# Secondary syphilis: a multisystem disease not to be forgotten

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## INTRODUCTION

Syphilis is a sexually-transmitted disease caused by the spirochaetal organism *Treponema pallidum*, and is characterized by the appearance of a painless indurated ulcer at the site of inoculation – the primary chancre. Secondary syphilis occurs 2–6 months after the primary chancre and results from haematological dissemination of the organism. As a result, nearly any organ system may be involved, giving rise to protean signs and symptoms which commonly mimic other diseases.

The authors present a case of secondary syphilis with multisystem involvement and concomitant human immunodeficiency virus (HIV) infection. Also discussed are the implications of HIV infection on the course and treatment of syphilis.

## DISCUSSION

The number of cases of infectious syphilis reported at genitourinary clinics in the UK has risen from 0.5 to 3.0 per 100 000 of the population between 1995 and 2001 (Public Health Laboratory Service et al, 2002). Therefore, physicians need to consider the diagnosis in any patient who presents with multisystem disease.

Secondary syphilis usually presents with fever, malaise, lymphadenopathy, and a macular exanthem progressing to a coppery-red papular eruption affecting the trunk, palms and soles. The primary chancre may go unnoticed. The psoriasiform eruption over the palms and soles in this case is usually seen in patients from the African sub-continent (World Health Organization, 1982).

## CASE REPORT

A 42-year-old homosexual man presented with a 3-month history of painful mouth ulcers and a hyperkeratotic, erythematous scaly rash affecting his palms and soles (*Figure 1*). He also had a 2-month history of bilateral anterior tibial pain, balanitis and a panuveitis. There was a recent history of a non-specific urethritis and a past history of shingles. In addition to the rash affecting his palms and soles, he had facial seborrhoeic dermatitis, mucosal ulceration with leukoplakia, and a balanitis with phimosis. A tender firm lump was noted over his left anterior shin. He was apyrexial and there was no lymphadenopathy or hepatosplenomegaly.

Routine investigations revealed a raised erythrocyte sedimentation rate of 42 mm/h, associated with a polyclonal rise of immunoglobulins with a normal full blood count and C-reactive protein. A plantar skin biopsy showed numerous plasma cells in addition to lymphocytes within the papillary dermis (*Figure 2*). A Warthin–Starry stain for bacteria was negative. At the same time as the skin biopsy his vision worsened with bilateral mid-peripheral retinitis in addition to panuveitis. The skin biopsy showing numerous plasma cells and the mid-peripheral distribution of the retinitis were highly suggestive of secondary syphilis.

The diagnosis of secondary syphilis was confirmed by a positive venereal disease research laboratory (VDRL) titre of 1:256, in association with a positive fluorescent treponemal antibody (FTA) test and treponema pallidum haemagglutination assay. He was also found to be positive for human immunodeficiency virus with a CD4 (t-helper cell) count of 145 x $10^6$/litre (10.5%), and a viral load of 115 305 copies/ml. X-rays of his tibial bones revealed bilateral lytic cortical lesions, in keeping with a syphilitic osteitis. The firm tender lump over his left shin corresponded to a cortical lesion with a marked periosteal reaction (*Figure 3*).

He was given a 10-day course of high-dose intravenous benzylpenicillin, after which his skin and mucosal lesions had almost resolved. The initial ocular inflammatory reaction settled quickly but visual acuity deteriorated 2 days after the commencement of penicillin, thought to result from an intraocular Jarisch–Herxheimer reaction. This complication was treated with a tapering dose of oral prednisolone, starting at a dose of 60 mg/day. His visual acuity subsequently returned to normal leaving a residual typical 'salt and pepper' scarring in the fundus (*Figure 4*).

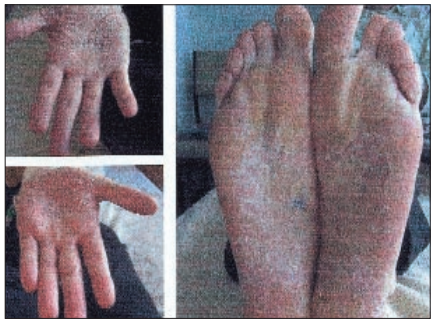
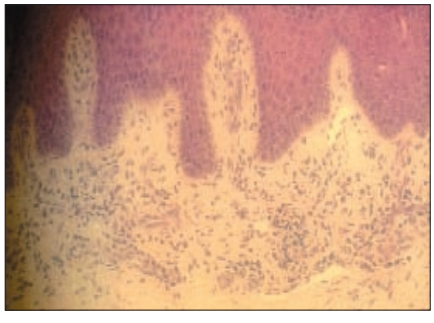


***Figure 1. Scaly symmetrical eruption over palms and soles.***

Histological examination of skin biopsies taken from lesions of secondary syphilis commonly show a high percentage of plasma cells within the dermal inflammatory cell infiltrate. Although several histological patterns have been associated with secondary syphilis, the presence of numerous plasma cells, with or without granuloma formation, warrants syphilis serology testing. In addition to skin involvement, there was evidence of mucosal, ophthalmological and musculoskeletal involvement in this case.

The mucosal lesions of secondary syphilis are known as 'mucous patches'.

