Macular degeneration associated with a novel Treacher Collins tcof1 mutation and evaluation of this mutation in age related macular degeneration

Treacher Collins syndrome (TCS) results from defects in a nucleolar trafficking protein (Treacle) coded for by the TCOF1 gene. The purpose of this report is, firstly, to describe an isolated male with TCS associated with macular degeneration who also had a novel TCOF1 gene mutation and, secondly, to evaluate this mutation in a well characterised cohort of 95 patients with age related macular degeneration (AMD).

Case report
A 44 year old man presented with a 1 month history of metamorphopsia. He had minimal dysmorphic features but was noted to have an antimongoloid slant of the palpebral fissures with mild flattening of the midface. Sensorineural deafness had been diagnosed from childhood but the external ears were normal in appearance. Best corrected visual acuity was 6/9 (−2.25 DS) right eye and 6/24 (−1.50 DS) left eye. Ocular examination revealed bilateral posterior embryotoxon with adhesions between iris and Schwalbe's line, and iris hypoplasia. No eyelid colobomata were present. Posterior segment examination (fig 1) revealed atrophic macular degeneration in both eyes and a choroidal neovascular membrane (CNV) in the left eye confirmed on fluorescein angiography. No drusen were seen in either eye. Mutation screening of TCOF1 gene was instigated because his facial appearance and deafness suggested possible TCS. A mutation was identified in exon 13 (2055 del AG), which is predicted to create a premature stop codon. In view of this unique genotype and phenotype we wished to evaluate whether this mutation in the TCOF1 gene was commonly associated with macular degeneration. Ninety five white patients with AMD were therefore screened for the 2055 del AG mutation by denaturing high performance liquid chromatography (dHPLC), using the DNA from our patient with TCS as a positive control (fig 2). The spectrum of AMD in this cohort was AREDS grade I (21 patients); AREDS grade II (20 patients); AREDS grade III (19 patients) and AREDS grade IV (35 patients). No abnormal chromatograms were detected in any of these patients.

Comment
Ophthalmological features in TCS may be extensive, but rarely involve intraocular structures. Common features include astigmatism, defective inferior lateral angle of the orbit, caudal displacement of the superolateral orbit, coloboma of the lateral part of the lower lid, pseudocoloboma of the eyelids, lateral canthal dystopia, nasolacrimal obstruction, orbital and limbal dermoids, and microphthalmos. Hansen et al6 have observed bilateral iris, choroid, and optic nerve colobomata. Cataracts, lacrimal duct atresia, pupillary ectopia, distichiasis, and uveal colobomas have been reported less frequently. A solitary case with aniridia, sclerocornea, and retinal maldevelopment has also been reported.7 We believe this is the first report of atrophic macular degeneration and CNV demonstrated in a patient with a proved molecular diagnosis of TCS.

Disease expressivity is highly variable in TCS, ranging from the clinically undetectable to death in the perinatal period. The late clinical presentation in our case may be explained by the mild phenotype in the spectrum of TCS. The TCS Collaborative Group first identified different mutations in the TCOF1 gene in each of five unrelated families with TCS. All of the mutations were predicted to result in a premature stop codon leading to premature termination of the protein product. Since then over 100 disease causing mutations have been reported throughout the TCOF1 gene in patients with TCS, which represented a detection rate of 60%. Our patient has a 2055 del AG mutation in exon 13 of the TCOF1 gene which has not been previously reported. We speculate that there may be a causal relation between the mutation and the macular degeneration seen in our patient with TCS.

The specific role of TCOF1 in the molecular pathogenesis of TCS remains elusive, but mechanisms such as abnormal neural crest cell migration and abnormal cell death seem important. TCOF1 is expressed in the human eye and apoptotic regression has been described in organs such as ears and kidneys in animal models of TCS. Therefore, it seemed possible that this TCOF1 mutation may also trigger cellular apoptosis resulting in atrophic macular degeneration. However, we tested for the presence of this mutation in 95 patients with AMD but did not identify any mutation carriers in this cohort.

