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Palmoplantar keratosis as a primary presentation of secondary syphilis

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ABSTRACT A 36-year-old man of Bangladeshi origin presented with a febrile illness, arthralgia, generalised lymphadenopathy and palmoplantar keratosis. Initially the patient denied any sexual contact, although investigations went on to confirm a diagnosis of secondary syphilis. Subsequently a sexual history was obtained which revealed he regularly attended male saunas and had receptive anal sexual intercourse.

KEYWORDS Men having sex with other men, palmoplantar keratosis, rapid plasma reagin (RPR), syphilis, *Treponema pallidum* particle agglutination (TPPA) test

DECLARATION OF INTERESTS No conflict of interests declared.

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CASE REPORT

A 36-year-old single man of Bangladeshi origin was seen in the medical clinic with a six-week history of headache and influenza-like symptoms and a rash of more recent onset. His headache was daily, centred on the crown of the head, had no other associated features and was relieved by paracetamol. He had additional symptoms of dry cough, generalised arthralgia and feeling hot and sweaty despite the prevailing cold weather. Two weeks earlier he had also noticed an erythematous rash on both palms, which was non-pruritic.

The patient was known to have β-thalassaemia trait and a past history of affective psychosis, with symptoms well controlled on olanzapine and citalopram.

On examination the patient was afebrile. A discrete maculo-papular, hyperpigmented rash with hyperkeratosis was observed, confined to the palms and soles bilaterally (Figure 1). He was also found to have bilateral inguinal and right supraclavicular soft, non-tender, mobile lymphadenopathy. There were no oral or genital lesions. All other systems were unremarkable.

Investigations confirmed the diagnosis of secondary syphilis with positive syphilis IgG/IgM screen and subsequently positive *Treponema pallidum* particle agglutination (TPPA) and rapid plasma reagin (RPR) tests. He was hepatitis B surface antigen (HBsAg), hepatitis A virus IgM, hepatitis C virus IgG and human immunodeficiency viral (HIV) load negative.

A detailed retrospective social history was sought. The patient admitted to use of marijuana but denied intravenous drug use, and said he smoked 20 cigarettes per week and drank approximately three pints of normal-strength lager per week. A sexual history was eventually obtained, which revealed he regularly attended male saunas and had unprotected receptive anal sexual intercourse.

The patient was informed of his diagnosis and counselled regarding his sexual health risk. He was started on a 28-day course of penicillin and has been referred to the genito-urinary clinic for further treatment, contact tracing and follow-up.

DISCUSSION

In 2006, 2,766 cases of infectious syphilis were diagnosed in the UK, a drop of 1% from 2005. This was mostly accounted for by a 19% drop among women, but there was a 2% rise among men.[1] Syphilis had been relatively rare in the UK, but numbers began to increase sharply during the late 1990s until 2005. The rise occurred in many geographical locations, including London, the North West, East and West Midlands, Yorkshire and the Humber, and Scotland, and is associated with increasingly unsafe sexual behaviour among men having sex with other men (MSM).

Our patient presented with features of secondary syphilis. The reason that he did not present with a chancre was thought to be because the original lesion could have been within the rectum or the oropharynx. It is common for chancres to go unnoticed as they are often painless. Approximately 25% of individuals with untreated infection develop a systemic illness, secondary syphilis.[2]

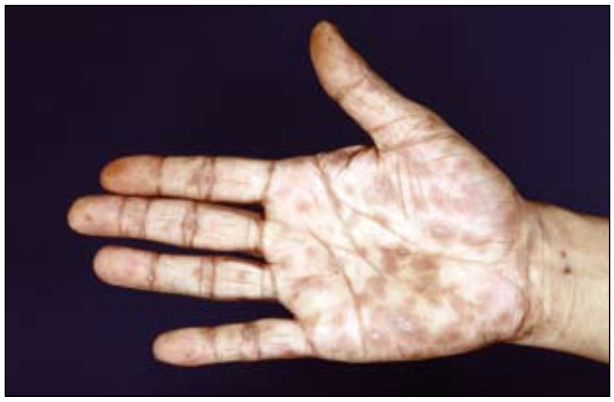
The Centers for Disease Control and Prevention estimate that approximately 64% of all cases of primary and secondary syphilis occur in MSM.[3] The rash is the most characteristic finding of secondary syphilis and can present in any form, except vesicles. Classically, the rash is a symmetrical macular, papular or maculo-papular eruption involving the entire trunk and limbs, including

