factor is at play in such situations. To our knowledge high astigmatism as a contributory factor to development of persistent epithelial defects post operatively, has not been previously considered.

R Singh, T Umaphathy, B B Kulkarni, H S Dua
University Hospital, Queens Medical Centre, University of Nottingham, Nottingham, UK
Correspondence to: Professor H S Dua, Division of Ophthalmology, University Hospital, Queens Medical Centre, B Floor, Eye ENT Centre, Nottingham NG7 2UH, UK; harminder.dua@nottingham.ac.uk
doi: 10.1136/bjo.2005.069260
Accepted for publication 23 March 2005

Reference

Non-tuberculous mycobacteria related infectious crystalline keratopathy
Non-tuberculous mycobacteria (NTM) or atypical mycobacterial keratitis is an uncommon condition causing indolent corneal ulceration. The infection mimics herpetic, mycotic, and Nocardia keratitis and diagnosis requires a high index of suspicion. We report two cases of NTM infection where the presenting sign was that of crystalline keratopathy. Both cases were diagnosed by microbial culture and successfully treated.

Case 1
A 44 year old white female contact lens wearer presented with a 3 week history of an inflamed eye with a 1.5 mm diameter area of corneal stromal infiltration. Vision was 6/6 in each eye. She was being treated with antivirals and later unsuccessfully with antibiotics and steroids. Three active stromal crystalline infiltrates appeared in the mid-stroma 3 weeks later (fig 1). Culture from a corneal biopsy revealed Mycobacterium chelonei. The keratitis responded to topical amikacin and amphotericin B, which was started on the suspicion of fungal keratitis, before microbial culture results were available. The keratitis resolved over a 4 week period and vision settled at 6/9.

Case 2
An 80 year old white woman with pseudoephphitic bollus keratopathy had a penetrating keratoplasty and was given systemic tacrolimus. Three months postoperatively she presented with endothelial dusting and a 1 mm mid-stromal abscess with a crystalline appearance (fig 2). A corneal scrape revealed acid fast bacilli for which she was commenced on topical ciprofloxacin and amikacin 2.5% but was slow to respond. Culture confirmed Mycobacterium chelonei resistant to amikacin. Topical moxifloxacin was added and oral clarithromycin commenced. Three months later, the ulcer healed with a clear graft but the vision did not improve (counting fingers) on account of pre-existing macular oedema.

Comment
Non-tuberculous mycobacteria cause indolent corneal ulceration resembling herpes virus, fungal, or Nocardia keratitis. The variable clinical presentations and poor susceptibility to conventional antibiotics usually results in a delay in diagnosis.1,4 The two common types of NTM causing keratitis are M chelonei and M fortuitum. The clinical features of NTM include pseudodendritic epithelial defects, subepithelial white fluffy infiltrates with crystalline satellite lesions and ulcers with an overhanging necrotic edge and a grey sloughed base.5 Keratic precipitates and endothelial deposits may appear. Early diagnosis is difficult and absence of organisms in smears and cultures does not exclude the diagnosis of NTM. Repeat scrapes or a corneal biopsy should be considered in all indolent corneal ulcers.

Amikacin has been the drug of choice in Nocardia and atypical mycobacterial infections.1,4 However, approximately 60% of patients will not respond to topical amikacin, as with our second case, and use of combination therapy with ciprofloxacin, gatifloxacin, moxifloxacin, and clarithromycin is recommended.1,4 Penetrating keratoplasty is performed when stromal infiltration is extensive5 but immunosuppression may pre-dispose to recurrent infection. Both our patients were treated successfully. The first patient had a good visual outcome but the second had poor vision due to pre-existing pathology. Successful treatment requires disease awareness, deferring the use of steroids when no organism has been isolated and use of effective antibiotics.

T Umaphathy, R Singh, H S Dua
Division of Ophthalmology and Visual Sciences, Queens Medical Centre, University Hospital, Nottingham, UK
F Donald
Department of Microbiology, Queens Medical Centre, University Hospital, Nottingham, UK

Correspondence to: H S Dua, Division of Ophthalmology, B Floor, Eye ENT Centre, University Hospital, Queens Medical Centre, Nottingham NG7 2UH, UK; harminder.dua@nottingham.ac.uk
doi: 10.1136/bjo.2005.069856
Accepted for publication 23 March 2005

References
Xanthogranulomatous disease in the lacrimal gland

We report three cases of adult lacrimal gland xanthogranulomatous disease that demonstrate the spectrum of this disorder and provide insight into immune dysfunction.

Case 1
A 23 year old asthmatic female had 1 year of bilateral, painless, lacrimal gland masses from polyclonal B cell (CD 20+) infiltration (fig 1A, B). The patient was asymptomatic for 18 months after external beam radiation (25 Gy in 10 fractions). While 7 months pregnant, painless lacrimal gland enlargement recurred, as firm, yellow, nodular masses (fig 1C). A second biopsy showed foamy histiocytes, Touton giant cells, and lymphoid infiltrate without necrobiosis (fig 1D). The orbital masses have remained stable 2 years after corticosteroids and surgical debulking. Systemic involvement included breast MALT type lymphoma 4 years after presentation.

Case 2
A 49 year old Brunei male had 10 years of bilateral, yellow, mildly steroid responsive, superolateral orbital masses (fig 2A). Previous biopsy showed benign, polyclonal lymphocytic proliferation in the lacrimal gland and eyelid xanthoma. Second eyelid and lacrimal gland biopsy demonstrated xanthomatous infiltrate involving obicularis and lymphocytes with some germinal centres, s100 negative, KP1 positive foamy histiocytes and Touton giant cells, respectively (fig 2B–D). Orbital findings improved with Solumedrol (3 g over 3 days), ciclosporin, and cyclophosphamide. The patient was lost to follow up after 6 months. Systemic associations included asthma, sinuitis, and polyclonal paraproteinaemia (increased z1 and z2, A globulin, and IgM).

Case 3
A 52 year old white female had 2 months of bilateral, yellow, lacrimal gland masses and dry eye (confirmed by Schirmer’s testing) (see fig 3A–C). Lacrimal gland biopsy demonstrated foamy histiocytes, Touton giant cells, chronic inflammation, bands of fibrosis, and necrobiosis. The lacrimal gland masses resolved at 2 years after treatment with Solumedrol (3 g over 3 days), methotrexate, pulsed cyclophosphamide, and topical 0.05% Solumedrol (3 g over 3 days), methotrexate, and ciclosporin (Restasis) (fig 3E–F). She is maintained on prednisone 40 mg per day, methotrexate 17.5 mg per week, and Restasis twice a day. Systemic associations included asthma, cervical, axillary, hilar lymphadenopathy, iliac, sacral, L4 sclerosis, and xanthogranulomatous disease of the breast for which she underwent mastectomy 3 months before presentation (fig 3D).