We acknowledge that it is possible that this macular finding is incidental to TCS and the TCOF1 mutation. The early age of onset of macular degeneration in this patient is also atypical for AMD. We also note that the macular degeneration seen in this patient is more severe than would be expected with his low degree of myopia. It is therefore possible that patients with TCS may have an increased risk of developing macular degeneration.

In summary, we describe a new clinical phenotype in a patient with molecularly proved TCS and a novel TCOF1 mutation. Although most cases of TCS present early in life, ophthalmologists need to review adults with TCS to see if macular degeneration is more widespread than reported. This mutation, however, does not appear to be implicated in AMD.

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Figure 1 Both eyes showing atrophic macular degeneration. The left eye in addition has subretinal hemorrhage (white arrow) with choroidal neovascularisation.

Figure 2 Mutation screening chromatograms. (A) A double peak is seen indicating the base pair mismatch in the proband. (B) A normal wave tracing from a screened AMD sample.
The age of 49 with a 4 year history of typical derma presented with a 9 month history of A 51 year old woman with known scleroderma with neovascularisation that responded to panretinal scatter photocoagulation. The disease is rare. We report for the first time subclinical and visual loss as a direct result of involvement of the posterior segment is often ophthalmic symptoms related to dry eyes. Patients with scleroderma experience vasculopathy in scleroderma. Bilateral ischaemic retinal vasculopathy in scleroderma

Bilateral ischaemic retinal vasculopathy in scleroderma Patients with scleroderma experience ophthalmic symptoms related to dry eyes. Involvement of the posterior segment is often subclinical and visual loss as a direct result of the disease is rare. We report for the first time a patient with a bilateral ischaemic retinopathy with neovascularisation that responded to panretinal scatter photocoagulation.

Case report
A 51 year old woman with known scleroderma presented with a 9 month history of increasing visual loss. She had presented at the age of 49 with a 4 year history of typical Raynaud's phenomenon and a 6 month history of symmetrical skin induration affecting her hands, feet, and face. Subsequently skin sclerosis extended over the chest wall and proximal limbs, typical of diffuse systemic sclerosis. She also had oesophageal involvement and interstitial lung fibrosis. Initially she responded well to symptomatic treatment, but 2 years later she developed worsening breathlessness and pulmonary hypertension was confirmed by right heart catheter. At the time of presentation to the eye clinic her blood pressure was well controlled and her blood sugars were normal. On examination, best corrected visual acuity was 6/9+2, N6 in the right eye and 6/12+2, N8 left eye. Anterior segment examination and intraocular pressures were normal.

Dilated fundal examination showed bilateral disc neovascularisation, multiple cotton wool spots, and marked venous tortuosity (fig 1). Fluorescein angiography showed marked bilateral capillary closure, disc neovascularisation, and left macular ischaemia (fig 2).

A left panretinal photocoagulation was performed the same day and the right treated similarly 2 weeks later. Two weeks later, there was no objective change in her acuities but fundal examination showed partial regression of the disc new vessels. She subsequently deteriorated systematically and died of cardiac failure secondary to pulmonary hypertension 30 months after her initial presentation.

Comment
Scleroderma targets many organs, including the skin, blood vessels, synovium, gastrointestinal tract, kidneys, heart, and lungs. The lesions of scleroderma are typified by inflammation and microvasculopathy, which in turn stimulate collagen overproduction and fibrosis.

Keratoconjunctivitis sicca is the most common ocular complication of scleroderma, present in up to 70% of cases, and may be complicated by foreshortening of the conjunctival fornices. Choroidal disease is also common in scleroderma; one series reported that 53% of cases had patchy areas of non-perfusion on fluorescein angiography (FFA), undetectable in all but one, on fundoscopy.

Another study showed capillars abnormalities and normal fundi in seven of 21 FFAs.

Retinopathy in scleroderma has been described in two patients. The first of these was thought to be related to uncontrolled systemic hypertension, with funduscopic findings of cotton wool spots, oedema, and haemorrhages. The second case, with normal blood pressure and normal fundi, was found to have histopathological changes through- out the retina consisting of extensive vacuolation in the nerve fibre, ganglion cell, and plexiform layers. Horan reported the ophthalmological findings in a series of 23 patients; only one patient was found to have a small superficial retinal haemorrhage, in the absence of vascular risk factors.

