Bilateral nodular sarcoid choroiditis with vitreous haemorrhage

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SUMMARY A 21-year-old black man with presumed systemic sarcoidosis had bilateral choroidal nodules, unilateral retinal neovascularisation and vitreous haemorrhage, and non-caseating granulomas on percutaneous liver biopsy. The choroidal nodules were serially documented by fundus photography and fluorescein angiography over a 22-month period. Fluorescein angiography was more accurate than ophthalmoscopy in demonstrating choroidal inflammation. The choroidal nodules resolved after systemic corticosteroid therapy. A vitreous haemorrhage occurred probably secondary to neovascularisation related to occlusion of an inferotemporal branch vein. The non-resolving vitreous haemorrhage and associated traction retinal detachment were treated with vitrectomy and membrane sectioning.

Sarcoidosis is an idiopathic, systemic, and non-caseating granulomatous disorder with protean clinical manifestations. The lymph nodes, lungs, eyes, skin, and viscera are common sites of involvement. Ocular involvement has been found to be from 20 to 50%, depending on the series.^{1,2} Anterior uveitis has always been found to be the commonest ocular manifestation of ocular sarcoidosis, occurring in 20 to 90% of patients with systemic sarcoidosis.¹⁻³ Involvement of the orbit, eyelids, cornea, lens, lacrimal sac, ciliary body,⁴ and motor nerves has also been reported.

Posterior segment involvement was considered rare in a large review series,² with posterior uveitis found in only 2.5% of patients. Other workers reported an incidence of posterior uveitis as high as 60%.³ It is widely acknowledged that fundus changes are frequently overshadowed by the concomitant anterior uveitis.⁵ Posterior segment manifestations include retinal vascular, chorioretinal, vitreous, and optic nerve inflammatory lesions, as well as retinal and vitreous haemorrhage.

We studied a patient with presumed systemic sarcoidosis, with bilateral nodular choroiditis, and left retinal neovascularisation with vitreous haemorrhage. We carefully documented the course

of the subretinal lesions by serial fundus photography and fluorescein angiography over a 22-month period; our documentation of these lesions is, to the best of our knowledge, more detailed than that of previously reported cases. The patient underwent vitreous surgery in the left eye for non-resolving vitreous haemorrhage and suspected traction macular detachment, and he had good recovery of vision.

Case report

On 24 January 1981 a 21-year-old black man in previously good health came to the University of Chicago Medical Center because of a marked decrease in left eye vision over the course of two days. There was no family history of ocular disease.

On ocular examination the best corrected visual acuity was right eye 6/6, left eye hand motions at 1 foot (30 cm). Tension by applanation was 12 mmHg in each eye, and motility was full. There was mild injection of the left bulbar conjunctiva. An occasional mutton-fat and an occasional pigmented punctate keratic precipitate were present in each eye. There was a mild degree of flare and cells in the anterior chamber of each eye. The right retrolental space was clear; the left retrolental space had a mild degree of cells and flare. Right ophthalmoscopy revealed about 20 ¼ to ½ disc diameter yellowish

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Fig. 1 14 January 1981. Multiple choroidal nodules in the posterior pole of the right fundus.

Fig. 2 14 January 1981. Confluent choroidal nodules in the posterior pole of the right fundus.

white, slightly elevated, sharply outlined subretinal infiltrates. They presumably involved the choroid along the superotemporal, superonasal, and inferotemporal vessels (Fig. 1). There were occasionally larger, more confluent patches of choroiditis (Fig. 2). Fluorescein angiography of these areas showed blockage of the background fluorescence in the early arteriovenous phase; in the later venous phase there was mild staining of the infiltrates (Figs. 3A, B). Temporally, several areas of the flat retiform retinal vessels were present.

The left fundus showed a large posterior vitreous haemorrhage inferotemporally, partially obscuring

the disc and macula. The disc was hyperaemic with blurred margins. The superonasal and superotemporal veins were mildly engorged, dusky, and slightly tortuous, with perivascular superficial haemorrhages. Temporal to the disc, retinal oedema and intraretinal haemorrhages were present (Fig. 4). Areas of early neovascularisation arose from veins throughout the fundus (Fig. 5). A diaphanous fibrous strand and two large ovoid preretinal haemorrhages were present superotemporally in the posterior pole (Fig. 6). Several focal, whitish yellow, $\frac{1}{4}$ to $\frac{1}{2}$ disc diameter lesions, similar in appearance

Fig. 3A

Fig. 3B

Fig. 3 14 January 1981. Fluorescein angiogram of right eye. A: In the early arteriovenous phase, blockage of the background fluorescence is present. B: In a later venous phase, there is mild staining of the infiltrates.

Fig. 4 14 January 1981. Disc hyperaemia with blurred margins, engorgement of superior veins, and retinal oedema and intraretinal haemorrhage temporal to the disc are present in the left fundus.

