be a risk factor. All of this, combined with the fact that patients are generally living longer, would make one expect an increased rate of incidence. However, given the dramatic rise in the number of recent reports of osteonecrosis occurring in association with HIV infection, the possibility that HAART can cause or, through its immunological effects, exacerbate the symptoms of osteonecrosis needs to be explored. Further studies clearly are needed to elucidate the pathogenesis and natural history of osteonecrosis in HIV-infected patients. We reemphasize that there is an association between osteonecrosis and HIV infection that must be recognized by clinicians who care for these patients, particularly since early detection and intervention is essential for a favorable outcome in the treatment of osteonecrosis, regardless of its cause.

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Manic Syndrome Associated with Efavirenz Overdose

Stir—Adverse effects on the CNS have been reported in 50% of patients who are given efavirenz for the treatment of HIV type 1 infection; the symptoms of “altered sensorium” that are associated with such infection include dizziness, headache, insomnia, depression, impairment of concentration, agitation, disturbing dreams, and somnolence [1]. Although the exact causal relationship between such adverse effects and treatment with efavirenz has not been determined, there also have been reports of severe depression, delusion, and inappropriate behavior, including suicide attempts, in a very small proportion of patients infected with HIV type 1 (<2%), predominantly those who have a history of mental illness or substance abuse [1]. Similar neuropsychiatric effects rarely have been associated with the administration of other antiviral treatments, such as interferon [2, 3] or zidovudine [4].

We describe a 33-year-old antiretroviral-naive woman who had asymptomatic HIV infection, a virus load of 3900 copies/mL, and a CD4+ lymphocyte count of 490 × 10⁶ cells/L. The patient, who had been recruited for participation in a clinical trial, began receiving antiretroviral treatment with abacavir, 300 mg q12h; nelfinavir, 1250 mg q12h; and efavirenz, 600 mg/day. Two days after initiation of treatment, she experienced mental dullness. On the night of the third day after initiation of treatment, she took an overdose of 90 tablets of efavirenz because she was “in search of new sensations.” She was admitted to the emergency department of the Hospital Clinic Universitari de Barcelona (Barcelona, Spain), where she showed good orientation with regard to time and place; however, she was unable to complete the rest of the Mental Status Examination because of psychomotor agitation. The patient showed other manic symptoms, including irritability, expansiveness, disinhibition, and aggressiveness. She also had a lack of insight and impaired judgment. The results of neurological and general physical examinations as well as the results of routine laboratory tests, including complete liver-and kidney-function examinations and lumbar puncture, showed no significant disturbances. MRI of the brain showed no significant changes.

The patient had no history of opportunistic disease, other disorders related to HIV infection or medication, or risk factors for CNS disease. The patient reported a personal history of cocaine abuse (such abuse occurred only on weekends) that had ended 1 year prior to admission to the hospital, but she reported no personal or family history of psychiatric illness or treatment. Screening of urine samples for illicit drugs yielded negative results. The patient received antipsychotic medication (risperidone, 1 mg q12h) and had rapid recovery within 48 h and full remission of symptoms within 5 days. Treatment with antipsychotic medications was then discontinued.

Given the close temporal relationship between treatment with efavirenz and the development of manic symptoms, and given that the patient had no history of mood disorders, we believe that this case of manic syndrome was most likely induced by use of efavirenz. Furthermore, the patient’s symptoms disappeared immediately after discontinuation of efavirenz therapy. Although antipsychotic medication was introduced, the patient’s rapid response to low dosages of risperidone (2 mg/day) suggests that suppression of efavirenz was the main determinant of the psychopathological recovery of the patient.

It is unlikely that other antiretroviral agents taken by the patient were responsible for the manic syndrome. No mood disturbances have been reported among patients treated with abacavir or nelfinavir [5], but such mood symptoms as aggravated depression, apathy, emotional lability, and euphoria were reported among patients who participated in clinical trials of efavirenz [1]. Furthermore, although the initial manifestations of manic syndrome occurred after the first dose of efavirenz was administered, the
overdose that was self-administrated by the patient may have contributed to the severity of the disorder. Conversely, no other abnormal findings of physical or laboratory examinations were associated with a dose of efavirenz that was ~30-fold greater than the usual prescribed dose. Other diagnoses, such as HIV encephalopathy, CNS opportunistic infection, or hepatic encephalopathy, were ruled out because of the normal laboratory findings, the immune status of the patient, and the quick improvement in the patient’s condition after discontinuation of efavirenz.

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