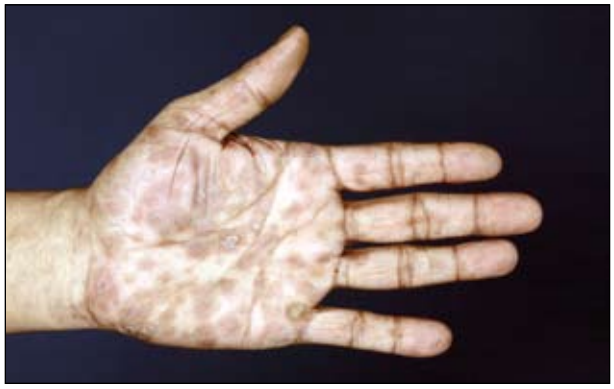
the palms and soles. Individual lesions are discrete red or reddish-brown and measure 0.5–2 cm in diameter. They are often scaly, but may be smooth and, rarely, pustular. The involvement of the palms and soles is an important clue to the diagnosis of secondary syphilis. The lesions may resemble the target lesions of erythema multiforme.[4] Large, raised, grey to white lesions occur in mucous membranes in the mouth and perineum, and may develop in some patients during secondary syphilis. These are referred to as condylomata lata, occur most often in areas proximate to the primary chancre and may reflect the direct spread of organisms from the primary ulcer.[5]

In addition to secondary syphilis, there are other diseases that present with a palmoplantar rash. The palmoplantar keratodermas share the common feature of palmar and plantar hyperkeratosis that manifests as thickening and scaling of the palms and soles. The general underlying defect in the majority of the palmoplantar keratodermas is the overproduction of a normal or an abnormal keratin in the palms and soles. The majority of cases are mild to moderate without systemic problems and with autosomal dominant inheritance.[6,7] Examples of these disorders include Howel-Evans syndrome, a rare autosomal dominant diffuse form with onset between five and 15 years of age.[7] It has been associated with the early development of oesophageal cancer. Another example is Vohwinkel syndrome, a rare autosomal dominant disorder in which patients may have autoamputation of the digits (pseudo-ainhum) and high-frequency hearing loss.

Another differential of a palmoplantar rash is palmoplantar pustulosis, which presents as a sterile vesiculopustular rash in shiny, erythematous, scaling areas of the palms and soles. As the rash dries up, it develops dry brown haemorrhagic scales. Palmoplantar pustulosis is usually chronic and symmetrical, and primarily affects women between 40 and 60 years of age. It is associated with psoriasis in 15–30% of cases and rarely with the SAPHO syndrome (synovitis, acne, pustulosis, hyperostosis and sterile osteomyelitis).[8]

The diagnosis of syphilis is difficult because *Treponema pallidum* cannot be cultured in the laboratory. Therefore, the disease must be identified by direct visualisation of the spirochete in clinical wet specimens or, more commonly, by serological testing. There are two types of serologic tests for syphilis: nontreponemal tests such as the Venereal Disease Research Laboratory (VDRL) test and the RPR test, and treponemal tests such as the fluorescent treponemal antibody absorption (FTA-ABS) test, the microhaemagglutination test for antibodies to *Treponema pallidum* (MHA-TP) and the TPPA. Newer techniques involving molecular methods are being increasingly used for the diagnosis of early syphilis.[9]





