BRIEF REPORTS

Primary Lamivudine Resistance in Acute/Early Human Immunodeficiency Virus Infection

Primary resistance of HIV to zidovudine was first described in 1992 [1] and has since been identified in up to 10% of antiretroviral-naive patients in some centers [2]. Primary resistance to nevirapine [3] has also been reported, but the prevalence of primary resistance to other agents in widespread use in clinical practice is unknown. We now report two cases of primary lamivudine resistance in two antiretroviral-naive patients who presented with acute HIV infection.

Patients with acute/early HIV infection (documented acquisition of infection in the previous 6 months) were recruited as part of an ongoing pilot study, initiated in March 1995. Patients have been recruited from community physicians, street clinics, sexually transmitted disease clinics, cohort studies of gay or bisexual men and intravenous drug users, and high-risk persons admitted to hospital. At the time of the initial evaluation, a blood sample was obtained for measurement of the CD4 cell count and the plasma virus load (Amplificor HIV Monitor kit; Roche Diagnostics, Mississauga, Canada).

For resistance testing, HIV RNA was isolated from the baseline plasma sample and then reverse-transcribed and amplified by use of primer NE1 (5′-CCCACACTTTCTGTATGTCATTGACAGTCCAGCT-3′) and primer A (5′-TGGTTGCACTTTAAATTTCCATGTCTCTATT-3′), respectively, under standardized conditions. Dilutions of this first PCR product were used as templates for specific PCR-based detection of the M184V mutation characteristic of resistance to lamivudine. This was done with primer 184 (5′-GTATCCACCTCTCCAACAGA-3′) and either primer 184M (5′-CAGACATAGTATACTCTATAAGCT-3′) or 184W (5′-CAGACATAGTATACTCTAT-3′), designed to selectively amplify viruses with the appropriate mutation at codon 184 (184M) or wild-type HIV (184W). Experimental controls (provided by J. Mellors) consisted of clinical plasma samples known to contain wild-type or mutant virus strains. Selective PCR findings were confirmed by formal sequencing of DNA obtained from the initial reverse transcription–PCR reaction.

The M184V mutation was identified at baseline in isolates taken from 2 of 35 patient samples. These consisted of 1 of 12 homosexual men (patient A), 0 of 17 injection drug users, and 1 of 6 heterosexual subjects (patient B).

Patient A is a 36-year-old man who presented 60 days after an acute retroviral syndrome that began 2 weeks after receptive anal intercourse with an unknown male partner. At the time of initial evaluation, the patient was well. Physical examination was entirely unremarkable. A test for HIV antibodies was positive. His baseline plasma virus load was 136,000 copies/mL of plasma, and his CD4 cell count was 190/μL (figure 1A). Therapy was initiated with zidovudine (500 mg/day) and lamivudine (300 mg/day). At week 8, the plasma virus load was 4,800 copies/mL. Saquinavir (enhanced oral formulation, 3,600 mg/day) was added at week 10. With this regimen, maximal virologic suppression was achieved (<400 copies/mL) and has been maintained to week 86, the most recent CD4 cell count being 1,020/μL.

Patient B is a 20-year-old man who presented 35 days after an acute illness that followed sexual contact with a female partner. Physical examination revealed oral candidiasis. He received local therapy with nystatin (to which the candidiasis responded), and an HIV antibody test was ordered, which was positive. Prior testing earlier in the year had yielded negative results. His baseline plasma virus load was 3,600 copies/mL, and his CD4 cell count was 380/μL (figure 1B). Therapy was initiated 5 weeks later with zidovudine (500 mg/day) and lamivudine (300 mg/day). By week 3, the virus load had fallen to unquantifiable levels but then increased to 970 copies/mL, and his treatment regimen was changed to stavudine (80 mg/day), didanosine (400 mg/day), and indinavir (2,400 mg/day) and then changed again to stavudine and lamivudine at week 18 because of intolerance. His plasma virus load was <400 copies/mL until week 36 and was then found to be 670 copies/mL after a recurrence of genital herpes. Four months later, while the patient is receiving the same therapy, his plasma virus load is 53,000 copies/mL.

