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References

- 1 Brodsky MC. Anomalies of the optic disc. In: Miller NR, Newman NJ, eds. *Walsh and Hoyt's clinical neuro-ophthalmology*. Volume 1. 5th ed. Baltimore: Williams and Wilkins, 1998:799-800.
- 2 Brodsky MC. Congenital optic disc anomalies. In: Taylor D, Hoyt G, eds. *Pediatric ophthalmology and strabismus*. 3rd ed. Baltimore: Elsevier-Saunders, 2005:637-8.
- 3 Margo CE, Hamed LM, Fang E, et al. Optic nerve aplasia. *Arch Ophthalmol* 1992;110:1610-3.
- 4 Storm RL, PeBenito R. Bilateral optic nerve aplasia associated with hydranencephaly. *Ann Ophthalmol* 1984;16:988-92.
- 5 Brodsky MC, Atreides SP, Fowlkes JL, et al. Optic nerve aplasia in an infant with congenital hypopituitarism and posterior pituitary ectopia. *Arch Ophthalmol* 2004;122:125-6.
- 6 Scott IU, Warman R, Altman N. Bilateral aplasia of the optic nerves, chiasm and tracts in an otherwise healthy infant. *Am J Ophthalmol* 1997;124:409-10.
- 7 Weiter JJ, McLean IW, Zimmerman LE. Aplasia of the optic nerve and disk. *Am J Ophthalmol* 1977;83:569-76.

Uveitis and a subretinal mass in a patient with chronic granulomatous disease

Chronic granulomatous disease (CGD) is a rare disorder of phagocytic inability to produce the respiratory burst needed to kill ingested micro-organisms.¹ CGD typically presents early in life with recurrent life threatening bacterial and fungal infections and tissue granuloma formation.² Prophylaxis with systemic antibiotics, antifungals, and interferon γ have been shown to significantly reduce infections.^{1,2} Ocular involvement occurs in about 25% of CGD patients. We report the clinicopathological findings of a subretinal CGD lesion.

Case report

A 4 year old boy developed recurrent, cultured positive, cutaneous bacterial infections (*Serratia* spp). Four years later, ocular examination revealed 20/200 in the right eye and 20/50 in the left eye, bilateral moderate vitritis, retinal oedema and pigmentary clumps, multiple chorioretinal scars, and a large chorioretinal scar in the left eye. Despite transient improvement on antibiotics and systemic and periocular corticosteroids, his vision became worse with persistent vitritis and retinal exudation in the left eye. Six months later the patient was found to have an abnormal nitroblue tetrazolium test diagnostic of CGD.

Another 6 months after the diagnosis of CGD he was referred to NIH where p47^{phox} deficiency was detected.¹ Evaluation revealed 20/100 in the right eye, 20/200 in the left, mild conjunctival injection, chemosis, 1+ anterior chamber flare in the both eyes, and trace cells in the left. Posterior segment showed bilateral 2+ vitreous cells and trace haze, disc hyperaemia and oedema, perivascular sheathing, peripheral chorioretinal scars, and bone spicules in both eyes (fig 1A). Additionally, the left eye showed diffuse retinal oedema with marked macular

Figure 1 Fundus photographs showing (A) vitreous haze, mild disc oedema and hyperaemia, diffuse retinal oedema and perivascular sheathing, pigment atrophy, and marked macular lipid exudation; and (B) a subretinal mass (asterisk) in the inferotemporal region, perivascular bone spicule, and intraretinal pigment migration in the left eye.

lipid exudation and an inferotemporal subretinal mass where a large chorioretinal scar had been noted previously (fig 1B). This mass was worrying for intraocular granuloma, abscess, or neoplasm. Fluorescein angiography showed generalised disc and retinal vascular leakage, and staining of the subretinal mass, which appeared solid and homogeneous with low to moderate reflectivity on ultrasonography.

The biopsy of the intraocular mass revealed glial and vascular inflammatory granulation tissues admixed with abundant spindle cells stained positive for actin and myosin (fig 2). No granuloma or malignancy was identified. Special stains and cultures of the vitreous and biopsy were negative for bacteria and fungi. Vitreal interleukin-6 (IL-6) (141 pg/ml) and IL-8 (26 pg/ml) were elevated.

