Hong Kong J. Dermatol. Venereol. (2012) **20**, 115-119

Case Report

The 2012 syphilis & HIV combo

二零一二年的梅毒與愛滋病病毒雙併

SS Kumar and S Lee 李啓焱

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.

我們報告一例男同性戀病患的梅毒及愛滋病病毒雙重感染的不尋常表現。其最先在頭皮出現平常的脂溢性皮炎；但不久即出現其他病灶及全身的症狀。病患的個人陳述引起性傳染病的懷疑，而繼後的檢查亦揭示了一個現代都會中的皮膚科性事典故。

Keywords: Eosinophilic folliculitis, great imitator, HIV, syphilis

關鍵詞：嗜酸性毛囊炎，超級模仿者，愛滋病病毒，梅毒

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.

Department of Dermatology, Concord Repatriation General Hospital, Sydney, Australia

SS Kumar, MBBS, BSc(Med)

S Lee, MBBS(Hons), DDM(Syd), FACD

Correspondence to: Professor Stephen Lee AM

Department of Dermatology, Concord Repatriation General Hospital, University of Sydney, NSW 2139, Australia

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

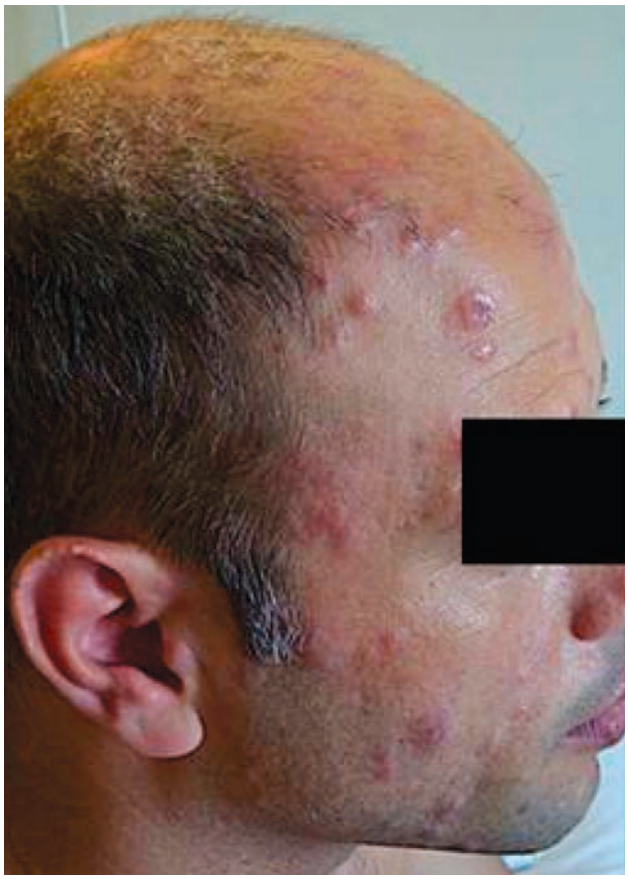

Figure 1. Psoriasiform lesions on the scalp and erythematous papules and nodules on the forehead and cheeks.

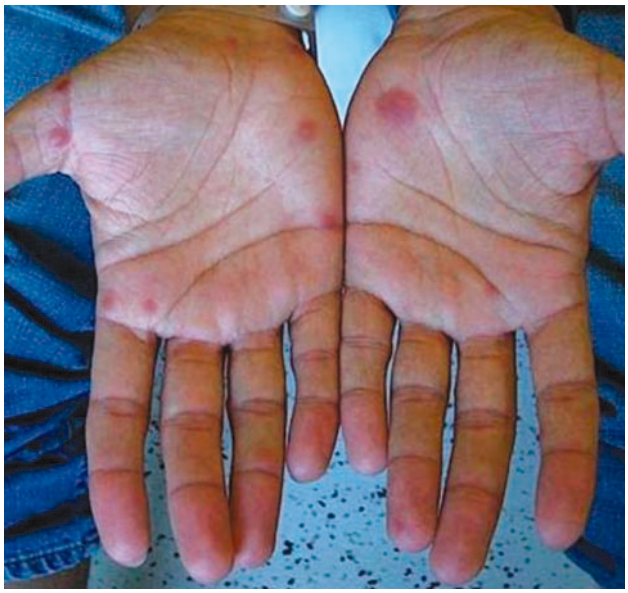

Figure 2. Characteristic lesions on the palms.