Comment
Adult xanthogranulomatous disease is a class II histiocytic disorder syndrome classifiable as adult onset xanthogranuloma (AOX), adult asthma and periocular xanthogranuloma (AAPOX), necrobiotic xanthogranuloma (NBX), and Erdheim-Chester disease (ECD). AOX is a solitary lesion. AAPOX has B cell mediated findings including adult onset asthma, lymphadenopathy, and paraproteinaemia. Ulcerative skin lesions, paraproteinaemia/myeloma, and silent internal organ disease characterise NBX. ECD is typified by lethal, retroperitoneal and bony sclerosis.

All our cases had asthma. Case 2 had elevated serum protein. Case 3 had lymphadenopathy, salivary gland enlargement, and bony sclerosis. Cases 1 and 3 had breast masses: MALT type lymphoma postdated orbital disease in case 1; xanthogranulomatous disease preceded orbital involvement in case 3. The first two cases could be classified as AAPOX. Case 3 had necrobiosis suggesting NBX, but had clinical features of AAPOX and lacked skin ulcers. These findings demonstrate the adult xanthogranulomatous syndromes are not mutually exclusive. Xanthogranuloma histology consists of non-Langerhans, lipid laden histiocytes, Touton giant cells, and varying degrees of lymphocytic infiltrate, fibrosis, and necrosis (necrobiosis). This infiltration replaced the normal lacrimal gland architecture causing mass effect and loss of tear production. This same process affected the breast in case 3.

The immune cascade leading to this histopathological appearance is unknown. Our previous work found a predominance of CD8 (cytotoxic) T cells in areas of fibrosis and lipophage accumulation. We postulated that CD8 cells activated histiocytes and fibroblasts. Relevant to this hypothesis, it is fascinating that polyclonal B cell (CD20+) infiltration, without gland destruction or foamy histiocytes, preceded the development of xanthogranuloma in cases 1 and 2 and in one case from the literature (fig 1B). An additional report was initially diagnosed as Sjögren’s syndrome, but lacked history.“

Figure 1 (A) T1 weighted axial magnetic resonance imaging (MRI) showing bilateral lacrimal gland enlargement. (B) Initial lacrimal gland biopsy showing a dense lymphocytic infiltrate with preserved ducts (haematoxylin and eosin stain, original magnification 4×). (C) Clinical photograph of yellow, recurrent mass, right orbit, 2 years after radiation treatment. (D) Second lacrimal gland biopsy showing Touton giant cells, foamy histiocytes, lymphocytes, and plasma cells (haematoxylin and eosin stain, original magnification 60×). (E) Clinical photograph of patient showing improvement 1 year after treatment.

Moreover, case 1 developed a monoclonal proliferation of B cells in the breast 1 year after the orbital xanthogranuloma.

Our cases are unusual because the orbital xanthogranuloma were limited to the lacrimal gland, which is devoid of fat. We found four similar reports (table 1). Perhaps immune dysregulation leads to tissue destruction, and the resultant cell membrane fatty acids are scavenged by malfunctioning histiocytes.

The best treatment for xanthogranulomatous disease is unknown. Our patients had some response to steroids, with cases 2 and 3 responding to B cell (cyclophosphamide) and T cell (ciclosporin) suppressors.

These cases raise questions regarding the pathogenesis of non-Langerhans histiocytes and demonstrate that histopathological and clinical findings must be used for diagnosis in the spectrum of disorders that is xanthogranulomatous disease.

H J Williams, W W L Chang
Department of Pathology, West Virginia University, Morgantown, WV, USA

A DiBartolomeo
Department of Rheumatology, West Virginia University, Morgantown, WV, USA

D Howarth
Department of Pathology, University of Toronto, Toronto, Ontario, Canada

Correspondence to: Jennifer A Sivak-Callcott, MD, West Virginia University Eye Institute, PO Box 9193, Morgantown, WV 26506, USA; jsivak@hsc.wvu.edu
doi: 10.1136/bjo.2004.063578

Accepted for publication 1 April 2005

None of the authors have any financial interests regarding this paper.

*Published posthumously.

## References


Management of phaeniciatic ophthalmomyiasis externa

Ophthalmomyiasis, maggot or fly larvae infestation of the eye, is a rare condition that can have variable presentation depending on the type of fly, the ocular structures involved, and the level of larval infiltration.

Case report

A 60 year old African-American male presented with a chief complaint of a swollen, moderately painful red right eye since 4 am that day. Ocular history was significant for foreign body lid trauma of unknown aetiology (presumably a rock or insect) 2 days earlier while riding his motorcycle without protective goggles.

Ocular examination revealed 20/20 vision in each eye with correction. Pupils, extraocular motilities, and confrontation fields were normal. Slit lamp evaluation revealed upper and lower lid oedema with mild erythema in the right eye. A 1.5 mm round ulcerated lesion was noted on the right outer canthal region that appeared to pulsate as the patient was examined in the slit lamp (fig 1). The left eye and other ocular structures in the right eye were unremarkable.

Upon external digital pressure of the ulcerated lesion, a foreign organism was seen to retreat into the ocular tissue. Manual forceps were used to remove a 1.0 cm long white segmented maggot (fig 2). This specimen was identified by an entomologist under a microscope, as being of the Calliphoridae family, *Phaenicia lucilia*, otherwise known as a screwworm fly.

The patient was given erythromycin ointment for use twice a day over the lesion. After 3 days, the patient returned with complete resolution of the lid oedema and erythema (fig 3).

Comment

Ophthalmomyiasis is generally caused by sheep botflies and flesh flies. The most commonly reported organism in the literature is *Oestrus ovis*, a botfly highly prevalent in sheep herding and farming communities. These flies typically lay their eggs on decaying organic material, but are also attracted to open mucopurulent human sores. Within 24 hours, these eggs hatch, producing larvae which then feed on human tissue. This case was somewhat unusual in that trauma was the mechanism by which the fly eggs were
deposited. Clinical features of external ophthalmomyiasis can include conjunctivitis, conjunctival hemorrhage, corneal abrasion, and iritis. Internal ophthalmomyiasis can produce vitreous haemorrhage, tractional retinal detachment, endophthalmitis, and hypopigmented linear and arcuate subretinal tracks. Some of the cases of presumed internal ophthalmomyiasis have been based on hypopigmented subretinal tracks without documentation of an actual maggot.

Treatment strategies depend upon the type of ocular involvement and the level of damage. In cases of external ophthalmomyiasis, manual forceps removal of the larvae is ideal. Ophthalmic ointment can be used to block the larva’s respiratory pore, thereby suffocating the organism to facilitate manual removal. Treatment strategies in cases of internal ophthalmomyiasis are case-specific, ranging from iridectomy, vitrectomy, and retinotomy to laser photocoagulation. This is the first reported case of ophthalmomyiasis externa by a screwworm fly, Calliphoridae Phaenicia sp successfully treated with manual forceps removal.