***Figure 2. Plantar skin biopsy showing numerous plasma cells infiltrating the dermis.***



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These are small macules or papules covered by a white to grey hyperkeratotic membrane. Spirochaetes may be demonstrated from smears of these lesions by dark ground microscopy.

The ophthalmological manifestations of syphilis include granulomatous conjunctivitis, uveitis, retinitis and optic atrophy (Aldave et al, 2001).

The differential diagnosis of retinitis in HIV-positive individuals includes syphilis, cytomegalovirus (CMV) infection, acute retinal necrosis secondary to herpes simplex virus (HSV) or varicella zoster virus (VZV), lymphoma, and toxoplasmosis. The mid-peripheral distribution of the retinitis was strongly suggestive of syphilis. In HSV and VZV the retinitis tends to start in the far periphery, toxoplasmosis may be associated with an old scar, and CMV infection usually has much less inflammation and is commoner at a lower CD4+ (t-helper cell) count. A vitreous sample had been taken for PCR (polymerase chain reaction) and was negative for HSV, VZV and CMV. In addition, serology for toxoplasmosis was negative.

Reiter's syndrome was included in the differential diagnosis given his non-specific urethritis, balanitis, human leucocyte antigen-B27 (HLA-B27) positivity, uveitis and the psoriasiform eruption which may have represented atypical keratoderma blenorrhagicum. Reiter's syndrome, however, is not associated with a retinits.

The musculoskeletal manifestations of secondary syphilis include polyarthralgias, polyarthritis, tenosynovitis, spondylitis, periostitis and osteitis. Bone involvement in secondary syphilis has been reported to occur in 0.15–9.7% of patients (Reginato, 1993). This patient had cortical lytic lesions in both tibial bones, in keeping with a syphilitic osteitis and periostitis. Other bones commonly involved include the skull and sternoclavicular bones.

Penicillin remains the treatment of choice for all stages of syphilis, but high-dose intravenous penicillin is necessary for both ocular and neurological complications (van Voorst Vader, 1998). All other forms of syphilis can be treated with intramuscular preparations of penicillin or oral erythromycin in penicillin-allergic patients.

The deterioration in this patient's visual acuity soon after the commencement of penicillin was felt to be a result of an intraocular Jarisch–Herxheimer reaction; there was an increase in intraocular inflammation associated with the visual loss, which responded rapidly to systemic steroids. Severe reactions are managed with systemic corticosteroid therapy and penicillin.

The presentation of syphilis may be more exuberant and atypical in the presence of HIV (Hutchinson et al, 1994). However, the majority of HIV patients present with similar manifestations as those without HIV infection, and have similar treatment responses. HIV infection has been associated with a more rapid progression of secondary syphilis to its tertiary stage. There have been many case reports of HIV patients with negative syphilis serology and the subsequent development of neurosyphilis within 2–3 years (Czelusta et al, 2000). It is important to note that the serological response may be impaired in the presence of concomitant HIV infection. Therefore in patients with clinical findings suggestive of syphilis but negative syphilis serology, alternative investigations such as direct fluorescent antibody testing or PCR analysis of lesional material should be performed.

This patient's antiretroviral therapy was deliberately delayed in order to avoid worsening of his intraocular inflammation secondary to the immune reconstitution syndrome (Furrer and Fux, 2002). The immune reconstitution syndrome describes worsening of neoplastic, inflammatory or infectious conditions secondary to a rise in the CD4 count after commencing anti-retroviral therapy. This phenomenon has been well described for tuberculosis, *Pneumocystis carinii* pneumonia, CMV infection, and Kaposi's sarcoma within the context of HIV infection.

## CONCLUSIONS

The numerous manifestations of secondary syphilis, as demonstrated by this patient, explain its ability to act as a 'great imitator' of many diseases. This case also highlights the importance of syphilis serology testing in patients presenting with multisystem disease. As HIV infection and syphilis have close epidemiological association, it is strongly recommended that patients with syphilis are offered HIV testing and vice versa. **HM**

*Figure 3. Left tibial X-ray demonstrating a lytic cortical lesion with a marked periosteal reaction.*

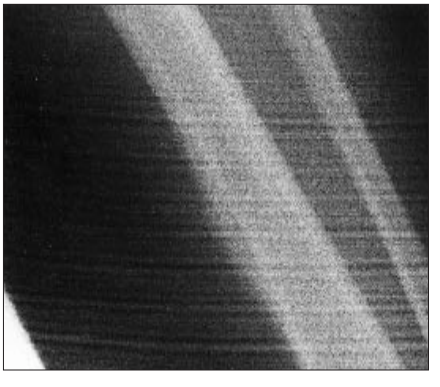
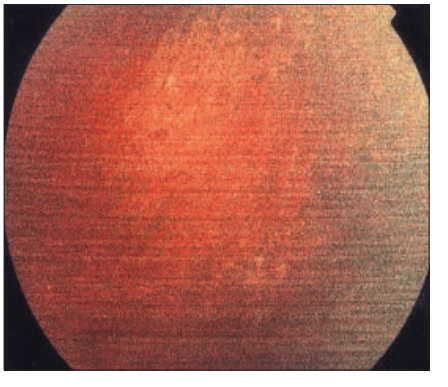


*Figure 4. Retinal photograph showing 'salt and pepper' scarring characteristic of syphilitic retinitis.*

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