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MILD, SELF-RESOLVING ACUTE LEPTOSPIROSIS IN AN HIV-INFECTED PATIENT IN THE PERUVIAN AMAZON

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Abstract

We report a case of acute, self-resolving leptospirosis presenting in a HIV-positive patient from the Peruvian Amazon. The patient presented with an undifferentiated acute febrile illness that resolved without treatment, diagnosed retrospectively as leptospirosis by serology and real-time polymerase chain reaction. Five months later, he was admitted because of a febrile illness with jaundice, hepatosplenomegaly, peripheral edema, and oral candidiasis. Because of the clinical suspicion of AIDS, stored sera of the previous admission were tested, and HIV seropositivity was confirmed, proving that the condition was present at the first admission. Acute leptospirosis in HIV coinfection is not inevitably severe, and there is probably a wide variation in clinical manifestations similar to what occurs in immuno-competent hosts.

CASE PRESENTATION

We report a case of a 34-year-old Peruvian man who attended the outpatient fever clinic of the Hospital Cesar Ga-rayar Garcia in Iquitos, one of the largest medical facilities in the Peruvian Amazon. He had a 6-day history of fever, headache, and generalized malaise. Initial physical examination did not reveal jaundice, hepatomegaly, or splenomegaly. Past medical history was unremarkable. He lived in the city, was unmarried, heterosexual, did not use illicit drugs, and worked as a truck driver. He reported seeing rats around his house. Thick and thin smears were negative for *Plasmodium* spp. Blood and urine samples were drawn for ELISA for leptospira, microscopic agglutination test (MAT), and real-time polymerase chain reaction (PCR) analysis in the context of an epidemiological study of leptospirosis established in the Peruvian Amazon.[1] Because he appeared clinically well, he was discharged home with antipyretics, scheduled for follow-up, and advised to return for any worsening of his condition.

One month later, a study nurse visited the patient at home for follow-up. His fever had relapsed 2 weeks after the initial visit to the fever clinic, but he did not seek medical care or take antibiotics. His fever resolved spontaneously. The results of the MAT panel from the first visit showed a titer of 1/1,600 against a newly identified leptospiral serovar, provisionally delineated Var10[2] (Matthias MA and others, manuscript in preparation; Segura ER and others, in press). ELISA for IgM was negative, but testing of the stored serum and urine samples using a TaqMan-based real-time PCR[3] revealed the presence of *Leptospira* in the urine sample at an

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estimated concentration of 868 leptospires/mL, confirming that the patient indeed had had acute leptospirosis. Repeat testing of serum by ELISA for leptospira and serum and urine by real-time PCR at follow-up were negative while the MAT titer decreased to 1/100, consistent with resolving infection.

Five months later, the patient returned to the same hospital because of sudden onset of fever, jaundice, edema below the umbilicus, and odynophagia. Remarkable findings on admission physical exam included oral mucosal candidiasis and severe wasting, as well as hepatomegaly and splenomegaly. These findings suggested advanced HIV infection. After he gave oral and written consent, the stored serum from the first fever clinic visit was found to be positive for anti–human immunodeficiency virus I antibodies by ELISA and Western blot. The underlying medical reason for the second admission remained undiagnosed but was not related to leptospirosis, as serologic, culture, and nucleic acid tests for *Leptospira* infection were negative, indicating complete resolution of the previous infection. CD4 count was not performed due to lack of resources. He recovered progressively with supportive care and was discharged home. He died at home several months later; autopsy was not performed.

DISCUSSION

Leptospirosis is a zoonotic disease that occurs worldwide but with a higher prevalence in tropical areas in both developed and developing countries.[1] It occurs both in rural and urban settings. Clinical manifestations range from asymptomatic seroconversion to acute undifferentiated fever to severe presentations with jaundice, renal failure, and pulmonary hemorrhage. To our knowledge, this is the sixth reported case of leptospirosis in patients with HIV infection and the second in the English language literature.[4–7] Although this patient had no AIDS-defining conditions before his first fever clinic visit, his advanced presentation at subsequent hospital admission and his rapidly progressive and ultimately fatal course make it almost certain that he had AIDS at the time of his acute episode of leptospirosis.

This case is particularly notable because previously reported patients with acute leptospirosis and HIV coinfection had severe clinical courses. Clinical manifestations differed between patients, variably including meningitis, renal insufficiency, acute respiratory distress syndrome, and hypotension as main manifestations.[4–7] All patients recovered fully from leptospirosis, except one who had residual renal insufficiency. In contrast, the patient reported here experienced a clinical course of leptospirosis consistent with the more common presentation of acute self-resolving undifferentiated fever. Many believe that humoral immunity, primarily against leptospiral lipopolysaccharide (LPS), mediates recovery from acute leptospirosis and protects against reinfection.[8] As a T-independent antigen, leptospiral LPS would be predicted to induce antibodies in the absence of $CD4^+$ T cell help,[9] explaining the high MAT titer during acute infection despite likely advanced HIV-driven immunodeficiency. The high MAT titer cannot be dismissed as HIV-related B cell polyclonal proliferation with hypergammaglobulinema, as an etiologic diagnosis (real-time PCR) definitely demonstrated infection. The patient recovered from acute leptospirosis without antibiotic treatment, without acute complications or sequelae, and without requiring hospitalization. Acute leptospirosis was retrospectively confirmed by a molecular diagnostic technique conducted on-site in the Peruvian Amazon, which has been demonstrated to be very sensitive and specific, detecting pathogenic *Leptospira* to ~10 organisms per specimen without cross-detecting other pathogens or non-pathogenic *Leptospira*.[3]

We conclude that acute leptospirosis in HIV coinfection is not inevitably severe and that there is probably wide variation in clinical manifestations similar to what occurs in immuno-competent hosts. Clinical presentations and complications likely depend on a combination of virulence potential differences that vary between pathogenic *Leptospira* and host genetics of

non–T-cell-dependent innate immune responses. A prospective cohort study in an HIV and leptospirosis dually endemic area would be necessary to establish definitively whether HIV infection alters the course of leptospiral infection, either acutely or in chronic infection, as it does for *Treponema pallidum*, the agent of another spirochetal disease, syphilis, which lacks the T-independent LPS antigen.[10]

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