Favorable Outcome of Severe Acute Hepatitis B in a Patient Treated with Antithrombin III and Antiviral Therapy

To the Editor—A 47-year-old man was admitted to our institution with severe acute hepatitis B (SAHB). The patient had suffered deep venous thrombosis of both lower extremities 2 years previously, and 2 mutations (C677T and A1298C) in the gene for methylenetetrahydrofolate reductase (MTHFR) were detected. Moreover, the family history was positive for thrombophilic states—his mother had thrombosis of the central retinal vein. The clinical course demonstrated a gradual worsening, with encephalopathy and progression to fulminant hepatic failure occurring during the first week after admission. The bilirubin level rose to 314 μmol/L (reference range, 0–20 μmol/L), and the alanine aminotransferase level rose to 87.5 μkat/L (reference range, 0–0.8 μkat/L). Moreover, a significant deterioration in coagulation parameters was apparent: the prothrombin time was 21.3 s (reference range, 10.9–15.3 s), the international normalized ratio was 1.85 (reference range, 0.80–1.20), the D-dimer level was 1380.0 ng/mL (reference range, 0–250 ng/mL), and the antithrombin III (AT III) level was 31% (reference range, 81%–130%). The initial therapy was aimed at combining antiviral treatment with improvement of the coagulation disorder. The patient received low-molecular-weight heparin, intravenous vitamin K, and 4 transfusion units (1000 mL) of fresh frozen plasma followed by 2000 IU of AT III concentrate and 100 mg of lamivudine (Zeffix) daily for viral suppression. This therapeutic approach led to a prompt correction of coagulopathy and to favorable clinical, biochemical, and virological responses over the next several days. Seroconversion to antibody against hepatitis B e antigen was recorded on the 11th day of lamivudine therapy; 5 weeks later, the biochemical and coagulation test results were normal, and hepatitis B surface antigen was undetectable. Lamivudine therapy was stopped after the second negative hepatitis B surface antigen test result, which was obtained 1 month later.

SAHB is an intermediate state between acute hepatitis B with a moderate course and progression to fulminant hepatic failure. The following criteria for the diagnosis of SAHB have been proposed by Schmilovitz-Weiss et al [1]: (1) the presence of hepatic encephalopathy, (2) a serum bilirubin level ≥10.0 mg/dL (≥170 μmol/L), and (3) an international normalized ratio ≥1.6. The combination of 2 or more of these criteria is considered to be diagnostic. According to Tillmann et al [2], only 1 criterion is required for the diagnosis of SAHB: a prothrombin time ≤36% of normal (or either an international normalized ratio ≥2.0 or an absolute prothrombin time ≥23 s). The disturbances in blood coagulation are sequelae of the involvement of the coagulation and fibrinolysis pathways. Hemorrhage complicating the course of SAHB is due to reduced synthesis of clotting factors and inhibitors of coagulation and fibrinolysis. Less is known about AT III levels during the course of SAHB; AT III supplementation is therefore debatable. However, we chose more aggressive anticoagulation therapy for our patient with extremely low AT III levels and a potential thrombophilic state (ie, MTHFR deficiency and a history of deep venous thrombosis), and this therapy led to a rapid improvement in clinical status and laboratory parameters.

It is worth noting that the fulminant course of SAHB is associated with an exaggerated immune response, which might be modulated by the strong anti-inflammatory effects of AT III [3]. Thus, the close monitoring of AT III levels and the combination of antiviral agents and AT III concentrate in the treatment of SAHB could be beneficial.

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References


On Changes in Cancer Mortality among HIV-Infected Patients: Is There an Excess Risk of Death from Pancreatic Cancer?

