CASE REPORT

Syphilitic jaundice: a rare manifestation of the secondary stage presenting a missed opportunity to prevent ocular syphilis

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SUMMARY

The classical presentation of secondary syphilis comprises skin rashes, mucosal ulceration and lymphadenopathy. However, this disseminated stage can also present with symptoms and signs of ocular, neurological, pulmonary, renal, musculoskeletal and digestive tract disease.

We report the case of a gay man who presented with icteric hepatitis. Although he underwent an exhaustive series of investigations (some of which were invasive), syphilis was not initially considered in the differential diagnosis. His jaundice resolved spontaneously, but he subsequently developed an acute optic neuritis. Early syphilis is relatively common in men who have sex with men (MSM). Prompt diagnosis and treatment in this case would have prevented ocular involvement. Syphilis testing should be considered in all MSM presenting with unexplained symptoms and signs.

BACKGROUND

Dissemination of the spirochaete bacterium *Treponema pallidum* in the secondary stage of syphilis classically produces a triad of clinical signs, namely skin rashes, lymphadenopathy and mucosal ulceration. Although subclinical hepatitis in the secondary stage is not uncommon, frank jaundice is rare. Ocular involvement can also be seen as part of the spectrum of 'early neurosyphilis'.

We report a case of a young man who presented with icteric syphilitic hepatitis and subsequently developed optic neuritis. Prompt diagnosis of the syphilis would have prevented the development of ocular syphilis in this patient.

CASE PRESENTATION

A 36-year-old British man, who has sex with men, presented to a walk-in clinic with a 3-week history of nausea, pharyngitis, malaise, abdominal pain, weight loss, night sweats and an itchy skin rash. He was previously well and took no medication. He used no recreational drugs and drank alcohol in moderation. He had not travelled abroad for over 1 year and had no pets.

Physical examination revealed jaundice, a macular rash on his thorax, cervical and postauricular lymphadenopathy, and right upper quadrant abdominal tenderness.

He was admitted to hospital under a surgical team. Blood tests confirmed cholestatic hepatitis. Having excluded extrahepatic biliary obstruction

on ultrasound scanning, his care was transferred to the gastroenterology team. Serological tests for viral causes of hepatitis were negative, apart from a positive cytomegalovirus (CMV) IgM antibody test. He was referred to the department of infectious diseases. At this time he was feeling much better and the rash and jaundice had resolved. It was thought that the positive CMV result was a false-positive as on repeat testing, some weeks later, CMV IgM and IgG were negative. Treponemal serology was however reactive. He was then referred to the department of sexual health.

At this time he complained of a recent-onset right-sided headache and blurred vision in his right eye.

On examination, there were no mucocutaneous signs of syphilis, but his right optic disc appeared oedematous. Neurological examination was otherwise normal. An urgent ophthalmic referral confirmed optic neuritis. Neuroimaging of the head was normal and cerebrospinal fluid (CSF) studies confirmed neurosyphilis.

INVESTIGATIONS

At initial presentation serum bilirubin was 35 µmol/L (0–20), alanine aminotransferase 291 µ/L (7–40) and alkaline phosphatase 946 µ/L (30–130). Liver function and clotting tests were normal. Serological tests for hepatitis viruses A, B, C and E and HIV were negative initially and at interval testing. Tests for antibodies to Epstein-Barr virus were IgG-positive, IgM-negative, and CMV IgM-positive and IgG-negative (subsequently IgM-negative and IgG-negative on repeat testing).

