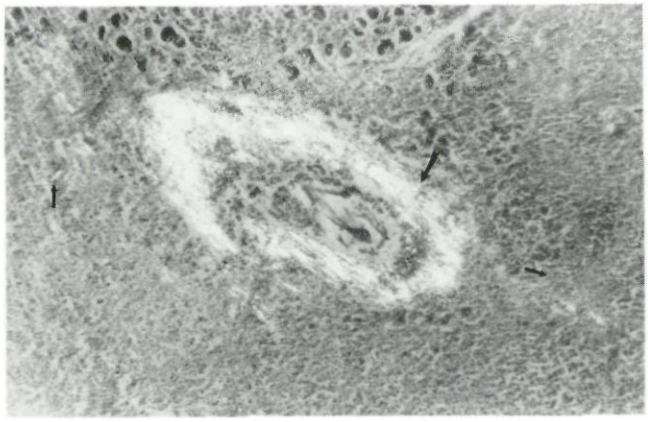

FIG. 1. Apple-green birefringence under polarized light showing perivascular *(large arrow)* and parenchymal *(small arrow)* amyloid deposits in the pancreas.

mention pancreatic involvement in a series of 229 patients with systemic amyloidosis. In an autopsy series of 30 patients with systemic amyloidosis, the pancreas was examined in only nine; only one of four patients without multiple myeloma or macroglobulinemia was noted to have pancreatic involvement, although no further histologic or pathologic information was given (5). Our patient had both acute hemorrhagic pancreatitis and amyloidosis involving the pancreas.

Clinical and laboratory findings suggestive of amyloidosis in a patient with progressive intrahepatic cholestasis of unknown cause include macroglossia, hepatosplenomegaly, proteinuria, congestive heart failure, orthostatic hypotension, carpal tunnel syndrome, and peripheral neuropathy. Thrombocytosis is common and is attributed to functional hyposplenism (with Howell-Jolly bodies on peripheral smear). The thrombin time is often prolonged, and may be the most consistent coagulation abnormality, but does not appear to predispose the patient to bleeding (1). Cholestatic jaundice appears to be an uncommon but ominous mode of presentation in systemic amyloidosis; a serum direct bilirubin greater than 1 mg/dl is associated with a median survival of only 2.1 months (2).

Serum protein electrophoresis is often unhelpful in establishing the diagnosis of amyloidosis. Often, a monoclonal spike may not be seen on serum protein electrophoresis, due to urinary losses of protein (2). A combination of serum and urine immunoelectrophoresis can increase the diagnostic yield (1, 2). Although fat pad biopsy is one of the tests commonly used to make the diagnosis, and is reported to have a sensitivity of 85% (8), this test was negative on two occasions in our patient. Other tissues that may yield a diagnosis of amyloidosis include rectum, bone marrow, and liver (6). Liver biopsy in patients with hepatic amyloidosis may carry an increase risk of bleeding (2).

Liver histology may demonstrate amyloid infiltration in the hepatic parenchyma, periportal regions, and in perivascular areas (1, 3). Amyloid deposition in the intrahepatic bile ducts and in peribiliary regions has also been described recently (9); however, pancreatic involvement has not often been reported.

In conclusion, a case of fatal hepatic and pancreatic systemic amyloidosis with an initial presentation of cholestatic jaundice due to hepatic infiltration by amyloid is described. Patients presenting with this form of primary or systemic amyloidosis have a poor prognosis, and often die within weeks of presentation. Fat pad biopsy, though less risky than biopsy of other organs, may be falsely negative. We speculate that ERCP may carry an increased risk of pancreatitis in patients with amyloidosis, possibly due to amyloid infiltration in the pancreas.

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ELEVATED α-FETOPROTEIN IN ASSOCIATION WITH LOSS OF SERUM HBeAg

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INTRODUCTION

Serum α-fetoprotein (AFP) is widely used in clinical practice as a useful marker for hepatocellular carcinoma in patients with acute liver disease, chronic liver disease, and cirrhosis (1). Recognition of an elevated serum AFP usually results in an extensive evaluation to determine whether hepatic cancer is present. False-positive elevations in serum AFP occur in all categories of liver disease but are most common in patients with chronic hepatitis B infection (2). In this report we describe two patients with chronic hepatitis B infection who developed elevation in serum AFP to levels greater than 500 ng/ml shortly before serum HBeAg converted from positive to negative.

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METHODS

Case 1

A 32-yr-old male from Korea presented to an outside institution in October 1989 complaining of fatigue and anorexia. Laboratory evaluation revealed AST 664 IU/L, ALT 1166 IU/L, alkaline phosphatase 186 IU/L, and bilirubin 1.2 mg/dl. His serum was HBsAg positive, anti-HBs negative, and anti-HAV IgM negative.