Postoperatively the patient developed a rhegmatogenous retinal detachment within a month and became blind in the left eye. The uveitis was controlled with prednisone and cyclosporin. Vision in the right eye maintained 20/80 without visual field or electroretinogram worsening during 3 years of follow up.

Comment

CGD with an incidence of 1/200 000 live births is caused by a congenital defect in phagocyte reduced nicotinamide adenine dinucleotide phosphate (NADPH) oxidase production of superoxide and related species.¹ This multi-component enzyme system is composed of cytosolic proteins (p47^{phox}, and p67^{phox}, p40^{phox}, and rac1/2) and membrane proteins (gp91^{phox} and p22^{phox} that form cytochrome b558), which assemble at membrane sites upon cell activation.³ The X linked CGD is caused by mutation in gp91^{phox} (60% of cases), while the

Figure 2 Microphotographs showing the subretinal mass that is composed of (A) glial component (asterisk), a cluster of inflammatory cells and hyalinised fibrous stroma (two asterisks) admixed with pigment clumps and small vessels (haematoxylin and eosin, original magnification, $\times 100$), (B) typical granulation tissue with proliferating capillaries and lymphoplasmacytic inflammatory cells in hyalinised stroma (haematoxylin and eosin, original magnification, $\times 400$), and (C) local proliferation of smooth muscle highlighted by positive staining for myosin (black), a marker for smooth muscle within the fibrovascular tissue (avidin-biotin-complex immunoperoxidase with anti-human myosin B antibody, original magnification $\times 200$).

autosomal recessive forms are caused by mutations in other genes.⁴ Patients with p47^{phox} deficiency (30% of cases), as in our patient, often have a milder clinical course than patients with X linked defects.

Ophthalmic manifestations of CGD include blepharoconjunctivitis, keratitis, optic neuropathy, and chorioretinal scars.⁵⁻⁷ Active chorioretinal lesions, vitreous haemorrhage, and retinal detachment are noted infrequently.⁸ Anterior segment involvement is presumably caused by inadequate control of normal flora, whereas the chorioretinal lesions are hypothesised to be the sequelae of infectious microemboli or granulomas. Pathological studies of intraocular CGD specimens have not demonstrated micro-organisms.⁹ Vitritis with active chorioretinal lesions progressing to panuveitis with an exudative retinal detachment has been reported in one CGD patient; histopathology of the eye showed choriocleral granuloma.⁸

Another feature of CGD involves poor wound healing.¹⁰ Therefore, subretinal granulation tissue mass in our case may represent an abnormal reparative response to previous chorioretinal injury. The absence of infection or granuloma, intravitreal pro-inflammatory cytokines, and improvement with immunosuppression suggests that his ocular disease is probably the result of aberrant inflammatory responses. Routine ocular biopsy is not recommended as part of standard ophthalmic evaluation.

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References

- 1 Segal BH, Leto TL, Gallin JI, *et al.* Genetic, biochemical, and clinical features of chronic granulomatous disease. *Medicine (Baltimore)* 2000;**79**:170–200.
- 2 Johnston RB Jr. Clinical aspects of chronic granulomatous disease. *Curr Opin Hematol* 2001;**8**:17–22.
- 3 El-Benna J, Dang PM, Gougerot-Pocidalo MA, *et al.* Phagocyte NADPH oxidase: a multicomponent enzyme essential for host defenses. *Arch Immunol Ther Exp (Warsz)* 2005;**53**:199–206.
- 4 Clark RA, Malech HL, Gallin JI, *et al.* Genetic variants of chronic granulomatous disease: prevalence of deficiencies of two cytosolic components of the NADPH oxidase system. *N Engl J Med* 1989;**321**:647–52.
- 5 Palestine AG, Meyers SM, Fauci AS, *et al.* Ocular findings in patients with neutrophil dysfunction. *Am J Ophthalmol* 1983;**95**:598–604.
- 6 Goldblatt D, Butcher J, Thrasher AJ, *et al.* Chorioretinal lesions in patients and carriers of chronic granulomatous disease. *J Pediatr* 1999;**134**:780–3.
- 7 Djalian AR, Smith JA, Walsh TJ, *et al.* Keratitis caused by *Candida glabrata* in a patient with chronic granulomatous disease. *Am J Ophthalmol* 2001;**132**:782–3.
- 8 Valluri S, Chu FC, Smith ME. Ocular pathologic findings of chronic granulomatous disease of childhood. *Am J Ophthalmol* 1995;**120**:120–3.
- 9 Grossniklaus HE, Frank KE, Jacobs G. Chorioretinal lesions in chronic granulomatous disease of childhood. Clinicopathologic correlations. *Retina* 1988;**8**:270–4.
- 10 Eckert JW, Abramson SL, Starke J, *et al.* The surgical implications of chronic granulomatous disease. *Am J Surg* 1995;**169**:320–3.