Acknowledgements

Thanks to Kipling Will and David Faulkner for their assistance from the University of California, Berkeley. Entomology Department. Thanks to A Bitanga for the photographs. Thanks also to Thomas Lietman for his help with the manuscript.

N Huynh, B Dolan
San Francisco VA Medical Center, CA, USA
S Lee, J P Whitcher
Proctor Foundation, CA, USA
J Stanley, J P Whitcher, S Lee
UCSF Department of Ophthalmology, CA, USA
Correspondence to: Dr Scott Lee, UCSF Department of Ophthalmology, CA 94122, USA; selee@itsa.ucsf.edu
doi: 10.1136/bjo.2005.071597
Accepted 1 April 2005

References

The legal requirement for driving in the United Kingdom is met following pupil dilatation

Dilatation of the pupil (mydriasis) is a core component of a comprehensive ophthalmic examination and is becoming part of the eye examination routine for optometrists in the United Kingdom. As many patients drive to attend their examinations, concerns have been raised regarding the effects of pupillary dilatation on driving and whether or not the visual standard for driving has been met after dilatation. Therefore, we investigated the effect of mydriasis on the visual standard for driving a private vehicle in the United Kingdom.

Report

Twenty adult subjects (mean age 24 years) with normal or corrected to normal visual acuity participated in the study. A selection of six different pairs of number plates (black on white and black on yellow), which contained 50 letters, were free from signs of ocular disease. Given the small effect of mydriasis on visual acuity, all subjects passed the number plate test both before and after dilatation and irrespective of the number of subjects (four of 28) did not pass the number plate test after mydriasis. However, subjects in our study were relatively young, wore the appropriate refraction and accommodation and were free from signs of ocular disease. Given the small effect of mydriasis on visual acuity, it is not surprising that, for our subjects, mydriasis did not affect the UK visual standard for driving. Notwithstanding the relatively small loss in visual acuity, most subjects in our study reported a slight or moderate effect of mydriasis on their vision. Nevertheless, all subjects but one felt confident enough to drive home.

Wood et al have shown that mydriasis has a measurable decrease on real life driving performance, specifically on the detection and recognition of low contrast road obstacles and the ability to navigate around them. These findings, together with our results, suggest that satisfying the UK visual standard for driving does not preclude a decrease in driving performance. Therefore, all patients should be advised that although the visual standard for driving may be met following mydriasis, caution is advised when driving after pupillary dilatation.

\[ \text{Confident to drive?} \]

\[ \text{Yes} \]

\[ \text{No} \]

\[ \text{Not applicable} \]

\[ \text{Not available} \]

Table 1 Monocular (RE and LE) and binocular (BE) visual acuity results

<table>
<thead>
<tr>
<th>Subject</th>
<th>Age (years)</th>
<th>Pre-dilatation</th>
<th>Post-dilatation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>RE</td>
<td>LE</td>
</tr>
<tr>
<td>1</td>
<td>23</td>
<td>6/4.8</td>
<td>6/4.8</td>
</tr>
<tr>
<td>2</td>
<td>23</td>
<td>6/6</td>
<td>6/6</td>
</tr>
<tr>
<td>3</td>
<td>21</td>
<td>6/6</td>
<td>6/6</td>
</tr>
<tr>
<td>4</td>
<td>23</td>
<td>6/6</td>
<td>6/6</td>
</tr>
<tr>
<td>5</td>
<td>24</td>
<td>6/6</td>
<td>6/6</td>
</tr>
<tr>
<td>6</td>
<td>36</td>
<td>6/6</td>
<td>6/6</td>
</tr>
<tr>
<td>7</td>
<td>23</td>
<td>6/6</td>
<td>6/6</td>
</tr>
<tr>
<td>8</td>
<td>27</td>
<td>6/6</td>
<td>6/6</td>
</tr>
<tr>
<td>9</td>
<td>22</td>
<td>6/6</td>
<td>6/6</td>
</tr>
<tr>
<td>10</td>
<td>21</td>
<td>6/6</td>
<td>6/6</td>
</tr>
<tr>
<td>11</td>
<td>20</td>
<td>6/6</td>
<td>6/6</td>
</tr>
<tr>
<td>12</td>
<td>23</td>
<td>6/6</td>
<td>6/6</td>
</tr>
<tr>
<td>13</td>
<td>22</td>
<td>6/6</td>
<td>6/6</td>
</tr>
<tr>
<td>14</td>
<td>20</td>
<td>6/6</td>
<td>6/6</td>
</tr>
<tr>
<td>15</td>
<td>26</td>
<td>6/6</td>
<td>6/6</td>
</tr>
<tr>
<td>16</td>
<td>22</td>
<td>6/6</td>
<td>6/6</td>
</tr>
<tr>
<td>17</td>
<td>24</td>
<td>6/6</td>
<td>6/6</td>
</tr>
<tr>
<td>18</td>
<td>22</td>
<td>6/6</td>
<td>6/6</td>
</tr>
<tr>
<td>19</td>
<td>22</td>
<td>6/6</td>
<td>6/6</td>
</tr>
<tr>
<td>20</td>
<td>23</td>
<td>6/6</td>
<td>6/6</td>
</tr>
</tbody>
</table>
of these small fragments was performed with a forceps. Complete meticulous removal of the buckle was encountered that disintegrated the hyperintensity of the mass on T2 weighted MRI. The mass in the medial intraconal space. The presentation of hydrated MAI buckles are varied. They can become extremely loose and migrate anteriorly, or enlarge in situ and present as orbital masses. Since complications do not occur until many years after the orbital surgery, the history of a retinal detachment repair may not be elicited. In addition, these loose buckles usually do not indent the globe and may not be recognised as being present on indirect ophthalmoscopy. Radiological imaging may be helpful. MRI T1 weighted images of a hydrated buckle reveal a well defined, hypointense mass, while T2 weighted images reveal a hyperintense mass as a result of high water content. (In contrast, silicone element will be black on MRI images.)

Removal of hydrated MAI buckles can be very difficult. Careful sub-Tenon dissection should be carried out since any pressure on the buckle can lead to its fragmentation. The procedure is often complicated because of the extremely friable nature of these buckles. Cryo-probe has been used successfully in some cases for removal of the buckles. Le Rouic et al demonstrated that removal of MAI buckles with a cryoprobe is a safe and effective technique with lower fragmentation rate compared to the use of forceps. The cryo-probe allows the water in the swollen explant material to freeze, which helps to reduce fragmentation. In conclusion, ophthalmologists should be aware of the possible complications of the MAI hydrogel buckles. Knowledge of the MRI characteristics of hydrated MAI buckles may be helpful in identifying them in the event they present as a space occupying orbital mass.