Abdominal ultrasound scanning excluded hepatobiliary obstruction but demonstrated inflamed appearances of the liver and slight enlargement of the spleen. Magnetic resonance cholangiopancreatography was normal. CT scans of the thorax/abdomen/pelvis revealed small-volume lymph nodes in the neck, axilla and chest. A lobulated centrally necrotic mass (probably lymphatic) was seen in the right cardiophrenic area and a centrally necrotic mass along the left lateral chest wall. Needle aspiration of cervical and mediastinal lymph nodes showed reactive histological changes but no evidence of lymphoma. Serological tests showed rapid plasma reagin (RPR) test positive at >1:128 and *T. pallidum* particle agglutination

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test (TPPA) positive at >1:5120. CSF testing showed the following: RPR positive at 1:2, TPPA >1:5120, lymphocytes 35 cells/mm³, polymorphs <1, erythrocytes <1 and protein 0.79 g/L (0.1–0.4).

A magnetic resonance head scan was normal and the lymphadenopathy seen on CT scanning resolved after syphilis treatment.

DIFFERENTIAL DIAGNOSES

Jaundice

Hepatobiliary tract obstruction, viral hepatitis, lymphoma, drugs, alcohol.

Optic neuritis

Demyelinating pathology, neuromyelitis optica, autoimmune disorders, Lyme disease, cat scratch fever, measles, mumps and herpes simplex virus.

TREATMENT

The patient was treated with a 14-day course of intramuscular procaine penicillin G 1.8 Mu and oral probenecid 500mg four times a day, in line with the British Association of Sexual Health and HIV treatment guidelines for neurological syphilis.¹ A 3-day course of oral prednisolone 40mg daily was started 24 hours before starting antibiotics.

He also received 1% cyclopentolate hydrochloride and 0.1% dexamethasone eye-drops.

OUTCOME AND FOLLOW-UP

After treatment, the patient's serum RPR rapidly achieved a four-fold drop, indicating serological cure of syphilis. A post-treatment lumbar puncture is planned to ensure neurological cure. In the first few months after treatment, he remained lethargic and low in mood and was absent from work for a significant time. He remains under review by the ophthalmology team, and although his vision improved after treatment it has not returned to normal.

DISCUSSION

Sexual health clinics offer HIV and syphilis tests to all patients, irrespective of their sexuality.

The incidence of early (infectious) syphilis is, like HIV, much higher in men who have sex with men than in the heterosexual population. The classical presentation of secondary syphilis comprises skin rashes, mucosal ulceration and lymphadenopathy.² From the outset this patient was open about being a man who has sex with man, and although he presented with two elements (skin rash and generalised lymphadenopathy) of the classical triad of signs, syphilis was not considered.

The secondary stage can also manifest with ocular, neurological, pulmonary, renal, musculoskeletal and digestive tract disease. While subclinical hepatitis is thought to occur in up to 10% of patients with secondary syphilis, icteric hepatitis has been reported only rarely.^{3–6}

Although ocular syphilis remains uncommon, the exponential rise in rates of infectious syphilis seen in developed countries

in the last 20 years has resulted in increasing reports of syphilitic eye disease. The authors of the British Ocular Syphilis Study (BOSS) estimated that ocular syphilis occurred in 0.6% of cases of early syphilis.⁷ This figure is similar to that reported in the USA.⁸ Optic neuritis was diagnosed in 24% of patients in the BOSS study, although panuveitis was the most common diagnosis, affecting 41.3% of patients.

Although our patient underwent an exhaustive series of investigations (some of which were invasive), syphilis serology was not performed until 12 weeks after his initial presentation.

Early diagnosis and treatment of syphilis would have prevented ocular involvement.

In 2016 diagnoses of early syphilis in England reached their highest level since 1949.⁹ In light of this increase, it is more important than ever that physicians in specialties other than sexual health are aware that the great imitator may challenge their diagnostic skills.

Learning points

- ▶ The incidence of syphilis, like HIV infection, is disproportionately high in men who have sex with men (MSM).
- ▶ Syphilis is an uncommon cause of icteric hepatitis.
- ▶ The occurrence of signs of secondary syphilis such as skin rashes and lymphadenopathy (and in this case jaundice) may presage more serious complications such as ocular syphilis.
- ▶ MSM presenting with unexplained symptoms and signs should be tested for syphilis.

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