Case report of three consecutive lues maligna infections in an HIV-infected patient

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Abstract
Lues maligna is a rare presentation of an infection with Treponema pallidum. Here we report three lues maligna infections with severe dermatological manifestations in a single HIV-1 infected individual. Despite the start of highly active antiretroviral therapy and a substantial increase in CD4 cell count after the first episode, he developed consecutive episodes. We assume a specific immunological predisposition to react to T. pallidum in this patient.

Keywords
Lues maligna, reinfection, HIV-1, skin manifestation, CD4 cell count, Treponema pallidum

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Introduction
Syphilis infections are frequent among HIV-infected individuals, especially men who have sex with men; however, it seldom presents with lues maligna. This clinical entity represents a rare dermatologic manifestation of secondary syphilis and is also known as ‘ulcero-nodular syphilis’ or ‘malignant syphilis’. Reinfection is a possibility, however this has not been described in HIV infection. Here we describe an HIV-infected individual who developed malignant syphilis with three consecutive infections.

Case report
A bisexual man in his 40s presented to our infectious diseases outpatient department for skin lesions three times (in 2010, 2012 and 2014). He had been diagnosed with HIV infection in 2003. With each episode, the patient suffered from non-specific symptoms such as headache, malaise and subfebrile temperatures. Striking was a disseminated exanthema presenting with ulcerating nodules (Figure 1(a)) for months. The patient’s skin in 2010 (Figure 1(b)) showed multiple disseminated polymorphic lesions all over the body without itchiness. In 2012, the skin lesions were not as many as two years before but the rate of ulceration increased. In 2014 (Figure 1(c)), the skin manifestations were even less but got bigger and more ulcerated. The serological tests proved active syphilis in every case. Treponema pallidum particle agglutination assays (TPPA) for syphilis were positive (2010: 320,000, 2012: 1.28 million, 2014: 320,000) and rapid plasma reagin (RPR) titre increased (2010: 1:128, 2012: 1:32 and 2014: 1:256). Lumbar puncture was performed and neurosyphilis was excluded. The patient reported promiscuous unprotected sexual contacts in the past. Each time he was treated with ceftriaxone 2 g intravenously once daily for three weeks due to the extensive dermatologic manifestation. To prevent a Jarisch–Herxheimer reaction we added oral prednisolone 1 mg/kg body weight only for the first day of treatment. The non-specific flu-like symptoms disappeared quickly within days. All skin lesions healed, partly with scars within three weeks (Figure 1(d)). RPR titres slowly decreased (to 1:4 after the first episode and to 1:16 after the second episode. The patient did not return to our outpatient department after the treatment of the third episode).

He started highly active antiretroviral therapy (HAART) consisting of raltegravir 400 mg bid,

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darunavir 800 mg qd, ritonavir 100 mg qd and tenofovir 245 mg qd with the first episode in 2010. His CD4 cell count increased from 360 \( \mu l^{-1} \) (22%) to 506 \( \mu l^{-1} \) (44%) and his viral load ranged between <50 and 200 copies/ml while on HAART. Written informed consent was obtained regarding the publishing of clinical data and images.

**Discussion**

Lues maligna is predominantly found in immunodeficient patients such as patients with HIV or AIDS but also occurs in immunocompetent individuals. The classic lesion of lues maligna is an oval, papulopustular skin lesion with well-demarcated borders sometimes covered with a lamellar crust (Figure 1(a)), but myriad clinical presentations of this disease also exist. Differential diagnosis includes vasculitis, lymphoma, leishmaniasis, pyoderma gangrenosum and varicella zoster infections among others. Although the clinical manifestations of lues maligna are complicated and severe, the response to antibiotic treatment (benzathine penicillin or ceftriaxone) is excellent.

Interestingly, the patient presented here developed the course of malignant syphilis three times despite the start of HAART after the first episode. As he received adequate antibiotic treatment with ceftriaxone, we assume reinfection for the two following episodes. To our knowledge, this is the second case reported after the first case report in 1978. An immunocompromised state, a certain virulent bacterial strain or a unique characteristic of the immune response is discussed as reasons for malignant syphilis. In our patient, the CD4 count improved after HAART start and he had three independent infections which render a virulent strain three times in a row unlikely. Therefore, our hypothesis is that the patient’s immune system is predisposed for developing this kind of reaction to *Treponema pallidum*.

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