Hypertensive retinopathy and branch vein and artery occlusions have been described and it has been noted by several authors that the retinopathy is more florid than would be expected with the level of recorded blood pressure. Our patient developed pulmonary hypertension secondary to a fibroproliferative pulmonary vasculopathy. It is well recognised that other vascular beds (renal, digital, and gut) also have intimal proliferation and fibrosis in scleroderma, and it is likely that this was the pathological process underlying the patient’s eye disease.

To our knowledge, this is the first report of frank bilateral ischaemic retinopathy in association with scleroderma and the first to document neovascularisation at the disc with a beneficial response to laser photocoagulation.

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References
An Arg311Gln NR2E3 mutation in a family with classic Goldmann-Favre syndrome

Goldmann-Favre syndrome (GFS) is one of the rarest inherited vitreoretinal dystrophies that manifests with hemeralopia, degenerative vitreous changes, peripheral and central retinoschisis, a liquefied vitreous cavity with preretinal band-shaped structures, macular oedema, cataract formation, and an abnormal electroretinogram (ERG). The term “clumped pigmented retinal degeneration” (CPRD) describes a group of patients with decreased night and peripheral vision who have round and irregular clumps of pigment in the mid-peripheral fundus with little or no evidence of bone spicule formation. This pattern of pigmentation occurs in retinitis pigmentosa (RP) with preserved para-arteriolar retinal pigment epithelium (PPRPE), enhanced S-cone syndrome (ESCS), and GFS, and these disorders share common mutations in the NR2E3 gene, which is involved in retinal cell fate determination.

We present clinical and molecular genetic studies of a family from the United Arab Emirates with a classic GFS phenotype and a mutation in the NR2E3 gene.

Case reports

Two affected siblings and two unaffected siblings from a consanguineous family in which there were nine unaffected siblings were examined. GFS was diagnosed according to previous clinical descriptions of the disease. Complete ocular examinations, fluorescein angiography (FA), ERG, and optical coherence tomography (OCT) were done. ERGs were performed according to ISCEV recommendations.

Blood samples were obtained to study the NR2E3 gene after informed consent was secured following explanation of the procedures; all studies conformed to the standards of the institutional review board at the Cleveland Clinic Foundation and the Declaration of Helsinki.

DNA was extracted from leucocytes and the coding exons of the NR2E3 gene were amplified using polymerase chain reaction (PCR) with published primers and methodology. Sequencing was accomplished using an automated sequencing unit (Beckman-Coulter, CEQ 2000).

Case 1 had a best corrected visual acuity of 20/200 right eye with +0.25+0.35x135 and 20/400 left eye with +1.00 sphere, and case 2 had a best corrected visual acuity 20/60 right eye with −3.75+2.25x0.80 and 20/50 left eye with −2.75+2.75x0.85. External ocular examination, pupillary reaction, applanation tonometry, and slit lamp biomicroscopy were within normal limits. Both patients had macular schisis and yellowish lesions, some with pigmented edges, deep to the neurosensory retina in both eyes (fig 1A and 1B). Both patients had prominent macular oedema in both eyes detected on FA and OCT (fig 1C and 1D). ERGs obtained to low intensity stimuli presented to the dark adapted eye were not different from the baseline. When a high intensity stimulus flash was used, large amplitude ERGs were obtained (fig 2). These responses had an abnormally slow waveform. Unlike control subjects, the presence of a steady adapting field had a modest effect on ERG amplitude and almost no effect on ERG waveform in the two patients. Flicker ERGs were also slower than control.

Both patients were homozygous for a point mutation 932 G > A in exon 6, leading to an Arg311Gln change in the NR2E3 protein (fig 3). One of the unaffected siblings carried one mutant allele and the other was not a carrier.

Comment

NR2E3 encodes a retinal nuclear receptor and is part of a large family of nuclear receptor transcription factors involved in signaling pathways for photoreceptors. This retinal nuclear receptor, limited to the outer nuclear layer of the human retina, has been shown to regulate pathways involved in embryonic...
development, as well as maintain proper cell function in adults. The homonymous mutation, Arg311Gln, in exon 6 of the NR2E3 gene causes ENCS, CPCR, and by previous reports. Sharon et al reviewed the literature and found that exon 6 is where most disease mutations are found. The mechanism for the phenotypic variability associated with the Arg311Gln mutation is unclear but NR2E3 appears to have a role in determining photoreceptor phenotype.

