Case report

Secondary syphilis presenting with acute unilateral vision loss and a widespread maculopapular rash

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SUMMARY

Syphilis infection has shown a marked resurgence over the past several years. Ocular involvement is a rare complication of syphilis, occurring in approximately 1% of cases. We present the case of a man in his 50s who presented to hospital with acute unilateral vision loss and a widespread maculopapular rash. Ophthalmological examination showed unilateral optic disc swelling and bilateral vitritis. Intracranial imaging revealed no acute pathology. Initial blood tests were normal apart from mildly elevated inflammatory markers. A comprehensive autoimmune and infection screen revealed positive syphilis serology. The patient was subsequently treated for syphilis with ocular involvement with a course of intravenous benzylpenicillin, resulting in rapid symptomatic improvement. This case highlighted the importance of considering syphilis infection as part of the differential diagnosis for unexplained multisystemic symptoms, such as loss of vision in combination with dermatological involvement.

BACKGROUND

Syphilis infection has shown a marked resurgence over the past several years. Public Health England reports that in 2017, there were 7137 reported diagnoses of syphilis in England, representing an increase of 20% relative to 2016 and an increase of 148% compared to 2008.¹ Men who have sex with men are disproportionately affected by syphilis: in 2017, 90% of syphilis cases in London were among this population group, with 32% of cases diagnosed at the primary stage, 30% at the secondary stage and 38% at the early latent stage.²

Ocular involvement is a rare complication of syphilis, occurring in approximately 1% of cases.³ Given the rising rates of syphilis, it is important for physicians not only to be aware of this potential complication but also to remember that visual loss may in fact be the first presentation of syphilis in acute medical settings. Early diagnosis and prompt, effective treatment can lead to the return of visual acuity and help to prevent further complications.

We present the case of an immunocompetent patient who presented to our hospital with unilateral vision loss. An extensive search for an aetiology identified positive syphilis serology.

CASE PRESENTATION

A man in his 50s presented to the emergency department of his local eye hospital with a history of sudden onset painless loss of vision in his left

eye. Initial examination revealed bilateral vitritis and some left optic disc swelling, but a definitive cause could not be identified. He was subsequently referred to our hospital's medical team for urgent review and further investigation.

He described a central dark, red spot with preserved peripheral vision in his left eye, which he had noticed on waking. Over the next 48 hours, the dark spot increased in size and he subsequently presented to hospital. He otherwise reported feeling well in the preceding weeks, denied any constitutional symptoms and was not able to recall any obvious precipitating factors for his symptoms. There was no history of headache, aura or traumatic head injury.

His medical history included long-standing myopia, for which he had a stable lens prescription for several years, and hypertension. He was adherent to regular anti-hypertensives and reported that his blood pressure was well controlled on treatment. He had not recently started any new medications. There was no history of any allergies or drug reactions. He was a regular smoker. He had a history of male sexual partners and had not been sexually active for several months. He reported that his most recent screen for sexually transmitted infections and blood-borne viruses had been negative.

Examination of the cardiovascular, respiratory and gastrointestinal systems was normal. Neurological examination was normal apart from the aforementioned visual loss in his left eye. Examination of the skin revealed a very faint maculopapular rash across his upper limbs and back ([figure 1](#)). He had not previously noticed the rash and reported no previous history of dermatological conditions. He was afebrile and all observations were within normal range.

INVESTIGATIONS

Initial blood tests revealed normal full blood count, renal function, liver function and coagulation screen. Erythrocyte sedimentation rate was elevated at 37 mm/hour and C reactive protein was mildly elevated at 11.6 mg/L. Urinalysis revealed microscopic haematuria.

A CT scan of the brain did not demonstrate any acute abnormalities. Subsequent MRI of the brain showed some old lacunar infarcts which were not thought to be the cause of the patient's acute presentation. CT angiogram showed some atheromatous disease and a 2 mm anteriorly pointing aneurysm in the right middle cerebral artery bifurcation. Following discussion with the stroke physicians,

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Figure 1 Image of the patient's subtle maculopopular rash on the right arm.

the patient was started on secondary prevention therapy with a statin and the antiplatelet agent clopidogrel.

The patient was subsequently reviewed again by the ophthalmologists while an inpatient. During this review, a new small area of visual loss in the nasal field of the right eye was identified, although the patient himself had not previously noted this. Vitreous cells were also noted in both eyes. The ophthalmologists made a diagnosis of intermediate uveitis with perivasculitis, the origin of which was still unclear.

Due to the unexplained microscopic haematuria, widespread rash and vitreous cells seen on ophthalmoscopy, additional blood tests were requested. An autoimmune vasculitis screen was negative. IgA, IgG, IgM and complement (C3 and C4) levels were normal. A blood-borne viral screen was negative for HIV, hepatitis A, hepatitis B and hepatitis C infections. Lyme serology was negative. As part of the systemic screen, a tuberculosis (TB) enzyme-linked immune absorbent spot blood test was sent. This was found to be positive. The patient was assessed for active TB and no evidence of active infection was identified. TB did not fit clinically with the presentation. The patient was assumed to have latent TB, since he had not been treated for TB previously. This may require treatment in the future if he requires immunosuppression, but it was not implicated in this acute presentation.

