Case Report

The 2012 syphilis & HIV combo

二零一二年的梅毒與愛滋病病毒雙併

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We report a case of a homosexual male patient with an unusual presentation of syphilis and HIV co-infection. The initial skin problem on the scalp appeared banal and seborrhoeic. However, this soon became multifocal and general symptoms developed as well. The patient's personal history signalled the possibilities of sexually transmitted diseases. Subsequent investigations unfolded a modern dermatological tale of sex in a city.

Keywords: Eosinophilic folliculitis, great imitator, HIV, syphilis

Introduction

The historical epithet for syphilis as "the great imitator", a term first coined by Sir William Osler in 1897, remains appropriate today. With its often complex and varied clinical presentations, the diagnosis of syphilis should always be considered in the at-risk patient. In addition, there has been a worldwide escalation in the number of reported cases since 2001 and that has not abated. Indeed syphilis, which was first recognised in the 15th century, has well and truly re-established its position as an important global disease.

Case report

We report a 37-year-old patient who presented with a three-month history of night sweats and constitutional symptoms. The patient had migrated to Australia from India 13 years previously. He was a homosexual male who had had unprotected sexual intercourse, as well as intravenous drug use. He had never had investigations for HIV, hepatitis or other sexually transmitted infections.

This patient was initially admitted to hospital with fever, weight loss, myalgia and arthralgia. Chest imaging demonstrated bilateral lung opacities in
the absence of any respiratory symptomatology. The dermatology team was consulted when he developed psoriasiform plaques on his right parietal scalp, followed by multiple tender, erythematous plaques on his scalp, upper body and palms that rapidly disseminated (Figures 1 and 2). Multiple erythematous nodules then appeared on his genitalia, including a symptomatic ulcer. He had no palpable lymphadenopathy, or any evidence of ocular or oral mucosal involvement. Based on the history and cutaneous findings, the dermatology team favoured the possibility of HIV infection, eosinophilic folliculitis and secondary syphilis.

A skin biopsy from a scalp lesion was taken to help elucidate the likely diagnosis. The biopsy showed a predominantly granulomatous pattern extending into the subcutis. The granulomas were non-necrotising, and were centred on neurovascular bundles, with a surrounding lymphocytic infiltrate. Some vessels showed endothelial cell swelling, but no intimal fibrosis was seen. Plasma cells were not prominent. Multiple stains for micro-organisms including a Ziehl-Neelsen stain, periodic acid-Schiff stain and a Warthin-Starry stain were all negative. Mycobacterial polymerase chain reaction (PCR) was negative on the tissue sample. Despite the negative special stains, the histologic appearance was most consistent with infective causes including atypical mycobacteria, fungi and syphilis, although systemic granulomatous disorders such as sarcoidosis could not be entirely excluded histologically (Figure 3). In view of the above findings, the patient was tested for HIV and found to be HIV ELISA and Western blot positive. He was also found to have a very strongly positive syphilis rapid plasma reagent titre and positive syphilis antibody enzyme immunoassay screen, confirming a diagnosis of secondary syphilis. The remainder of the screen for sexually transmitted infections was negative.

The patient was commenced on intravenous benzylpenicillin. After two days of intravenous

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**Figure 1.** Psoriasiform lesions on the scalp and erythematous papules and nodules on the forehead and cheeks.

**Figure 2.** Characteristic lesions on the palms.
therapy there was pleasing clinical improvement. He was discharged with ten days of one gram daily intramuscular procaine penicillin to be administered as an outpatient by his general practitioner. His cutaneous lesions began to fade within a week and at dermatology follow-up two months later, the skin lesions had resolved completely. His systemic symptoms had also resolved. On discharge, his HIV viral load count was 15,197 copies RNA/ml and his CD4 T lymphocyte count was 480x10^6/L. He was reviewed by both the immunologists and infectious disease physicians who commenced him on anti-retroviral therapy. At present he is generally well and without any skin problems.

Discussion

Syphilis, a disease caused by the spirochete Treponema pallidum, continues to be an important and increasingly prevalent public health problem with an estimated annual global incidence of 12 million.\(^1\) After declining to historically low levels in the 1990s, rates of syphilis began to increase again in 2001, largely amongst homosexual men.\(^2,3\) Indeed syphilis has re-emerged and resurfaced among homosexually active men in Sydney, leading to a 10-fold increase in the number of syphilis notifications in inner Sydney between 1999 and 2003.\(^4\)

Data from the Centers for Disease Control and Prevention in the United States showed that this trend has continued through to 2007 with 64 percent of reported cases being in homosexual or bisexual men.\(^5\) This is likely to have been fuelled by increased risk-taking behaviour and related to optimism generated by improved HIV treatment, modified sexual networks due to the internet and "recreational" drug use.\(^1\) HIV-positive men represent between 40-54% of reported cases.\(^4,6\) Individuals who are infected with HIV are particularly susceptible to contracting and spreading syphilis and are often unaware of either diagnosis.\(^7\) This combined sexual health problem has been well demonstrated in our patient.