Mutations in NR2E3 result in retinal disorganisation as a result of defective development, known as S-cone fragility, or abnormal maintenance of mature photoreceptors in adults. This abnormal retinal architecture is evidenced phenotypically as macular retinoschisis, as in GFS. From a clinical perspective, OCT testing in our patients has provided information about the location and extent of retinoschisis typically found in the neurosensory retina in GFS and supports one previous report. Our study corroborates previous reports that the classic GFS phenotype results from mutations in the NR2E3 gene, and more notably the right blindness and clumped retinal pigment deposits should raise suspicion that a patient may have a mutation in the NR2E3 gene.

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References

IVF babies with ROP at higher gestational age and birth weight: implications of changing screening criteria
There is interest in reducing the criteria for retinopathy of prematurity (ROP) screening below the current guidelines of less than 32 weeks gestation and birth weight less than 1501 g. Here we present three babies conceived by IVF who were close to the limits of the current criteria and could not be identified should such changes be made.

Case reports
A female baby, twin 2 of an IVF pregnancy, born at 31+4 weeks with a birth weight of 1.27 kg developed bilateral stage 3 ROP with mild vascular changes (pre-plus disease), but did not reach the threshold for treatment. A male baby, twin 1 of an IVF pregnancy, born at 31+5 weeks with a birth weight of 1.265 kg developed 4+4 ROP that although sub-threshold was considered to require treatment. This was undertaken at 44 weeks postmenstrual age (PMMA) and he responded well to laser therapy, with regression in both eyes.
A female baby, triplet 2 of an IVF pregnancy, born at 32 weeks with a birth weight of 1.31 kg developed bilateral stage 3 ROP. There was minimal vascular congestion and the retinopathy resolved spontaneously.

Comment
Babies born after assisted conception are more likely to be born pre-term and of lower birth weight. This appears to be the result of increased numbers of multiple births with assisted conception (23% compared to 1% of those conceived naturally); both birth weight and gestational age fall in direct relation to the multiplicity of the pregnancy. However, even singleton births resulting from assisted conception are more likely to be premature and of low birth weight than those conceived naturally.

Watts and Adams reported that IVF infants with ROP had lower gestational age and birth weight than those IVF infants who did not develop ROP. They also reported that assisted conception using IVF appears to be a risk factor for development of threshold ROP. Additionally, they reported a non-statistically significant increased risk for the IVF infants with stage 3 ROP to have a higher gestational age and birth weight than those who did not have ROP. In a large series, reported no difference in the incidence or severity of ROP between singleton and multiple gestation babies.

The different outcomes of assisted conception have been postulated to be because the gametes are exposed to a variety of drugs, physically manipulated, nurtured in potentially hazardous conditions, and perhaps placed in an inappropriate uterine environment.

Retinopathy of prematurity may affect larger and more mature babies who are conceived by IVF than those who are not. The three babies described here all developed ROP despite gestational ages greater than 31 weeks and birth weights greater than 1200 g. If the criteria for ROP screening are changed in the future, it is possible that some babies who develop ROP might fall outside the guidelines for screening.

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References

A novel mutation in the RDS gene in an Italian family with pattern dystrophy
The term “pattern dystrophy” (PD) of the retina refers to a group of inherited dystrophies characterised by deposition of abnormal pigment at the level of retinal pigment epithelium (RPE). Several studies have correlated PD with mutations in the RDS gene. Therefore,
mutations in the same RDS gene have been reported to be associated with other retinal diseases. Here we report the clinical features of an Italian family (fig 1) affected by autosomal dominant PD associated with a new mutation in the RDS gene.

