Orbital varices and orbital wall defects

Orbital varices are a vascular hamartoma typified by a plexus of low pressure, low flow, thin walled and distensible vessels that intermingle with the normal orbital vessels. If freely communicating with the orbital circulation, engorgement of varices can occur by increasing venous pressure through the Valsalva manoeuvre, bending posture, coughing or straining and these, in turn, lead to the clinical characteristics of variable proptosis, intermittent pain, and orbital haemorrhage.

Observation is usually warranted for small lesions, but surgical intervention may be necessary in advanced cases: indications for surgical intervention include non-resolving episodes of thrombosis, severe disfiguring proptosis or displacement of the globe, and optic nerve compression. Surgery can be extremely difficult, as varices are very friable and intimately intermixed with normal orbital structures; there is also a significant risk of visual loss as a result of haemorrhage or optic nerve damage, the latter being generally caused by vascular compromise.

Orbital varices can extend up to the dural space and involve the frontal lobe parenchyma

Case series

The orbital database, at Moorfields Eye Hospital, was used to identify patients with a clinical diagnosis of low pressure orbital varices and their orbital imaging (computed tomography and/or magnetic resonance image) was reviewed. Images were examined for evidence of orbital expansion, osseous defects of the orbit, nose or sinuses, and anomalies of the frontal lobes. Patients who had either orbital or intracranial surgery before the date of imaging were excluded from the investigation.

The clinical diagnosis of orbital varices was identified in 310 patients, and imaging was available for 223 patients (72%). Six patients with previous orbital or intracranial surgery were excluded and nine cases (4%) had associated anomalies of the neighbouring orbital walls (table 1).

Four cases (patients 1–4) were associated with “pitting” of the orbital wall secondary to orbital varices (fig 1A). Another three cases (patients 6–8) were associated with enlarged superior orbital fissure and two cases (patients 5 and 9) with multiple orbital roof “defects” (fig 1B). Orbital varices were present up to the dural space in two cases (patients 4 and 5).
One patient (case 2) had thinning of the superonasal quadrant of the orbital wall, nasal orbital wall pitting, and a low ipsilateral cribriform plate, when first seen at age 21 in 1981 (fig 1E, F). On repeat imaging 20 years later (2001), this patient was noted to have developed proptosis, a defect in the superonasal wall of the orbit, and a new mid-line nasal encephalocoele (fig 1J, L).

Comment
Fine cut (3 mm) orbital CT scans easily delineate varices and diagnostic phlebitis, which occur from thrombus formation, and provide an excellent natural contrast between brain, bone, and varix. The typical findings for varices include an ill defined multiloculated mass, with some patchy contrast enhancement, in communication with the neighbouring orbital circulation; diffuse expansion of the orbital walls is well recognised in some cases, especially in childhood lesions.

Several factors may have biased the study population: many are symptomatic patients, having been referred from other ophthalmic units in consideration for surgical intervention. The apparent incidence of orbital wall defects (4%) in our series may, therefore, be a slight overestimate. In a minority of patients, orbital varices may be associated with orbital wall defects, and such defects may, eventually, lead to an encephalocoele formation. Clinicians should be aware of these, apparently unreported, associations before embarking on surgical intervention for orbital varices.

Table 1 Characteristics of nine patients with orbital wall defects in association with orbital varices

<table>
<thead>
<tr>
<th>No</th>
<th>Side</th>
<th>Age (years) at referral</th>
<th>Sex</th>
<th>Main location of orbital varix</th>
<th>Expansion of orbit</th>
<th>Absent walls</th>
<th>Ethmoid</th>
<th>Cribriform</th>
<th>Frontal</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Left</td>
<td>6</td>
<td>M</td>
<td>Medical and extensive superomedial</td>
<td>Present</td>
<td>Small roof defect</td>
<td>Pitted bone and smaller ethmoid</td>
<td>L-low R-normal</td>
<td>Dips low at cribriform</td>
</tr>
<tr>
<td>2</td>
<td>Right</td>
<td>21</td>
<td>F</td>
<td>Extraconal-medial</td>
<td>Present</td>
<td>Tiny thin area SNQ</td>
<td>Pitted bone and smaller ethmoid</td>
<td>R-low L-mild</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Left</td>
<td>62</td>
<td>M</td>
<td>Superomedial</td>
<td>Present</td>
<td>Pitted roof and small defects of veins</td>
<td>Compressed</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>4</td>
<td>Right</td>
<td>58</td>
<td>M</td>
<td>Panorbit intraconal and extrasomal</td>
<td>Present</td>
<td>Post superior wall and pitted bone</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>5</td>
<td>Right</td>
<td>47</td>
<td>M</td>
<td>Panorbit intraconal and extrasomal</td>
<td>Absent</td>
<td>Posterior orbital roof</td>
<td>Normal</td>
<td>Normal</td>
<td>Varices up to dural space</td>
</tr>
<tr>
<td>6</td>
<td>Right</td>
<td>14</td>
<td>F</td>
<td>Posterior intraconal, superior extrasomal</td>
<td>Present</td>
<td>Enlarged SOF</td>
<td>Normal</td>
<td>Normal</td>
<td>Varices into frontal lobe</td>
</tr>
<tr>
<td>7</td>
<td>Left</td>
<td>40</td>
<td>M</td>
<td>Posterior intraconal</td>
<td>Present</td>
<td>Enlarged SOF and small lateral wall</td>
<td>Slightly smaller</td>
<td>Unknown</td>
<td>Normal</td>
</tr>
<tr>
<td>8</td>
<td>Left</td>
<td>37</td>
<td>F</td>
<td>Posterior intraconal and extrasomal</td>
<td>Present</td>
<td>Very enlarged SOF, patchy SNQ defects posteriorly</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>9</td>
<td>Left</td>
<td>66</td>
<td>M</td>
<td>Extrasomal–superior (large)</td>
<td>Present</td>
<td>Posterior orbital roof</td>
<td>Slightly smaller</td>
<td>Normal</td>
<td>Normal</td>
</tr>
</tbody>
</table>

