Uveitis due to secondary syphilis

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SUMMARY The incidence of uveitis caused by syphilis has fluctuated during the past century. This paper suggests ways in which the diagnosis of this condition may be helped by reactions to chemotherapy. It also reports on a 22 year old woman presenting with anterior uveitis due to secondary syphilis, who rapidly developed bilateral papilloedema on starting antisyphilitic chemotherapy. She later developed psychiatric symptoms which were partly the result of corticosteroid treatment.

Introduction

Although syphilitic inflammation of the iris was reported as early as 1815 by Adam Hunter of Edinburgh,¹ Jonathan Hutchinson's famous papers describing keratitis and uveitis (or as it was then commonly called "iritis") in congenital and acquired syphilis did not appear until 1858-9 and 1873 respectively.^{2,4} By 1918 when Igersheimer produced his monograph on ocular syphilis,⁵ there was an extensive literature on the subject although in many cases the exact aetiology of uveitis was vague. The table shows that the proportion of cases purporting to be primarily due to syphilis varied from 1.2% to 80% in 18 studies of patients with uveitis published over 100 years.⁶

In 1931 Moore, whilst advocating care in the interpretation of all findings including serological tests before diagnosing syphilitic iritis, also stressed the need for a higher index of suspicion of syphilis.⁷ Although Perkins had found the incidence of syphilitic uveitis to be only 1.2% in 1961,⁸ the number of new cases of early infectious syphilis reported had risen from 1199 in England and Wales in 1961 to 1630 in England alone in 1979.^{9,10} In three reports concerning the proportion of patients known to have syphilis developing uveitis, a more reliable measure of the incidence of this complication, the percentages ranged from 1.6% to 4.5%.^{7,11,12} In a recent report Zwink and Dunlop diagnosed uveitis, mainly asymptomatic, by slit lamp examination in

TABLE Percentage of cases of uveitis considered to be primarily caused by syphilis⁶

Year	Author	% Cases of uveitis due to syphilis
1853	von Arlt	17
1905	Campbell	70
1911	Butler	22
1913	Lang	6
1914	Goulden	9
1921	Clapp	82
1923	Irons and Brown	6
1925	Newton	13
1925	Elschnig	20
1925	Weiss	55
1925	Bruns	70
1930	Gilbert	16.6
1931	Gifford	16.9
1932	O'Leary	6
1937	Copps <i>et al</i>	8
1941	Guyton and Woods	10.5
1958	Schlaegel	3
1961	Perkins	1.2

50% of a series of patients with secondary syphilis, suggesting that syphilitic uveitis is much more prevalent than previously appreciated.¹³

Chemotherapy may help to unmask syphilitic uveitis in one of two ways; either with the occurrence of a Jarisch-Herxheimer reaction to treatment with antibiotics or through the anti-inflammatory effect of corticosteroids.

The ocular Herxheimer reaction following treatment with arsenicals was described and discussed very fully by Zimmerman in 1928.¹⁴ He explained that, as in the syphilitic process in general, the Herxheimer response in the eye was an intensification of an active lesion, an activation of a quiescent lesion, or the unexpected appearance of changes in structures previously without clinical evidence of

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pathology. In 1923 Toulant had suggested the Herxheimer reaction as a means of diagnosing syphilitic lesions in the eye,¹⁵ but in 1946 Klauder and Dublin found that it was certainly not an absolute criterion in the differential diagnosis of syphilitic anterior uveitis.¹⁶

McFaul and Catterall (1971) described a case of panuveitis in which high dosage systemic corticosteroids cleared the vitreous haze revealing the characteristic changes of syphilitic choroidoretinitis.¹⁷ Similar reports, in which secondary syphilis was overlooked as a cause of uveitis until the condition was well advanced, and the anti-inflammatory effect of steroids helped to establish the diagnosis, have since come from north America.¹⁸⁻²⁰

This report describes a case of secondary syphilitic uveitis with papilloedema and subsequent psychiatric symptoms. Although there are no similar reports, it is possible that this condition may occur more frequently than has hitherto been appreciated.

Case report

A 22 year old unmarried woman was first seen at the Royal Liverpool Hospital on 3rd June 1980, having been seen earlier that day at St Paul's Eye Hospital. There she had given a history of sore eyes for a week and a rash for four weeks (diagnosed elsewhere as pityriasis rosea and treated with ultraviolet therapy). The ophthalmologist found bilateral anterior uveitis, which was more severe in the left eye, with a visual acuity of 6/9. No gross abnormality had been found on fundal examination, which had been limited because of photophobia. As the ophthalmologist had in the previous twelve months seen three similar patients in whom a diagnosis of secondary syphilis had later been established, he referred her to the sexually transmitted diseases (STD) clinic after starting local treatment with steroids and mydriatics without waiting for the results of her serological tests.

On examination she had a copper coloured macular rash, bilateral anterior uveitis and accompanying photophobia, generalised peripheral lymphadenopathy, and some patchy hair loss. There was no genital abnormality. The results of her serological tests were available two days later and were typical of late secondary syphilis. The blood Wasserman reaction, the fluorescent treponemal antibody absorption (FTA-ABS) test, the Venereal Disease Research Laboratory (VDRL) test (1/256), and the *Treponema pallidum* haemagglutination assay (TPHA) (1/64) all gave positive results.

After explaining the diagnosis, treatment (with daily intramuscular injections of 600,000 U procaine penicillin for 10 days) was started and she was

warned about a possible Herxheimer reaction. The following day she reported a mild Herxheimer response and mentioned that her sight had deteriorated. This was explained as probably being caused by the eye drops and she reattended the ophthalmological outpatient department. There the ophthalmologist found florid bilateral disc swelling with reduced visual acuity (6/18). It was suggested that, while this might be due to the Herxheimer reaction, a neurological opinion should be obtained to exclude the possibility of a space occupying lesion and she was transferred to the Regional Neurological Unit.