Hydrated scleral buckle: a late complication of MAI explants
Several long term complications have been reported with MAI scleral buckles,\(^1\)\(^2\) a synthetic hydrophilic scleral buckling element, first introduced in the 1970s.\(^1\) We present a case of an extruding, hydrated MAI scleral buckle that presented as an orbital lesion. The magnetic resonance imaging (MRI) characteristics of the hydrated MAI buckle are also described.

Case report
An 81 year old woman was referred to the orbital service for evaluation of a freely mobile non-painful subconjunctival lesion in the left eye present for at least a year. The extracocular movement was full but with a small left exotropia in primary gaze. Anterior segment examination revealed a firm, nodular subconjunctival lesion in the superomedial quadrant. The diagnosis of extruding scleral buckle versus a large orbital conjunctival inclusion cyst was entertained. She, however, denied a history of retinal detachment repair.

The patient underwent MRI of the orbits with and without gadolinium infusion which revealed a 2.5 × 0.7 cm elongated, elliptical mass in the medial intraconal space. The hyperintensity of the mass on T2 weighted images, indicative of high water content, led to the mistaken radiological diagnosis of a cystic, fluid filled lesion (fig 1). Intraoperatively, a swollen intact segmental buckle was encountered that disintegrated into small and large pieces when grasped with a forceps. Complete meticulous removal of these small fragments was performed (fig 2).

Comment
MAI hydrogel explant is made of poly(methyl acrylate-co-2-hydroxyethyl acrylate) crosslinked with ethylene diacrylate with 15% acrylate-co-2-hydroxyethyl acrylate crossed linked with mitochondria DNA (mtDNA) mutations in complex I.\(^1\) We describe a patient with LHON plus dystonia who had a severe complex I respiratory defect with no pathological mtDNA mutation, implying a mitochondrial abnormality of nuclear origin.

Complex I respiratory defect in LHON plus dystonia with no mitochondrial DNA mutation
Leber hereditary optic neuropathy (LHON) sometimes occurs with dystonia\(^3\) in association with mitochondrial DNA (mtDNA) mutations in complex I.\(^1\) We describe a patient with LHON plus dystonia who had a severe complex I respiratory defect with no pathological mtDNA mutation, implying a mitochondrial abnormality of nuclear origin.

Case report
The proband was healthy until age 17 years when she developed progressive right sided weakness followed 3 years later by a left hemiparesis with involuntary posturing of the left arm and leg. Intelligence was average, and she finished grade 6 at school. Her parents were unrelated, and she had five healthy siblings.

Neuro-ophthalmological examination at age 23 documented excellent afferent and efferent visual functioning with no Kaiser-Fleischer ring. Optic discs were hyperaemic and slightly elevated with peripapillary telangiectasias in both eyes (fig 1A and B). She had modest right sided visual field loss, diffuse hyper-reflexia greater on the right, bilateral Babinski signs, and dystonic posturing on the right while walking.

On return 21 months later, she reported that the vision of both eyes had declined 9 months previously. Visual acuity was 20/100 in both eyes with poor colour vision in both eyes, a mild left afferent pupillary defect, and bilateral optic atrophy with no residual hyperaemia or peripapillary telangiectasias (fig 1C). Gait was somewhat worse, and she was modestly dystarhric. Vision did not improve during 18 months of follow up.

Normal laboratory studies included haemoglobin, liver and renal function, serum lactate, pyruvate, and 24 hour urine copper excretion. Cerebral spinal fluid (CSF) lactic acid was slightly elevated (2.8 mmol/l with normal range 0.6–2.2 mmol/l), and brain MRI revealed abnormalities in both basal ganglia (fig 1D). After signing informed consent, the proband, her mother and father, and four siblings had blood drawn for DNA extraction, polymerase chain reaction amplification, and sequencing of the entire mitochondrial genomic coding region as previously described.\(^1\) Sequence results were compared to Mitomap (www.mitomap.org/mitomap/mitoseq.html), the human mitochondrial genome database (www.genpat.uu.se/mitDB), GenBank (www.ncbi.nlm.nih.gov/Genbank/index.html), and

References
a normal control group of 119 people with no medical problems, who share similar ethnicity with the proband. Mitochondrial respiratory function in complexes I, III, IV, and V was assessed in the proband and one unaffected sibling using a previously described flow cytometric functional analysis method.

The proband, her siblings, and their mother had one mtDNA sequence variant recognised as a polymorphism in the Japanese population, which was not present in the 119 normal controls of similar ethnicity. Thirteen previously reported homoplasmic mtDNA polymorphisms were detected in the proband, her family, and the control group. The proband, but not her unaffected brother, had a severe respiratory defect in complex I (fig 1E, F, and G).

**Comment**

This young woman’s initial examination was significant for normal vision with hyperaemic optic discs, pseudopapilloedema, and peripapillary telangiectasias. She went on to develop bilateral optic nerve injury typical of LHON. She also had progressive basal ganglion and upper motor neuron disease culminating in bilateral spasticity, a broad based and unsteady gait, dystonia, and dysarthria. Her clinical course, elevated CSF lactate, normal urinary copper excretion, and severe complex I respiratory defect imply a mitochondrial mechanism for optic nerve and brain injury.

Mitochondrial complex I dysfunction in the absence of a pathologica mtDNA mutation provides presumptive evidence of a mitochondrial abnormality of nuclear origin. Complex I dysfunction has been identified in patients with sporadic focal dystonia, and at least one familial generalised dystonia syndrome had a defined nuclear mutation affecting a mitochondrial protein. Other patients with LHON plus dystonia have had complex I mtDNA mutation(s), so this patient broadens the genetic circumstance in which the phenotype may be expected.

**References**


**Retinal haemorrhages in a young patient with homocysteinuria**

The most common ocular complication in homocysteinuria is lens subluxation. We present a patient with homocysteinuria who developed subhyaloid haemorrhages during pars plana vitrectomy/lensectomy for a subluxated lens in the right eye. She had also developed preretal and intraretal haemorrhages in her fellow eye 6 months earlier,
after phacoemulsification of the subluxed lens. No preoperative or intraoperative anticoagulation was used for either eye surgeries.

Case report
A 12 year old girl with homocysteinuria presented with decreased vision in the right eye as a result of an anteriorly luxated lens causing pupillary block glaucoma with an intraocular pressure (IOP) of 50 mm Hg. The posterior segment was normal. She had undergone phacoemulsification and anterior vitrectomy for a subluxed lens caused by subluxated lens in the fellow eye 6 months earlier. Retinal examination postoperatively revealed preretinal and intraretinal haemorrhages in the mid-periphery (fig 1), which cleared spontaneously over the next 5 months.