Syphilis also remains an important public health concern in other parts of the world. The World Health Organization has demonstrated a significant increase in new cases of syphilis in North America, Europe, Africa, the Middle East, Latin America, the Caribbean, Central Asia and Southeast Asia.\(^8\) In China, a national surveillance programme demonstrated that after the virtual eradication of syphilis in the 1960s to the 1980s, syphilis has re-emerged with a total of 74,000 cases of primary and secondary syphilis diagnosed in 2005 alone.\(^9\)

Syphilis has generally been accepted and referred to as "the great imitator" because of its broad spectrum of clinical manifestations.\(^10\) In the parallel world of clinical dermatology, the senior author notes that adverse cutaneous drug reactions come close as a burgeoning and ubiquitous imitator.

In this case report, we note that there are characteristic cutaneous manifestations which have been captured in Table 1. To begin with, there is usually an incubation period during which there are no associated symptoms. The typically painless chancre or ulcer of primary syphilis then

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**Figure 3.** A punch biopsy from the scalp demonstrating non-necrotising granulomas.
appears at the site of inoculation, accompanied by regional lymphadenopathy, up to three months after infection begins. Shortly after, syphilis develops into a systemic infection. Cutaneous manifestations typify secondary syphilis, with eruptions that are characteristically macular, maculopapular, papular or annular. However, Wolff acknowledges that uncommonly lesions of secondary syphilis and a chancre of primary syphilis can occur concomitantly, and that atypically genital chancres may be painful. In our patient, the cutaneous features of secondary syphilis in fact appeared before the syphilitic chancre at the likely site of his inoculation. In addition he had a penile ulcer that was tender. This illustrates the variability in clinical presentations that can occur. As a consequence clinicians can be somewhat confounded.

Apart from the clinical diagnostic limitations and challenges, the histological findings of syphilis have been described as protean and non-specific. The common finding of granulomas as demonstrated in our patient, is not, in itself, helpful diagnostically. In reality, the list of differential diagnoses is lengthy and varied. Nevertheless, it may be useful to include a list of cutaneous problems associated with HIV infection, as shown in Table 2.

Of particular note in this case is the differential diagnosis of eosinophilic pustular folliculitis. Classic eosinophilic pustular folliculitis, or Ofuji's disease, is a chronic and relapsing dermatosis that is predominantly reported in East Asian populations and commonly associated with HIV infection. It is an eosinophilic infiltration of hair follicles that responds well to treatment with indomethacin. Clinically, the disease typically begins as small papules, which enlarge and coalesce into a large plaque mainly distributed in seborrhoeic areas including on the face, upper

<table>
<thead>
<tr>
<th>Primary syphilis</th>
<th>Secondary syphilis</th>
<th>Tertiary/late syphilis</th>
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<tr>
<td>• Localised chancre at the site of inoculation</td>
<td>• Disseminated infection manifesting as a macular, maculopapular, papular or annular eruption anywhere on the body</td>
<td>• Nodular or papulosquamous plaques that may ulcerate</td>
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<tr>
<td>• Occurs ten days to three months after infection begins</td>
<td>• Can be papulosquamous, pustular or acneiform</td>
<td>• Occurs late in untreated syphilis</td>
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<td>• Occurs two to ten weeks after appearance of the primary chancre</td>
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Table 2. Cutaneous problems related to HIV infection

- Acute retroviral syndrome
- Kaposi’s sarcoma
- Reiter’s syndrome
- Eosinophilic folliculitis
- Primary or recurrent herpes zoster
- Disseminated molluscum contagiosum
- Cutaneous findings of hepatitis C in a co-infected patient
- Other sexually transmitted and infective causes – bacterial, mycobacterial, viral, fungal and parasitic
- Adverse cutaneous drug eruptions
- Florid and resistant seborrhoeic dermatitis
back, and upper extremities. The eruptions are often associated with peripheral blood eosinophilia.

From a global health perspective, the use of penicillin for all stages of syphilis has resulted in dramatic decreases in the incidence of syphilis and associated morbidity and mortality over the last 65 years. However, global persistence of syphilis and its recent re-emergence are grim reminders that there is no room for complacency in the ongoing efforts to eliminate this problem. Importantly, the HIV and syphilis epidemics have been described as reflecting an "epidemiological synergy" whereby each infection modifies the natural history of the other and possibly mutually enhancing transmission.1 Not only are syphilis incidence rates higher among HIV-infected patients, but evidence suggests that HIV-infected patients have a poorer response to therapy than HIV-negative patients, and are frequently diagnosed with more advanced stages of the disease.3 In addition, reinfection with syphilis is higher among HIV-infected patients, possibly as a result of unsafe sexual behaviour among this cohort. This emphasises the need to screen HIV-infected patients regularly and to educate patients that there is no immunity gained from prior infection with syphilis.

**Conclusion**

Syphilis, with its varied clinical manifestations, remains "the great imitator" in medicine. Consequently, an incorrect or missed diagnosis is not uncommon. From a public health perspective it is important to note that this once quiescent disease is increasing in frequency again. This is accompanied by a disturbing pattern of HIV co-infection, with up to 40-54% reported cases of syphilis in inner Sydney,4,5 and 28% in the United States occurring in HIV positive men.6 Our case illustrates the importance of careful history taking and the recognition of diagnostically distinctive clinical manifestations. Lest we forget: when in doubt always consider the diagnosis of syphilis and HIV in the at-risk patient.

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**References**