patient showed continued clinical improvement, the fungemia resolved, and she was extubated. On day 8 of treatment, the dosage of intracolonic vancomycin was tapered to every 8 hours, while parenteral metronidazole was changed to oral metronidazole and continued for 2 weeks.

C. difficile is the cause of approximately 25% of all cases of antibiotic-associated diarrhea and the major etiology for pseudomembranous colitis (1). Notably, pseudomembranes are not always present in *C. difficile* colitis, and 10% of cases are not detected when direct visualization is limited to flexible sigmoidoscopy (2). In one study of recipients of allogenic stem cell transplants, the rate of *C. difficile* infection was 13% (3). The source of infection can be either endogenous or exogenous, with onset of symptoms between the start of antibiotic therapy and within 60 days of antibiotic discontinuation (4). Severe cases may be associated with fulminant colitis, toxic megacolon, hyperpyrexia, intestinal perforation, leukemoid reaction, and death (5).

Although uncommon, the toxic form of pseudomembranous colitis usually requires surgical intervention, and has been associated with a crude mortality rate of 35% (5). The indications for surgery include fulminant disease, colonic perforation, toxic megacolon, and failure of medical therapy (5). Our patient, who had severe fulminant *C. difficile* colitis and a colonic wall that was thickened by 2.5 cm, responded to aggressive, nonstandard medical management. The role of intracolonic vancomycin in severe *C. difficile*–associated pancolitis deserves further consideration as an alternative to surgery or as a bridge to surgery in severely ill patients (6).

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ATORVASTATIN-INDUCED REVERSIBLE POSITIVE ANTINUCLEAR ANTIBODIES

To the Editor:

The cholesterol-lowering 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase inhibitors, or statins, have sustained benefits in the treatment of patients with hypercholesterolemia, and have been shown to decrease the incidence of coronary events in primary and secondary prevention. Although generally safe and well tolerated, they have been associated with secondary effects, such as hypersensitive reactions, vasculitis, and minor systemic autoimmune syndromes. There have been several reports of patients who developed lupus-like syndromes or vasculitis after treatment with statins (1–6). Atorvastatin is a new and effective HMG-CoA reductase inhibitor (7), which has a safety profile similar to that of other statins. We report a case of positive antinuclear and antihistone antibodies in a 26-year-old man who was treated with atorvastatin.

The patient had cryptorchidism during childhood, as well as benign intracranial hypertension as an adolescent. He had hypercholesterolemia in 1998 (total cholesterol, 335 mg/dL; low-density lipoprotein [LDL] cholesterol, 254 mg/dL), for which he was treated with atorvastatin, administered orally at 20 mg daily. In November 1999, he visited the family physician because of a 4-week course of constitutional symptoms and slight headaches. He tested positive for antinuclear antibodies, and was admitted to our systemic autoimmune diseases unit for further study. The patient reported possible recent photosensitivity; he did not have fever, discoid rash, alopecia, aphthous ulcers, Raynaud's phenomenon, vasculitis, arthralgias, arthritis, myositis, seizures, psychosis, or pleural pain. The standard laboratory data were normal and reported an absence of leukopenia, thrombocytopenia, anemia, and proteinuria. Laboratory studies disclosed the following values: total cholesterol, 206 mg/dL; LDL cholesterol, 133 mg/dL; thyroid-stimulating hormone, 4.57 μIU/mL (normal range, 0.26 to 4 μIU/mL); and free thyrosine, 1.01 ng/dL (normal range, 0.65 to 1.9 ng/dL). Antinuclear antibodies were positive and revealed a speckled pattern (1/320); antihistone antibodies were also positive (276 IU/mL). C3 complement was 114 mg/dL, and C4 complement was 17 mg/dL. Antibodies to double-stranded deoxyribonucleic acid (dsDNA), Sm, Ro/SSA, La/SSB, RNP, Scl-70, centromere, and ribosomal P0 were negative or within normal range. In December 1999, because of possible drug-induced antinuclear antibodies, atorvastatin was replaced with a bile acid–sequestrating agent. Cholesterol levels remained within the normal range. The patient was asymptomatic (Table).

This patient may represent a new case of positive antinuclear and antihistone antibodies after treatment

Table. Evolution of Antinuclear and Antihistone Antibodies

Date	Antinuclear Antibodies	Antihistone Antibodies
December 1999	1/320, speckled pattern	276 IU/mL
March 2000	1/160, speckled pattern	232 IU/mL
June 2000	1/80, speckled pattern	Negative
November 2000	Negative	Negative
January 2001	Negative	Negative

with atorvastatin, without symptoms of lupus. Our patient did not have symptoms of lupus or other autoimmune diseases; the acute constitutional symptoms reported, although similar to those described in most patients with drug-related lupus (8,9), may have been due to a nonrelated viral syndrome. The presence of positive antinuclear antibodies was insufficient to establish drug-related lupus. We might have been presented with a more complete clinical picture if the patient had received the drug for a longer time.

Neither the prevalence of drug-related lupus nor its frequency after treatment with statins is known (1). The serological evolution observed in our patient was similar to the transient clinical description in other cases of drug-related lupus after administration of statins. Symptoms resolved a few months after stopping the drug, although some patients did require a short course of prednisone (10). Many drugs have been associated with drug-related lupus, and this is one example of the environmental-autoimmune disease relation. Because of the increased use of treatments involving statins, clinicians should be aware of possible adverse effects.

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HEPATITIS B VIRUS–ASSOCIATED APLASTIC ANEMIA FOLLOWED BY MYELODYSPLASTIC SYNDROME

To the Editor:

Aplastic anemia complicating viral hepatitis is a rare but well-documented phenomenon. Although most cases are caused by a non-A, non-B, or non-C agent (1), aplastic anemia has been associated with hepatitis B virus (2–4). Hepatitis B virus can be detected in tissues other than hepatocytes, including circulating mononuclear cells, bone marrow cells, and the spleen (5,6). In vitro exposure of bone marrow to hepatitis B virus results in a dose-dependent inhibition of hematopoietic stem cells (6). Furthermore, several studies have implicated a possible etiologic role of hepatitis B virus in hematopoietic malignancies, such as myelodysplastic syndrome and acute myeloid leukemia (7–9). Successful management of aplastic anemia has led to the long-term survival of many patients who later developed clonal disorders, such as acute myeloid leukemia and myelodysplastic syndrome (10). We report a case of a patient with hepatitis B virus and aplastic anemia, who developed myelodysplastic syndrome over the course of 9 years.

A 52-year-old Japanese woman was admitted to Sapporo Medical University Hospital, Japan, in May 1991, presenting with shortness of breath and purpura. Routine laboratory tests on admission revealed pancytopenia (hemoglobin, 8.3 g/dL; leukocyte count, 1.6×10^9/L; and thrombocytes, 31×10^9/L) and an elevated alanine aminotransferase level of 47 IU/L. Both surface and envelope antigens for hepatitis B virus were positive, whereas antibodies to both hepatitis A (IgM) and C were negative. Bone marrow biopsy (Figure 1) revealed hypocellularity without any other abnormality, a normal karyotype, and a low uptake by ^{111}InCl scintigraphy. Her condition was diagnosed as hepatitis-associated aplastic anemia. She underwent a blood transfusion, and was treated with prednisolone 30 mg/d, which was later tapered to 5 mg/d. Although she underwent an initial remission, she gradually developed hypoproteinemia, pancytopenia, hyperammonemia, pleural effusion, and ascites. A diagnosis of cirrhosis was made. Dur-