HCV RNA were positive. Since 1998, she had been taking stavudine, lamivudine, and nevirapine. In December 2000, she was admitted for jaundice, ascites, and elevated liver enzyme levels. Tests for HBsAg, anti-HBc IgM, and HBeAg were positive. HBV DNA level was 4.2 log copies/mL. Test for HCV RNA was negative. The CD4 count was 118 cells/mm^3 and plasma HIV RNA level was 6.3 log copies/mL. Two months later, therapy with zidovudine and lamivudine was reintroduced. HBV DNA levels dropped rapidly to undetectable levels, and anti-HBe was present. Retrospectively, HBV DNA was undetectable (lower detection limit $<$1000 copies/mL) 3 years and 1 year before liver decompensation.

Transmission of HBV infection from blood and organ donors with isolated anti-HBc was not detected by DNA amplification in most reports (3,4). Yet it has been observed that some liver transplant recipients developed acute HBV infection even when the donor was negative for HBsAg, or positive for anti-HBc alone or for both anti-HBc and anti-HBs. Indeed, at the Digestive Disease Week 2000, Marusawa et al reported detecting HBV DNA in liver samples from 24 of 32 healthy, related liver donors with negative tests for HBV antigens and genomes, a normal alanine aminotransferase test, and anti-HBc. The detected HBV genomes included covalently closed circular DNA and pregenomic RNA, the replication intermediate of HBV. In our 2 patients, HBV DNA was also undetectable by PCR in blood serum before hepatitis B reactivation, the alanine aminotransferase test was normal, and anti-HBc was the only marker of HBV infection.

In HIV-positive patients, hepatitis B reactivation has been reported in patients who were positive for HBsAg and who had recovered fully from HBV infection and developed anti-HBs (5). Patients with isolated anti-HBc, even with a negative HBV DNA test, are also at risk of sudden HBV reactivation and subsequent severe hepatic failure.

Firouzé Bani-Sadr, MD
Anne Maillard, MD
Diane Ponscarme, MD
Catherine Scieux, MD
Jean Michel Molina, MD
Hôpital Saint Louis
Paris, France

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RETROVIRAL REBOUND SYNDROME WITH MENINGOENCEPHALITIS AFTER CESSATION OF ANTIRETROVIRAL THERAPY

To the Editor:

In patients with chronic human immunodeficiency virus (HIV) infection, interruption of highly active antiretroviral therapy (HAART) may be associated with symptoms mimicking those of primary HIV infection (1–3). We report a case of retroviral rebound syndrome with severe meningoencephalitis after treatment interruption.

A 47-year-old man tested HIV-1 seropositive in 1999. In February 2000, he was asymptomatic, his CD4 cell count was 280/μL, HIV plasma viral load was 270,000 copies/mL, and he had begun antiretroviral therapy with stavudine, lamivudine, ritonavir, and indinavir. On October 2000, peripheral neuropathy was diagnosed. Blood examination showed elevated hepatic aminotransferase levels and a lactate level of 53.1 mg/dL, which was consistent with lactic acidosis. Antiretroviral therapy was thus stopped. One month later, he presented with progressive fever, asthenia, weight loss of 6 kg, severe myalgias, and dysuria. Clinical examination revealed fever (39°C), purpuric rash on both legs, and mental confusion. Blood examination showed 7200 leukocytes/μL (neutrophils, 32%; lymphocytes, 53%) and no inflammatory syndrome. Hepatic aminotransferase levels were 92 U/L (normal $<$56 U/L), and CD4 cell count was 265/μL. A cerebrospinal fluid examination showed a normal glucose level, a protein level of 1.2 g/L, and a leukocyte count of 45 cells/μL (lymphocytes, 93%). Cerebrospinal fluid cultures for bacteria, mycobacteria, and fungi were negative, as were tests by polymerase chain reaction for herpes simplex virus, varicella-zoster virus, cytomegalovirus, and JC viruses. Serologic tests for parvovirus B19 and *Rickettsia* were negative. Cerebral and medullar examinations by magnetic resonance imaging were normal. Electroencephalogram revealed bilateral slow waves. Clinical outcome was marked by progressively more intense confusion and by seizures. Treatment with antituberculous agents and acyclovir did not improve symptoms. HIV viral load was 78,000 copies/mL in plasma and 317,000 copies/mL in cerebrospinal fluid, suggesting that clinical symptoms could be due to a rebound of HIV infection. Antiretroviral therapy was restarted on January 26, 2001, with lopinavir, ritonavir, and saquinavir, but without nucleoside analogs because of recent lactic acidosis. Clinical outcome was favorable, with cessation of fever and myalgia after 1 week of treatment. After 2 months of therapy, Mini-Mental

State Examination, electroencephalogram, and cerebrospinal fluid examination were normal. HIV viral load, which was 2800 copies/mL in plasma and 77,000 copies/mL in cerebrospinal fluid after 1 month of treatment, was undetectable in plasma (<200 copies/mL) after 2 months of treatment.

