

Post kala azar uveitis

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SUMMARY Three patients who developed bilateral anterior uveitis at the end of, or soon after, the apparently successful treatment of visceral leishmaniasis are described. The uveitis gave rise to secondary glaucoma in 2 of the patients, and in the third patient the eye lesions were associated with an episode of post kala azar dermal leishmaniasis.

Ocular complications of kala azar are uncommon.^{1–5} Little distinction is sometimes made between the various species and clinical forms of human leishmaniasis. Actual case reports are very rare. In a paper that now seems to be available only as an abstract,⁶ 2 patients with iritis, one of whom also had retinal haemorrhages, and a third patient with papillitis are described. Recupero⁷ reviewed previous reports and described retinal haemorrhages in 6 children with kala azar. Superficial haemorrhages and cytooid bodies were seen in the retinae of a patient with kala azar probably acquired in Spain.⁸ McKie Reid¹ mentions in addition a central retinal vein thrombosis, a keratitis, and a chronic iritis. In all these the eye lesions have been a presenting feature of the kala azar. They regressed, together with the systemic illness, on treatment with pentavalent antimony.

Somerset³ states that involvement of the eye in post kala azar dermal leishmaniasis is exceedingly rare, but notes that there may be signs of chronic iritis.

Three patients seen at the Kenyatta National Hospital, Nairobi, during the last 8 years have developed anterior uveitis as a late complication of kala azar.

Case reports

CASE 1

A 37-year-old male Mkamba living in the area of Makuani, the centre of a recently^{9,10} noted epidemic of kala azar, first became ill in 1976. Kala azar was diagnosed in 1977, and he was treated with 60

injections of Pentostam (sodium stibogluconate) at an up-country hospital. Although he felt better, the spleen, of which he had been very much aware, did not recede completely. In 1978 the spleen enlarged again and he was treated at another up-country hospital with a further 60 injections of Pentostam. The spleen disappeared. A few days after discharge from that hospital he noted pain in both eyes together with deteriorating vision. He was referred to this hospital 3 months after the onset of the eye symptoms.

On examination visual acuity was restricted to the ability to count fingers at 1 metre (RE) and to detect hand movements at 30 cm. (LE). Refraction was +1 dioptre in both eyes. The conjunctivae appeared red with marked ciliary injection, the lower thirds of the corneal epithelia were oedematous, and numerous pigmented precipitates were seen in the lower thirds of the corneal endothelia. The anterior chambers contained a moderate number of tiny cells moving in the caloric stream, and a moderate flare was noted. Gonioscopy revealed circular peripheral anterior synechiae bilaterally. In both eyes the lens, posterior vitreous, retina, and posterior uvea were free from inflammation, but oedema of the macula and early glaucomatous cupping of the discs were noted. The intraocular pressures measured 52 mmHg (RE) and 42 mmHg (LE) with Goldmann's applanation tonometer.

On general examination the patient appeared to be in good health. The body temperature was normal, he was not anaemic, and his liver and spleen were not palpable. A few small hypopigmented macules on the forehead (Fig. 1) had been observed to develop during the preceding weeks by the patient. The leishmanin skin test and the Mantoux test were both positive. Results of investigations

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included haemoglobin 17.2 g/dl, leucocytes $5.6 \times 10^9/l$ with a normal differential, a platelet count of $255 \times 10^9/l$, a serum albumin level of 35 g/l and a globulin level of 38 g/l. A bone marrow aspirate was examined but no parasites were seen. There was no sugar or protein in the urine, and the blood urea was 42 mg/100 ml (6.97 mmol/l). The USR (syphilitic screening test) and a leishmanial fluorescent antibody test were negative, though the serum for this latter test was collected 8 months after the apparent cure of the visceral leishmaniasis.

Maximal standard therapy, namely, acetazolamide, mannitol infusions, systemic and topical corticosteroids, and trabeculectomy, was given for 2 months with little if any benefit. The surgical relief of intraocular pressure was associated with intra- and preretinal haemorrhages and lasted only for some 3 weeks because of the persistent inflammation.

He was then treated with Pentostam, 6 ml daily by intramuscular injection for 30 days. Systemic and local corticosteroids and acetazolamide were continued. On 2 occasions cyclocryotherapy was used to control rising intraocular pressures, still around 40 mmHg in both eyes.

The uveitis steadily improved on this regimen, and 5 months after admission he was discharged on acetazolamide, 125 mg 4 times daily, and corticosteroid eyedrops. The intraocular pressures measured 20 mmHg (RE) and 14 mmHg (LE). Visual acuity with correction was 6/60 (RE) and 1/60 (LE). In both eyes the anterior chamber showed some flare, but no cells were seen. The marked cupping of both discs persisted.

CASE 2

This patient was a 49-year-old male Mkamba from northern Kitui, the area of a major epidemic of kala azar that began shortly after the second world war.¹¹ He was not seen by us, but his records came to light while we were reviewing the records of patients with kala azar seen at the Kenyatta National Hospital over the last few years. He became ill in October 1972 and was admitted to this hospital in March 1973. He complained of periodic fever, weight loss and a mass, the spleen, in the left hypochondrium. Leishman-Donovan (L-D) bodies were seen in a marrow aspirate. Pentostam, by intramuscular injection, was given for 2 10-day courses of 6 ml daily and for a third course of 10 ml daily for 14 days. Ova of *Schistoma mansoni* were found on stool examination, and hycanthone 75 mg by intramuscular injection was given on 2 occasions a week apart. He improved, and a repeat marrow aspirate was normal.

