CASE REPORT | LIVER

Amyloidosis: A Rare Cause of Severe Cholestasis and Acute Liver Failure

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ABSTRACT

Although hepatic involvement in light chain–associated amyloidosis is common, clinical manifestations of hepatic amyloidosis are rare. In most cases, hepatomegaly serves as a clue to diagnosis. We report a unique case of a 48-year-old man from China with jaundice and noncirrhotic portal hypertension, with rapidly progressive liver failure, in the absence of hepatomegaly, secondary to systemic light chain–associated amyloidosis associated with multiple myeloma.

INTRODUCTION

Primary or light chain–associated (AL) amyloidosis is characterized by abnormal deposition of monoclonal immunoglobulin light chains in tissues and organs, with a wide range of clinical manifestations. Hepatic involvement in AL amyloidosis is seen in up to 90% of patients, with usually mild clinical manifestations, such as hepatomegaly and an elevated alkaline phosphatase level.[1–3] Findings of portal hypertension, jaundice, and acute liver failure are rare, and in the majority of these cases, hepatomegaly was present.[3–8] We present a unique case of systemic amyloidosis with acute liver failure, cholestatic jaundice, portal hypertension without hepatomegaly, and rapid progression to multiorgan failure.

CASE REPORT

A 48-year-old man from China with a history of hypertension, dyslipidemia, and type 2 diabetes mellitus, complicated with diabetic nephropathy, presented with a 1-month history of abdominal distension and bilateral pedal edema. He reported an episode of nonbloody diarrhea on a trip to Mexico requiring a short course of ciprofloxacin, but his symptoms had begun before this diarrheal illness. Physical examination revealed jaundice, ascites, and bilateral pitting pedal edema, without hepatosplenomegaly and other stigmata of chronic liver disease.

Initial investigations revealed cholestatic transaminitis with alkaline phosphatase (ALP) 1441 IU/L, gamma glutamic transferase (GGT) 1572 IU/L, bilirubin 41 μmol/L, alanine aminotransferase (ALT) 209 U/L, aspartate aminotransferase (AST) 272 U/L, and albumin 24 g/L. He had mild acute kidney injury with serum creatinine at 133 μmol/L. Otherwise, complete blood count, electrolytes, and international normalized ratio (INR) were normal. Viral serologies for acute hepatitis A to E, Epstein-Barr virus, cytomegalovirus, and HIV were negative. The patient was immune to hepatitis A, but not hepatitis B. Malaria, schistosomiasis, and strongyloides were ruled out. Antinuclear antibody, antimitochondrial antibody, anti–smooth muscle antibody, anti-liver-kidney microsomal antibody, alpha-1 antitrypsin, quantitative immunoglobulins, anti–neutrophil cytoplasmic antibody, angiotensin-converting enzyme level, and hemochromatosis genetic testing were negative. Peritoneal fluid analysis showed serum ascites albumin gradient of 1.9 g/dL consistent with portal hypertensive ascites. Ascitic fluid total protein was 8 g/L, and fluid albumin was less than 5 g/L. Despite high peritoneal fluid total protein, cardiac ascites was ruled out with cardiac echocardiogram showing no diastolic or systolic cardiac dysfunction. Peritoneal fluid culture and cytology were negative.

Figure 1. Abdominal computed tomography showing normal liver size with no cirrhotic changes.

Abdominal computed tomography revealed ascites and esophageal varices but no cirrhosis or hepatomegaly (Figure 1). Doppler abdominal ultrasound showed no evidence of portal or hepatic vein thrombosis. Magnetic resonance cholangiopancreatography demonstrated no biliary pathology. Although initially the cause for his noncirrhotic portal hypertension and jaundice was unclear, his liver enzyme trended down to AST 151 U/L, ALT 133 U/L, GGT 1035 IU/L, ALP 835 IU/L, total bilirubin 44 μmol/L, and INR 1.1, and his creatinine remained stable at 131 μmol/L. His ascites improved with paracentesis and gentle diuresis; therefore, he was discharged home with outpatient gastroenterology follow-up.

