Pathologically Confirmed Malignant Syphilis in an HIV-Infected Patient

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Abstract

We report a case of pathologically confirmed malignant syphilis in an HIV-infected patient. Physical examinations revealed ulceronecrotic skin lesions. Skin biopsies demonstrated syphilis spirochetes on immunohistochemical stain, and syphilis serological titers were positive. Treatment with intravenous penicillin G was begun, and complete resolution of the skin lesions was observed. A rapid plasma reagin titer test performed 3 months after treatment revealed a 4-fold reduction in the titer, indicating successful treatment.

Key words: malignant syphilis, HIV, ulceronodular skin lesions

Introduction

Malignant syphilis (lues maligna) is a rare presentation of secondary syphilis. The disease is characterized by a prodrome of fever, headache, and myalgia followed by a papulopustular eruption that rapidly transforms into necrotic, sharply marginated ulcers covered with hemorrhagic brown crusts that are organized in rupoid layers (1).

The incidence of malignant syphilis is low. Shulkin et al were able to identify only 14 cases of malignant syphilis in the English language literature since the early 1900’s (2). However, more cases of the disease have been reported since the HIV epidemic, suggesting that HIV-infected patients may be at an increased risk (2-15). A multicenter retrospective study of 11,368 HIV-infected patients in Germany found that 151 (1.3%) patients were concurrently infected with syphilis, and 11 (7.3%) of those patients had lues maligna (16).

Diagnosis of malignant syphilis can be a challenge since skin biopsy samples rarely show syphilis spirochetes (1). Here, we report a case of pathologically confirmed malignant syphilis in an HIV-infected patient.

Case Report

A 29-year-old homosexual HIV-infected man presented with a 3-week history of fever and multiple skin lesions. The patient reported that the skin lesions appeared first on his palms and soles, and gradually spread to his trunk and extremities. At the time of symptom onset, he was not on antiretroviral therapy (ART). The most recent CD4 cell count was 229 cells/μL, and the HIV viral load was 64,000 copies/mL. Physical examination revealed a painful, non-pruritic generalized papulopustular eruption on his trunk, as well as on his upper and lower extremities. The patient was prescribed valacyclovir for presumed disseminated varicella-zoster infection; however, 1 week later he was admitted for exacerbation of his skin lesions. Ulceronodular skin lesions covered with layers of thick, dirty-appearing crusts were observed all over his body, including his palms and soles (Fig. 1A, 1B). The patient’s genitalia were free of skin lesions. The oral mucosa was affected, and also manifested thrush. His physical exam was otherwise unremarkable. Serologic testing revealed a rapid plasma reagin (RPR) titer >1 : 64 and a Treponema Pallidum latex agglutination assay (TPLA) was positive. The patient had a negative syphilis se-
We present a case of pathologically confirmed malignant syphilis in an HIV-infected patient. We have previously reported a similar case which was also confirmed by biopsy specimen using immunohistochemical stain (11). To the best of our knowledge, there have been only 6 published cases in the English language literature of pathologically confirmed malignant syphilis in HIV-infected patients including ours (Table 1). We demonstrated the presence of spirochetes using immunohistochemical stain, while others used Warthin-Starry stain (2, 5, 8) and Steiner stain (9, 10).

The typical method for detecting spirochetes in tissue sections is through silver staining using either the Warthin-Starry or Steiner technique. However, spirochetes are often difficult to detect because this technique also stains melanin granules and reticulin fibers, resulting in marked background artifacts. In addition, silver staining is reported to have low sensitivity in detecting spirochetes in the dermis compared to the immunohistochemical stain (17, 18). Previous reports...
have shown that immunohistological stain is more sensitive and specific than silver stain for detection (18, 19). Furthermore, due to the near absence of background artifacts, rare dermal spirochetes could be visualized using this technique. Although serologic studies remain the cornerstone of syphilis diagnosis, immunohistochemical stain may be more useful than conventional methods in establishing the diagnosis.

However, the paucity of spirochetes in biopsy specimens makes the diagnosis of malignant syphilis a challenge for clinicians. There have been reports using the same staining mentioned previously that were negative for spirochetes. In the largest case series from Don et al, describing 6 HIV-infected patients with malignant syphilis, Warthin-Starry stain did not demonstrate spirochetes in any of the biopsy samples (3), and Tucker et al could not detect spirochetes using Steiner staining (7). Pleimes et al have reported that neither immunohistochemical staining nor DNA polymerase chain reaction revealed spirochetes (6). HIV infection seems to have no clinical impact on the absence of spirochetes in biopsy specimens, since the demonstration of spirochetes in HIV-negative patients has also been reported to be rare (20-22).

In addition to the characteristic gross and microscopic morphology, the diagnostic criteria for malignant syphilis includes a strongly positive RPR titer, a severe JHR, and rapid resolution of the lesions with antibiotics (21). JHR was not evident in the present case, but all other diagnostic criteria were fulfilled. The patient’s lack of JHR may have been related to his concurrent immunosuppression, which may have been the reason in previous reported case (7). RPR was positive in our case; however, substantial variations have been reported in patients with HIV-infection. There was a case of malignant syphilis with negative RPR titer from prozone phenomenon (23), and cases with extremely high titers (2, 24).

The diverse clinical manifestations of syphilis also contribute to the diagnostic difficulties. Syphilis has often been called “the great imitator” because so many of the signs and symptoms are indistinguishable from those of other diseases. Previous reports of malignant syphilis had initial diagnoses of disseminated varicella-zoster, herpes simplex, or meningococcemia (3). The present case was initially diagnosed as disseminated varicella-zoster. Malignant syphilis can even resemble a malignant disease, such as mycosis fungoides (5). Moreover, clinical symptoms can vary; skin lesions may or may not be accompanied by symptoms such as pain or pruritus.

The resurgence of syphilis and its high co-infection rate with HIV has been reported in recent years (25, 26). Fortunately, the prognosis of malignant syphilis is usually good with penicillin treatment (1). However, without treatment, the infection will progress to the latent and possibly late stages of the disease, which have a poor prognosis. Although skin and mucous membrane lesions are characteristic of secondary syphilis, other symptoms, including fever, lymphadenopathy, pharyngitis, alopecia, malaise and muscle aches can be manifested and can also provide diagnostic clues to clinicians. Therefore, prudent history and physical examination, along with the knowledge of malignant syphilis, are essential in making an accurate diagnosis.

In this report, we have described a pathologically confirmed malignant syphilis in an HIV-infected patient. Physicians must take note that ulceronodular skin lesions are symptoms of malignant syphilis, and their presence should also raise the clinical index of suspicion for HIV co-infection.

The authors state that they have no Conflict of Interest (COI).

References
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