Cerebrospinal fluid (CSF) findings showed: pressure 110 mm Hg, total protein concentration 20 mg/100 ml; glucose concentration 3.7 mmol/l; erythrocytes $<5 \times 10^6$ /l; lymphocytes 18×10^6 /l; TPHA positive results (1:10); FTA-ABS weakly reactive results. On computed tomography (CT) no space occupying lesion or other abnormality was found. Her visual acuity had fallen to 6/24 and, because of the risk of permanent visual damage, the neurologist advised high dosage systemic corticosteroid treatment. She was then transferred to St Paul's Eye Hospital and retinal photographs were taken that showed blurring of the disc margin, a slight increase in the venous calibre, and retinal oedema involving the posterior pole (the signs were particularly pronounced on the left) (figs 1 and 2).

A week later the uveitis was resolving, although the disc swelling and visual acuity had not improved and she had developed depression and disorientation for time and space. She became more withdrawn,

FIG 1 Retinal photograph of left eye.

FIG 2 Retinal photograph of right eye.

lethargic, dysphasic, and then paranoid. Two weeks after her first attendance she was reported to be showing suicidal tendencies. She was transferred to the acute psychiatric assessment unit at the Royal Liverpool Hospital where an electroencephalogram showed no organic cerebral change. Organic psychosis as a result of steroid treatment was diagnosed. Over the following ten days her corticosteroids were gradually tailed off, during

which time her depression lessened. The disc swelling subsided more gradually and her visual acuity improved. Fluorescein angiography confirmed the optic disc oedema (figs 3-7). The capillaries in the surface of the disc were ill defined because of fluorescein dye leakage. The disc showed fluorescence as a result of exudation of fluid. There was, however, no significant active retinal leakage, presumably because at this stage the condition was resolving. She was discharged eight weeks after her first visit and when seen four weeks later at St Paul's Eye Hospital her optic discs and visual acuity were normal.

Discussion

There is ambiguity in the definition of papilloedema. In neurology it is merely a descriptive term indicating disc swelling without reference to the underlying cause.²¹ Ophthalmologists, however, consider that papilloedema is passive disc swelling, caused by raised intracranial pressure which embarrasses the normal venous return to the optic disc, but does not affect visual acuity in the first instance. In 1911 Paton and Holmes differentiated between papilloedema and optic neuritis in which disc swelling is associated with inflammation and loss of vision.²²

When papilloedema, in the ophthalmological sense, was suspected in this patient the possibility of raised intracranial pressure had to be investigated urgently. The cerebrospinal fluid pressure and

FIG 3 Fluorescein angiogram No 1 of left eye.

FIG 4 Fluorescein angiogram No 2 of left eye.

FIG 5 *Fluorescein angiogram No 3 of left eye.*

protein content were normal, however, and CT showed no space occupying lesion. It seems likely that the disc oedema was the result of a syphilitic process exacerbated by a Herxheimer reaction. Meningovascular involvement is common in secondary syphilis and is characterised by nocturnal

headaches with occasional vomiting (symptoms which our patient disclosed on close questioning by the neurologist).

It would have been difficult to rule out optic perineuritis, a rarely diagnosed inflammation of the optic nerve sheath sparing the subjacent optic nerve.²³ In this condition, which is an extension of syphilitic meningitis, the visual symptoms are non-specific but the optic discs are swollen. There are positive serological findings and normal cerebrospinal fluid pressure.

Ischaemia of the optic nerve head following vasculitis in low grade syphilitic meningitis would not have been incompatible with $18 \times 10^6/l$ lymphocytes in the CSF. Her discs were not pale and fluffy as expected in ischaemia, however, but engorged and pink suggesting an inflammatory lesion.

Syphilitic optic neuritis could have produced this appearance, but the original reduction in visual acuity was probably not sufficiently acute for the diagnosis of this condition, which is rare in secondary syphilis. Her early field changes were not obvious and, once her psychotic symptoms had developed, were not assessable. Although testing the visual evoked response might have shown altered optic nerve function,²⁴ this procedure was considered unjustified particularly as disc swelling has been reported, even in the apparent absence of posterior uveitis accompanying anterior uveitis of bacterial, autoimmune, and other aetiologies.²⁵

In some cases cystic degeneration occurs after

FIG 6 *Fluorescein angiogram No 4 of left eye.*

FIG 7 *Fluorescein angiogram No 5 of left eye.*

longstanding macular oedema.²⁶ Such a macular cyst was reported in our patient's left eye on several occasions as the disc swelling subsided.

The severe reduction in visual acuity reported after the Herxheimer reaction could be ascribed either to vitreous haze in panuveitis or to a central scotoma due to macular oedema.

Her psychosis was considered to be an adverse drug reaction resulting from treatment with systemic corticosteroids. Paranoid delusions and a noticeable alteration of mood with schizoid-like states are characteristic of this reaction.²⁷ The start and withdrawal of treatment certainly coincided with the waxing and waning of her symptoms. There may have also been several contributory factors to her psychosis. The cerebral meninges had probably been involved in the syphilitic process; and impaired memory, apathy, confusion, and partial aphasia are only some of the many signs and symptoms of such involvement.²⁸

This case illustrates the importance of interdisciplinary cooperation in the diagnosis and treatment of secondary syphilis in which generalised infection may result in highly specialised problems.

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