In January 1990, his serum transaminases were normal. In April 1990, he was referred to the University of Michigan Medical Center for continued symptoms of fatigue, anorexia, and right upper quadrant pain which were not as prominent as his symptoms in October (see Fig. 1). He did not have fever, chills, arthralgias, myalgias, history of jaundice, or change in stool color. His wife and two sisters were anti-HBs positive. On physical examination, there were no stigmata of chronic liver disease. His liver was 9 cm by percussion and not palpable. His serum laboratory tests were as follows: AST 316 IU/L, ALT 639 IU/L, total bilirubin 1.2 mg/dl, alkaline phosphatase 138 IU/L, AFP 796 ng/ml, HBsAg positive, anti-HBs positive, HBeAg positive, anti-HBe negative, anti-HBc positive, anti-HCV negative by ELISA, anti-HDV negative, anti-HAV IgM antibody negative, and anti-HIV negative. A liver biopsy revealed lobular hepatitis with lymphocytic infiltrate and scattered necrotic hepatocytes, disordered lobular architecture and bridging periportal fibrosis which extended focally into sinusoids. Cirrhosis was not present. A repeat serum AFP was 1451 ng/ml. An ultrasound of the liver was normal, and CT scan of the abdomen revealed a possible 2- to 3-mm nodule in the right lobe of the liver. A selective celiac, superior mesenteric, and supraselective proper hepatic arteriogram was normal. In November 1990, he reported a significant improvement in his symptoms. There was a marked decline in AFP and transaminases, and his serum HBeAg was negative. In February and June of 1991, he felt well.

He again complained of lassitude in February 1992. His laboratory tests showed: AST 140 IU/L, ALT 279 IU/L, alkaline phosphatase 99 IU/L, total bilirubin 0.9 mg/dl, serum AFP < 3.5 ng/ml. A liver biopsy in May 1992 showed focal scarring with mild superimposed inflammation and hepatocyte necrosis but no cirrhosis. Immunostaining demonstrated HBsAg but not HBcAg.

Case 2

A 51-yr-old school teacher sought medical attention for persistent nausea and lassitude in October of 1990. Serum transaminases and bilirubin were elevated, whereas serum alkaline phosphatase was normal. He was serum HBsAg and HBeAg positive. There were no risk factors for HBV infection, and his past medical history and family history were unremarkable. He did not smoke or use alcohol. Physical examination revealed mild palmar and scleral icterus. His liver span was 14 cm by percussion and extended 2 cm below the right costal margin. His symptoms of weakness and lassitude continued throughout 1991, and he was unable to return to work. A liver biopsy in December 1991 showed a mixed inflammatory cell infiltrate consisting of neutrophils, plasma cells, and lymphocytes with bridging necrosis and cirrhosis. Immunohistochemistry stains for HBs Ag were positive. In January 1992, he was serum HBeAg and anti-HBe positive. Serum HBV DNA was negative and serum AFP was 532 ng/ml. A CT scan showed the liver to be of normal size and configuration without evidence of malignancy. Tortuous veins in the hilum were suggestive of portal hypertension. Over the next 42 days, his serum transaminases fell (Fig. 1), and the serum AFP declined to 21 ng/ml. On repeat testing, he was HBsAg positive, HBeAg negative, and anti-HBe positive.

DISCUSSION

Serum AFP is used as a marker of hepatocellular carcinoma (HCC), both for individual case finding and as a screening tool. A National Institutes of Health clinical conference recommended that people with hepatitis B (HBsAg positive) and chronic liver disease undergo routine screening with serum AFP levels and ultrasound every 3–4 months (3). These two cases illustrate the sequence of a sudden rise in serum transaminases and AFP in patients with chronic hepatitis B infection. To the physician caring for these patients, this suggests the presence of HCC.

In a prospective study of a well-defined cohort of liver disease patients, Liaw *et al.* (2) followed 537 people with