Case reports

The proband I-1 is a 76 year old man who referred with progressive reduction of visual acuity at approximately 50 years of age; he showed an uncorrected visual acuity of 20/400 in the right eye and 20/100 in the left eye in lateral gaze position. Examination of the retina showed pink optic nerve heads, normal retinal vessels, retinal pigmented epithelial, and choriotapicalis atrophy in the peripapillary regions bilaterally and an extensive geographic atrophy that involved the posterior pole within the vascular arcades demarcated from healthy appearing tissue in the periphery (fig 2A). Confocal scanning laser ophthalmoscope (cSLO) fundus autofluorescence imaging showed a central well circumscribed loss of autofluorescence corresponding to the atrophic area. Patient I-1 had abnormal rod and cone electroretinogram (ERG) responses (scotopic blue flash: 166 V; normal 379 (SD 104) μV photopic: 43.5 μV; normal 210 (86) μV. The electro-oculogram (EOG) cannot be performed.

Patient II-1, a 46 year old woman, at examination did not have any subjective visual complaint. She presented with a best corrected visual acuity of 20/20 in the right eye with a refraction of −0.75D, and 20/20 in the left eye uncorrected. At fundus examination, she showed a normal optic disc and retinal vessels in both eyes, with a characteristic yellowish subfoveal lesion with five “butterfly-shaped” radiating arms. On autofluorescence imaging, the fundus yellowish linear deposits in macular region are shown to be more fluorescent than the background (fig 2B). The yellowish butterfly-shaped lesions correspond to a radial hypofluorescence in the macular area, enclosed by a faint hyperfluorescence, revealed by fluorescein angiography. Scotopic ERG tracing was reduced at 185 μV while the photopic tracing was in the normal range at 135 μV; the EOG revealed a decreased Arden ratio (RE 1.53; LE 1.60; normal ratio >1.65). Patient II-2, a 45 year old woman, at 44 years of age complained of metamorphopsia, and 1 year later she reported a reduced central visual acuity. At examination, she had a visual acuity of 20/20 in both eyes.

Figure 1 Pedigree of family with autosomal dominant pattern dystrophy. Square: male; circle: female; solid symbol: affected; open symbol: unaffected.

Figure 2 (A) Posterior pole of patient I-1, showing the sharply demarcated atrophy of retinal pigmented epithelium and inner choroid at the macula and around the optic disc. (B) Autofluorescence imaging of patient II-1, showing, in the macular region, linear radial fluorescent deposits corresponding to funduscopic yellowish butterfly-shaped lesions.

Amsler grid test revealed a waviness in the central field of the right eye. Fundus examination demonstrated normal disc and vessels. The perifoveal region had a lightly yellowish spots clustered at the level of the foveal and perifoveal area; the periphery was of healthy appearance. On autofluorescence imaging the macular lesions showed a high level of autofluorescence that better defined the abnormalities observed by ophthalmoscopy. A fluorescein angiography showed a hypo-fluorescent area in the macular region with a hyperfluorescent halo. There was a normal ERG (scotopic blue flash: 376 μV; photopic: 218 μV) and EOG such as colour vision testing.

Comment

The new mutation, described here, lies very close to the cysteine position 166 and 166 residues that have been suggested to be important for the ability of the peripherin protein to keep normal flattened outer segment disc morphology. The morphological changes associated with RDS mutations causing pattern dystrophies of the macula ranged from mild depigmentation of the fovea to advanced geographic atrophy or choroidal neovascularisation. In this study the two younger patients (II-1 and II-2) showed typical lesions of “butterfly-shaped” pattern dystrophy while the oldest one (I-1) had a severe geographic atrophy of the retina probably as an advanced evolution of lesions showed by his daughters. The missense mutation in the RDS gene described in this report is associated with a relatively severe manifestation of PD in affected family members. The identification and further characterisation of mutations in the RDS gene may yield insight into the function of the peripherin protein, the pathogenesis of PD and other retinal dystrophies, and the development of treatment for these disabling visual disorders.

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References


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Preventing exposure keratopathy in the critically ill: a prospective study comparing eye care regimes

Microbial keratitis has been reported among critically ill patients and the need for effective eye care in the intensive care unit (ICU) has been recognised for some time. However, dility, eye care regimes are not always evidence-based and there is no clear consensus defining the best form of eye care. A recent survey in the United Kingdom found that 75% of ICUs used Geliperm routinely as eye care, with 25% using ocular lubricants. Although Geliperm was originally designed as a wound dressing and there is no evidence to support its use in eye protection. Lacrilube, however, has been shown to be effective in reducing exposure keratopathy in sedated and paralysed patients. This prospective comparative study aims to assess the prevalence of corneal surface disease in ICU and the effectiveness of two different eye care regimes at preventing corneal surface disease.