SNQ = superonasal quadrant; SOF = superior orbital fissure.

Exenteration of invasive conjunctival squamous cell carcinoma

Ocular surface squamous neoplasia (OSSN) includes conjunctival intraepithelial neoplasia with dysplasia, carcinoma in situ and conjunctival squamous cell carcinoma (SCC). Beside ultraviolet B irradiation identified as an risk factor, OSSN is associated with human papillomavirus type 16 and 18 (HPV-16, HPV-18). The exact role and possible prognostic value of p53 overexpression is unclear and little is known about its expression during the development of conjunctival SCC.

Comment
The high recurrence rate of OSSN of 9–64% after resection seems to depend on the histopathological grade and status of surgical margins. HPV-16 and HPV-18 are considered risk factors. Previous biopsies had revealed conjunctival dysplasia. On examination, the tumour of the ocular and tarsal conjunctiva of the lower lid covered the entire corneal surface (fig 1A).

Patient 2
A 90 year old patient presented with a 2 year history of an extensive conjunctival papillomatous tumour of the left eye covering three quarters of the cornea with visual acuity of light perception. A full thickness biopsy was performed.

Both patients underwent orbital exenteration including removal of the eyelids. Histopathologically the lesion proved to be a well differentiated papillomatous tumour. The clinical, ophthalmological and histopathological diagnosis of OSSN was confirmed.

The exophytic tumours of patient 2 was predominantly intraepithelial with foci of subepithelial invasion. Focal tumour anaplasia was observed in the otherwise moderately differentiated tumour with squamous cell differentiation.

Immunostaining of both specimens revealed strong p53 (monoclonal mouse-anti-human p53-protein DO-7, Dako) over-expression (>26% of epithelial cells) and low expression of p21 (<6% of epithelial cells) of the invasive region of the tumour indicating an inactivating p53 mutation (fig 1C). While in patient 1 expression for p53 was found in all epithelial layers, in patient 2 it was expressed suprabasally. In contrast, both p53 and p21 showed moderate reactivity in the dysplastic region up to the middle layer of the tumour (fig 1D). In the apical layer epithelial cells were occasionally p21 positive.

Immunostaining for HPV (HPV screening antibody, Virofem Diagnostica, Germany) was positive in patient 1.

References
The tumour suppressor gene p53 has been found to be inactivated in over 50% of human cancers. In OSSN, overexpression of p53 has been previously reported in some SCC of the conjunctiva and lacrimal sac by immunohistochemistry, in situ hybridisation, and polymerase chain reaction. We decided to examine the whole family to determine if familial articular chondrocalcinosis was present.

Our results of two exenterated advanced stages of SCC emphasise the necessity to remove dysplastic OSSN completely to prevent progression to invasive carcinomas. Identification of inactivating p53 mutations may indicate an increased risk for invasiveness. Therefore immunohistochemical analysis of biopsy specimen may help in the management of these tumours.

References


Familial pseudotumoral sclerochoroidal calcification associated with chondrocalcinosis

Sclerochoroidal calcification is the deposition of calcium at the level of the sclera and choroid. Two entities have been described: metastatic calcifications resulting from deposition of calcium in normal tissues caused by phosphocalcic metabolism abnormality such as primary and secondary hyperparathyroidism, pseudohyperparathyroidism, hypervitaminose D, vitamin D intoxication, hypophosphataemia, sarcoidosis, Barter syndrome, and Gietelman syndrome; and dystrophic calcifications caused by secondary deposition of calcium in abnormal tissues despite normal serum levels of calcium and phosphate.

Sclerochoroidal calcifications can also be idiopathic. We describe the first case of hereditary form of sclerochoroidal calcifications associated with familial articular chondrocalcinosis.

Case report

A 69 year old man was admitted to the department of ophthalmology in November 1999 with gradual deterioration of vision in both eyes. He had a medical history of idiopathic familial chondrocalcinosis. His father, brother, and son were treated for the same disease.

On examination, best corrected visual acuity was 20/20 in both eyes (fig 1). Slit lamp examination of the ocular surface confirmed the calcific nature of the lesions.

References


www.bjophthalmol.com
The brother’s funduscopy revealed multiple bilateral, extrafoveal pseudotumoral white choroidal masses (fig 2, top). The son’s funduscopy revealed plaque-like and only slightly elevated lesions seen in the midperiphery (fig 2, bottom). Ultrasonograms confirmed the calcific nature of these lesions.

