The association between syphilis, leprosy, and human immunodeficiency virus (HIV) is not well documented, and the emergence of isolated cases raises the interest and indicates that this triple coinfection can occur. We report the case of a 42-year-old man from Rio de Janeiro, Brazil, who presented with erythematous papules on the trunk, back, and upper and lower extremities; an erythematous plaque on the upper abdomen; and an erythematous violaceous plaque on the right thigh with altered sensitivity. Laboratory investigation showed a reagent VDRL test (1:512) and positive test results for Treponema pallidum hemagglutination. Treatment with benzathine penicillin (2,400,000 U intramuscularly) was started (2 doses 1 week apart). On follow-up 40 days later, the lesions showed partial improvement with persistence of the plaques on the right thigh and upper abdomen as well as a new similar plaque on the back. Further laboratory examinations showed negative bacilloscopy, positive HIV test, and histologic findings consistent with tuberculoid leprosy. The patient was started on multidrug therapy for paucibacillary leprosy with clinical improvement; the patient also was monitored by the HIV/AIDS department. We emphasize the importance of clinical suspicion for a coinfection case despite the polymorphism of these diseases as well as the precise interpretation of laboratory and histopathology examinations to correctly manage atypical cases.

**Syphilis, Leprosy, and Human Immunodeficiency Virus Coinfection: A Challenging Diagnosis**

Claudia Fernanda Dias Souza, MD; Eduardo Bornhausen-Demarch, MD; Aline Gesualdo Prata, MD; Felipe Cupertino de Andrade, MD; Mariana Paulsen Fernandes, MD; Marcia Regina Araújo Lopes, MD; José Augusto da Costa Nery, MD, PhD

**Practice Points**
- Observe the patient as a human being, regardless of his/her social class, race, or sexual preference.
- As health care professionals, keep up-to-date through continuing medical education.
- Provide health education on sexually transmitted diseases and infectious diseases, giving patients an understanding of self-protection.

Syphilis, a chronic systemic infection caused by Treponema pallidum, usually is sexually transmitted and is characterized by periods of active disease or latency. The primary lesion typically arises after an incubation period of 2 to 6 weeks and usually is attributed to local lymphadenopathy. The secondary stage, caused by intense bacterial growth, is associated with the development of disseminated mucocutaneous lesions and generalized
lymphadenopathy, followed by a latent period of a subclinical infection lasting many years. In approximately 33% of untreated cases, the tertiary stage starts after a long period with mucocutaneous and musculoskeletal lesions, aortitis, and/or symptomatic central nervous system disease.\(^1\)

Leprosy, a chronic infectious disease caused by *Mycobacterium leprae*, was first described in ancient Indian texts of the sixth century BC.\(^2\) Clinically, leprosy is characterized by signs and symptoms usually confined to the skin, resulting from the impairment of peripheral nerves and/or worsening of health in reactional cases. As the disease evolves, other organs may be affected. The characteristic *M leprae* tropism for peripheral nerves and certain immunologically mediated reactional states is the main cause of morbidity in leprosy. When left untreated, leprosy tends to cause typical disabilities that have resulted in a deep social stigma due to the person-to-person transmission of disease. With early diagnosis and adequate antibiotic therapy, patients now can have productive lives, and the visible manifestations or deformities caused by the disease are largely preventable.\(^1\)

The interaction between human immunodeficiency virus (HIV) and leprosy is not fully understood. The incidence rate of leprosy is not higher in HIV patients. The clinical course of leprosy is not changed by coinfection with HIV. In fact, most reports show no clinical, immunological, or histological changes with HIV coinfection, and therefore there is no need for changes in leprosy management. However, HIV-positive patients are more likely to contract syphilis, making it more difficult to treat.\(^3,4\)

