Clinical Manifestations of Discordance between Cerebrospinal Fluid and Plasma HIV-1 Loads

Str—The demonstration of discordance between HIV-1 evolution in CSF and plasma (with greater drug resistance occurring in the CSF, as described by Tashima et al. [1]) underscores the importance of recognizing the CNS as a distinct compartment. This is particularly important with respect to obscure white matter encephalopathy, as is illustrated by the following description of a woman who developed progressive encephalopathy that was characterized by a high CSF HIV-1 load, despite the presence of reasonably well-controlled plasma viremia, and who experienced remission of encephalopathy coincident with a reduction in the CSF HIV-1 load.

In September 2000, a 34-year-old woman was seen at Jacobi Medical Center (Bronx, NY); she had a CD4 cell count of 2 cells/mm³ and an HIV-1 load of 58,194 copies/mL (as determined by RT-PCR; Roche Amplicor), and she had previously developed cryptococcal meningitis in 1994. She manifested tremulousness and muttering. Examination of the CSF revealed a WBC count of 46 cells/mm³ (98% lymphocytes), a protein level of 148 mg/dL, and a glucose level of 50 mg/dL. Results of CSF PCR for the detection of JC virus and cytomegalovirus were negative, as were the results of repeated cultures and serologic tests. Because of its ability to penetrate the CNS, efavirenz was added to the patient’s regimen of lopinavir/ritonavir, lamivudine, and abacavir, despite the persistence of a K103N mutation that resulted from prior receipt of efavirenz.

The patient experienced transient improvement in her condition, but, by June 2002, she experienced further deterioration despite maintaining a CD4 cell count of 212 cells/mm³. In addition to cognitive dysfunction, she manifested hyperreflexia with sustained clonus and nearly constant fine myoclonus, exacerbated by action, that involved her extremities and trunk and prevented ambulation. During a 2-week period, her condition worsened. The patient could no longer ambulate. She was disoriented and confused, as was evidenced by her speech, which was characterized by nearly in comprehensible muttering. Examination of the CSF revealed the following findings: a WBC count of 156 cells/mm³ (80% lymphocytes), a glucose level of 37 mg/dL, and a protein level of 200 mg/dL; results of repeated CSF cultures, serologic tests, and PCR (for the detection of JC virus, herpes simplex virus, and varicella-zoster virus) were negative. The plasma HIV-1 load was 7392 copies/mL. By contrast, her CSF HIV-1 load was 266,667 copies/mL.

Biopsy of nondominant frontal white matter obtained from the patient’s brain showed HIV encephalitis without viral inclusions, necrosis, demyelination, or the presence of microorganisms. The ART that the patient was receiving was intensified, according to her plasma HIV-1 genotype. Zidovudine and tenofovir were added to therapy, and administration of efavirenz was stopped. The patient’s condition improved remarkably. In July 2002, she was alert, oriented, and ambulatory, and she had fluent speech; she had no abnormal movements or sustained clonus. Examination of the CSF revealed a WBC count of 20 cells/mm³ (100% lymphocytes), a protein level of 112 mg/dL, and a glucose level of 48 mg/dL. The CSF HIV-1 load decreased to 248 cells/mm³, and the plasma HIV-1 load was <50 copies/mL.

Levels of HIV-1 in plasma typically are substantially higher than those in CSF, as demonstrated by 5 cases reported by Tashima et al. [1] and by additional cases reported elsewhere [2, 3]. Among patients with dementia, CSF HIV-1 levels are elevated, compared with those of patients without dementia [3, 4]; CSF HIV-1 levels may also exceed plasma levels in up to 80% of patients with dementia [5]. Logically, the occurrence of discordance between CSF and plasma virus loads and genotypes would presage the occurrence of discordance between the virologic responses of CSF and plasma to ART. The effectiveness of ART, with respect to HIV encephalopathy, may not be adequately characterized by the plasma virus load. Further studies will determine the role of measuring the CSF HIV-1 load and determining the HIV-1 genotype for patients with HIV encephalopathy. It is fortunate that this patient had a favorable response without the benefit of a CSF HIV-1 genotype.