A syphilis serology test was sent on the second day of admission. The results of this, which were available 3 days later, were positive: the rapid plasma reagin was positive at a titre of 1:256 and *Treponema pallidum* particle agglutination was positive. Significant blood test results are summarised in table 1.

Due to concerns over the possibility of neurological involvement, a lumbar puncture was undertaken. The opening pressure was normal, the cerebrospinal fluid (CSF) protein level was elevated at 0.57 g/L (normal reference value 0.15–0.45 g/L) and

Table 1 Summary of key blood test results

Test	Result	Normal reference value
Haemoglobin	143 g/L	130–168 g/L
White cell count	$10.0 \times 10^9/\text{L}$	$4.2\text{--}10.6 \times 10^9/\text{L}$
Neutrophils	$5.6 \times 10^9/\text{L}$	$2.0\text{--}7.1 \times 10^9/\text{L}$
Lymphocytes	$3.1 \times 10^9/\text{L}$	$1.1\text{--}3.6 \times 10^9/\text{L}$
Monocytes	$1.1 \times 10^9/\text{L}$	$0.3\text{--}0.9 \times 10^9/\text{L}$
Eosinophils	$0.1 \times 10^9/\text{L}$	$0.0\text{--}0.5 \times 10^9/\text{L}$
Erythrocyte sedimentation rate	37 mm/hour	0–10 mm/hour
C reactive protein	11.6 mg/L	0.0–5.0 mg/L
Ferritin	896 µg/L	20–300 µg/L
Vitamin B ₁₂	263 ng/L	160–800 ng/L
Folate	2.5 ng/mL	>2.7 ng/mL
Thyroid stimulating hormone	0.84 mU/L	0.30–4.20 mU/L
Free thyroxine (T4)	13.0 pmol/L	9.0–23.0 pmol/L
Glucose	6.4 mmol/L	3.0–7.8 mmol/L
Glycated haemoglobin (HbA1c)	32 mmol/mol	20–41 mmol/mol
ACE	43 IU/L	10–70 IU/L
Complement C3	1.41 g/L	0.70–1.70 g/L
Complement C4	0.34 g/L	0.16–0.54 g/L
IgA	3.85 g/L	0.80–4.00 g/L
IgG	15.8 g/L	5.3–16.5 g/L
IgM	1.05 g/L	0.50–2.00 g/L
Serum protein electrophoresis	No abnormality detected	
Antinuclear antibody	Negative	
Antineutrophil cytoplasmic antibodies	Negative	
HIV 1 and 2 antibodies	Negative	
Hepatitis A IgM	Negative	
Hepatitis B surface antigen	Negative	
Hepatitis C antibody	Negative	
Tuberculosis enzyme-linked immune absorbent spot	Reactive T-spot: spots>20; PHA+	Spots: 0–5 non-reactive, 6–8 borderline, >8 positive PHA: +Weak PHA reaction, ++Moderate PHA reaction, +++Strong PHA reaction (saturated response)
Borrelia burgdorferi IgG and IgM	Negative	
Syphilis serology	Positive	
Rapid plasma reagin	Positive at a titre of 1:256	
<i>Treponema pallidum</i> particle agglutination	Positive	

the CSF culture was negative. CSF testing for syphilis was not done. The lumbar puncture had already been completed before the syphilis serology results were available. The complete lumbar puncture and CSF results are summarised in table 2.

DIFFERENTIAL DIAGNOSIS

The initial differential diagnosis for the patient's acute painless visual loss included retinal detachment, vitreous haemorrhage, optic neuritis, central retinal vein occlusion, central retinal artery occlusion and internal carotid artery occlusion. Radiological investigations excluded an acute cerebral infarction. Subsequently, taking together the positive syphilis serology, widespread rash and visual symptoms, the patient was diagnosed with secondary syphilis with ocular involvement 4 days after his initial presentation to hospital. Of note, the patient reported no genitourinary symptoms.

Table 2 Lumbar puncture results

Test	Result	Normal reference value
Opening pressure	18.5 cm H ₂ O	10–25 cm H ₂ O
CSF appearance	Slightly bloodstained	
CSF microscopy	Four white cells; 1760 red blood cells	Up to five white cells; up to five red blood cells
CSF culture	No growth	
CSF glucose	3.9 mmol/L	1.8–4.7 mmol/L
Serum glucose	6.4 mmol/L	3.0–7.8 mmol/L
CSF protein	0.57 g/L	0.15–0.45 g/L
Serum protein	78 g/L	64–83 g/L
CSF IgG	79 mg/L	0–40 mg/L
CSF albumin	373 mg/L	0–320 mg/L
Serum IgG	16.3 g/L	5.5–14.5 g/L
Serum albumin	45 g/L	33–47 g/L
CSF IgG:albumin ratio	0.21	0.00–0.25
CSF:serum (IgG:albumin)	0.58	0.00–0.85
CSF protein electrophoresis	Both CSF and serum IgG were oligoclonal and showed a similar electrophoretic pattern, indicating a source of oligoclonal IgG outside the central nervous system	
CSF HSV PCR	Negative	
CSF VZV PCR	Negative	
CSF enterovirus PCR	Negative	

CSF, cerebrospinal fluid; HSV, herpes simplex virus; VZV, varicella-zoster virus.

