Erythema Multiforme-like Targetoid Lesions in Secondary Syphilis

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Sir,
Syphilis has variable clinical courses, diverse manifestations and histological patterns, commonly mimicking those of other diseases, which were recognized long before Sir William Osler dubbed syphilis "the great imitator" (1). We report here erythema multiforme (EM)-like targetoid lesions in secondary syphilis.

CASE REPORT

A 37-year-old woman presented with a 6 week history of pruritic targetoid lesions, which were violaceous, erythematous plaques in an annular pattern, 1–2 cm in size, on both palms (Fig. 1). She had no prior history of medication or herpes simplex infection before the skin lesions occurred. All other physical findings were normal. The clinical findings suggested EM.

Skin biopsy performed on the palm was consistent with interface dermatitis, and showed hyperkeratosis, lymphocytic exocytosis, and vacuolization of the basal layer. A mild perivascular lymphohistiocytic infiltrate without plasma cells was present throughout the papillary dermis (Fig. 2). Proliferation of endothelial cells and a perivascular dermal infiltrate containing plasma cells, which are histological hallmarks of syphilis (2), were not seen. Warthin-Starry stain of the skin biopsy specimen was negative for spirochetes. To provide a direct association between *Treponema pallidum* and the targetoid skin lesions, polymerase chain reaction (PCR) technology was used to detect treponemal genomic DNA in the skin lesions. The 47-kDa lipoprotein gene (GenBank accession no. M88769 and M27493) (3, 4) for *T. pallidum* was amplified using 40 cycles of 94°C for 1 min, 58°C for 1 min, and 72°C for 1 min. The final product was separated on 2% agarose gel, stained with ethidium bromide, and visualized by BioPrint/Bio1D (Vilber Lourmat, France). A 658 bp band of the PCR product specific for *T. pallidum* was present only in the skin biopsy specimens from this patient, as in the positive control, but not in the negative control (Fig. 3).

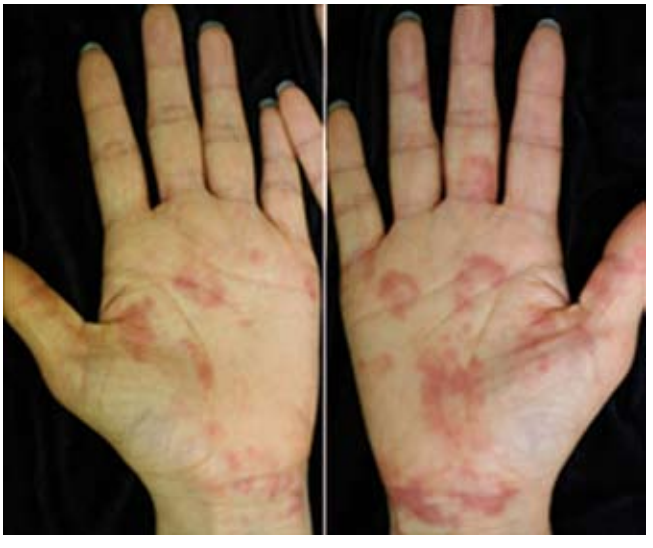

Fig. 1. Targetoid and polycyclic plaques on both palms.

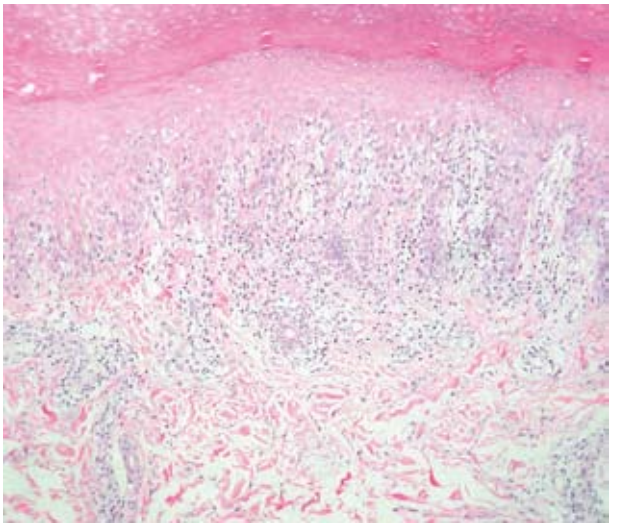

Fig. 2. Skin biopsy performed on the palm was consistent with interface dermatitis, and showed hyperkeratosis, lymphocytic exocytosis, and vacuolization of the basal layer. A mild perivascular lymphohistiocytic infiltrate without plasma cells was present throughout the papillary dermis (HE; original magnification ×100).

