PROGRESSIVE BLINDNESS DUE TO POSTERIOR UVEITIS FOLLOWING ANTISYPHILITIC TREATMENT FOR INTERSTITIAL KERATITIS*†

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A Case Report

Case B14682 a married man, aged 44 years, reported initially to the Venereology Department in 1952, having been referred by the ophthalmologist with right interstitial keratitis of 6 weeks' duration and a positive blood Wassermann reaction (WR).

Investigations revealed no clinical abnormalities other than right interstitial keratitis and a strongly positive Wassermann reaction. The cerebrospinal fluid was normal and no clinical or personal data relevant to this patient or to his family, wife, or children, indicated whether his infection was acquired or congenital.

Ophthalmological Picture in Relation to Antisyphilitic and Local Treatment

Phase I. Right Interstitial Keratitis (July, 1952-July, 1953).—Between these dates he had had a right interstitial keratitis which had been treated locally with 1 per cent. atropine drops twice daily and subconjunctival injections of cortisone, 10 mg. twice weekly. During this time he received three courses of penicillin (18 mega units) and three courses of bismuth.

The right eye, in spite of treatment, showed slowly progressive corneal infiltration and vascularization. In May, 1953, an anterior choroiditis was observed with initial clearing of the cornea.

Phase II. Bilateral Interstitial Keratitis (July, 1953–October, 1954).—In July, 1953, the left eye developed a quickly progressive interstitial keratitis and in a week or two was as severely involved as the right had been. However, both eyes responded dramatically to the cortisone drops and there was a normal regression in both, except for a mild flare-up when the cortisone drops were discontinued for a short spell in 1954.

The patient had been given altogether 36 mega units penicillin, six courses of bismuth, and two courses of mercury.

Phase III. Stage of Retrogression (October, 1954–February, 1956).—Gradual regression of the interstitial keratitis occurred, local treatment with atropine and cortisone drops being continued.

During this period, there were two mild relapses of stromal activity in the left eye in June, 1955, and September, 1955, when cortisone drops were inadvertently discontinued. With resumption of the drops, there was again a quick response to treatment.

Phase IV. Posterior Uveal Complications (February, 1956).—At this time, while still on maintenance cortisone drops four times daily, the patient complained of sudden loss of vision in the right eye. The vitreous was completely opaque, obscuring all fundus detail. By May, 1956, it had cleared sufficiently to show a massive, destructive, diffuse, exudative process—a generalized posterior uveitis—the whole chorio-retina to beyond the equator now being replaced by an area of atrophy and fibrosis with surrounding pigmentary changes. The visual acuity was bare perception of light.

The left fundus was normal in February, 1956, and the visual acuity in the left eye was 6/6. Careful observation of this eye was made during the next few weeks; the first signs of trouble were noted on May 2, 1956, when a few cells were seen in the vitreous with the suspicion of an early juxta-papillary lesion on the nasal side of the disk. This did not develop as a typical juxta-papillary choroiditis, but, leaving a zone of clearance about half a disk diameter about the nervehead, this exudative process progressed slowly and relentlessly to form a halo with a feathered edge around the disk; then its advancing edge, fringed by a sprinkling of small, flat haemorrhages, encroached on the macular area with off-shoots extending along the slightly congested main veins. The visual acuity in the left eye is now reduced to 6/60.

Additional antisyphilitic treatment was commenced in Phase IV, in the form of two courses of prednisone-ACTH-penicillin therapy. Each course comprised 20 mega units Triplopen* and 40 units ACTH gel twice-weekly, together with prednisone over a 53-day period. Initially, the daily dosage of prednisone was purposely kept at a high level, 60 mg. for the first 4 days, followed by a daily maintenance dosage of 30 mg., and eventually reduced to 5 mg. daily, the tailing-off process lasting for from 7 to 10 days. This seemed to have little effect on the disease, but the impression was received that, after discontinuing prednisone therapy, there was a slight

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* Benethamine, procaine, and sodium penicillin, Messrs. Glaxo Laboratories.
speeding-up in the progress of the posterior uveitis in the left eye. This may, however, have been coincidental with macular involvement.