Since medical therapy was ineffective in the right eye, she underwent pars plana lensectomy and vitrectomy. As the core vitrectomy was initiated, small subhyaloid haemorrhages were noted to develop in the mid-periphery. The vitrectomy settings were changed to a high cutting speed and low aspiration but the haemorrhages continued to form. Induction of the posterior vitreous detachment was aborted when peripapillary intraretinal haemorrhages were noted to develop.

On the first postoperative day, a 2 day diameter subhyaloid haemorrhage (not seen at the end of the surgery) was noted in the macula (fig 2). All haemorrhages resolved spontaneously over the next 10 weeks.

Comment
The precise mechanism of action of homocysteine on the vascular tree is not well understood. Elevated homocysteine levels can cause endothelial disruption, structural damage by toxic effects on the intima and media, increased oxidation of low density lipoproteins, and alterations of clotting factors leading to a hypercoagulable state.3 Histopathological data derived primarily from animal models demonstrate smooth muscle cell hypertrophy and hyperplasia of the arteries.3 Postmortem studies of hyperhomocysteinaemic patients have shown intimal and medial thickening with disruption of the internal elastic lamina of small and large vessels.4 Histopathology of small arteries reveal focal proliferation of connective tissue with increased fibroblasts, collagen, and irregular elastic fibres.5 These changes may contribute to the fragility of small arteries and capillaries.

Valsalva retinopathy sometimes occurs with general anaesthesia. We do not believe this patient experienced this mainly because Valsalva retinopathy is bilateral. The retinal haemorrhages occurred only in the operated eye and not the fellow eye each time the patient underwent surgery.

The haemorrhages noted postoperatively in the left eye may have occurred because of ocular decompression retinopathy. An acute lowering of IOP can decrease the resistance of the retinal and choroidal circulation, temporarily overwhelming the capacitance of the capillary bed and resulting in multiple endothelial leaks and intraretinal haemorrhages.6 Hyperhomocysteinaemia can affect the autoregulation of small arteries.7 This may have contributed to the development of retinal haemorrhages in the left eye. The subhyaloid haemorrhages in the right eye, however, were unlikely to be related to ocular decompression retinopathy since no haemorrhages were observed during pars plana lensectomy, but these developed soon after vitrectomy was initiated. Minimal traction transmitted to the internal limiting membrane and nerve fibre layer by the vitrectomy may have caused the extremely friable superficial capillaries to rupture. Indeed, defects in retinal vascular autoregulation due to homocysteinuria, may have contributed to the development of the observed haemorrhages.

We hypothesise that individuals with chronic hyperhomocysteinaemia are at an increased risk for retinal haemorrhages because of homocysteine mediated destructive changes in small vessel walls and an autoregulatory defect that results in extreme capillary fragility.

Figure 1. Fundus photographs of the left eye 3 days after undergoing phacoemulsification and anterior vitrectomy for an anteriorly subluxated lens. Multiple ovoid subhyaloid preretinal and intraretinal haemorrhages are noted in the mid-periphery of the retina.

Figure 2. Fundus photographs of the right eye 1 day after pars plana vitrectomy and pars plana lensectomy for an anteriorly subluxated lens. A 2 disk diameter subhyaloid haemorrhage is seen in the macula along with one preretinal haemorrhage temporal to the macula. Photographs of other mid-peripheral retinal haemorrhages could not be taken owing to the patient’s non-cooperation.

Internet based ophthalmology service: impact assessment
In 2003, the Department of Health, Western Australia, commenced a teleophthalmology service between Carnarvon Regional Hospital (CRH) and Lions Eye Institute (LEI) at City of Perth (at 940 km), pioneering the use of remote, interactive consultations in ophthalmology. This assessment (a) reports the impact of teleophthalmology service on patient diagnosis, management, outcomes, and satisfaction; and (b) estimates the costs of teleophthalmology service.

Case report
An internet based system (www.e-icare.com) developed and evaluated at LEI, was used to store and transmit multimedia data to a secure, central database.7 Practitioners at CRH collected these data, which included patients’ demographic details, medical history, and ocular images. A portable slit lamp developed at LEI,8 tonometer (Keeler Pulsair 3000, Japan), and digital retinal camera (Canon CR-45NM, Japan) were also used. A questionnaire and interview approach assessed the satisfaction of the patients and practitioners. Estimation of costs analysed additional activity data and associated costs.

During the 12 month study period, there were 118 teleophthalmology consultations (42% men, 58% women, mean age 42 years, range 4–73 years). Most patients (53%) became aware of the service through local media, while health professionals in Carnarvon referred 36% for teleophthalmology consultation. Of the 118 cases, 3% of the patients used teleophthalmology for emergency consultation, 94% for testing for glaucoma and diabetic retinopathy: 3% of the cases were for expert second opinion and postoperative follow up.

Teleophthalmology proved to have impact on all the patients, by improving the eye care facility at CRH itself, instead of the need to travel 940 km to the city. Following teleconsultation, only 3% of patients were referred to a city hospital. While 53% of patients had no abnormalities detected, 3% of patients received treatment at CRH itself. The ophthalmologist recommended regular follow up for 36% of patients seen by telemedicine.

References

"This work was supported by Research to Prevent Blindness Inc, the Lions Eye Research Foundation of New Jersey, and the Eye Institute of New Jersey."
The teleophthalmology consultation cost per patient, at current efficiency level, is $279.96 including fixed cost. A cost neutral analysis estimated, at optimal efficiency, of 352 patients per annum, cost per patient would decrease to $107.72. In the remote area, without teleophthalmology, the cost to the service provider for a face to face consultation with an ophthalmologist in CRH and at LEI, City of Australia, Mr Francisco Chaves (health economist), received an award from University of Western Australia. The project is a technical and clinical success and one that led to direct potential benefit for patients in terms of improved outcomes, as well as considerable educational experience for the participating medical practitioners. However, current assessment brought to light the importance of redefining utilisation criteria in order to achieve efficiency. For example, 126 patients per annum are required for a cost effective teleophthalmology service while the current efficiency rate is 118 per annum (2.2 patients per week). Better coordination between the local healthcare workforce and CRH may increase the number of teleophthalmology consultations, which in turn will help to achieve break even or even establish net savings. Overall, this assessment indicates that the success of teleophthalmology will be based upon identifying the requirements of the service and using appropriate technology.

Acknowledgements

Supported by an IPRS Scholarship and UPA(IS) Award from University of Western Australia. The authors thank the Department of Health, Western Australia, Mr Francisco Chaves (health economist), and Ms Beth Hudson for her support and assistance especially in data collection. The authors also thank the patients, clinical staff, and administrative officers in CRH, Carnarvon and at LEI, City of Perth for their assistance.