Two months later, he was readmitted with deteriorating liver and renal function with nephrotic-range proteinuria (4.33 g/d). Blood work showed bilirubin 277 μmol/L, ALP 974 IU/L, GGT 932 IU/L, INR 1.5, albumin 11 g/L, and creatinine 288 μmol/L. Common etiologies for fulminant liver failure were ruled out
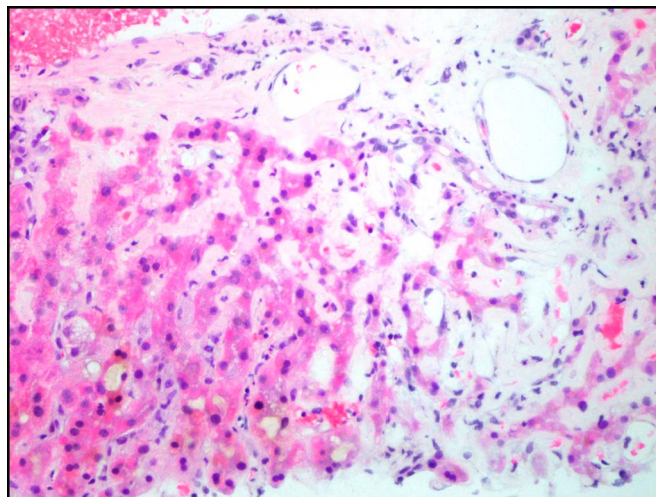

Figure 2. The liver biopsy shows sinusoidal space occupied by extensive deposition of the eosinophilic amorphous material. There is also perivascular deposition (hematoxylin and eosin stain, 200×).

again. Transjugular liver biopsy showed hepatic amyloidosis with extensive amorphous deposits within sinusoidal space (Figure 2). Because of procedural technical issues, hepatic venous pressure gradient and wedge pressure could not be measured. Congo red stain confirmed the presence of perisinusoidal and perivascular amyloid deposition with characteristic apple-green birefringence under the polarizer (Figure 3). Serum and urine protein electrophoresis with immunofixations were normal, but he had elevated serum-free kappa light chains at 2010 mg/L and free lambda light chains at 64.9 mg/L, in keeping with a free light chain monoclonal gammopathy. Bone marrow biopsy revealed plasma cell neoplasm with plasmacytosis of 30%–40% and amyloid deposition consistent with multiple myeloma. Upper endoscopy was performed for reported dysphagia and variceal surveillance, noted on imaging. Multiple yellow esophageal aphthous ulcerations were noted (Figure 4). Biopsies of the ulcers revealed amyloid depositions (Figure 5).

A screening echocardiogram demonstrated evidence of new diastolic dysfunction, hyperdynamic ejection fraction of 75%, and elevated brain natriuretic peptide (17,739 ng/L). He subsequently had a cardiac magnetic resonance imaging,
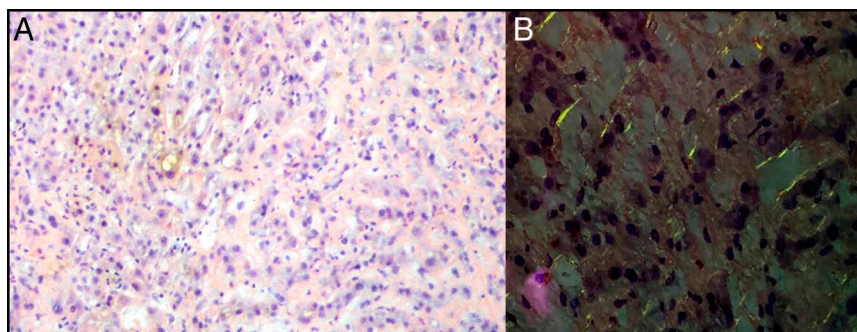

Figure 3. Liver biopsy showing (A) the sinusoidal and perivascular space (Congo red stain, 100×) and (B) apple-green birefringence (Congo red stain, 200×).
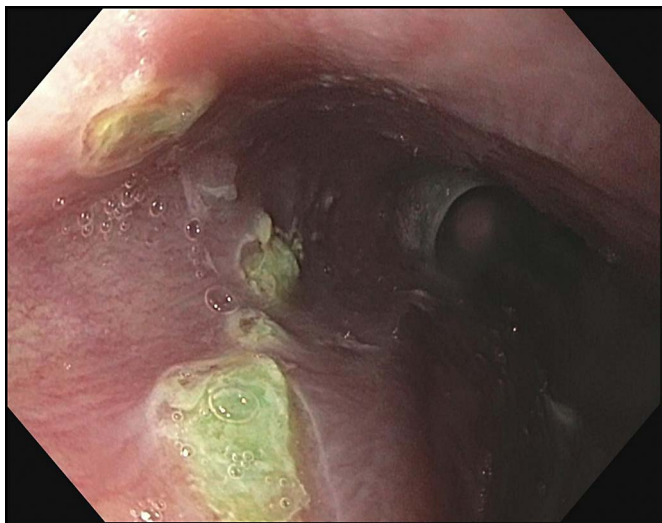
Figure 4. Upper endoscopy shows 3–4 mm yellow ulcerations within the mid-esophagus.