Comment

In 1997, Shields et al described a case of sclerochoroidal calcifications in a normocalcaemic patient who had chondrocalcinosis. We first describe a familial case of sclerochoroidal calcifications associated with calcium pyrophosphate dihydrate (CPPD). In this family, autosomal dominant inheritance is highly likely because there are affected individuals in each generation, there is male to male transmission, and every affected member has an affected parent.

Inheritance in sclerochoroidal calcifications has never been described; however, hereditary forms of chondrocalcinosis have already been described.

In our report, a patient had a 24 year follow up showing a progressive involvement of the macular area, suggesting a growth of the calcifications. Two types of calcifications have been described previously, the plaque-like and the pseudotumoral type.

To our knowledge, it has never been determined if the plaque-like lesions evolve into tumour-like lesions. In 1992, Schachat and associates reported 10 cases with follow up ranging from 7 months to 10 years, for whom no change in the lesion was seen. This is the first observation with 24 years of follow up suggesting a possible evolution of plaque-like lesions to pseudotumoral lesions.

We suggest that every patient affected by familial chondrocalcinosis should have an ophthalmic examination to detect sclerochoroidal calcification. These lesions seem to be evolving in time with possible involvement of the macula. Choroidal neovascularisation is also a vision threatening complication of sclerochoroidal calcifications. Our case suggests the need to perform ophthalmological examination in patients and family members of patients affected by chondrocalcinosis.

S Bouboul, T Bourcier, J-P Heligon, P Houiller, M Ullern, M Abitbol, V Borderie, L Laroche CHNO des XV-XX, 28, Rue de Charenton 75571 Paris Cedex 12 Paris, France

Correspondence to: Dr Sandrine Boutboul, CHNO des XV-XX, 28, Rue de Charenton 75571 Paris Cedex 12 Paris, France; skewronek@free.fr

doi: 10.1136/bjo.2003.039925

Accepted for publication 15 December 2003

References


Whole body PET/CT imaging for detection of metastatic choroidal melanoma

Metastatic choroidal melanoma typically presents in the liver. Therefore, liver enzyme assays are the most common haematological evaluation performed after treatment.

In 1985, The Collaborative Ocular Melanoma Study required periodic medical evaluations including a physical examination, liver function studies, a complete blood count, and a chest x-ray. If liver enzymes exceeded 1.5 times normal, computed tomography (CT) of the abdomen was required. If low attenuation hepatic nodules suggested metastatic disease, fine needle aspiration biopsy of the liver tumours provided cytopathological confirmation.

Positron emission tomography (PET) is a molecular imaging technique that uses radiolabelled molecules to image metabolic activity in vivo. When whole body PET was combined with computed radiographic tomography (CT), PET/CT put anatomy and function on the same page making practical a new era of physiological imaging.

This study examines the ability of positron emission tomography combined with computed tomography (PET/CT) to allow for detection of previously occult metastatic melanoma.

Case report

A 77 year old woman presented with a 15.4 x 15 mm width and 13.2 mm high collar button shaped choroidal melanoma with a large secondary retinal detachment in her right eye. Her preoperative medical evaluation...
Two years later a follow up medical evaluation revealed elevated liver function studies (table 1) and a chest x ray showed a pleural effusion. CT of the abdomen with contrast revealed a large liver metastasis. PET/CT imaging was able to reveal multiple bony metastases that were not seen on the CT portion of the examination. Both CT and PET showed a large liver metastasis. Since it is a physiological assay, PET also demonstrated the metabolic activity of the metastatic tumours (fig 1).

Comment

In this case, whole body PET/CT was found to be capable of uncovering metastases not seen with abdominal CT alone. This led us away from considering regional perfusion of the liver, hepatic resection, and towards systemic treatment. Therefore, when PET/CT identifies extrahepatic involvement, it can have a significant impact on the management of patients with metastatic choroidal melanoma.

PET/CT could also be used for initial staging. Early detection of occult metastases

<table>
<thead>
<tr>
<th>Table 1 Patient characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical</td>
</tr>
<tr>
<td>General Subcutaneous tissue</td>
</tr>
<tr>
<td>Nodes</td>
</tr>
<tr>
<td>Lungs</td>
</tr>
<tr>
<td>Liver</td>
</tr>
<tr>
<td>Kidney</td>
</tr>
<tr>
<td>Bone</td>
</tr>
</tbody>
</table>

Figure 1 On the left, the CT demonstrates the anatomy; on the right the PET shows areas of hypermetabolism (glucose uptake); in the middle the two images are fused. PET/CT revealed enlarged para-aortic lymph nodes and a subcutaneous nodule in the anterior abdominal wall. The PET imaging portion of the PET/CT was able to reveal multiple bony metastases that were not seen on the CT portion of the examination. Both CT and PET showed a large liver metastasis.
offers the potential to avoid ineffective and expensive enucleations, radioactive plaques, proton irradiation, eye wall resections, or laser treatment. Local therapies would be abandoned in favour of systemic treatments.

Another issue related to PET/CT is cost. Up to five times more than CT of the abdomen, PET/CT is only covered (Medicare) for melanoma staging/restaging when the stage of the cancer remains in doubt after completion of conventional imaging (or if the clinical management would differ depending on the PET findings). Since PET/CT revealed hepatic foci in this case, it changed our clinical approach. There is little doubt about the improved ability of PET/CT to detect lesions; the real issue is cost and if the results will change outcomes.