S Kumar, M-L Tay-Kearney, I J Constable, K Yogesan

Lions Eye Institute, University of Western Australia, Nedlands, WA 6009, Australia

Correspondence to: Sajeesh Kumar, Lions Eye Institute, University of Western Australia, 2 Verdun Street, Nedlands, WA 6009, Australia; sajeeshk@cyllene.uwa.edu.au

Ethical approval was obtained from the University of Western Australia Human Ethics Committee and the Western Australia Aboriginal Health Information Ethics Committee.

doi: 10.1136/bjo.2005.072579

Accepted for publication 12 April 2005

Competing interests: none declared

References


Temperature sensitive oculocutaneous albinism associated with missense changes in the tyrosinase gene

Oculocutaneous albinism (OCA) describes a group of autosomal recessive disorders characterised by reduced or absent pigmentation of the eye, skin, and hair as a result of a congenital reduction in melanin synthesis. Additional findings in the eye include decreased visual acuity, nystagmus, iris transillumination, hypopigmentation of the uveal tract and retina pigment epithelium, foveal hypoplasia, and abnormal decussation of the optic nerve fibres at the optic chiasm leading to a lack of binocular vision. Type I OCA results from mutations in the tyrosinase gene and leads to either total absence of tyrosinase activity (OCA Ia) associated with absence of pigmentation (“tyrosinase negative”), or a marked reduction in tyrosinase activity (OCA Ib) associated with reduced pigmentation (“tyrosinase positive” or “yellow albinism”). We report a new case of the rare variant temperature sensitive albinism and our identification of missense mutations in the tyrosinase gene, not previously found in this form of albinism.

Case report

The patient, a 31 year old woman, was referred to us for genetic advice. She had originally presented at 6 weeks old with nystagmus and white hair; her parents both have dark hair and olive skin. The diagnosis of oculocutaneous albinism was made at 9 months. As she grew older the hair of her head darkened and, particularly in her teens, the hair on her lower legs and forearms darkened. As an adult she has light blonde hair, darker eye lashes and eyebrows, white axillary and pubic hair, but strongly pigmented hair on forearms and lower legs (fig 1). When examined in the clinic she had reduced visual acuity (6/36 bilaterally), marked iris translucency, and an albinotic retina with foveal hypoplasia bilaterally. Visually evoked potential revealed crossed asymmetry consistent with oculocutaneous albinism. We made a diagnosis of temperature sensitive albinism and searched for mutations in the tyrosinase gene. Blood was taken, with informed consent, from the patient and her parents and DNA extracted using standard techniques. Using polymerase chain reaction we amplified each of her tyrosinase gene exons and sequenced the entire coding region and intron-exon boundaries. Our patient did not have the R422Q mutation previously reported in patients with this phenotype and also did not have two other mutations known to be temperature sensitive.1 We did identify two missense mutations: R217Q and A355P, in exons 1 and 3 respectively (fig 2). The exon 1 mutation had been inherited from her parents.

Figure 1 Clinical photographs of patient. Note the yellow blonde hair, dark eyebrows, and strongly pigmented forearm hair. (Photograph reproduced with permission of the patient.)
pigmentation. No description of the distribution of the pigment is given, with “little apparent pigmentation” but with no description of the distribution of the pigmentation. Neither has previously been associated with a temperature sensitive phenotype.

Comment
Temperature sensitive albinism is a rare variant, first described in 1991, and subsequently associated with a particular missense mutation in the tyrosinase gene. The mutation, R422Q, results in a temperature sensitive trafficking defect preventing the translocation of the mutant tyrosinase into melanosomes. Thus, at 37°C mutant R422Q tyrosinase is retained in the endoplasmic reticulum and degraded by proteasomes and no pigment is produced. At lower temperatures (31°C) the enzyme can be successfully translocated into the melanosomes and some pigment is produced. At lower temperatures (31°C) the enzyme can be successfully translocated into the melanosomes and some pigment is produced. Patients with albinism are reviewed later in this developing phenotype will not be noted.

Choroidal neovascularisation associated with meningioma
This report documents the occurrence in three patients of subretinal choroidal neovascular membranes (CNVM) ipsilateral to meningiomas involving the optic nerve. We propose that the association might not be coincidental.

Case 1
A 31 year old woman developed a central scotoma in the left eye that led to the diagnosis of a left sphenoid wing meningioma involving the optic canal. The tumour was resected and her vision returned to normal. At age 56 a generalised seizure led to recognition of a recurrence. When the recurrent tumour was resected it proved to be a malignant meningioma. She was then treated with proton radiation from a 10 MV source (using a three field technique – right lateral, left lateral, and superior). The total dose was 45 Gy administered in 25 fractions. Thereafter, on regular follow up eye examinations she had normal visual function, pupils, and fundi. At the age of 64 she had a single episode in which for several seconds she lost all vision in the left eye except for a nasal island. There were no residua but her ophthalmologist found a new fundus abnormality that prompted referral.

Her medical history included migraine and a cutaneous malignant melanoma. There was no pertinent family history.

The patient’s visual acuities were 20/15 in each eye. Her colour vision ( Ishihara) and pupils were normal. The Goldmann visual field of her right eye was full but she had a relative inferior altitudinal defect to the 12e white stimulus in the left eye. There was no evidence of development of the left eye with normal orbital resiliency. Fundus examination of the left eye revealed a peripapillary superotemporal retinal elevation associated with lipid exudation. Echography showed a 1.1 mm of elevated retina adjacent to the left disc with normal acoustics. The rest of her neuro-ophthalmological examination was normal. There was hyperfluorescence in the area of disc elevation with late leakage of dye on fluorescein angiography consistent with a peripapillary CNVM (fig 1). At that time magnetic resonance imaging (MRI) scans showed no evidence of recurrent meningioma.

Five years later the vision declined to 20/30 in the left eye. There was neither optic atrophy nor optic disc swelling, but a left afferent pupillary defect and dyschromatopsia were observed. MRI showed that the sphenoid meningioma had recurred and involved the intracanalicular and posterior orbital segments of the left optic nerve. There also was enlargement of the posterior bellies of the left inferior and lateral rectus muscles.

Case 2
An 89 year old woman had cataract surgery on her left eye in December 2000 and her right eye in February 2001. She initially saw well following surgery; however, in August...
2001 she noted blurring of the vision in her left eye and a peripapillary CNVM was discovered. Despite two laser applications the patient’s vision continued to worsen.

Her medical history included rheumatic heart disease, hypertension, and hypercholesterolemia. In February 2001 she had endocarditis complicated by a left hemiplegia. There was no family history of any pertinent disorder.

Her visual acuities were 20/20 in the right eye and 7/200 in the left. She had dyschromatopsia of the left eye with 2 mm of proptosis and a relative afferent pupil defect. Goldman perimetry revealed a full visual field in the right eye and only a residual nasal island in the left. The fundus of the right eye was normal without drusen. Her left optic disc was atrophic and the left was normal. There were no macular drusen. She failed to respond to laser photocoagulation and proton beam radiation. Vision failed to 2/200 and the left disc became oedematous. MRI scanning showed bilateral optic nerve sheath enlargement and gadolinium enhancement of the mid and posterior segments of both optic nerves and extension of the lesion on the right side over the planum towards the chiasm. The lesions were interpreted as primary optic nerve sheath meningiomas.