demonstrating reversal of the nulling pattern, suggestive of a diffuse cardiac amyloid infiltration. Ultimately, the patient was diagnosed with systemic AL amyloidosis associated with multiple myeloma with liver, gastrointestinal tract, heart, and presumably renal involvement. Given systemic amyloidosis, he was not a candidate for liver transplant. He was then started on cyclophosphamide-bortezomib-dexamethasone chemotherapy, but his hepatic and renal dysfunction further deteriorated with worsening ascites and dialysis-dependent renal failure, not well tolerated due to persistent hypotension. He had multiple episodes of agitation and
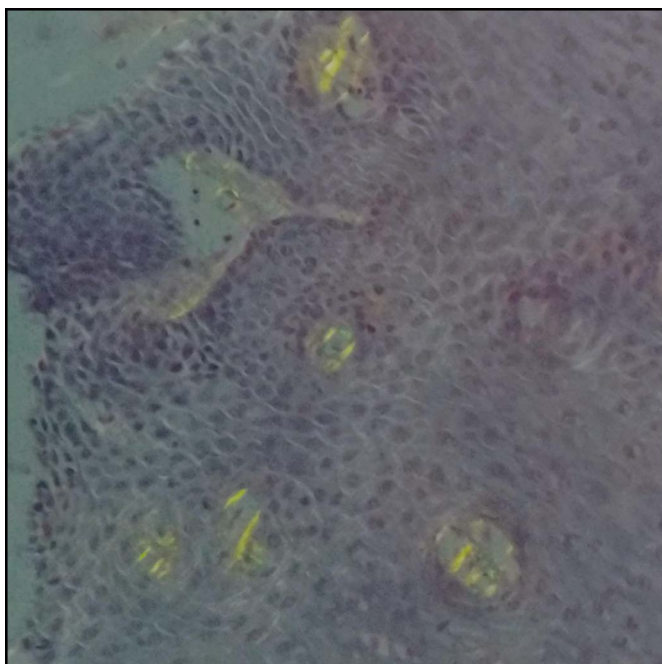
delirium but no overt hepatic encephalopathy. He was then transferred to the palliative care unit for supportive management and subsequently died of multiorgan failure, 3 months after his initial presentation.

DISCUSSION

Loudin et al demonstrated hepatic involvement in up to 95% of AL amyloidosis postmortem.[9] Hepatomegaly, seen in 57 to 83% of patients, and elevated ALP are the most common findings.[3,10] Cholestatic jaundice and portal hypertension are less frequent.[3,9] Acute liver failure secondary to hepatic amyloidosis is quite rare and is usually accompanied by massive hepatomegaly.[5–8,11–14] Hepatomegaly with infiltrative diseases serves as a clue to diagnosis. We hereby present a unique case of AL amyloidosis with significant hepatic dysfunction and rapidly progressive disease without hepatomegaly. The patient also had multiple esophageal ulcerations with amyloid deposits, which is rarely documented.[15] This case may suggest that the degree of liver functional abnormality does not always correlate with the extent of hepatic amyloid infiltration.[16] Although the prognosis of systemic amyloidosis remains poor, earlier diagnosis may improve survival, with sequential liver and stem cell transplantation and systemic chemotherapy.[3,14,17]

DISCLOSURE

Author contributions: HJ Kim wrote the manuscript. W. Xiong provided the pathology images. M. Tomaszewski, EC Lam, and S. Moosavi edited the manuscript. S. Moosavi is the article guarantor.

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Figure 5. Biopsy of the esophageal ulcerations under the polarizer confirms the presence of amyloid deposits (Congo red stain, 200×).

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