This study goes one step further than CT, MRI, or PET alone. By combining whole body PET and CT, this examination joins anatomy and function in one examination (fig 1). The relative efficacy of PET/CT to locate metastases should be evaluated within the framework of a prospective study.

P T Finger, M Kurli
The New York Eye Cancer Center, New York, USA

P T Finger, M Kurli, P Wesley, L Tena
The New York Eye and Ear Infirmary, New York, USA

P T Finger, L Tena
St Vincent’s Comprehensive Cancer Center, New York, USA

P T Finger, K R Kerr
Beth Israel Medical Center

P T Finger, A Pavlick
New York University School of Medicine, New York, USA

Correspondence to: Paul T Finger, MD, The New York Eye Cancer Center, 115 East 61st Street, New York, NY 10021, USA; pfinger@eyecancer.com

doi: 10.1136/bjo.2003.039289

Accepted for publication 1 January 2004

This work was supported by The EyeCare Foundation and Research to Prevent Blindness, New York, USA.

References


Trans-Tenon’s retrobulbar triamcinolone infusion for small choroidal neovascularisation

Intravitreal and sub-Tenon’s corticosteroids are being evaluated for the treatment of choroidal neovascularisation (CNV). We reported on the efficacy of triamcinolone acetonide administered as a trans-Tenon’s retrobulbar infusion (triamcinolone infusion) in reducing inflammation in uveitic eyes. Here we evaluated the same treatment in eyes with small subfoveal CNV.

Case reports

Triamcinolone infusion was performed in 22 eyes of 22 patients with subfoveal CNV of greatest diameter less than or equal to 1 disc diameter (DD). The diagnoses were age related macular degeneration (AMD) in 14 eyes, idiopathic CNV in four eyes, polypoidal choroidal vasculopathy (PCV) in three eyes, and punctate inner choroidopathy (PIC) in one eye. One AMD eye had undergone ablative argon laser photoacoagulation for CNV previously, but no other eyes had received previous treatment. The median post-triamcinolone infusion follow up was 7.5 months (range 4–27 months). Pretreatment fluorescein angiography (FA) revealed predominantly classic CNV in 12 eyes and predominantly occult CNV in 10 eyes. Records were reviewed retrospectively and did not require institutional review board approval. Informed consent was obtained before each procedure.

The patient’s eye was prepared with povidone-iodine and sterile drapes applied. After topical anaesthesia, conjunctiva and Tenon’s capsule were incised in the inferotemporal quadrant. A 23 gauge curved blunt cannula approximately 2.1 cm in length (#HS-2764, Handaya Co, Ltd, Tokyo, Japan) was inserted to the hub into sub-Tenon’s space and 20 mg (0.5 ml) triamcinolone acetonide (Bristol Pharmaceutical, KK, Tokyo, Japan) was infused. The wound was left unsutured and 0.5% levofloxacin was instilled topically three times a day for 1 week.

Onset of CNV fibrosis was observed in 14 eyes (64%) by 3 months post-triamcinolone infusion (fig 1). Rates of fibrosis were 50% (7/14 eyes) for AMD, 100% (4/4 eyes) for idiopathic CNV, 67% (2/3 eyes) for PCV, and 100% (1/1 eye) for PIC. Fibrosis did not correlate with CNV size or lesion composition. FA performed at 3 months showed decreased leakage in 12 eyes (59%), no change in five eyes (23%), and increased leakage in five eyes (23%). Best corrected visual acuity (VA) at 3 months for all eyes improved by 0.2 logarithm of the minimum angle of resolution (logMAR) in four eyes (18%), remained unchanged in 13 eyes (59%), and worsened by 0.2 logMAR in five eyes (23%). The median decimal VA for all eyes was 0.30 before treatment (range 0.08–1.0) and 0.24 at 3 months after treatment (range 0.05–1.2). Of the 14 eyes with AMD, the VA at 3 months improved by ≥0.2 logMAR in one eye (7%), remained...
unchanged in 10 eyes (71%), and worsened by >0.2 logMAR in three eyes (21%). In these AMD eyes, the median decimal VA was 0.30 before treatment (range 0.08–1.0) and 0.20 at 3 months after treatment (range 0.05–0.7). Complications such as intraocular pressure elevation, infection, or cataract progression were not noted in any eyes.

Comment
This interventional case series shows that trans-Tenon's retrobulbar infusion of triamcinolone acetonide resulted in lesion fibrosis in the majority of eyes with small CNV, efficacy being best for idiopathic CNV or CNV related to PIC. The mechanism of action of triamcinolone acetonide in inhibiting CNV growth probably involves several pathways. The effect of corticosteroids in inhibiting inflammatory cells that participate in the neovascular response probably has a prominent role. 1 Triamcinolone acetonide has specifically been shown to inhibit basic fibroblast growth factor induced migration and tube formation of choroidal microvascular endothelial cells. 2 Furthermore, triamcinolone acetonide inhibits choroidal neovascularisation induced by laser trauma in a rat model. 3 Finally, triamcinolone acetonide may decrease vascular permeability, thereby decreasing influx of serum proteins that may contribute to an angiogenic microenvironment. 4 Longer follow up and greater numbers of cases in a randomised clinical trial are needed to confirm these results.