Fig. 6 14 January 1981. Two large ovoid preretinal haemorrhages superotemporally in the left fundus. The diaphanous fibrous strand overlying the haemorrhage is not visible in the photograph.

to those seen in the fellow eye, were noted along the superotemporal arcade.

On systemic examination the patient had mild posterior cervical and inguinal lymphadenopathy. The liver was enlarged to 12 cm and the tip of the spleen was palpable.

A percutaneous needle biopsy of the liver revealed non-caseating granulomas surrounded by non-specific inflammatory cells. The acid-fast

bacillus stain and cultures for mycobacteria and fungi revealed no organisms. The combined clinical, laboratory, and histopathological findings were consistent with systemic sarcoidosis.

The patient was started on prednisone, 60 mg orally every day, on 20 January 1981. Topical therapy included atropine 1% drops twice daily and prednisolone acetate 1% drops four times a day to both eyes.

Fig. 5 14 January 1981. Areas of early neovascularisation seen nasally in the left fundus.

Fig. 7 29 January 1981. No choroidal nodules are present on fundus photography of the posterior pole of the right eye.

Fig. 8 29 January 1981. Fluorescein angiography of the right eye. The late phase of the angiogram, showing persistent staining of choroidal nodules.

At ocular examination on 29 January 1981 the patient's visual acuity was right eye 6/6, left eye counting fingers at 1 foot (30 cm). Although the majority of the right choroidal infiltrates resolved clinically (Fig. 7), fluorescein angiography showed staining in the macular region (Fig. 8), corresponding to areas previously visible on ophthalmoscopy. In the left eye the vitreous haemorrhage dispersed, and a yellow-red reflex was visible. As the right eye

improved, the prednisone was gradually reduced over the course of 14 months.

The left vitreous haemorrhage failed to clear for at least eight months. On A and B scan ultrasonography there was a possible traction macular detachment (Fig. 9). A left vitrectomy was performed on 18 August 1981. The vitreous haemorrhage was excised and removed. A superotemporal preretinal fibrous strand was severed from its connection with the posterior vitreous. Postoperatively the visual acuity was left eye 6/7.5. Superotemporally there was a preretinal strand which represented an isolated epicentre (Fig. 10), and there were macular striae (Fig. 11).

On follow-up examination at one year the patient had no ocular or systemic complaints. Visual acuities were right eye 6/6, left eye 6/6. The right fundus was normal. In the left eye there was a sheathed vein superotemporally, adjacent to the previous preretinal membrane. In the midvenous phase of the right eye fluorescein angiogram there were two distinct areas of hyperfluorescence superior to the macula. In the late phase of this angiogram the hyperfluorescence faded, suggestive of atrophy of the retinal pigment epithelium (Figs. 12A, B).

Discussion

There were multiple elevated choroidal nodules present in both eyes. Geeraets *et al.* described four

Fig. 9 On A and B scan ultrasonography of the left eye, there is possible traction macular detachment.

Fig. 10 20 August 1981. Preretinal membrane superotemporally causing traction on an adjacent venule.

Fig. 11 20 August 1981. Macular striae present postoperatively in the left fundus.

groups of choroidal nodules.⁶ The first group has a few circumscribed areas of fundus involvement, with flat $\frac{1}{4}$ disc diameter round lesions, often located close to retinal vessels. Lesions in the second group are not always related to blood vessels, appear more irregular in shape, and are more numerous. The third group shows more generalised fundus changes, and larger and more confluent areas of exudative choroiditis are also present. The fourth group has additional factors such as preretinal and intraretinal

haemorrhage associated with different stages of chorioretinitis. Our case more closely resembles the fourth group.

Initially fluorescein angiography of the nodules showed blockage of the background fluorescence in the early venous phases; in the later venous phases there was mild staining of the infiltrates, which only faded slowly. This fluorescein pattern suggested active choroidal inflammation. Some choroidal nodules that were seen on fluorescein angiography

Fig. 12A

Fig. 12B

Fig. 12 20 November 1982. A: Midvenous phase of fluorescein angiogram of the right eye. Two distinct areas of hyperfluorescence are present superior to the macula. B: In the late phase the hyperfluorescence fades, suggestive of atrophy of the retinal pigment epithelium.

were not detected by ophthalmoscopy. Nine days after the beginning of systemic steroid therapy there was almost complete resolution of the choroidal nodules ophthalmoscopically, though fluorescein angiography continued to show a few areas of involvement.