Five months later when seen in the outpatients

department he was generally well, no hepatosplenomegaly was noted, but he complained of poor vision. The findings were of a granulomatous uveitis with secondary glaucoma. Vision without correction was 6/60 (RE) and 6/36 (LE). Both eyes showed ciliary injection, oedema of the corneal epithelia, especially on the right, and large precipitates on the corneal endothelia.

The intraocular pressures were 46 mmHg (RE) and 34 mmHg (LE) as measured by Goldmann's applanation tonometer. Treatment with depot corticosteroids, steroid eye drops, and acetazolamide was apparently successful, as the subsequent notes make no reference to eye symptoms or signs.

Three years later he was admitted with an operable malignancy of the stomach. The liver and the spleen were not palpable. The patient was not seen again at this hospital.

CASE 3

This patient, a boy, developed kala azar at the age of 2 years when living on the wall of the northern part of the Kenyan Rift Valley near Kapenguria. He was seen, aged 5 years, by one of us (PHR) after repeated unsuccessful courses of Pentostam and pentamidine. Splenic smears showed enormous numbers of L-D bodies. He received 3 30-day courses of Pentostam and a 3-month course of amphotericin B combined with 5-fluorocytosine, with some clinical improvement, but L-D bodies persisted in the splenic aspirate. A few days after completing a further 30-day course of Pentostam he developed an illness typical of post kala azar dermal leishmaniasis, with fever, malaise, conjunctivitis and a diffuse maculopapular rash, initially resembling measles, but becoming nodular with lesions some 4 mm across. The rash was especially on the face but also on the trunk and arms. Nodules were seen on the sclera, but the fundi appeared normal. L-D bodies were demonstrated both in skin scrapings and stained sections of the skin lesions. Pentostam was restarted and the rash cleared quickly, having been present for 4 weeks. The general malaise worsened, and investigation of this revealed that he was uraemic (blood urea 230 mg/100 ml = 38 mmol/l). The Pentostam was stopped on the 15th day of this final course, and he slowly recovered. Ten weeks later, although he was parasitologically cured and in good general health, he continued to complain of poor vision. Ciliary injection was still present, and ophthalmological examination disclosed corneal oedema and nodular iritis, especially inferiorly, in both eyes. A diagnosis of anterior uveitis with nodular iritis was made, and treatment with hydrocortisone and atropine eye drops given.

The boy was discharged home. Follow-up was difficult, but so far as can be ascertained no further complications developed.

Discussion

Although the last decades of ophthalmological history have taught us to be careful in postulating an aetiological connection between uveitis and some general disease, it is probable that the time relationship of the onset of the uveitis to the kala azar in these 3 patients is more than coincidental.

The first patient developed eye symptoms a few days after completing a curative course of Pentostam. The date of onset of the uveitis in the second patient is less certain, but must have been at some time during the weeks following cure. In the third patient the uveitis was apparently a part of post kala azar dermal leishmaniasis. Thus unlike the 2 patients described by Salvati,⁶ the uveitis occurred at or shortly after the conclusion of the systemic illness, post kala azar uveitis.

A consideration of the pathogenesis of the uveitis must be speculative, but an association with post kala azar dermal leishmaniasis seems likely. In the third patient the uveitis and the post kala azar dermal leishmaniasis appeared to be integral. In the first patient the rash on the forehead was in keeping with the East African form of post kala azar dermal leishmaniasis,¹²⁻¹⁵ though it should be noted that depigmentation of the lashes and/or a patchy depigmentation of the skin in association with chronic uveitis, such as in sympathetic ophthalmitis and in the Vogt-Koyanagi syndrome, is an observation of considerable age.¹⁶

The East African form of post kala azar dermal leishmaniasis occurs at the end of successful treatment or during the ensuing months. It is possible, though more difficult than in the Indian form,^{17,18} to demonstrate parasites in the skin. The demonstration of these parasites suggests that the apparent parasitological cure of kala azar is relative rather than absolute. Post kala azar dermal leishmaniasis may be the outward sign of an immunological change, from the parasite-tolerant anergic state of kala azar to a parasite-intolerant state, manifest initially by much cellular reaction in the neighbourhood of parasites or sensitised cells, and then by parasitological cure or at least by a massive reduction in the parasite population. *Leishmania donovani* might be well tolerated in the anterior uvea during the anergic phase, but at the time of 'cure' these same parasites might form the focus of a uveitis. Such tiny lesions as we have described might be insignificant in other tissues such as the skin, but

in the anterior uvea will be obvious and may cause glaucoma and blindness.

Treatment is uncertain. Although the improvement in the first patient seemed to date from the introduction of Pentostam, the uveitis of the second patient probably recovered without the use of Pentostam, and in the third patient the eye lesions persisted despite the response of the post kala azar dermal leishmaniasis to Pentostam. The mode of action of pentavalent antimonials in kala azar remains unknown. Both a direct leishmanicidal effect and stimulation of the reticuloendothelial system seem improbable,¹⁹ and there are difficulties in accepting that chemotherapeutic activity depends on the reduction of pentavalent to trivalent antimony in the body.²⁰ If our speculations are correct, the inflammation could be expected to subside in due course without treatment, but perhaps not before irreparable damage had been done. Pentostam, or a similar pentavalent antimonial, and corticosteroids would seem to be sensible initial treatment, together with standard therapy for glaucoma should this develop.

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