Elizabeth R. Jenny-Avital1 and Cathy Chuang2
1AIDS Consultation Service and 2Department of Neurology, Jacobi Medical Center, Bronx, New York

References
Urban Trench Fever in a Healthy Man from the Southeastern United States

Str—Bartonella quintana (formerly, Rochalimaea quintana) has recently emerged as an important cause of opportunistic infection in HIV-1–infected patients [1]. Nonimmunosuppressed individuals with ectoparasite (Pediculus humanus humanus) [2] infestation also have an increased risk for B. quintana bacteremia and/or endocarditis [3, 4]. Here, I report a case of classic trench fever in a healthy man who had a low risk of human body lice infestation.

A 43-year-old healthy man presented with a 3-week history of hectic fever (temperature range, 39°C–41°C) that occurred daily at midday, profound diaphoresis, and severe malaise. He had no response to treatment with cefuroxime, trimethoprim-sulfamethoxazole, and ceftriaxone. Acute weight loss (∼7 kg), incapacitating fatigue, frontal headache, and progressive pain in the deep thigh and calf occurred. At the time of examination, the man appeared to be ill; nontender inguinal lymph nodes were palpable bilaterally, and the lymph nodes were matted and had a doughy consistency. Splenomegaly (>15 cm) was confirmed by CT. Findings on a chest radiograph were normal. The WBC count was 12,500 cells/mm³, the platelet count was 269,000 platelets/µL, and the aldolase level was 16.3 U/L.

Extensive necrosis and prominent lymphocytic tissue infiltration were observed in an inguinal lymph node biopsy specimen, whereas examination of a specimen from a bone marrow biopsy showed reactive mature plasma cells and atypical lymphocytes. The findings of full-body gallium-67 citrate scanning and echocardiography were noncontributory. Serologic workup revealed negative results for the detection of HIV-1; human T cell lymphotropic virus 1; IgG and IgM for Toxoplasma gondii, Yersinia pestis, Histoplasma capsulatum, Bartonella henselae, and Ehrlichia chaffensis; and IgM for human cytomegalovirus and Epstein-Barr virus. Fever resolved 4 days after treatment with doxycycline (200 mg iv daily) was initiated. The B. quintana serum IgM level was 40 U (as determined by EIA; normal control subjects had a B. quintana serum IgM level of <12 EIA U). Two weeks later, the serum IgM level was 19 EIA U. Blood cultures were sterile for 4 weeks. Serum B. quintana IgM became undetectable 6 weeks after the completion of 1 week of therapy with doxycycline. Fatigue resolved gradually. No recurrence of urban trench fever was noticed 2 years later.

Systemic bartonellosis due to B. quintana has emerged and, recently, reemerged as an important cause of bacteremia and endocarditis in nonimmunosuppressed patients in the United States and Europe [5]. Urban trench fever is a disease that primarily involves the inner-city homeless population [3]. Symptoms may vary from those associated with the original description of trench fever (febrile illness with prominent deep leg pain and marked prostration) [6] or those associated with the recently described syndrome of fever, weight loss, bacteremia, and endocarditis [5]. In this patient, classic features of trench fever led to empiric institution of appropriate antimicrobial therapy; bacteremia or endocarditis was not present.

In most instances, person-to-person transmission of B. quintana via infected human body lice is reported among socioeconomically disadvantaged homeless individuals with poor personal hygiene [3]. Other persons at risk include patients who have the risk factors of chronic alcoholism, malnutrition, and/or injection drug abuse and who reside in overcrowded, unsanitary inner-city dwellings [5]. The patient described here did not have any known risk for P. humanus humanus infestation, and how he became infected is not known. Trench fever is a reemerging infection, and a high level of suspicion is needed to promptly identify and treat this potentially disabling disease, even in individuals at low risk.

Amar Saftar*  
Department of Medicine, University of South Carolina School of Medicine, Columbia

References


* Present affiliation: Department of Infectious Diseases, Infection Control, and Employee Health, University of Texas M. D. Anderson Cancer Center, Houston.

Reprints or correspondence: Dr. Amar Saftar, Dept. of Infectious Diseases, Infection Control, and Employee Health, 402, The University of Texas M. D. Anderson Cancer Center, 1515 Holcombe Blvd., Houston, TX 77030 (aasafdar@mdanderson.org).

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