A A Okada, T Wakabayashi, E Kojima, Y Asano, T Hida
Kytor Eye Center, Kyorin University School of Medicine, 6–20–2 Shinkawa, Mitaka, Tokyo, Japan

Correspondence to: A A Okada, MD, Department of Ophthalmology, Kyorin University School of Medicine, 6–20–2, Shinkawa, Mitaka, Tokyo 181–8611 Japan; askoda@kpuj.affrc.go.jp

doi: 10.1136/bjo.2003.039719

Accepted for publication 6 January 2004

References

Retinoblastoma in a child conceived by in vitro fertilisation

As the number of infants born through in vitro fertilisation (IVF) grows, there is increased interest regarding the long term effects of IVF and other assisted reproduction techniques on such offspring. Recent reports have noted cancer in children born after IVF or fertility drug use (table 1). 1

In 2001, retinoblastoma was reported to occur in a child born through IVF in Israel. 1 Since then, an additional report documented four cases from the Netherlands. 2 Here we add a sixth case and the first from the United States. Of these children four had unilateral retinoblastoma and two bilateral disease (table 2).

During 2002, a 16 month old child was referred to The New York Eye Cancer Center with no known family history of eye disease. She had a blind right eye with neovascular glaucoma. Intraocular pressures were 35 mm Hg in the right eye, and 14 in the left. Examination of the anterior chamber of the right eye revealed cells on the corneal endothelium and iris neovascularisation. While ophthalmoscopic examination of the right eye was not possible because of opaque media, ultrasonography revealed a dense calcified mass in the posterior pole (fig 1). Computed radiographic tomography demonstrated tumour calcification with no evidence of extrascleral or optic nerve extension. Post-enceulmatation histopathology confirmed the diagnosis of retinoblastoma. 3 The parents did not approve genetic studies of the child.

Further history revealed that this child was born through IVF with a donor egg and the father’s sperm. In order to carry the child, the postmenopausal mother received oestrogen and progesterone before and during gestation.

Table 1 Anomalies and cancers reported in offspring of IVF

<table>
<thead>
<tr>
<th>Condition</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neuroectodermal tumours</td>
<td>White et al</td>
</tr>
<tr>
<td>Neuroblastoma</td>
<td>Kramer et al</td>
</tr>
<tr>
<td>(Note: associated with the use of fertility drugs only)</td>
<td>Michalek et al</td>
</tr>
<tr>
<td>Retinoblastoma</td>
<td>Moll et al</td>
</tr>
<tr>
<td>Hepatoblastoma</td>
<td>Melamed et al</td>
</tr>
<tr>
<td>Clear cell kidney</td>
<td>Toren et al</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>Kojima et al</td>
</tr>
<tr>
<td>Transposition of the great arteries</td>
<td>Berg et al</td>
</tr>
<tr>
<td>Neural tube defects</td>
<td>Lancaster</td>
</tr>
</tbody>
</table>

Several types of congenital anomalies and cancers have been reported in the literature, primarily in the form of case reports. The relation between IVF and these conditions is not definitively established.

Table 2 Retinoblastoma in children born through IVF

<table>
<thead>
<tr>
<th>Reference</th>
<th>Sex and age at diagnosis</th>
<th>Eye</th>
<th>Causality of subfertility</th>
<th>DNA 13q14 analysis</th>
<th>Assisted reproductive technique</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antebay et al</td>
<td>M, 30</td>
<td>Unilateral</td>
<td>Normal</td>
<td>Normal</td>
<td>IVF with donor sperm</td>
</tr>
<tr>
<td>Mall et al</td>
<td>M, 15</td>
<td>Unilateral</td>
<td>Normal</td>
<td>Normal</td>
<td>IVF</td>
</tr>
<tr>
<td>Mall et al</td>
<td>F, 34</td>
<td>Unilateral</td>
<td>Normal</td>
<td>Normal</td>
<td>IVF</td>
</tr>
<tr>
<td>Mall et al</td>
<td>M, 8.5</td>
<td>Unilateral</td>
<td>Normal</td>
<td>Normal</td>
<td>IVF</td>
</tr>
<tr>
<td>Mall et al</td>
<td>F, 32</td>
<td>Unilateral</td>
<td>Normal</td>
<td>Normal</td>
<td>IVF</td>
</tr>
<tr>
<td>This report</td>
<td>F, 16</td>
<td>Unilateral</td>
<td>Normal</td>
<td>Normal</td>
<td>IVF</td>
</tr>
</tbody>
</table>

References
1 White et al. 2 Kramer et al. 3 Michalek et al. 4 Moll et al. 5 Melamed et al. 6 Kojima et al. 7 Berg et al. 8 Lancaster.
Retinoblastoma is the most common intraocular cancer of childhood and affects approximately 300 children each year in the United States. Retinoblastoma is a manifestation of a de novo deletion or mutation of the q14 band of chromosome 13, occurring as a second hit during embryogenesis or the result of two hit deletions in retinal cells. In that it could be the result of chromosomal breakage and deletions in IVF born children, surveillance of retinoblastoma incidence in children born through IVF is warranted.  