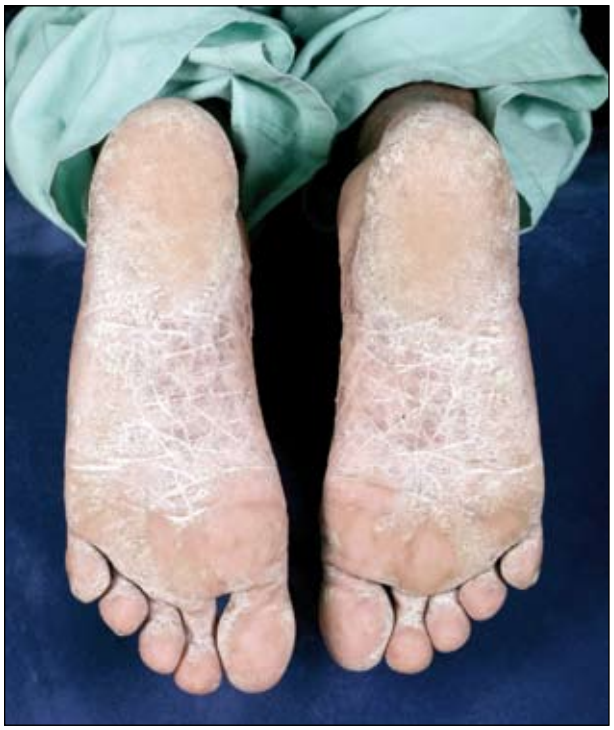


FIGURE 1 A 36-year-old man of Bangladeshi origin presented with a febrile illness, arthralgia and generalised lymphadenopathy. The soles of his feet and the palms of both hands showed a discrete maculo-papular hyperpigmented rash with hyperkeratosis.

Potentially most interesting is a multiplex polymerase chain reaction (M-PCR) assay that can simultaneously detect *Treponema pallidum*, *Haemophilus ducreyi* (the aetiologic agent of chancroid) and herpes simplex.[9]

Another PCR test using sequences of the DNA polymerase I gene had a sensitivity and specificity of 95.8% and 95.7%, respectively, in 112 genital ulcer specimens. This test did not cross-react with nonpathogenic treponemal species or other spirochetes.[10]

In a recent study, biopsy samples from skin lesions of 12 patients with secondary syphilis were examined.[11] Diagnosis of syphilis was based on clinical presentation, dark-field microscope analysis and serological tests. Using a polyclonal antibody directed against *Treponema pallidum*, the presence of *Treponema pallidum* in 90% of the samples studied with the bacteria was located in the epidermis and the upper dermis. The *Treponema pallidum* 47-kDa surface protein gene could be amplified by PCR in 75% of the skin lesions. When combining both techniques, *Treponema pallidum* was detected in 92% of the samples from patients with secondary syphilis but not in the control samples. These findings suggest that both immunohistochemistry and PCR could be useful for the diagnosis of secondary syphilis, and may be helpful in some rare cases when serological assays have failed to detect *Treponema pallidum* antibodies.

KEYPOINTS

- This case illustrates the importance of taking a detailed sexual history in patients presenting with a rash.
- Syphilis, although less common in the general population, is still common in men who have sex with other men.

REFERENCES

1 Health Protection Agency. *STIs annual data 1997–2006*. Available from http://www.hpa.org.uk/web/HPAweb&HPAwebStandard/HPAweb_C/1195733775264

2 Clark EG, Danbolt N. The Oslo study of the natural course of untreated syphilis: an epidemiologic investigation based on a re-study of the Boeck-Bruusgaard material. *Med Clin North Am* 1964; 48:613–23.

3 Fenton KA, Wasserheit JN. The courage to learn from our failures: syphilis control in men who have sex with men. *Sex Transm Dis* 2007; 34:162–5.

4 Kim YY, Lee JH, Yoon SY et al. Erythema multiforme-like targetoid lesions in secondary syphilis. *Acta Derm Venereol* 2007; 87:381–2.

5 Hicks CB, Sparling PF. Pathogenesis, clinical manifestations and treatment of early syphilis. In: Rose BD, editor. *UpToDate*. Waltham, MA: UpToDate; 2007.

6 Itin, PH, Lautenschlager, S. Palmoplantar keratoderma and associated syndromes. *Semin Dermatol* 1995; 14:152–61.

7 Lucker, GP, Van de Kerkhof, PC, Steijlen, PM. The hereditary palmoplantar keratoses: an updated review and classification. *Br J Dermatol* 1994; 131:1–14.

8 Kahn MF, Chamot AM. SAPHO Syndrome. *Rheum Dis Clin North Am* 1992; 18:225–46.

9 Beyrer C, Jitwatcharanan K, Natpratan C et al. Molecular methods for the diagnosis of genital ulcer disease in a sexually transmitted disease clinic population in northern Thailand: predominance of herpes simplex virus infection. *J Infect Dis* 1998; 178:243–6.

10 Liu H, Rodes B, Chen CY et al. New tests for syphilis: rational design of a PCR method for detection of *Treponema pallidum* in clinical specimens using unique regions of the DNA polymerase I gene. *J Clin Microbiol* 2001; 39:1941–6.

11 Buffet M, Grange PA, Gerhardt P et al. Diagnosing *Treponema pallidum* in secondary syphilis by PCR and immunohistochemistry. *J Invest Dermatol* 2007; 127:2345–50.