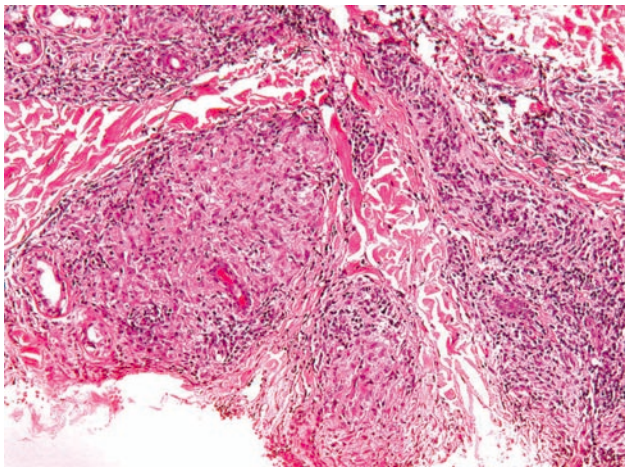

Figure 3. A punch biopsy from the scalp demonstrating non-necrotising granulomas.

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 re-surfaced 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

appears at the site of inoculation, accompanied by regional lymphadenopathy, up to three months after infection begins.[11] Shortly after, syphilis develops into a systemic infection. Cutaneous manifestations typify secondary syphilis,[7] with eruptions that are characteristically macular, maculopapular, papular or annular.[12] 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.[11] 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.[13] 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.[14,15] 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 1. Cutaneous manifestations of syphilis

Primary syphilis	Secondary syphilis	Tertiary/late syphilis
• Localised chancre at the site of inoculation • Occurs ten days to three months after infection begins	• Disseminated infection manifesting as a macular, maculopapular, papular or annular eruption anywhere on the body • Can be papulosquamous, pustular or acneiform • Occurs two to ten weeks after appearance of the primary chancre	• Nodular or papulosquamous plaques that may ulcerate • Occurs late in untreated syphilis

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.[16] 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.

Acknowledgement

The authors wish to thank Dr Stephen Mann, FRCPA, for his valuable assistance in the preparation of this manuscript.

References

1. Douglas JM. Penicillin treatment of syphilis: clearing away the shadow on the land. JAMA 2009;301:769-71.
2. Rouphael NG, Moanna A, Rimland D. Seronegative syphilis in an AIDS patient: Case report and review of the literature. Infect Dis Clin Pract 2008;16:330-1.
3. Horberg MA, Ranatunga DK, Quesenberry CP, Klein DB, Silverberg MJ. Syphilis epidemiology and clinical outcomes in HIV-infected and HIV-uninfected patients in Kaiser Permanente Northern California. Sex Transm Dis 2010;37:53-8.
4. Jin F, Prestage GP, Kippax SC, Pell CM, Donovan BJ, Kaldor JM, et al. Epidemic syphilis among homosexually active men in Sydney. Med J Aust 2005;183:179-83.
5. Weinstock H. Syphilis in the United States, epidemiology and emerging issues. Paper presented at: 2008 National STD Prevention Conference, 2008 March 10-13; Chicago (IL), USA.
6. Farley CK, Hocking TS, Medland N. Syphilis: back on the rise, but not unstoppable. Med J Aust 2005;183:172-3.
7. Hildreth CJ, Lynm C, Glass RM. Syphilis. JAMA 2009; 301:792.
8. Hook EW, Peeling RW. Syphilis control--a continuing challenge. New Engl J Med 2008;351:122-4.
9. Chen ZQ, Zhang GC, Gong XD, Lin C, Gao X, Liang GJ, et al. Syphilis in China: results of a national surveillance program. Lancet 2007;369:132-8.
10. Dourmishev LA, Dourmishev AL. Syphilis: Uncommon presentations in adults. Clin Dermatol 2005;23:555-64.
11. Wolff K, Johnson R, Suurmond D. Fitzpatrick's colour atlas and synopsis of clinical dermatology: 5th ed. New York: McGraw-Hill 2005. pp. 911-3.
12. Kim JS, Kang MS, Sagong C, Ko JY, Yu HJ. An unusual extensive secondary syphilis: condyloma lata on the umbilicus and perineum and mucous patches on the lips. Clin Exp Dermatol 2009;34:e299-301.
13. Mullins A, Randall M. The great imitator: A case of concurrent primary and secondary syphilis: Poster 163. J Cutan Pathol 2009;36:151-2.
14. Lankerani L, Thompson R. Eosinophilic pustular folliculitis: case report and review of the literature. Cutis 2010;86:190-4.
15. Sufyan W, Tan KB, Wong ST, Lee YS. Eosinophilic pustular folliculitis. Arch Pathol Lab Med 2007;131: 1598-601.
16. Zetola NM, Engelman J, Jensen TP, Klausner JD. Syphilis in the United States: an update for clinicians with an emphasis on HIV co-infection. Mayo Clin Proc 2007; 82:1091-102.