Methods

Three main types of eye care are instituted at the discretion of nursing staff: (1) simple eye toilet; (2) Lacrilube alone; (3) Geliperm alone.

Patients admitted over a 4 month period were examined at weekly opthalmology ward rounds for signs of ocular surface disease. All patients who spent less than 3 days on the unit and with primary orbital injury were excluded. The type of eye care regime was recorded as well as greatest vertical diameter of the palpebral aperture (mm), conjunctival chemosis, and length of stay. The cornea was assessed by instillation of fluorescein and viewing with cobalt blue light using an indirect ophthalmoscope and 20 dioptre lens. Corneal damage was graded from 1–6 according to severity using a previously described grading system (table 1). Conjunctival chemosis was graded from 1–3 (table 2) The sedation score and number of days that the patient were in the ICU were also recorded. Any patient found to have a compromised cornea was removed from the study and treated with prophylactic antibiotic ointment.

Result

Forty seven patients were recruited. A total of 24 were found to have exposure keratopathy (50%). These results are summarised in table 3. Twenty four patients were identified who received basic eye toilet alone (no Lacrilube or geliperm). Of these, 13 patients (54%) were found to have exposure keratopathy. Ten patients were treated with Geliperm alone and of these nine (90%) were found to have exposure keratopathy. In general, more severe keratopathy was seen in the Geliperm group. Statistical comparison of the three groups indicated that Lacrilube is more effective than Geliperm or basic eye care alone (Fisher’s exact test p = 0.04), and more effective than Geliperm (Fisher’s exact test p = 0.001). No significant variance was detected in the groups between sedation score (p = 0.45 Kruskal-Wallis) and number of days in the ICU (p = 0.09 Kruskal-Wallis). No skew in the distributions of ocular surface disease.

Comment

Microbial keratitis is almost always preceded by compromise of the corneal epithelium. The immune defences of the eye are predominately innate and consist of a combination of mechanical, anatomical, physiological, and barrier defence mechanisms. These include an intact corneal epithelium and the constant blinking action of the eyelids. The tear film also has important antimicrobial components such as lactoferrin, β lyso and immunoglobulins.

ICU patients are often sedated and paralysed leading to incomplete eyelid closure. Critical illness is frequently associated with capillary leak and fluid retention that causes peripheral oedema and conjunctival oedema. As a result, these patients are susceptible to exposure keratopathy. The breakdown of the ocular surface of the eye is known to predispose to opportunistic infection. There have been many reports of Pseudomonas and Acinetobacter infections causing microbial keratitis among the critically ill. It is thought that procedures such as endotracheal suctioning may lead to aerosol inoculation of the susceptible patients’ corneal surface by respiratory tract organisms. The need for effective eye care has been recognised for some time and although data exist to compare moist chamber treatments with ocular lubricants, no data exist to compare the efficacy of polyacrylamide Hydrogel (Geliperm) and ocular lubricants. We also note that Geliperm has been designed as a wound dressing and does not have a devices licence for eye care.

Our data suggest that the use of Lacrilube is more effective than Geliperm or basic eye care. Further research is clearly needed in this area.