Case 3
A 47 year old woman noticed that she had a painless visual disturbance of her right eye “like looking through a glass of water.” The symptom persisted, and 2 months later she awoke with a blind right eye. An MRI scan was interpreted as normal and her blindness was ascribed to optic neuritis. She was treated with a course of corticosteroids during which she recovered some vision but her vision failed again after the steroids were discontinued and thereafter she was unable to see light.

She had a history of asthma and obesity. Her father had age related macular degeneration.

At the age of 49 she noticed metamorphopsia in the left eye, and a large, elevated, extrafoveal CNVM was found. Echography revealed 1.3 mm of elevation, which was acoustically normal. Vision was then 20/20. The right optic disc was atrophic and the left was normal. There were no macular drusen. She failed to respond to laser photoacoagulation and proton beam radiation. Vision failed to 3/200 and the left disc became oedematous. MRI scanning showed bilateral optic nerve sheath enlargement and gadolinium enhancement of the mid and posterior segments of both optic nerves and extension of the lesion on the right side over the planum towards the chiasm. The lesions were interpreted as primary optic nerve sheath meningiomas.

Comment
Choroidal neovascularisation has been associated with macular degeneration, histoplasmosis, pathological myopia, angioid streaks, optic nerve drusen, optic nerve pits, pseudotumour cerebri, chronic inflammation, infection, malignant melanoma, choroidal osteomas, choroidal naevi, photocoagulation, and choroidal rupture. A break in Bruch’s membrane seems to be a common feature in CNV, but the exact pathogenesis remains a subject of debate.

While we cannot eliminate the possibility that the association of CNV with meningiomas and CNV in our patients is merely by chance, several observations suggest otherwise. In each case the fundus of the fellow eye was free of drusen, let alone more substantive evidence of macular degeneration. None of the patients had a disorder known to predispose to CNV. There has been one report of CNV after radiation but in that case the patient also had significant radiation retinopathy. Other irradiated patient (case 1) had no evidence of radiation retinopathy and the radiation portals spared the eye. One of our patients was only 49 years old when the membrane was recognised. In two of our patients the membrane was peripapillary.

Schatz et al published the histopathological findings in a patient with a primary optic nerve sheath meningioma in which there was a CNV. However, their patient had chronic disc oedema and venous collaterals and had antecedent age related macular degeneration in both eyes. Shields et al described an instance of CNV in a child with an optic nerve glioma. That patient’s disc was also oedematous. Peripapillary CNV has been described with chronic disc oedema of other causes as well, but two of our patients never had disc swelling and the third developed disc oedema only after the CNV was recognised.

How might a meningioma cause an ipsilateral CNV? The pathophysiological mechanism by which these two conditions occur together is unclear. It is possible that the tumour tissue could have invaded the eye. CNV has been associated with other tumours involving the choroid. Ocular invasion was not evident on ultrasound (cases 1 and 3) or MRI scans but absence of proof is not proof of absence. In the case of Schatz et al there were small foci of the meningioma in the peripapillary sclera and retrolaminar optic nerve, which were not seen before enucleation. Dutton reviewed meningiomas involving the optic nerve and primary optic nerve sheath meningiomas. CNV was not mentioned as a presenting sign. None the less, he calculated 3.7% of 477 reported cases described intraocular invasion by meningiomas. Other authors have reported histopathological cases of meningioma invading the optic nerve and disc.

We believe that the association of CNV with ipsilateral meningiomas in our patients was not one of chance. The presumed mechanism is invasion of the globe by the tumour sufficient to cause the CNV but below threshold for detection by MRI, ultrasound, or ophthalmoscopy.

M S Lee
Cale Eye Institute, The Cleveland Clinic Foundation, Cleveland, OH 44195, USA

S Lessell
Neuro-ophthalmology Unit, Massachusetts Eye and Ear Infirmary, Harvard Medical School, Boston, MA 02114, USA

Correspondence to: Michael S Lee, MD, Cale Eye Institute/1-32, The Cleveland Clinic Foundation, 9500

Figure 1 Patient 1. Retinal elevation and lipid exudation superotemporal to the left optic disc (top left). Venous laminar (top right), arteriovenous transit (bottom left), and late phases (bottom right) of the fluorescein angiogram demonstrates peripapillary hyperfluorescent area growing in size and fluorescence consistent choroidal neovascularisation.
Intraoperative visual experiences of cataract patients can be both pleasant and unpleasant

We read with interest Zia et al’s article, which highlights a professional artist’s and a poet’s respective renditions of their visual experiences during phacoemulsification and intraocular lens implantation under local anaesthesia. While it is unclear from the report whether the artist’s elaborate drawing resembling a “colourful monkey” was associated with a pleasant or frightening visual experience, it appears from the poem that the poet’s visual experience was most probably frightening. The frightening experience may also lower patients’ satisfaction with the surgery.1 2

The poet’s experience reported by Zia et al reminds us that the intraoperative visual experience during cataract surgery can be pleasant for some patients.3 In fact, our experience has shown that the majority of patients find their visual experiences pleasant and, in some cases, the visual experience actually increases their satisfaction with the surgery. In a recently reported randomised controlled trial conducted in India involving 304 patients who underwent phacoemulsification under general anaesthesia, 79% of patients who had phacoemulsification under general anaesthesia reported that their satisfaction with the surgery increased because of their visual experiences, whereas only two patients (0.6%) experienced a decrease in satisfaction. The remaining 88 patients (89.8%) reported that their visual experience did not affect their satisfaction with the surgery. Some of the patients who had cataract surgery under general anaesthesia commented on the “fantastic colours” that they experienced. In another study, 138 patients (85.8%) who had phacoemulsification under general anaesthesia reported that their satisfaction had decreased as a result of the visual experiences and the remaining 138 patients (80.8%) experienced no change in their satisfaction. An additional observation is from videotaped interviews conducted by one of us (CMK) with several leading ophthalmic anaesthesiologists in the United States who had cataract surgery under local anaesthesia themselves. The video recordings were made during the annual scientific meeting of the Ophthalmic Anaesthesia Society held in Chicago in October 2004. The videos clearly showed these leading ophthalmologists seeing pleasant and beautiful images during their surgery. In summary, patients may experience pleasant or unpleasant visual sensations during cataract surgery under local anaesthesia. Further investigation is warranted to help ascertain how we can reduce the possibility of the experience being unpleasant or frightening.