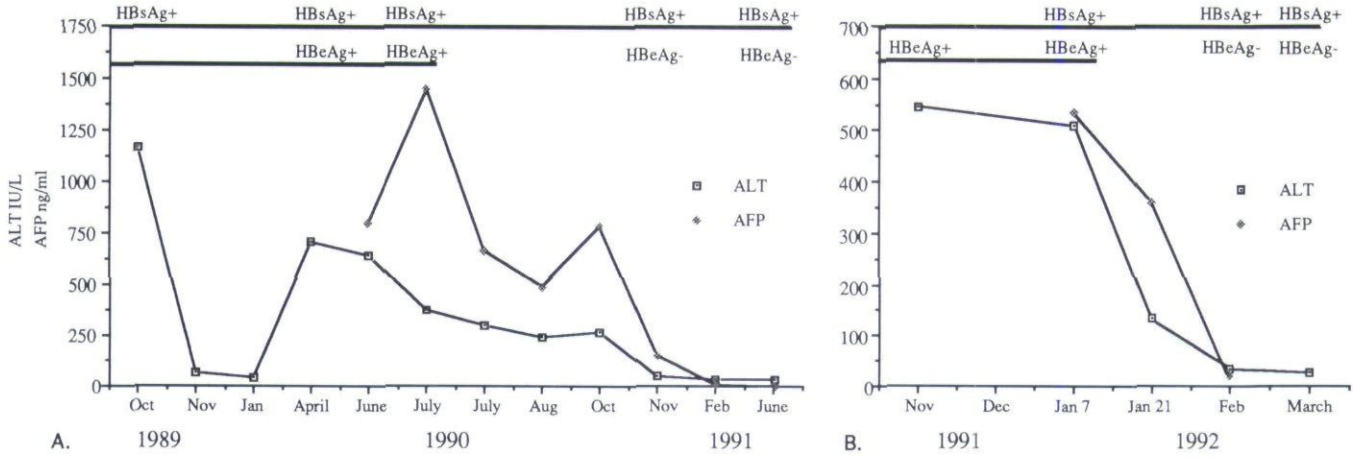

FIG. 1. The course of each patient's ALT and AFP over time is outlined above. *A*, case 1; *B*, case 2.

chronic hepatitis for elevations in AFP (435 of whom were HBsAg positive). During an average follow-up of 2 yr, 197 HBsAg-positive patients (46% of HBsAg-positive patients) and 18 HBsAg-negative patients (17% of HBsAg-negative patients) developed an elevated AFP level. An AFP greater than 100 ng/ml occurred in 19% of HBsAg-positive patients, compared with 1.9% of HBsAg-negative patients. Elevated AFP was associated with an increase in transaminases (ALT > 200 IU/L) in most cases (83%). HCC was found in only one of 167 patients with an elevated AFP and ALT, whereas HCC was found in six of 40 patients with elevated AFP without an elevated ALT. An AFP of > 100 ng/ml in an HBsAg-positive patient with an elevated ALT had a predictive value of about 0.6% for HCC, whereas the predictive value for a similar patient without a rise in ALT was 42%. Patients who were HBsAg negative were much less likely to develop an elevated AFP, but if they did, the predictive value for HCC was high. In a smaller retrospective study by DiBisceglie and Hoofnagle (4) of patients with chronic hepatitis B, elevations in AFP associated with exacerbation of transaminases had a predictive value for HCC of 0%, but without an exacerbation the predictive value was 50%.

Regarding our two cases, this information suggests that the findings of elevated transaminases and serum AFP levels probably represent a hepatitic response in association with loss of serum HBeAg and not HCC. Both DiBisceglie and Hoofnagle (4) and Liaw *et al.* (5) have observed the contemporaneous exacerbation of hepatitis, elevation of AFP, and loss of HBeAg from serum. Moreover, in the longitudinal prospective study of 237 HBsAg-positive persons by Liaw *et al.*, transient elevations in transaminases were common, and in general did not indicate loss of HBeAg, whereas the combination of elevated ALT and AFP (> 100 ng/ml) was so associated. These data suggest that it is clearance of serum HBeAg rather than ongoing hepatitis that is associated with increases in AFP.

In summary, elevated AFP has a low predictive value for hepatoma in HBsAg-positive patients who have accompanying elevations in transaminases, but has a high predictive value in those who do not have elevated transaminases. Clearance of HBeAg in particular appears to be associated with a transient hepatitis and marked elevation of AFP. Armed with this knowledge, physicians can reduce the need for repetitive investigations for HCC and the accompanying anxiety for the patient when elevated transaminases and AFP are encountered in a HBsAg, HBeAg-positive individual. For those patients, we would suggest that, if a suitable imaging study has not revealed a liver mass, the physician should follow the clinical course with particular attention to the HBeAg/anti-HBe status, since loss of HBeAg may be recognized by serial observation only.

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DIFFUSE GASTROINTESTINAL DYSMOTILITY IN A PATIENT WITH RHEUMATOID ARTHRITIS

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INTRODUCTION

Gastrointestinal motility abnormalities have been reported with connective tissue disorders (1). The most characteristic changes are diminished lower esophageal sphincter (LES) pressure and low-amplitude simultaneous distal esophageal contractions in progressive systemic sclerosis (PSS) (1). Small intestinal motility abnormalities may also occur in scleroderma (2).

Rheumatoid arthritis is a chronic progressive articular disease that can have extra-articular manifestations (3). Although decreased distal esophageal contraction amplitude and LES pressure have been reported (4), other gastrointestinal tract involvement is uncommon.

We describe a patient with classic rheumatoid arthritis and diffuse gastrointestinal dysmotility involving the esophagus, stomach, small intestine, and colon. This patient experienced temporary symptomatic improvement with the somatostatin-analog octreotide and a prolonged amelioration of symptoms with the prokinetic agent cisapride.

CASE REPORT

A 58-yr-old white female with a 22-yr history of rheumatoid arthritis, a history of interstitial lung disease, pericarditis, and reflux esophagitis, presented with 7 months of increasing episodes of abdominal pain and distension with nausea and vomiting.

Physical examination revealed a distended abdomen without masses, rebound, rigidity, fluid wave, or hepatosplenomegaly; bowel sounds were normal. Extremities showed several swan neck deformities, bilateral ulnar deviation at the metacarpophalangeal joints, and subcutaneous nodules on the extensor surfaces of the antebrachium.

Abdominal obstruction series showed prominent loops of

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