TREATMENT

A clinical decision was made to treat the patient on an inpatient basis. The patient was treated with a 14-day course of intravenous benzylpenicillin and a 3-day course of high-dose oral prednisolone at the time of antibiotic initiation by the genitourinary medicine team. He made a good clinical recovery with almost complete return of vision in his left eye. During his inpatient admission, a respiratory viral PCR screen identified incidental influenza A infection, for which he was treated with a short course of oseltamivir.

OUTCOME AND FOLLOW-UP

Two months following discharge from hospital, the patient was reviewed in the ophthalmology clinic, where the optic disc swelling was noted to have resolved and the bilateral vitritis had improved. Repeat ophthalmology review after a further 2 months revealed that the patient had a persisting small patch of blurred vision in his left eye, minimal vitreous inflammation and no other symptoms. The ophthalmologists advised that the symptoms would likely resolve over time and discharged the patient from further ophthalmology follow-up.

DISCUSSION

Syphilis is an infection caused by the spirochete bacterium *T. pallidum*. Acquired syphilis is divided into four stages⁴:

1. Primary infection: characterised by a painless ulcer, or chancre, typically found in the anogenital region with localised lymphadenopathy; although it should be noted that perioral or oral chancres are also being seen more commonly.
2. Secondary infection: signalled by more systemic involvement; often heralded by a rash (papular, macular or both), which is more common on the trunk, upper limbs, hands or soles, but can affect any part of the body and may be subtle in appearance; the start of multiorgan involvement can also be seen at this stage.

3. Latent stage: typically no signs or symptoms.
4. Tertiary syphilis: as signs and symptoms of secondary infection disappear, there may be widespread organ involvement, including neurological, cardiovascular and gummatous disease; complications may be fatal.

Ocular manifestations of syphilis may occur at any stage of the disease. These include anterior, intermediate or posterior uveitis; panuveitis; retinitis; interstitial keratitis; placoid chorioretinitis; papillitis; retinal vasculitis; and cranial nerve and optic neuropathies.^{3,5} Syphilitic uveitis has been shown to be associated with inflammatory ocular hypertension syndrome.⁶ The British Ocular Syphilis Study, a prospective epidemiological study, demonstrated that intraocular syphilis has an annual incidence of 0.3 per million adults in the UK, with bilateral ocular involvement affecting 56% of patients and panuveitis being the most common diagnosis, affecting 41.3% of patients.⁷

Visual symptoms may be the presenting feature of multisystem disease caused by syphilis. It has been reported that ocular symptoms develop after a median time of 11 months from the time of syphilis infection onset⁸ and that ocular syphilis may precede a diagnosis of systemic syphilis in half of syphilis patients.⁹ For patients presenting with ocular syphilis, the most common concurrent complaints are a skin rash and headache.³ The diagnosis of ocular syphilis should prompt screening for underlying immunosuppression, specifically undiagnosed HIV infection: a systematic review has shown that a diagnosis of ocular syphilis led to HIV infection being diagnosed in 52% of cases.¹⁰

Ocular syphilis is treated in the same way as neurosyphilis. As per British Association for Sexual Health and HIV guidelines, the recommended treatment regimen consists of either procaine penicillin 1.8–2.4 MU intramuscularly once daily plus probenecid 500 mg orally four times per day for 14 days; or benzylpenicillin 1.8–2.4 g intravenously every 4 hours for 14 days. In addition, 40–60 mg of prednisolone should be administered once daily for 3 days, starting 24 hours prior to commencement of antibiotics.⁴ While it has been suggested that the administration of steroids may reduce the risk of the Jarisch–Herxheimer reaction during anti-treponemal antibiotic therapy, the evidence underlying the benefits of concomitant steroid therapy remains unclear.¹¹

Ensuring prompt diagnosis of syphilis will reduce the likelihood of complications such as ocular involvement. Diagnostic delay runs the risk of long-term visual problems developing. Given the rising incidence of syphilis infection and the potential for ocular complications when syphilis is untreated, it is

Learning points

- ▶ Visual symptoms may be the presenting feature of multisystem disease.
- ▶ When patients present with acute visual loss, a comprehensive medical history should be elicited which incorporates questions to exclude a possible infective aetiology.
- ▶ Unexplained multisystemic symptoms, such as loss of vision in combination with dermatological involvement, should prompt investigations for autoimmune causes, blood-borne viruses and syphilis infection.
- ▶ Patients with serologically confirmed syphilis may not necessarily recall or report a history of acute genitourinary symptoms; a high index of clinical suspicion should be maintained.

important for physicians to consider the infection as part of the differential diagnosis when reviewing patients presenting with unexplained ocular symptoms, particularly in the presence of other systemic symptoms such as dermatological involvement. Prompt diagnosis and treatment should result in rapid clinical improvement.

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