References

Elevation in adduction of the right eye
trochlea to the medial canthal tendon was
described, its association with ethmoidal
sheath as the cause of restriction to
subsequent reports have alternatively pro-
scribed varied abnormalities in both
conjunctival and acquired Brown syndrome such as
traumatic or iatrogenic scarring, avulsion of
Brown syndrome were identified: trochlear
displacement of the trochlea, cyst in the superior oblique
tendon, inferior displacement of the lateral
rectus muscle injury following frontal and
inferior rectus muscle injury following frontal and
Complications of blepharoplasty. Ophthalmic
4 Hermann JS. Acquired Brown’s syndrome of
inflammatory origin. Arch Ophthalmol
1979;96:1228–32.
5 Whitefield L, Isenberg DA, Brazier DJ, et al.
Acquired Brown’s syndrome in systemic
lupus erythematous. Br J Rheum
6 Lacy PD, Bhogin M, Colarvey MP, et al.
Acquired Brown’s syndrome caused by a fronto-
ethmoidal mucocele. Aust N Z J Surg
resolution magnetic resonance imaging
demonstrates varied anatomical abnormalities in
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Ocular presentation of the
SAPHO syndrome
SAPHO syndrome (synovitis, acne, pustulosis,
hyperostosis, and osteitis) is a seronegative
spondylarthropathy. The term, introduced in 1987, describes a syndrome with various previous pseudonyms: multi-
local recurrent osteomyelitis; arthritis with
acne; and osteitis with pustulosis palmaris and plantaritis.1 Skeletal changes are com-
monest in the chest wall and skull involve-
ment is uncommon.2 We present an unusual
case of orbital SAPHO syndrome.

Case report
An 18 year old woman presented with
5 months’ retrobulbar pain, 2 weeks’
decreased vision, and a protruding appear-
ance of her left eye. Previous medical history
included thoracic spinal osteomyelitis aged 7.
Her grandfather had suffered from a multi-
local recurrent osteomyelitis.
Visual acuity (VA) was 6/6 right eye and
6/9 left eye. There was 3 mm left axial
proposis with restricted elevation. Pupil
reactions, colour vision, and funduscopic were
normal in both eyes. CT scan showed lytic
bone lesions and soft tissue swelling around the
left anterior clinoid process and sphenoi-
dal wings (fig 1A).

The episode was treated with oral NSAIDS.
Three months later repeat CT showed the
previously observed lytic areas had become
sclerotic (fig 1B). A bone scan showed uptake in
the left orbit and the area of the spine
previously affected by osteomyelitis.
Ten months after the left sided presenta-
tion she developed headache for 2 days,
diplopia, and decreased right vision. VA
was 6/36 right eye, with 1 mm proptosis,
2 mm ptosis, and restricted right eye abduc-
tion. Pupil reactions, colour vision and
funduscopic were normal. CT and MRI
(figs 1C and 2) revealed multiple lytic areas around the right anterior clinoid process and
sphenoid wings. Prominence of the
right superior orbital vein and optic nerve
sheath indicated a degree of orbital apex
syndrome. Treatment was with oral NSAIDS

References
1 Brown HW. Congenital structural muscle
anomalies. In: Allen JH, ed. Strabismus
ophthalmic symposium. St Louis: CV Mosby,
2 Rosenbaum AL, Astle WF. Superior oblique and
inferior rectus muscle injury following frontal and
Complications of blepharoplasty. Ophthalmic
4 Hermann JS. Acquired Brown’s syndrome of
inflammatory origin. Arch Ophthalmol
1979;96:1228–32.
5 Whitefield L, Isenberg DA, Brazier DJ, et al.
Acquired Brown’s syndrome in systemic
lupus erythematous. Br J Rheum
6 Lacy PD, Bhogin M, Colarvey MP, et al.
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Figure 1 Preoperative versions of subject in nine diagnostic positions of gaze, demonstrating
underelevation on adduction of the right eye.

Figure 2 Orbital contrast MRI showing non-
enhancing 3–4 cm mass of the right ethmoidal
sinus having an intraorbital extraconal extension.

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Differential diagnosis includes Propionibacterium acnes have been suggested. Broad spectrum antibiotic treatment has not been shown to be effective. 
Radiologically, combinations of osteolysis, bone infarction-like lesions, and hyperostosis are seen. 
Fibrotic hyperostosis, a process which occurs produced a good outcome.

The pathogenesis is poorly understood. 
Eight months later biopsy of a left temporal bone lesion showed a mixture of fibrous tissue, foci of inflammation, and new bone formation. She has not developed any dermatological lesions.

**Comment**

Diagnosis of SAPHO syndrome depends on one of the following being present: (1) multifocal osteitis without skin manifestations; (2) sterile joint inflammation associated with pustules of palms or soles, psoriasis, acne, or hidradenitis; (3) sterile joint inflammation associated with focal osteitis without skin manifestations. 
The pathogenesis is poorly understood. Fibrotic hyperostosis, a process which occurs alone in fibrous dysplasia, follows an initial acute osteolysis. Histologically a mixture of bone necrosis, new bone formation, fibrosis, and inflammation are seen. 