Serological tests for syphilis showed venereal disease research laboratory test titres of 1:32, and the fluorescent treponemal antibody absorption test IgM and *T. pallidum* haemagglutination assay were reactive.

DISCUSSION

In the case described here, the cutaneous manifestations, the result of the Warthin-Starry stain, and the pathological findings could not provide a direct association between the skin lesions and secondary syphilis. However, the patient was diagnosed as having secondary syphilis because of high titres in the serological

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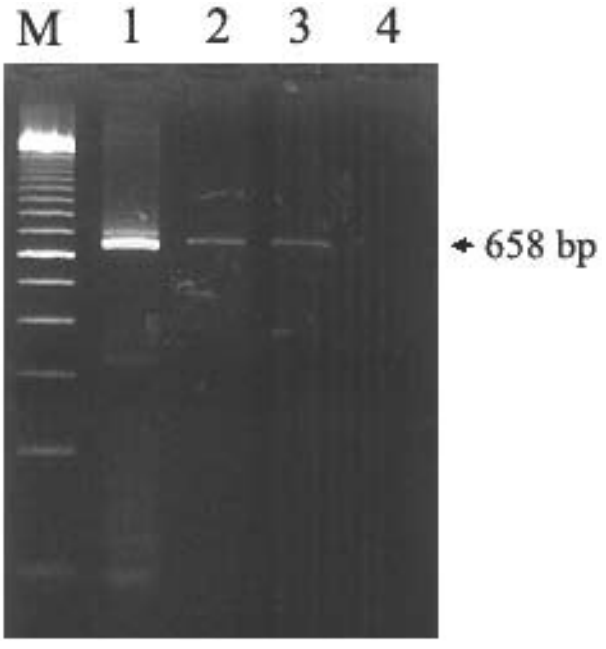

Fig. 3. Polymerase chain reaction (PCR) detection of *T. pallidum*-specific DNA. The position of the 658 bp PCR product is indicated by an arrow. M: 100 bp DNA size marker. Lane 1: *T. pallidum* positive control. Lanes 2 and 3: the skin biopsy specimen from secondary syphilis. Lane 4: negative control.

test for syphilis and demonstration of *T. pallidum* in the tissue by PCR.

The patient was treated with benzathine penicillin G (2.4 million units) by intramuscular injection once weekly for 3 consecutive weeks. One month after initiation of therapy, her skin lesions resolved, leaving post-inflammatory hyperpigmentation .

EM is a self-limited, usually mild and relapsing exanthematous reaction of the skin that has been considered to be a hypersensitivity reaction in a host manifesting an immune response to various aetiological factors capable of generating foreign antigen, primarily infectious agents or drugs (5). *T. pallidum* is a rare aetiological agent of infection-related EM. EM typically occurs 7–14 days after appearance of a recurrent herpes lesion and is characterized by an acute, self-limited course of less than 4 weeks' duration (5). In the case described here the skin eruption persisted for more than 6 weeks. It is likely that the development of EM-like lesions in this case was a reaction to *T. pallidum*. Two reports of EM-like lesions of syphilis have been published in English. Lee & Lee (6) reported EM-like targetoid lesions on both the forearms and the palms of a 37-year-old woman with secondary syphilis, and demonstrated numerous spiral *T. pallidum* in the epidermis and around the dermal blood vessel by immunoperoxidase staining. Wu et al. (7) reported EM-like bullous targetoid lesions in early congenital syphilis by using PCR, and detected *T. pallidum* in the skin lesion.

It is thought that the skin lesions of secondary syphilis are induced by an allergic reaction, since few *T. pallidum* are found in secondary syphilis by conventional detection methods such as dark-field microscopy, silver staining, immunofluorescence or rabbit infectivity test (8). However, demonstration of *T. pallidum* in the skin lesions by PCR, and abundant infiltrating T cells and macrophages, indicates that the skin lesions of secondary syphilis might be caused by direct spirochete invasion rather than by an allergic reaction (9). Therefore, the appearance of EM-like targetoid lesions may be caused by stimulating a specific immune response against *T. pallidum*, which may play a role in the pathogenesis of EM-like conditions (9). To the best of our knowledge, this is the first reported case in which *T. pallidum* has been demonstrated by PCR in EM-like targetoid lesions induced by secondary syphilis.

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