The spread of HIV in the 1980s led to the resurgence of rare diseases, such as progressive multifocal leukoencephalopathy, *Rhodococcus* infection, and other CD4-dependent opportunistic diseases, and also influenced the natural course of other diseases such as syphilis, resulting in the modification of clinical forms, changes in laboratory tests, and cases of rapid progression to later stages. Thus diagnosis of syphilis in the HIV era became much more difficult.\(^1,5\)

Syphilis and leprosy share common characteristics, such as cutaneous lesions with high polymorphism, that hinder the differential diagnosis and laboratory tests, which are not clear in certain situations and interfere with the confirmation of the clinical diagnosis. The most frequent signs of both diseases are cutaneous in nature and can manifest in virtually all forms of dermatologic lesions (eg, macules, papules, nodules, tubercles, plaques, infiltrations). These nonspecific lesions can arise in both diseases in various forms or stages either alone or in various combinations, making clinical diagnosis a challenge. Secondary syphilis usually manifests as localized or diffuse symmetric mucocutaneous lesions and painless generalized lymphadenopathy. Cutaneous lesions of tuberculoid leprosy, on the other hand, usually consist of brownish or reddish brown plaques that are clearly demarcated and hypesthetic, often with erythematous elevated edges. In the affected area, there is usually a lack of cutaneous components (eg, sweat glands, hair follicles); therefore, the lesion is dry, scaly, and anhidrotic.\(^1,6\)

We report a case of syphilis, leprosy, and HIV coinfection, which is not well represented in the literature. These diseases, which are endemic in Brazil, may have clinical similarities, making the diagnosis a challenge.

**Case Report**

A 42-year-old man from Rio de Janeiro, Brazil, presented for treatment of “red spots” on his skin that had developed 2 weeks prior; he also reported tingling in the hands and feet and a mild fever. Physical examination revealed erythematous papules on the trunk (Figure 1), back, and upper and lower extremities; an

---

**Figure 1.** Widespread exanthema of red papules (papular syphilide).

**Figure 2.** Early bounded plaque on the right thigh with marked alteration of thermal, tactile, and pain sensitivity.
erythematous plaque on the upper abdomen; and an erythematous violaceous plaque on the right thigh with altered sensitivity (Figure 2). Laboratory investigation showed a reagent VDRL test (1:512) and positive test results for *T pallidum* hemagglutination. Treatment with benzathine penicillin (2,400,000 U intramuscularly) was initiated, 2 doses 1 week apart. On follow-up 40 days later, the lesions showed partial improvement with persistence of the plaques on the right thigh and upper abdomen (Figure 3) as well as a new similar plaque on the back. Laboratory investigation included bacilloscopy, a complete blood cell count, liver and kidney function, and HIV serology. Bacilloscopy was negative and HIV serology was positive (2 enzyme-linked immunosorbent assay and Western blot test reagents). Other tests revealed no abnormalities. We also performed biopsies on plaques from both the thigh and abdomen, which showed findings consistent with tuberculoid leprosy (Figure 4). The patient was started on multidrug therapy for paucibacillary leprosy, as recommended by the World Health Organization, with clinical improvement (Figures 5 and 6). Physiotherapy evaluation revealed disability grade 0. The patient also was monitored by the HIV/AIDS department.

**Comment**

Although scarce, reports of clinical and pathologic findings in patients with active syphilis and HIV infection suggest that granulomatous infiltrates are common during the short stage of secondary syphilis in HIV-positive patients. Other histopathologic details have been reported in a case of syphilis...
suggesting leprosy. Granulomatous lesions are characteristic of tertiary syphilis, but small granulomas with Langhans giant cells can be found in early lesions. The inflammatory infiltration of some nerve branches is one of the alterations that can be seen on cutaneous lesions of secondary syphilis.

A study of 51 patients in a leprosy hospital identified no significant association between leprosy and HIV, but the spread of other sexually transmitted diseases was suggested because patients living apart in this community may constitute potential reservoirs of these diseases.