Turner *et al.*⁷ described retinal nodules which leaked fluorescein. Serial documentation of these lesions, however, was not undertaken. Early staining and late leakage from retinal vessel walls in areas of periphebitis and staining of periphebitic nodules have been previously noted.⁸ Serial fundus photography of one area of marked periphebitis was performed in one patient with ocular sarcoidosis, but fluorescein angiography was not done.⁹ Fluorescein angiography, performed in two patients with unilateral macular chorioretinal granulomas, revealed staining of the inflammatory mass with fluorescein leakage of the dye into the neurosensory space.¹⁰ Both patients, who had no retinal neovascularisation or vitreous haemorrhage, were treated with systemic corticosteroids. One year follow-up fluorescein angiography in both cases revealed complete disappearance of the abnormal leakage with only transmission defects due to the disturbance within the pigment epithelium. We have clearly documented, by serial fundus photography and fluorescein angiography over a 22-month period, the course of bilateral choroidal nodules in sarcoidosis treated with systemic prednisone.

Histopathologically Laval¹¹ has described nodules of epithelioid cells in the choroid in patients with ocular sarcoidosis. However, Gass and Olson¹² have suggested that many of the lesions interpreted clinically as focal sarcoid choroiditis are actually due to granulomas between the retinal pigment epithelium and Bruch's membrane.

Active sarcoid choroidal nodules are an indication for treatment with systemic corticosteroids, starting with moderately large doses (60 to 100 mg of prednisone daily), and tapering according to the clinical responses.¹³ The ophthalmoscopic and angiographic changes are the primary means for assessing therapeutic efficacy. One should exercise caution in tapering the systemic corticosteroid dose when there is angiographic evidence of activity in the absence of ophthalmoscopic signs. In the present case we slowly decreased the systemic corticosteroid dose with the ophthalmoscopic resolution of the majority of choroidal nodules while closely monitoring the fluorescein angiogram for total resolution.

The second prominent feature of our case was the left eye vitreous haemorrhage. Several mechanisms of haemorrhage have been described in sarcoidosis. Geeraets *et al.* observed waxy exudate accumulation on contiguous vessels leading to branch vein

occlusion.⁶ Such occlusion can directly result in deep and superficial retinal haemorrhage and vitreous haemorrhage or predispose to late onset neovascularisation, either peripherally or at the optic disc, with subsequent retinal or vitreous haemorrhage.¹⁴ Goldberg and Newell¹⁵ described a 23-year-old black man with sarcoidosis who initially had a unilateral superotemporal branch vein occlusion which had been replaced by a fibrous band. Six weeks later they noted a white mass and new blood vessels extending three disc diameters into the vitreous from the inferonasal margin of the optic disc.

A non-specific periphebitis retinae, similar in its manifestations to Eales' disease, has been described in sarcoidosis by many authors^{3, 16} and documented by fluorescein angiography.¹⁷ It seems probable that vascular involvement in areas of chorioretinal sarcoid inflammation has accounted for some of the manifestations attributed to perivasculitis retinae in the past.³

Asdourian and coworkers have described angiographically seafan neovascularisation and vitreous and retinal haemorrhage in three black patients with sarcoidosis without other systemic disease.⁵ They postulated that the periphebitic process may be the cause of stasis, hypoxia, and a secondary vasoproliferative stimulus.

In the present case the patient had a large left posterior vitreous haemorrhage, two large ovoid preretinal haemorrhages, and a striate haemorrhage overlying white centres. Engorged, tortuous veins, a strand of fibrous tissue, and multiple areas of flat neovascularisation were present. An inferotemporal venous occlusion or haemorrhage from retinitis proliferans may have accounted for the large preretinal and posterior vitreous haemorrhages. The prognosis was guarded owing to the possibility of fibrous tissue proliferation associated with traction macular detachment.

Steroid therapy was not initially directed at the vitreous haemorrhage but rather at the nodular choroiditis which accompanied it. However, in a case of bilateral sarcoid optic disc neovascularisation without haemorrhage, neovascular fronds were found to respond promptly to oral prednisone therapy.¹⁸ Furthermore, Spalton and Sanders¹⁹ had two patients with bilateral optic disc neovascularisation, which disappeared with adequate steroid therapy and produced no sequelae.

Photocoagulation has not been widely used in the treatment of neovascularisation secondary to sarcoidosis. In one case of disc neovascularisation argon laser photocoagulation of retinal avascular areas was followed by regression of the disc vessels.¹⁵ Asdourian and associates⁵ described one patient with a seafan type of sarcoid neovascularisation

treated with focal argon laser photocoagulation. Although the neovascular process was successfully ablated, a neovascular tuft returned in six months. Spalton and Sanders¹⁹ have emphasised that ocular inflammation should be well controlled with steroids before any laser treatment is attempted.

In our case a vitrectomy was performed when the left vitreous haemorrhage did not resolve despite six months of steroid therapy. Important technical consideration included the careful removal of the central vitreous and all preretinal membranes and fibrous strands. If this had not been done, proliferating fibrovascular tissue would have led to further retinal traction and detachment.^{20,21}

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