This observation is consistent with a retroviral rebound syndrome with meningoencephalitis after cessation of HAART. The onset after treatment interruption, rapid resolution after treatment reinstitution, clinical presentation similar to acute retroviral syndrome of primary HIV infection, mononuclear leukocytosis, and high HIV viral load strongly suggested retroviral rebound syndrome. Five patients who had the syndrome after interruption of antiretroviral therapy have been reported (1–3). Their symptoms occurred a mean of 24 days (range, 10 to 42 days) after HAART interruption. As in our patient, their main clinical manifestations included fever, asthenia, sweats, and myalgias, as well as pharyngitis, rash, adenopathy, headache, aseptic meningitis, and diarrhea. The mean CD4 cell count was 271/μL (range, 86 to 410/μL) and mean HIV plasma viral load was 620,000 copies/mL (range, 31,000 to 1,600,000 copies/mL). A favorable outcome was achieved in all patients a mean of 14 days (range, 10 to 21 days) after HAART reinstitution.

Although the frequency of treatment interruption in patients with chronic HIV infection is high because of nonadherence, adverse effects, or structured therapeutic interruption, there have been few reported cases of retroviral rebound syndrome. Only two cases have been reported in trials of structured treatment interruption (4). It is possible that the syndrome is underdiagnosed because it may present as a flu-like syndrome and have a favorable outcome without treatment, as in the case of acute HIV infection (5,6). Nonetheless, physicians should be aware of this unusual and potentially severe syndrome after interrupting antiretroviral therapy in HIV-infected patients.

Guillaume Breton, MD
Xavier Duval, MD
Anne Gervais, MD
Pascale Longuet, MD
Catherine Leport, MD, PhD
Jean-Louis Vildé, MD
Department of Infectious and Tropical Diseases
Bichat Claude Bernard Hospital
Paris, France

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RECURRENT EXTRAINTESTINAL *CLOSTRIDIUM DIFFICILE* INFECTION

In contrast to its propensity for causing intestinal infections (1), *Clostridium difficile* has rarely been isolated from extraintestinal sites (2). Apart from a few case reports and small case series (3–6), the clinical features of extraintestinal *C. difficile* infections have not been studied systematically. Despite the pronounced cytopathologic effect of *C. difficile* toxin on the colonic mucosa, the organism probably has a low pathogenic potential outside the intestinal tract (7). Extraintestinal infection may also be underdiagnosed because the organism is fastidious. We report a case of recurrent extraintestinal abscesses due to *C. difficile* infection. We also reviewed all published reports of extraintestinal infections and summarize the clinical and pathological characteristics of these infections.

A 65-year-old woman with end-stage renal disease was admitted with fever and pain in the left hip. She had previously been admitted 6 months earlier with fever, confusion, and weakness, together with left upper quadrant tenderness. She had leukocytosis (white blood cell count, 34.2 $\times$ 10^6/L). Blood cultures were positive for *C. difficile.* A computed tomographic (CT) scan revealed a 9- $\times$ 11-cm splenic abscess, which tested positive for the same organism. She was treated successfully with splenectomy and intravenous metronidazole.

The patient continued, however, to experience multiple episodes of fever, confusion, generalized weakness, and left hip pain, prompting the current admission. Her white blood cell count was again elevated, at 16.3 $\times$ 10^6/L. Blood cultures and stool *C. difficile* toxin assays were repeatedly negative. A CT scan showed a left iliacus muscle abscess. The abscess was drained, and culture of the fluid was positive for *C. difficile.* The patient was treated with intravenous metronidazole. She had a good clinical outcome and was discharged in stable condition.

Our review of the literature showed 59 cases of extraintestinal *C. difficile* infections. They present in three main forms: bacteremia with or without focal infection, intra-abdominal infections, and extra-abdominal abscesses. The organism was isolated in pure culture only in a minority (32%) of cases, and recovered in a context of polymicrobial infection (bacteremia or abscess) in 40