To the Editor—A recent article from France published in Clinical Infectious Diseases suggested that non–AIDS-related cancers have played an increasing role in mortality among human immunodeficiency virus (HIV)–infected people during the highly active antiretroviral therapy (HAART) era (13.0% of all deaths in 2000 and 20.7% in 2005 were attributed to non–AIDS-defining cancers) [1]. We were impressed with the observation of an increased frequency over time of deaths due to solid neoplasms among HIV-infected people in France, particularly of deaths due to pancreatic cancer. On the basis of clinical documentation, pancreatic cancer emerged as one of the types of cancers with the highest relative increase (from 0.32% of all deaths in 2000 to 1.09% in 2005, a 3.4-fold higher frequency).

In their article, however, Bonnet and colleagues did not provide mortality rates, and a comparison of the observed site-specific number of deaths with the ex-
pected number from a general population of the same age and sex was not done. This might have affected the trend assessment, because age-related residual confounding might have partially determined the increase in non–AIDS-defining cancers (ie, the median age of HIV-infected people was 46 years in 2005 and 41 years in 2000) [1].

Taking advantage of population-based data used for assessing post-AIDS survival in Italy [2], we compared the number of observed deaths due to pancreatic cancer among persons given a diagnosis of AIDS with the expected number. Briefly, data on all Italian citizens receiving a diagnosis of AIDS from 1999 through 2005 were linked with the Italian Mortality Database (December 2006 version) to update their vital status and to identify conditions present at death (for details on the linkage procedure, see Dal Maso et al [3]). The number of person-years at risk of death was computed from the date of AIDS diagnosis to the date of death or to 31 December 2006. The number of observed deaths attributable to pancreatic cancer (C25 in International Classification of Diseases, Tenth Revision) was divided by the expected number, which was computed from age- and sex-specific mortality rates for the Italian general population during the years 2000–2003. Thus, the standardized mortality ratio and its 95% confidence interval for death from pancreatic cancer among people with AIDS versus the general population were computed.

Of the 8537 Italian patients, aged 25–54 years, given AIDS diagnoses from 1999 through 2005 (who accumulated 31,437 person-years at risk of death), 2634 died. Five patients had pancreatic cancer at death, versus an expected number of 0.92. The corresponding standardized mortality ratio was 5.42 (95% confidence interval, 1.71–12.74), suggesting that Italian patients with AIDS had a statistically significant higher risk of dying from pancreatic cancer than did the corresponding general population.

This finding from Italy seems to confirm the substantial burden of pancreatic cancer in the risk of death among people with HIV/AIDS noted during the HAART era in France. It is in accordance with a 2.5-fold higher incidence of pancreatic cancer among HIV-infected people reported in the United States during the HAART era [4], but it contrasts with incidence data from Italy, where no excess risk for pancreatic cancer was observed during the pre-HAART era compared with the HAART era [3].

Because HAART use has been associated with an elevated frequency of diabetes [5], which is a well-established risk factor for pancreatic cancer in the general population [6], one can speculate that HAART use may, in the long run, increase the risk of death from pancreatic cancer in HIV-infected people. On the other hand, the improved survival of HIV-infected people resulting from the use of HAART increases the probability of their developing several types of cancers. Assessing the cancer mortality burden is now a major concern for HIV-infected people, and we agree with Bonnet and colleagues that future studies should better address the issue of HAART use and causes of death, particularly cancer.

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References


Is Acquisition of Methicillin-Resistant Staphylococcus aureus an Occupational Hazard for Medical Students?

To the Editor—Exposure to microbes is an inherent risk of working in patient care settings. In view of its increasing incidence in the general population, acquisition of methicillin-resistant Staphylococcus aureus (MRSA) is a special concern for health care workers [1, 2]. Medical students comprise a unique population at risk for MRSA acquisition. During the first 2 years of medical school, most students have little patient contact. In contrast, the third and fourth years traditionally involve substantial patient contact in hospitals and clinics. No study has analyzed whether this patient exposure creates a risk of MRSA carriage for US medical students.

To address these issues, we evaluated MRSA carriage rates among medical students at a community-based medical