Erythema multiforme (EM) is self-limiting inflammatory disease, characterized clinically by “target” or “iris” skin lesions, and pathologically by vacuolar alteration of basal cells with many necrotic keratinocytes in the epidermis. Pathological confirmation is often required to differentiate EM from many other diseases that may manifest targetoid lesions. EM often occurs in association with various drugs or infections, most commonly herpes simplex virus (HSV) and, less commonly, mycoplasma or other infections (1). Recent studies showed that HSV-associated EM (HAEM) begins with fragmentation of HSV DNA, followed by transport of the DNA fragments to distant skin sites by peripheral blood mononuclear cells (2, 3). Although syphilis and EM are relatively common, syphilis-associated EM appears to be very rare. We describe here a case with such rare association.

**CASE REPORT**

In September 2009, a 20-year-old man presented with a 4-day history of a pruritic eruption. Examination revealed oral ulcers and coalescing erythematous to violaceous maculopapules with targetoid morphology on the trunk and proximal extremities (Fig. 1). EM was the provisional diagnosis. Histopathology of a targetoid lesion showed vacuolar interface dermatitis with many necrotic keratinocytes, consistent with EM (Fig. 2A). His drug history was unremarkable. HSV serology was checked, along with the skin biopsy. Serology for HSV types 1 and 2 was IgG-positive but IgM-negative. A week later, he was found to have oral candidiasis as well as multiple scaly erythematous plaques on the palms and soles, raising the suspicion of secondary syphilis and HIV infection, which were confirmed by positive syphilis serology (VDRL 1:256; TPHA 1:5120) and HIV antibody by Western blot. CD4 count was reduced to 209/ml. Further inquiry revealed a 3-year history of unsafe bisexual contacts with multiple partners, and a penile ulcer noted in mid-July. Biopsy of a sole lesion showed psoriasiform dermatitis with infiltration of lymphocytes and neutrophils in the epidermis and papillary dermis without necrotic keratinocytes, features compatible with secondary syphilis. Immunohistochemistry (IHC) stain (1:100, CP135A, Biocare Medical®, CA, USA) demonstrated numerous spirochetes in the sole specimen (not shown) but few in the EM specimen (Fig. 2B). Additional PCR study was performed on the genomic DNA extracted from paraffin tissue sections using primers designed for Treponema pallidum polA (4). A specific band of 377-bp product (confirmed by direct DNA sequencing) was detected in both specimens (Fig. 2C). Because of a weakly positive penicillin skin test, the patient was treated with doxycycline 100 mg twice daily for 28 days. The rash improved greatly in 5 days. Two months later the VDRL titre was 1:128.

**DISCUSSION**

In this report, we described a pathology-confirmed case of EM occurring in a HIV-positive bisexual young man with serology- and pathology-confirmed secondary syphilis. We are aware of only 3 other cases of EM-like lesions in association with syphilis, which were confirmed by VDRL titres of 1:32 or higher and positive demonstration of spirochete microorganisms or *T. pal*
The mechanism involved in the *T. pallidum*-induced EM is unclear. The finding of a few spirochetes in the EM lesion in our case suggests an antecedent bacteremia. We surmise that the EM lesions might have either developed *de novo* or evolved from the pre-existing maculopapular lesions of early secondary syphilis. Previously, the lymphocytic infiltrate in HAEM has been shown to be CD4+ predominant, in contrast to CD8+ predominance in drug-associated EM (3). The EM lesion in our patient showed a CD8+ predominant infiltrate (not shown), which might simply reflect the patient’s abnormal lymphocyte subpopulations due to his HIV infection. On the other hand, the HIV-induced altered immunity might have led to an abnormal local immune response to *T. pallidum*. In conclusion, the present case highlights that EM may occur in association with secondary syphilis and cause confusion between the two diseases. Syphilis should be considered in the differential diagnosis in HIV patients presenting with EM or targetoid skin lesions.

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**The authors declare no conflict of interest.**

**REFERENCES**