Pain is the commonest symptom, usually controlled with NSAIDS alone. Second line agents are pamidronate (anti-osteoclastic and anti-inflammatory) and corticosteroids. Third line agents include sulfasalazine, colchicine, and methotrexate. 

This case had the intriguing feature of bilateral optic canal involvement. Management with NSAIDS and pamidronate produced a good outcome.

**References**


**BOOK REVIEW**

Management of Cataracts and Glaucoma


Overall, this is an excellent book. It is a concise, informative discussion of the major issues surrounding the management of cataracts and glaucoma. It covers current opinion on this topic, including controversies and new treatment modalities; it is both stimulating and thought provoking. Each chapter is written by one or two highly regarded glaucoma experts and thus it is has a very broad perspective on this subject. The contributors present their strategic thinking, surgical techniques, and share their “pearls of wisdom.”

This is an extremely worthwhile text for the glaucoma subspecialist and general ophthalmologist. In some respects it is perhaps too advanced for the junior trainee, although it has detailed surgical instructions and photographs and would be valuable for those learning glaucoma surgery.

In the first chapter ophthalmic anaesthetists discuss the philosophy and challenges of ophthalmic anaesthesia in routine, paediatric, and sick individuals. This is a very detailed and informative presentation of the different anaesthetic modalities for cataract and glaucoma surgery. Next, cataract surgery in patients with pre-existing glaucoma is discussed. It mentions the specific hazards encountered in cataract surgery in patients with pre-existing glaucoma, with special techniques to counter them. It also covers cataract surgery in patients with previous glaucoma surgery including drainage devices. Both of these chapters were very educational and well written.

Keith Barton considers “trabeculectomy alone.” In particular, he addresses situations in which trabeculectomy alone may be appropriate, and also the potential negative aspects. There is a detailed description of his...
surgical technique, including discussion of releasable sutures and antimetabolites. A brief discussion of intraoperative hazards and postoperative complications is included. This chapter is particularly educational for those learning trabeculectomy surgery.

Aqueous drainage implants are covered by Richard Hill and George Baerveldt. They are presented in detail, including surgical techniques, postoperative care, and the treatment of complications. This chapter is excellent, especially for those who insert drainage devices infrequently.

Next there is a detailed discussion of non-penetrating glaucoma surgery (NPGS). The techniques include deep sclerectomy, implants (collagen, hyaluronic acid, and acrylic), viscocanalostomy, and Nd-YAG goniopuncture. Again there is detailed discussion of the surgical techniques, including excellent illustrations. Complications and their management are covered well. The authors presented this technique in such glowing light that I wondered why we aren’t all performing non-penetrating glaucoma surgery? One criticism is that these procedures are presented as being “safer but not less efficient (when performed by a NPGS trained surgeon) than trabeculectomies.” There are numerous studies which have demonstrated that when comparing NPGS and trabeculectomies, lower pressures were achieved with traditional surgery; however, they do support the observation that complication rates are lower with NPGS. Also trabeculectomies have a higher probability of success over time, thus trabeculectomy could be more suitable for patients with higher intraocular pressure levels or longer life expectancies. Also I think there was inadequate emphasis on the greater technical difficulties encountered with NPGS.

One site versus two site combined cataract and glaucoma surgery is discussed at length. Joseph Caprioli and Michelle Banks present a very useful algorithm for the surgical approach to patients with cataract and glaucoma, and when to proceed to cataract surgery alone, combined surgery, or trabeculectomy alone.

There are two interesting and useful chapters looking at combined cataract-aqueous drainage device surgery and combined cataract-non-penetrating glaucoma surgery. Their benefit here is that there is a discussion of issues that are not often addressed in other texts or studies.

Overall, this book presents a concise, well written, up to date, and comprehensive review of the management of cataracts and glaucoma. This is a book I definitely recommend.

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An Arg311Gln \textit{NR2E3} mutation in a family with classic Goldmann-Favre syndrome

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