One report in the literature described a triple coinfection of syphilis, leprosy, and HIV. It was reported in Paraguay as borderline leprosy.

In another study, a biopsy of a plaque revealing a granulomatous infiltrate distributed around vessels, appendages, and nerve fibers, which was suggestive of tuberculoid leprosy, led the physicians to start therapy for leprosy. Because the patient showed no improvement after 3 months of specific treatment, the physicians reviewed the histopathology and a hematoxylin and eosin stain revealed plasmacyte cell infiltration among the dermal vessels and between the granuloma cells, suggestive of syphilis, which had not been detected before. Further, a VDRL test was reactive.

It has been speculated that HIV and M leprae coinfection may exacerbate the pathogenesis of leprosy lesions and/or lead to increased susceptibility to leprosy, as seen in tuberculosis; however, to our knowledge, this point has not been proven. In contrast, initiation of highly active antiretroviral therapy (HAART) has been reported to be associated with anecdotal activation of M leprae infection and exacerbation of existing leprosy lesions. To determine if HAART is associated with worsening of the manifestations of leprosy, a cohort of leprosy patients recruited between 1996 and 2006 at the Oswaldo Cruz Foundation (FIOCRUZ) Leprosy Outpatient Clinic in Rio de Janeiro was studied longitudinally. The conclusion was that HAART and immune reconstitution were critical factors driving the development and/or clinical appearance of leprosy lesions.

Vinay et al. reported that the incidence of leprosy in patients on HAART treatment was 5.22 per 1000 person-years (95% confidence interval, 2.25-10.28). This high incidence suggests that there should be regular examination of HIV-infected individuals for clinical signs of leprosy.

Some data suggest that immune-mediated reactions that complicate leprosy occur at a higher frequency in patients with coinfection. Reports exist of leprosy presenting as immune reconstitution disease among patients commencing HAART. We speculate that this paradox may relate to differences between the activation state and rates of cell turnover within leprosy and tuberculosis granulomas that differentially affect the susceptibility of the granulomas to HIV.
penicillin based on clinical and neurologic examination as well as lumbar puncture, which showed no changes. Dissenting opinions of expert centers may exist in relation to such treatment due to HIV coinfection, but here we followed the protocol of the World Health Organization, keeping the standard treatment as in non-HIV patients and also in relation to leprosy. Both the frequency and the severity of neurologic involvement in secondary syphilis are greatly increased in patients with HIV. Somewhat surprisingly, there is little evidence to suggest that the dermatologic manifestations of secondary syphilis are more striking in HIV-infected patients or that there is an increase in syphilitic hepatitis, arthritis, or osteitis.  

Despite the availability of efficient drugs, early diagnosis and effective treatment strategies have not been enough to achieve the goal of eliminating leprosy and syphilis as public health concerns. The socioeconomic component contributes to maintaining leprosy as an endemic disease. Treatment strategies must consider social, cultural, and economic aspects to be successful. Identifying the origin of beliefs established and rooted into people's thoughts is important for understanding the problems related to treatment (eg, low adherence). In the 1940s and 1950s, the prevalence of syphilis decreased following the introduction of penicillin; however, the incidence started to rise again in the 1960s and 1970s with the sexual liberty encouraged by the use of oral contraceptives and a change in people's habits and values. Thus changes in sexual behavior, such as reducing the number of partners, and the methodical use of contraceptives are needed. It also is essential to diagnose and treat infected patients early, offer counseling services that are sensitive to the sociocultural and anthropological aspects of the disease, and increase disease detection and intervention efforts. 

Conclusion 

Few reports in the literature show coinfection of secondary syphilis, tuberculoid leprosy, and HIV infection. In our patient, the simultaneous presence of these diseases was demonstrated by the clinical history and laboratory investigation. We emphasize the importance of clinical suspicion for coinfection despite the polymorphism of these diseases as well as precise interpretation of laboratory and histopathology examinations to correctly manage atypical cases. 

REFERENCES 