The disappointing outcome of prednisone-ACTH-penicillin therapy in this case would appear to parallel the experience of Mazzini et al (1955), who found that large doses of penicillin together with cortisone and ACTH yielded disappointing results in the treatment of a patient suffering from syphilitic posterior uveitis of congenital origin.

Aetiology

The fundamental question to be answered at the outset is whether or not the posterior uveitis was due to syphilis. Although this was a relatively frequent complication of interstitial keratitis 20 years ago, it has become, in our experience, a rarity since the advent of cortisone, only two cases having been seen in recent years.

Points in favour of a syphilitic aetiology were:

(1) The elimination of other causes.

(2) The development of the left posterior uveitis followed the classical atypical pattern of syphilitic posterior uveitis as described by Leber (1915).

(3) It was established, by the three relapses directly following the withdrawal of cortisone, that the interstitial keratitis, although controlled by cortisone, was still dormant.

(4) In the presence of a recently active anterior chorioretinitis as part of the interstitial keratitis, it is reasonable to assume that the development of the posterior uveitis may be an extension of the same process and the same disease.

In the elimination of other causes, the classification of uveitis given by Woods (1949) was adopted; this classification is not universally accepted, but it served as a practical basis for the elimination of other aetiological factors.

Woods’ Classification

A. Granulomatous: Tuberculosis, spirochaetosis, brucellosis, toxoplasmosis, sarcoidosis, and virus infections.

B. Non-granulomatous: Due to bacterial allergy (streptococcal, gonococcal, etc.).

(1) Woods (1956).—Whereas in 1941 tuberculosis accounted for 79 per cent. of granulomatous cases and syphilis for 16 per cent., in 1953 toxoplasmosis accounted for 26 per cent., tuberculosis for 22 per cent., and syphilis for 7 per cent.

(2) Smith and Ashton (1955).—In 200 cases, none of which resulted from syphilis, special care was taken to eliminate toxoplasmosis (skull x ray, dye test, and complement-fixation tests negative) and tuberculosis.

On these premises, assuming a syphilitic aetiology, why did such a fulminating bilateral posterior uveitis follow bilateral interstitial keratitis, especially when this had been treated with 36 million units penicillin and six courses of heavy metal, a dose greatly in excess of antisyphilitic therapy advocated by some members present at this meeting?

It is unlikely that the explanation lies in the inability of spirillicidal drugs to kill the spirochaete in the uveal tract, so preventing the development of an immunity. It seems much more logical to assume that the posterior uveitis was a syphilitic allergic manifestation, just like interstitial keratitis. With reference to this theory, it is interesting to note that Woods (1949) maintains that the non-granulomatous types of uveitis may be due to bacterial hypersensitivity.

This does not explain, however, the progressive malignity of the posterior uveal lesion when the interstitial keratitis was apparently controlled. Did the local application of cortisone influence this development? This might have been so, from the inefficacious use of cortisone in Phase I—by conjunctival injection instead of frequent local applications of drops which are now employed. Alternatively, should we regard this as an extreme degree of hyper-sensitivity of the individual to syphilis antigen, or is it merely a poor reaction of the tissues to the hormone?

The same, however, would seem to be true in the case of systemic hormone treatment; this is in agreement with most of the more recent reports that the acute anterior segment inflammations respond most readily to all types of steroid therapy, but that the reaction of posterior segment inflammations to hormone therapy is indifferent (Duke-Elder and Ashton, 1951).

Summary

This case clearly illustrates the following well-recognized facts:

(1) Penicillin and heavy metal therapy in massive doses has no effect on the course of interstitial keratitis.

(2) Local cortisone therapy gives a dramatic improvement in interstitial keratitis, but premature withdrawal or insufficient maintenance dosage rapidly produces relapses; adequate treatment must be continued over a long period, i.e. the expected active self-limiting course of the untreated condition.
(3) Local cortisone therapy has no place in the treatment of a posterior uveitis.

(4) Systemic cortisone therapy is of very doubtful efficacy in the treatment of chronic uveitis.

It is not universally recognized that local cortisone therapy may produce a complete remission of signs in the anterior segment of the eye in interstitial keratitis, while at the same time an acutely progressive destructive lesion may be invading the posterior segment.

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