Ocular decompression retinopathy following trabeculectomy with mitomycin C associated with familial amyloidotic polyneuropathy

Familial amyloidotic polyneuropathy (FAP), a disorder inherited in autosomal dominant fashion, is characterised by systemic accumulation of polymerised mutated amyloidogenic TTR (ATTR) in peripheral nerves and in organs.¹ We report two patients with FAP ATTR Y114C (a point mutation, from tyrosine to cysteine, at codon 114) who developed diffuse retinal haemorrhages immediately after uncomplicated trabeculectomy with mitomycin C (MMC).

Case reports

A woman underwent vitrectomy for vitreous opacity associated with FAP ATTR Y114C in the left eye when she was 34 years old and in the right eye when she was 35 years old. Neurological examination revealed that she had polyneuropathy and autonomic dysfunction, and she underwent liver transplantation at 34 years old. Thereafter, intraocular pressure (IOP) in the left eye gradually increased and visual field loss progressed. Trabeculectomy with MMC in the left eye was performed when she was 39 years old. Preoperative IOP was 43 mm Hg despite maximal medical therapy. On the next postoperative day, IOP was 5 mm Hg, and fundus examination revealed scatter retinal haemorrhages in the periphery and posterior pole (fig 1). The haemorrhages had completely resolved and visual acuity was 20/20 in the left eye.

A woman underwent vitrectomy for vitreous opacity associated with FAP ATTR

Y114C when she was 45 and trabeculectomy in the right eye at another hospital when she was 46, respectively. At 48, vitrectomy in the left eye was performed. She underwent liver transplantation at 50. Thereafter, IOP in the left eye gradually increased and non-penetrating trabeculectomy with MMC was performed when she was 51. However, IOP increased postoperatively, and trabeculectomy with MMC was added. IOP before the additional trabeculectomy was 37 mm Hg despite maximal medical therapy. On the next postoperative day, IOP was 5 mm Hg, and fundus examination revealed scatter retinal haemorrhages in the periphery and posterior pole involving the fovea. Although haemorrhages had almost resolved during the follow up period, visual acuity decreased from 20/20 to 20/50.

Comment

Retinal haemorrhages are a rare complication after filtration surgery.^{2–6} Fechtner *et al* reported this condition for the first time under the descriptive term of ocular decompression retinopathy.² Affected patients are typically young, but not exclusively, with relatively high preoperative IOP, a very low postoperative IOP, and advanced cupping. Elevated IOP levels are generally significantly high in cases of secondary glaucoma related to FAP,⁷ and diffuse retinal haemorrhages immediately after uncomplicated trabeculectomy with MMC are noted in both cases. One possible mechanism is hypothesised to be caused by a loss of autoregulation of retinal vessels, which overwhelms their capacity to respond to changes in IOP, resulting in retinal haemorrhages.² Our cases had an autonomic dysfunction as a systemic symptom, further increasing the susceptibility to such a phenomenon. Also, although both

Figure 1 Scatter retinal haemorrhages in the periphery and posterior pole on the first postoperative day.