With the advent of assisted reproductive technology (ART) in 1977, American couples have increasingly turned to such treatments to overcome fertility problems. Nationwide, 99,629 procedures were performed in 2000 by ART. In that year, fertility treatments in which the egg and sperm are handled in the laboratory resulted in 25,228 live births and 35,025 infants. This report expands information on geography and determinants of both ART success and multiple birth risks (beyond the q14 band of chromosome 13, occurring as a second hit during embryogenesis or the result of two hit deletions in retinal cells). In that it could be the result of chromosomal breakage and deletions in IVF born children, surveillance of retinoblastoma incidence in children born through IVF is warranted.  

References

Angle closure glaucoma after laser photoagulation for retinopathy of prematurity

Infantile angle closure glaucoma (ACG) is a rare consequence of retinopathy of prematurity (ROP) and usually occurs a few years after laser treatment for ROP. A Medline search for ACG following laser photoagulation extracted only one case. In the case, ACG occurred in 2 weeks after laser photoagulation and although occurrence of iris bombe in both eyes was described, the mechanism for the ACG was not fully clarified.  

We present a case of bilateral ACG that occurred within a several weeks after the laser photoagulation for ROP. We shall discuss the importance of ultrasound biomicroscopy (UBM) in the diagnosis.

Case report

A baby girl, born at 25 weeks gestation weighing 796 g, was diagnosed with stage 2 plus, zone 2 ROP bilaterally at 33 weeks. Dioide laser photoagulation, 986 applications right eye and 629 left eye, with 200-240 mW, 0.4 second duration, was performed by a paediatric ophtalmologist. On the following day, severe hyphaema was observed bilaterally but there was no evidence of choroidal detachment by B-mode ultrasound sonography. Topical atropine and corticosteroid were started and she was
of the lens was also attached to the corneal endothelium (fig 2). Choroidal detachment and a retrolental mass were not observed by B-mode ultrasound sonography (fig 2).

Peripheral iridectomy was performed bilaterally (fig 1). Postoperatively, her peripheral anterior chamber deepened bilaterally although the lens in the right eye was still adherent to the corneal endothelium. Indirect ophthalmoscopy revealed normal cup to disc ratio. The IOP fell to normal levels bilaterally.

**Comment**

Shallow anterior chambers in ROP patients are known to be caused by various factors—for example, choroidal detachment after excessive photoocoagulation, development of retrolental mass, or relative increment in lens thickness, but usually the cause of shallow anterior chamber cannot be determined. In our case, the development of hyphaema after photoocoagulation induced posterior synechiae, and the iris bombe followed. The displacement of the anterior chamber structures was induced by the forward movement of the iris-lens diaphragm in the right eye, and the ocular fragility in prematurity baby may explain this deformity.

Vitreous haemorrhage is known to occur in 7.9% of ROP cases after photoocoagulation. In our case, there is a possibility that the hyphaema was derived from vitreous haemorrhage. Another possibility is an accidental photoocoagulation of persistent pupillary membranes and/or iridocorneal vessels caused the hyphaema. We are not aware of such morphological changes after photoocoagulation for ROP.

AGC that occurs immediately after retinal photoocoagulation in ROP patients is rare, but is still an important complication. In ROP patients, the lens and its ligament are weak, and therefore not only AGC but also lens displacement occurred. It is important that we be aware of the possible development of AGC following retinal photoocoagulation for ROP.

**Sequential treatment of central retinal vein occlusion with intravitreal tissue plasminogen activator and intravitreal triamcinolone**

Treatment for central retinal vein occlusion (CRVO) remains disappointing despite recently proposed intraocular surgical techniques. We previously introduced the use of intravitreal tissue plasminogen activator (TPA) for acute central retinal vein occlusion in 1999. Numerous investigators have confirmed its safety and suggested that it may have a beneficial role in the treatment of acute central retinal vein occlusion.

Although some studies in rabbits suggest the rabbit retina is not permeable to TPA,
investigators found the porcine retina was, in fact, permeable to TPA. Our clinical experience with intravitreal TPA in humans with CRVO and large submacular haemorrhages strongly suggests that intravitreal TPA does cross the human retina. Greenberg et al were the first to report the possible beneficial effect of intravitreal steroids on patients with chronic CRVO. This report describes a sequential treatment strategy for patients with CRVO who present early in the course of their disease and can be performed in the office while avoiding the risks of vitrectomy. It utilises intravitreal TPA in the acute phase of the vein occlusion to attempt clot lysis, and then treats any remaining vascular leakage with intravitreal triamcinolone.

Case report

A 59 year old obese, hypertensive flight instructor presented with a sudden decrease in vision for 7 days in the right eye. Vision was 20/400 right eye and 20/20 left eye. The patient was diagnosed with an acute CRVO in the right eye (fig 1A). The left eye was normal. After being advised of the risks and benefits, the patient elected to undergo intravitreal injection of TPA (75 µg). Thirteen days later, the patient noted marked improvement in vision with 20/60 vision. Thirty four days after the injection, the vision remained 20/30, but the patient still complained of metamorphopsia and blurry vision despite resolution of other findings of CRVO (fig 1C). Fluorescein angiogram (FA) revealed persistent macular oedema (fig 2A). Optical coherence tomography (OCT) showed the foveal thickness to be 331 µm with mild intraretinal oedema. After being advised of the risks and the benefits, the patient then underwent injection of intravitreal triamcinolone (4 mg). Six weeks after the intravitreal triamcinolone, the FA returned to normal and OCT showed decreased foveal thickness from 331 µm to 291 µm. The patient reported a significant improvement in vision with decreased metamorphopsia. Vision was 20/25 with no late leakage on the fluorescein angiogram (fig 2B).

