In the 1 November issue of the journal, Garlin and Sax [1] describe an HIV-infected patient “who developed retroviral rebound syndrome that led to death after antiretroviral treatment was stopped” (p. e83). In our opinion, the authors infer that treatment interruption had a key role in the clinical presentation of their patient’s illness and in his death; this assumption, essentially based on a temporal relationship, could be merely coincidental.

The patient’s antiretroviral therapy included stavudine and didanosine, taken for ~4 years, during which time the patient had chronic hepatitis C virus coinfection, a condition associated with mitochondrial stress and higher risk of drug toxicity [2]. This treatment has been associated with a >80% probability of hyperlactatemia [3] and a high risk of serious liver toxicity and lactic acidosis, which could potentially evolve to irreversible multiple-organ damage, despite treatment interruption. The patient’s clinical status at presentation was highly predictive of severe lactic acidosis in this context, and thus, treatment interruption was properly recommended. However, no mention is made about serial determinations of lactate or bicarbonate levels in this case report. HIV-associated lymphoma or mycobacterial disease could also cause or contribute to these clinical features, but no results of additional imaging studies, bone marrow examinations, or blood cultures for mycobacteria are provided.

After treatment was interrupted, the patient’s clinical condition continued to worsen, and bilateral lung infiltrates and embolic phenomena developed in the absence of specific clotting abnormalities or vasculitis. However, in the reported case, an exhaustive diagnostic evaluation to investigate other, more plausible possibilities, such as endocarditis, paradoxical embolism, or myocardial infarction, seemed warranted but is not reported. The normal findings of a bronchoalveolar lavage examination in this patient’s case is not enough to rule out other possible disorders, because the diagnostic yield of this procedure, though valuable, is limited [4]. Finally, the patient had cardiac arrest, which was most likely related to surgical stress in the context of a critical clinical condition.

We conducted a search of the Medline database with the term “acute retroviral syndrome,” plus generic terms such as “dyspnea,” “lung infiltrates,” and “embolism,” and we found absolutely no references. Moreover, in their review of the literature, Garlin and Sax [1] could not find any clinical report similar to that of their patient. If this article is to be accepted as the first report of treatment interruption–associated death, a plausible hypothesis linking retroviral rebound to the patient’s clinical presentation and his fatal outcome must be proposed, and other possible explanations must be reasonably ruled out. We think that, because these requirements are in no way accomplished in this case report [1], the title seems both unjustified and unnecessarily alarming.
Reply to Angel-Moreno and Perez-Arellano

Sr—In response to the letter by Angel-Moreno and Perez-Arellano [1] regarding our recent article [2], we agree that our case represents an exceedingly uncommon and morbid chain of events after discontinuation of antiretroviral therapy (ART). However, we did, in fact, conduct an exhaustive search for other unifying diagnoses, although limitations on the length of the article made it impossible to report every negative study result that was noted during our patient’s long, complex hospitalization. This patient never had significantly elevated lactate levels, although we, too, suspected mitochondrial toxicity caused by ART. He had transthoracic and transesophageal echocardiograms that did not show either signs of infective endocarditis or myocardial dysfunction consistent with infarction. We performed many blood cultures that revealed no growth of mycobacterial and fungal isolators. Several abdominal CTs showed no significant abnormalities and no evidence of hepatic steatosis; no signs of lymphoma or other malignancies were found either during cytological examination or during consultation with our oncology service.

This patient had many concomitant medical problems, including hepatitis C virus infection and diabetes mellitus, and he was a cigarette smoker; these, as well as cumulative drug toxicity, may very well have played roles in the cascade of events that led to death. His hypercoagulability may have preceded retroviral rebound syndrome, or it may have been triggered by other circumstances, but he had never had clinically apparent thrombotic events before. It is true that the temporal relationship of his marked deterioration to his discontinuation of ART provides only circumstantial evidence of a causal connection; however, the striking time line of his hospital course and rapid viral rebound, as well as the plausible physiological mechanism, led us to report his case. This patient came to us sick, but his condition rapidly became dramatically worse when we discontinued ART, which corresponded with a striking decrease in his absolute CD4 count and a spike in his HIV load. None of our investigations could explain his condition, and he then improved once ART was resumed, which added support for a relationship between his rapid viral rebound and his symptoms. Our supposition is that, for this already debilitated patient with comorbidities, the discontinuation of ART and resulting rapid rebound of viremia set in motion a systemic process that included an increased predilection for thrombosis that eventually led to his death.

Treatment interruptions may be necessary in order to manage drug toxicity, which was our intention regarding the care of this patient. The dramatic details of this case serve to illustrate an extreme form of retroviral rebound syndrome that, in this patient, who had several underlying disease processes, unfortunately resulted in a fatal outcome.

Acknowledgments


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References


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Cytomegalovirus Ileitis and Hemophagocytic Syndrome Associated with Use of Anti-Tumor Necrosis Factor-α Antibody

Sr—Recent reports of serious cytomegalovirus (CMV) infections in patients receiving treatment with infliximab have appeared [1, 2]. We report a case of acute CMV infection complicated by CMV ileitis and hemophagocytic syndrome.

A 22-year-old man with a history of Crohn’s disease presented with fever, nausea, and vomiting. He had previously required a total colectomy. His treatment included infliximab, which was given at 6-week intervals for 4 months, and 6-mercaptopurine. On presentation, his temperature was 39.4°C, his blood pressure was 90/52 mm Hg, his pulse was 93 beats/min, and his respiratory rate was 22 breaths/min. His initial WBC count was 1100 cells/μL, with 76% neutrophils and 17% lymphocytes. His hemocrit was 29%, and his platelet count was 62,000 cells/μL. Initial empirical treatment included liposomal amphotericin B, vancomycin, and aztreonam.

The patient’s clinical course was complicated by persistent, disseminated vascular coagulation and gastrointestinal hemorrhage. Endoscopy revealed ulcerations of the ileum, and immunostains of biopsy specimens were positive for CMV. Laboratory values included an anti-CMV IgM level of 5.46 (positive, >1.09) and an anti-CMV IgG level of 39 (positive, >6). Serum quantitative PCR was positive for CMV at 134,000 copies/mL. Other studies, including blood cultures and tests for antinuclear antibodies, toxoplasma IgG, Epstein-Barr virus, coccidioides antibodies, and HIV antibodies, yielded negative results.

Coagulopathy and hemorrhaging per-