It is not surprising that the first cases of transmission of resistant virus strains involved isolates with decreased susceptibility to zidovudine [1]. Additional cases of primary drug resistance have been slow to be identified but are now being described. The transmission of nevirapine-resistant HIV likely relates to the ease with which high-grade phenotypic resistance may develop in vivo [4]. A parallel can be drawn with lamivudine [5]. This study should not be taken as a measure of the prevalence of primary lamivudine resistance in British Columbia, as our study population was largely unselected. It is of interest that none of 17 injection drug users evaluated had primary drug resistance, and this should be monitored on an ongoing basis.

The prospective mapping of spread of primary drug resistance (to lamivudine and any other agents) may allow us to follow the spread of HIV infection in specific groups or communities. Comprehensive sampling of sentinel populations is being planned at a national level in Canada to begin to address these issues.

Brian Conway, Valentina Montessori, Danielle Rouleau, Julio S. G. Montaner, Michael V. O’Shaughnessy, Signe Fransen, Andrew Shillington, Owen Weislow, and Douglas L. Mayers
Figure 1. Serial plasma virus load measurements (copies/mL, ■), CD4 cell counts (cells/μL, ○), and antiretroviral therapy administered to patients A and B, HIV-infected patients with virus isolates with primary resistance to lamivudine (ddl = didanosine; D4T = stavudine; IDV = indinavir; SQV = saquinavir; 3TC = lamivudine; ZDV = zidovudine).

References

Massive Hemoperitoneum: A New Manifestation of Bacillary Peliosis in Human Immunodeficiency Virus Infection

Bartonella henselae and Bartonella quintana are agents recognized to be responsible for bacillary angiomatosis (BA) and bacillary parenchymal peliosis (BPP), two diseases characterized by unique vascular lesions affecting almost exclusively patients who are severely immunocompromised by HIV [1]. Histologic findings in BA consist of lobular proliferations of small blood vessels coated by enlarged endothelial cells. Although BA is most frequently found localized to the skin [1, 2], involvement of virtually every organ system has been reported [1]. Pathologic findings in BPP include dilated capillaries and blood-filled cavernous (peliotic) spaces involving the liver and spleen [1, 3]. We report a case of an HIV-infected patient with massive hemoperitoneum and hypovolemic shock as the main manifestation of hepatic BPP, complications not previously reported in this entity.

A 29-year-old man, seropositive for HIV, was admitted to the hospital because of fever and abdominal pain. The patient had a history of intravenous drug use until a few months before admission. A diagnosis of HIV infection had been made 8 years earlier, but the patient had never sought medical attention. He had had close contact with cats until recently. One month before admission, he was hospitalized because of low-grade fever, blurred vision in the right eye, dysarthria, and right hemiparesis. A CT scan of the brain revealed multiple small hypodense lesions distributed throughout both hemispheres, with no enhancement after administration of iv contrast. Results of CSF testing were normal. His serum was positive for antitoxoplasmic IgG antibodies at a titer of 1:300, and he had a CD4+ cell count of 41/mm³. The patient rejected a cerebral biopsy. He became clinically stable and was discharged while receiving treatment with pyrimethamine and sulfadiazine.

Six days after discharge, he was readmitted to the hospital because of fever, widespread abdominal pain, vomiting, and anorexia. On physical examination, the patient appeared severely ill, with a temperature of 38.5°C, diffuse abdominal tenderness, and marked hepatomegaly. Neurological findings remained unchanged in relation to those observed in the previous admission. The following laboratory values were noted: alkaline phosphatase, 2,774 U/L (normal range, 91–258 U/L); lactate dehydrogenase, 570 U/L (normal range, 230–460 U/L); WBCs, 1.8 × 10⁹/L; neutrophils, 1.2 × 10⁹/L; platelets, 28.8 × 10⁹/L; hemoglobin, 124 g/L. Bilirubin, aspartate aminotransferase, and alanine aminotransferase levels were normal, as was a chest radiograph. An abdominal CT scan revealed important liver enlargement, with a small hypodense lesion in the right hepatic lobe, and mild spleen enlargement. On the second hospital day, the patient developed hypovolemic shock and abdominal distension. His hemoglobin level...