Clostridium difficile Colitis: A Possible Cause of Unexplained Elevation of Serum Alkaline Phosphatase Levels in Patients with AIDS

Most elevations in serum levels of alkaline phosphatase (AP) in patients with AIDS result from hepatobiliary disorders, but unexplained elevations are also encountered [1, 2]. We describe marked elevations in serum levels of AP secondary to Clostridium difficile colitis in a patient with AIDS.

A 58-year-old male with AIDS presented to the hospital with a fever (temperature, 103°F). His medical history was notable for chronic diarrhea secondary to duodenal microsporidiosis, which was treated unsuccessfully with metronidazole. Findings on physical examination were unrevealing. The WBC count was 5,600/μL, and the AP level was 1,100 U/L. Levels of transaminases, bilirubin, albumin, γ-glutamyl transpeptidase (GGTP), and 5′ nucleotidase (5′NT) were normal, as was the prothrombin time. Radiological studies, including a bone scan, did not show any abnormalities, and multiple blood cultures were negative. The patient’s temperature normalized over 48 hours, and he was discharged.

Five days later, he was readmitted with fever, chills, and vomiting; the chronic diarrhea persisted. Physical examination revealed a temperature of 99.6°F, a normal abdomen, and blood in his stools. The WBC count was 4,200/μL with 34% neutrophils and 47% band forms. The AP level was 1,850 U/L; levels of liver transaminases remained normal. Plain abdominal films showed a dilated colon with thumbprinting; an ultrasonogram revealed a normal liver and biliary tree with moderate ascites; an abdominal CT scan showed colitis, pneumatosis, and ascites (figure 1). Sigmoidoscopy demonstrated the presence of yellow plaques; pseudomembranous colitis was confirmed by examination of biopsy specimens and by the results of a C. difficile toxin assay (titer, 1:1,000). The fever cleared with metronidazole therapy, the AP level decreased to 611 U/L, and repeated abdominal CT scan showed regression of the colonic inflammation previously evident and resolution of the ascites.

The patient received metronidazole for 14 days, and 1 week after the drug was discontinued, his fever recurred (temperature, 102°F). The chronic diarrhea was still present and unchanged in nature. The WBC count was 3,800/μL with 34% band forms, and the AP level had risen to 1,050 U/L. Empirical treatment with antibiotics was given but discontinued after blood cultures were found to be negative and the fever resolved. On repeated testing, the AP level was 2,140 U/L, the GGTP level remained normal, and the 5′NT level was 17 IU/L (normal, < 10 IU/L). A repeated C. difficile toxin assay was positive at a titer of 1:100. Treatment with vancomycin (125 mg po q.i.d.) was initiated and gradually tapered over 2 months. The patient remained afebrile, and the AP level declined to 136 U/L. After completion of therapy and at a 6-month follow-up evaluation, the serum levels of AP and GGTP remained normal. The chronic diarrhea subsequently resolved fol-

Figure 1. Axial CT images obtained with both oral and intravenous contrast media show extensive colonic wall thickening due to Clostridium difficile colitis in a patient with AIDS. a: At the level of the right kidney, both the ascending (black arrow) and the descending (white arrow) colon show wall thickening and submucosal edema. b: Thickening of the sigmoid colon is present with intraluminal stranding (black arrow) and pneumatosis (white arrow). Also note the presence of ascites (FL).
Following treatment with albendazole, obtained through a compassionate-use protocol (SmithKline Beecham Pharmaceuticals, Philadelphia).

Severe elevations in serum levels of AP are common in patients with AIDS and are usually attributable to hepatobiliary disorders [1]. However, ≤17% of patients have AP elevations to >1,000 U/L for which there is no obvious cause [2]. Liver biopsy fails to provide a diagnosis in ≤50% of such cases [3].

For our patient, the clinical history and negative bone scan argue against bone as a major source for the elevated AP levels. Although the mild elevation in the 5‘NT level at the patient’s second presentation suggests the liver as a possible source, the normal level of 5‘NT on his initial presentation, the persistently normal GGTP levels [4], and the normal hepatobiliary images argue against a major hepatobiliary source. Since treatment of C. difficile colitis led to complete normalization of AP levels, liver biopsy and endoscopic retrograde cholangiopancreatography were not indicated and, in all likelihood, would have been unrevealing. Finally, the striking temporal relation between AP levels and the presence, as well as severity, of C. difficile colitis strongly suggests that the colonic mucosa was the major source of the elevated AP levels.

An AP isoenzyme different from “tissue nonspecific” AP is produced by intestinal epithelium (IAP). There is a distinct fetal IAP [5], as well as a potentially different IAP that is released from the colon during various disorders [6–8]. Release of AP into serum is likely related to severity of inflammation. The severity of C. difficile colitis is greater in patients with AIDS and may be related to their lower absolute CD4 lymphocyte counts [9]. Our patient’s CD4 cell count was only 10/mm³, and the severity of the colitis was evidenced by his high fever, chills, hypotension, and pneumatosis intestinalis, a finding rarely reported for patients with AIDS [10].

When patients with AIDS present with increased levels of AP that are not attributable to the liver or bone, clinicians must consider processes that affect the intestinal tract and, more specifically, the colon, as the source for enzyme elevation.

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References