Comment

To our knowledge, this represents the first published case of CRVO treated sequentially with intravitreal TPA for the acute phase and intravitreal triamcinolone for the chronic phase. TPA is a drug that must be used early in the course of thrombus formation to be effective. We do not recommend its use for patients with chronic symptoms. Intravitreal steroids appear to decrease the blood-retinal barrier breakdown and macular oedema, but recurrent oedema may occur since the steroids do not appear to affect the thrombus itself.

J M L, J J K, M C Cheung
Ophthalmology, University of California at San Francisco, San Francisco, CA, USA
J M Lahey, J J K
Ophthalmology, Kaiser Permanente, Hayward, CA, USA
Correspondence to: J M Lahey, MD, Ophthalmology (Retina), Kaiser Permanente Medical Center, 27400 Hesperian Boulevard, Hayward, CA 94545-4299, USA; Mike.Lahey@kp.org
doi: 10.1136/bjo.2004.043406
Accepted for publication 3 February 2004

References

Severe post-laser suprachoroidal haemorrhaging in a diabetic patient receiving anticoagulants

Although the aetiology is not well understood, expulsive suprachoroidal haemorrhaging (ESH) is the most severe complications associated with intraocular surgery. Anticoagulants are considered a risk factor for spontaneous suprachoroidal haemorrhaging in cases with high myopia, age related macular degeneration, and diabetic retinopathy.2 However, ESH post photoocoagulation is extremely rare regardless of anticoagulant therapy. We have experienced a severe case of post-laser ESH correlated with anticoagulant therapy, which resulted in irreversible visual disturbance.

Case report

A 70 year old woman was diagnosed with pre-proliferative diabetic retinopathy based on fluorescein angiographic examinations. Two months before diagnosis she reported a sudden right eye cataract surgery. During the past 6 years, the patient received warfarin (4 mg/day) and aspirin (81 mg/day) because of atrial fibrillation after myocardial infarction. Laser photoocoagulation was performed in her right eye with a Nidek MC-7000, yellow-green laser. Operating conditions were 200–280 burns per session with a spot size 200 µm, exposure 0.2 seconds, power 100–120 mW using a Quadratropic contact lens (Volk, Tokyo, Japan). Treatment was separated into three partitions with a minimum 2 week interval between sessions. Three days after final photoocoagulation, the patient had a sudden visual loss to hand movements. In slit lamp examinations, the retina seemed to be attached to the posterior surface of the implanted intraocular lens. Severe choroidal detachment was found by fundus examination (fig 1). The B-mode ultrasonography showed massive haemorrhaging in the choroidal space (fig 2). In systemic examinations, multiple purple spots were observed in both her arms. Microhaematuria was also found. Blood examination revealed blood sugar 167 mg/dl; platelet number 179 000 ×10³/µl; PT% 19% (control 70–120); PTs 28.7 seconds; PT INR 4.72 (control 1); APTT 80.2 seconds (control 24.0–38.0); and bleeding time 5 minutes. Although surgery was planned to proceed as soon as the anticoagulant was washed out, her right eye lost all light perception before treatment.

Comment

We have described a case of ESH after laser photoocoagulation in a patient receiving anti-coagulant therapy. Laser photoocoagulation is known as an effective treatment for various ocular diseases and is a widely used, non-incision surgical procedure. However, a number of complications have been reported, with some citing an irreversible visual disturbance. On the other hand, anticoagulant therapy is prevalent after cardiac/brain infarctions, which necessitates a good coagulation system management. In the present case, the PT INR was extremely prolonged (a respected value of 2–3 is
appropriate for post-cardiac infarction). Presumably, choroidal microbleeding initiated by photoocoagulation persisted because of an overly suppressed coagulation system; blood pooled in the choroidal space, which assumed an ESH. To our knowledge there is only one other similar case reported by Khairallah et al. that showed post-laser choroidal haematoma in a diabetic patient treated with warfarin. Even though ESH incidence is low, extreme caution must be exercised when performing laser therapy in patients using anticoagulants, because of potentially serious outcomes. An age of 65 years or more, history of stroke, history of gastrointestinal bleeding, a serious morbidity condition (recent myocardial infarction, renal insufficiency, or severe anaemia), and atrial fibrillation are five high risk factors for major bleeding in outpatients treated with warfarin. If possible, preoperative coagulation system examinations are recommended for high risk patients receiving anticoagulant treatments.

A Mikawa, S Honda, I Sugita, N Okamoto, H Toda
Department of Ophthalmology, Kitano Hospital, Tazukekafukai Medical Research Institute, Osaka, Japan

Correspondence to: A Mikawa, Department of Ophthalmology, Kitano Hospital, Tazukekafukai Medical Research Institute, 2-4-20 Ougimachi, Kitaku, Osaka 530-8480, Japan; a-matsuo@kitano-hp.or.jp

doi: 10.1136/bjo.2004.043489
Accepted for publication 14 February 2004

References
1 Chak M, Williamson TH. Spontaneous suprachoroidal haemorrhage associated with high myopia and aspirin. Eye 2003;17:525-7
4 Yang SS, Arthur D, McDonald R. Massive spontaneous choroidal haemorrhage. Retina 2003;23:139-44

Figure 1 A fundus photograph of the patient after laser photoocoagulation. A severe choroidal detachment associated with secondary retinal detachment was found.