K-G Au Eong
The Eye Institute at Alexandra Hospital, National Healthcare Group, Singapore, The Eye Institute at Tan Tock Seng Hospital, National Healthcare Group, Singapore, Department of Ophthalmology, National University of Singapore, Singapore, Singapore Eye Research Institute, Singapore

References


Cigarette pack warning: it can send you blind!

The growing research implicating smoking in age related macular degeneration (AMD) prompted us to write an editorial in 1999 urging the Australian government to warn smokers of this little appreciated risk only if they smoke. In 2000, the Australian National Quit campaign ran an advertisement as part of a series titled “Every cigarette is doing you damage,” which explicitly addressed AMD. A website describes the campaign here in Australia (www.quitnow.info.au/script/eye.html) and the television ad may be downloaded (www.quitnow.info.au/smokescreen/smokescreen.html).

In 2006 the Australian government will require new mandatory pictorial pack warnings, one of which will be about AMD. This warning was one of the strongest tested among current smokers in the research conducted for the government before the announcement. The full report and other related information can be found at tobacco.health.
Immunology of the lacrimal gland, tear film and ocular surface

A short quotation (p 152) summarises the book: “These systems are all part of the multiple and redundant and protective mechanisms that maintain a functioning cornea.” Reflecting this complexity, chapters range from the pathogenesis of herpetic keratitis to dry eyes, to mucosal immunity and the use of topical ciclosporin, to tear film and contact lenses and, of course, inflammation. The book includes more unusual chapters on ocular surface: these integrate the eye into the upper aerodigestive tract. Parallels between lacrimal and salivary glands, which are not often conducted, focus attention to the inflammatory and immune processes common to these mucosae and the diagnostic markers they might offer.

Some chapters are dense and scholarly: “Sex, sex steroids and dry eye syndromes”: has no fewer than 232 references, and provides a “must read” synthesis of approaches, results and hypotheses of the research undertaken to understand sex related differences in lacrimal and meibomian gland (dys)function. Other chapters have a narrower focus: events leading to Acanthamoeba infections and candidates for therapy are presented in an very clearly.

Acanthamoeba infections and candidates for therapy are presented in an very clearly.

The next chapter deals with antimetabolites in filtration surgery; established antimetabolites are covered (5-fluorouracil and mitomycin C), new agents such as antibodies to TGF-β are also mentioned. The final chapter is on drainage implants, the Molteno, Baerveldt, and Ahmed implants are discussed. Finally the actual surgical techniques and the complications are well described.

Overall, this is an excellent book, it is concise, with only 163 pages of illustrated text, easy to read, and extremely pertinent to clinical practice. A text I thoroughly recommend for any trainee ophthalmologist or optometrist and anyone wanting a brief, contemporary revision text on the diagnosis and management of glaucoma. Although, fortunately or unfortunately, in the end it may only whet your appetite for more and leave you wanting more.

N Spencer
Bristo Eye Hospital, Lower Maudlin Street, Bristol BS1 2LX UK; bluegreeniris@hotmail.com

Glaucoma. 3rd ed.

This excellent text has been in print since 1989 and its longevity is testament to its high quality. This is the third edition, with a new co-author John Salmon. Since its previous edition over 8 years ago there have been many advances in both the genetics, and the diagnosis, monitoring and treatment of glaucoma. This text successfully updates the previous edition, and provides a concise, systematic, detailed and well balanced representation of modern glaucoma diagnosis and management.

This book is aimed at the trainee ophthalmologist and optometrist, although it is also good basic revision for the practising ophthalmologist. This is a comprehensive text in that each type of glaucoma is described in terms of its main clinical features and management. There are many colour illustrations and photographs; these help the reader to correctly interpret clinical signs and diagnostic tests. It also covers current controversies and new techniques such as non-penetrating glaucoma surgery. The landmark glaucoma studies and their significance are also mentioned. It is perhaps too brief in sections, particularly in the chapters looking at glaucoma diagnosis, perimeter, and imaging; however, adequate and key references are provided to allow further pursuit of these topics in more depth.

The text begins by covering the basic sciences including the physiology of aqueous secretion. Then there is a comprehensive definition and classification of glaucoma. The different types of glaucoma are described at length. Tonometry is covered well, including the range of tonometers, potential errors in tonometry, and calibration. Gonioscopy is discussed including angle structure identification and the different systems of angle classification.

Retinal nerve fibre and optic nerve head assessment is described briefly including the new imaging techniques of scanning laser tomography (Heidelberg retinal tomogram II), ocular coherence tomography (OCT), and scanning laser polarimetry (GDx nerve fibre analyser). The images or readouts produced by each machine are provided in colour along with a very brief description of their interpretation. The various modalities of perimeter are described, their interpretation is given, and new techniques such as the frequency doubling contrast test (FDT) and shortwave automated perimeter (SWAP) are discussed and examples provided.

Glaucoma medications are covered very well. Long standing medication are discussed as well as new treatment options, including combined topical preparations. Neuroprotective agents are covered with the recent research regarding these agents. There is a chapter on laser therapy which covers argon, diode, and selective laser trabeculoplasty, Nd:YAG laser iridotomy, and diode laser cyclodestruction.

Trabeculectomy surgery with early and late complications are discussed comprehensively. There is an excellent and concise chapter on non-penetrating filtration surgery, covering the most popular techniques—deep sclerectomy and viscosanastomosis.

The next issue of Community Eye Health (No 94) assesses the progress of Vision 2020 at the district level. 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; online edition: www.jceh.co.uk). Annual subscription (4 issues) UK £28/US$45. Free to developing country applicants.

NOTICES

World Ophthalmology Congress 2006 – Brazil
The World Ophthalmology Congress (which is replacing the International Congress of Ophthalmology) is meeting in February 2006 in Brazil.

For further information on the congress and committees, scientific program and coordinators of different areas are available at the congress website www.ophthalmology2006.com.br

Thoughts on Ophthalmology and Development
The Mathis Eye Foundation is a small, privately financed organisation, established 17 years ago by a former international banker who began his medical studies at age 40, with the specific intention of working in third world surgical ophthalmology. The Foundation’s experiences and lessons learned are presented in a 26 page bound summary entitled Thoughts on Poor World Ophthalmology Development, an often critical look at eye surgery programs in Latin America, Africa, and Haiti. To obtain this report without cost, please contact jheatherly@taylormathis.com.

Vision 2020
The latest issue of Community Eye Health (No 94) assesses the progress of Vision 2020 at the district level. 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; online edition: www.jceh.co.uk). Annual subscription (4 issues) UK £28/US$45. Free to developing country applicants.
Complex I respiratory defect in LHON plus dystonia with no mitochondrial DNA mutation

K K Abu-Amero, T M Bosley, S Bohlega and D McLean

Br J Ophthalmol 2005 89: 1380-1381
doi: 10.1136/bjo.2005.072819