Non-primary nail-plate syphilis in an HIV-infected patient

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Abstract
A 37-year-old Caucasian male, HIV-infected (CDC A2) in 2012 and on antiretroviral therapy, presented for a follow-up visit. On physical examination, a barely discernible light-colored macular rash was observed on the trunk, not involving the palms and soles. However, clear maculo-papular lesions were present over the proximal volar aspect of both forearms. Furthermore, well-demarcated purplish, opaque, rough, vertically ridged plaque-like lesions were observed over the proximal portions of fingernails. The patient reported that cutaneous and nail lesions had appeared about 2 months prior and that he had engaged in unprotected sex 5 months before. Serologic tests for syphilis resulted reactive. Intramuscular injection of benzathine penicillin G, 2.4 million units, was administered once a week for 3 weeks. One month after therapy, the rash was no longer present, and at 5 months, nail abnormalities had disappeared. The clinical findings, the serologic results, and the disappearance of skin and nail lesions after the administration of penicillin strongly suggest that this HIV-infected patient had secondary or early late syphilis with skin and nail-plate involvement. We are experiencing a resurgence of syphilis as well as an increase in unusual and/or forgotten clinical manifestations. Syphilis remains a diagnostically challenging disease.

Keywords
Syphilis, early latent, syphilis secondary, nail syphilis, HIV infection

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Introduction
Fingernail involvement is an extremely rare manifestation of syphilis and is more common during the primary phase of the infection, but it has been reported in all stages of the disease.1,2 Primary fingernail involvement in syphilis accounts for approximately 14% of all extragenital primary manifestations. It is generally the result of contact with an infected partner during sexual activity, but can also be diagnosed among health care personnel as result of direct contact with an infected patient.2 Non-primary fingernail manifestations of syphilis can exclusively involve the nail plate (syphilitic onychia) and include nail pitting, grooves, onycholysis, and/or onychogryphosis. Other reported fingernail manifestations include inflammation around the skin surrounding the nail (paronychia or perionychia), painful violaceous nodules, or abscesses around the nail folds.3-5

Case report
A 37-year-old Caucasian male, HIV-infected (CDC A2) in 2012 and on antiretroviral therapy (ART) with tenofovir/emtricitabine and efavirenz, was seen in December 2016 for a follow-up visit in our Infectious Disease department. At that time, the patient’s CD4 count was 505/µL and the viral load was <20 copies/mL. A physical examination evidenced an enlarged left inguinal lymph node, hepatosplenomegaly, and a barely discernible macular, pink rash on the trunk not involving the palms and soles, coexisting with maculo-papular lesions localized on the proximal volar aspect of both forearms (Figure 1(a) and (b)). Well-demarked purplish, opaque, rough, vertically ridged plaque-like lesions were also present on the proximal portions of some fingernails of both hands. The involved nails were friable. There was no discernible...
involvement of the periungual skin (Figure 1(c) and (d)). The patient reported the onset of these manifestations about 2 months prior. During the visit, the patient also reported that he had engaged in unprotected sex in July 2016. Laboratory tests evidenced erythrocyte sedimentation rate (ERS) of 26 mm/h, C-reactive protein (CPR) of 3.5 mg/dL (normal value [NV] < 0.5), gamma-globulins of 22%, hemoglobin of 12.1 g/dL, hematocrit of 35%, gamma-glutamyltransferase of 102 IU/mL (NV 7–49 IU/mL), and alkaline phosphatase of 334 IU/mL (NV 80–320 IU/mL). Hepatitis B, C, and A serology resulted negative. Syphilis serology, which had been negative in 2012, resulted reactive. Specifically, Rapid Reagin Test (RPR) and Treponema Pallidum Particle Agglutination Assay (TPPA) were positive, with titers of 1:32 and 1:5120, respectively. The patient was reactive to fluorescent treponemal antibodies and positive to anti-treponema IgM antibody. Intramuscular (IM) injection of benzathine penicillin G, 2.4 million units, was administered once a week for 3 weeks. A month later, the rash was no longer evident, while the fingernail lesions were reduced in size. At that time, RPR titer was 1:16 and anti-treponema IgM antibody was negative. Five months from the end of therapy, the fingernails were free of disease, with the exception of a linear scar on the left little fingernail (Figure 2(a) and (b)), and all the abnormal blood
test, including the liver enzymes, resulted normal. Six months after the end of therapy, RPR resulted reactive (titer 1:2).

Discussion
Secondary syphilis refers to that stage of *Treponema pallidum* infection when the greatest load of spirochete is present in the bloodstream and many other tissues. It appears several weeks after resolution of the primary chancre and lasts until the host develops some immune control. This stage includes a large diversity of signs and can mimic other diseases.1,6–9 Skin lesions are the most common manifestation1,6 and can include macular, maculo-papular, nodular, pustular, and papulo-squamous rash and a mix of all types. At the same time, any organ can be involved1,6–9 and also nails.1,3–5 The fingernail changes observed in this patient were similar to those known as onychia sicca syphilitica. They were confined to the nail plate itself and were not due to inflammation of the skin around the nail or the nail matrix.3 These types of nail lesions have been reported to occur as early as 6–8 months from infection to 10 years later and can be isolated.3

Early latent syphilis occurs in the first year of infection and is identified in a period of time in which relapsing clinical manifestation can be present, most often confined to skin and mucous membranes, with each relapse being less severe.6

Treatment of secondary syphilis is benzathine penicillin G, 2.4 million units, a single dose administered IM, while latent syphilis requires IM administration of benzathine penicillin G, 2.4 million units, once a week for 3 weeks.6 Despite the patient having reported skin and nail changes 2 months after having engaged in unprotected sex, in consideration of the fact that he had a paucisymptomatic picture, had not tested for syphilis during the previous 4 years, and had HIV co-infection, a condition known to be associated with a more severe, protracted, or relapsing syphilis disease, we decided to treat him for latent syphilis and administered benzathine penicillin G once a week for 3 weeks.6

In conclusion, the clinical findings, the serologic results, and the disappearance of skin and fingernail lesions after the administration of penicillin strongly suggest that this patient’s disease represents a rarely seen case of syphilis with skin involvement and non-primary nail-plate changes. Yearly serologic testing for syphilis is mandatory in HIV-infected patients, as well as in all patients who have engaged in risky sexual behavior.

We are experiencing a resurgence of syphilis along with an increase in unusual forgotten clinical manifestations. Syphilis remains a diagnostically challenging disease.

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Informed consent
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