Figure 2 The findings of B-mode ultrasound examination. A massive haemorrhage in the choroids is present.

MAILBOX

Authors’ reply

We appreciate the interest and many comments we have received regarding our recent article.1 In reply to the comments by Dr Vedantham, we acknowledge the paucity of experimental data to prove that accurate placement of corticosteroids into the sub-Tenon’s space provides good drug penetration into the eye. However, the studies to the contrary cited by Vedantham have all used needles to make such “accurate placement,” including the study by Jennings et al.,2 which utilised the technique described by Tessler.3 Use of needles represents not only a potential hazard to the eye in terms of accidental globe penetration, but also makes it much more difficult to place any sub-Tenon’s injection under the posterior Tenon’s capsule near the macula and/or around the optic nerve. It has been shown that many in our experience and for the sub-Tenon’s space merely end up somewhere in the orbit outside of Tenon’s capsule.4 We believe that our method using a 23 gauge blunt, curved, long cannula (the one we used was No HS-2764 by Handaya Co, Ltd, Tokyo, Japan) assures accurate placement into the target space, thereby increasing therapeutic efficacy and obviating the need for globe invasive procedures such as intraocular injection of corticosteroids, corticosteroid intravitreal implants, and/or therapeutic vitrectomy.

However, we are in agreement with Vedantham, in that ultimately corticosteroids placed outside of the eye may be more efficacious for the efficacy that may be obtained by corticosteroid placed inside the eye. Yet we have found such a high efficacy rate for the trans-Tenon’s retrobulbar infusion of triamcinolone acetonide in uveitis that we can conceive of no reason why this treatment should not be tried before such invasive injections that carry risks of severe complications are considered. For example, as also pointed out by Vedantham, the risks of intravitreous corticosteroid injections even include development of a rare form of mycobacterial endophthalmitis.5 Therefore, the risk to the eye of intravitreal procedures, especially when involving corticosteroid administration, cannot be taken lightly. Furthermore, we believe that the reason why sub-Tenon’s injections of corticosteroids have not become popular among retina specialists who for example treat diabetic macular oedema, is more likely related to the lower efficacy rate when using needles as opposed to the technique using an infusion cannula that we advocate. Lastly, obtaining the infusion cannula seems like a small inconvenience (and an even smaller cost) to the physician compared to the risk of doing intraocular injections of corticosteroids as a treatment of first choice as advocated by Vedantham. We strongly encourage all uveitis and retina specialists who have up until now been disappointed with the efficacy of their sub-Tenon’s corticosteroid injections, to make the effort to obtain an appropriate cannula and revise their technique before jumping to intravitreal procedures.

In reply to the first comment by Dr Mehta,6 we acknowledge the current WHO guidelines, revised for 2003, that include recommendations for extrapolmonary tuberculosis.7 However, we would also like to amend Mehta’s comment, in that the WHO admits in those guidelines that there are many
regimens with reported efficacy including a 6 month regimen of rifampicin (with streptomycin also given in the initial phase only) for meningeval tuberculosis. Furthermore, the WHO recommendations are for active extrapulmonary tuberculosis that has been diagnosed by specimen examination or strong clinical evidence, and give no recommendations for latent infection. As we have previously reported in a series on intracocular tuberculosis, systemic examination failed to identify a focus of active tuberculosis in the majority of our patients, and we have come to suspect that the uveitis we observed may be an immune response to latent tuberculosis antigen sequestered elsewhere. Therefore, the patients we described were given a diagnosis of "presumed intracocular tuberculosis," that is with uveitis presumed to be related to the Mycobacterium tuberculosis organism. Furthermore, we would like to clarify that in the cases of presumed ocular tuberculosis that received trans-Tenons retrobulbar triamcinolone infusion, this treatment was judged to be effective in two of three eyes. Regardless, since the focus of active or latent tuberculosis was never identified in our patients, a two drug regimen of isoniazid and rifampicin was used as a therapeutic trial for antituberculosis therapy. A similar therapeutic trial for ocular tuberculosis, albeit with isoniazid alone, has been previously advocated in Japan by Ishihara and Ohno.

With regard to the second comment, among the 16 patients who were receiving some form of systemic immunosuppressive therapy, we did not notice any difference in outcome when compared to patients who were not on immunosuppressive therapy. In other words, the efficacy of trans-Tenon's retrobulbar triamcinolone infusion was the same. However, we suspect that the recurrence rate after triamcinolone infusion may be different, and we are currently investigating this possibility.

A A Okada, T Wakabayashi
Kyorin Eye Center, Kyorin University School of Medicine, Tokyo, Japan
Correspondence to: Annabelle A Okada, Kyorin Eye Center, Kyorin University School of Medicine, Tokyo, Japan; aokada@po.iijnet.or.jp
doi: 10.1136/bjo.2003.038851
Accepted for publication 20 November 2003

References