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Untangling the Etiology of Ascites

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
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ADEF Michael Lopez-Molina
ADEF Ashok V. Shiani
ADEF Kellee L. Oller

Department of Internal Medicine, University of South Florida, Morsani College of Medicine, Tampa, FL, U.S.A.

Corresponding Author: Kellee L. Oller, e-mail: koller@health.usf.edu
Conflict of interest: None declared

Patient: Male, 72
Final Diagnosis: Systemic amyloidosis
Symptoms: —
Medication: —
Clinical Procedure: Liver biopsy
Specialty: Gastroenterology and Hepatology

Objective: Unusual clinical course

Background: Amyloidosis is a systemic disease known to affect a vast range of organs, including the liver, heart, and kidney. When infiltrating the liver, amyloidosis typically does not present with cirrhosis. Typical presentation includes hepatomegaly with some mild laboratory abnormalities.

Case Report: A 72-year-old man presented with a 2-week history of worsening abdominal, scrotal, and extremity swelling. He endorsed melanotic stools and intermittent dizziness with a 10-pound weight gain. Vitals revealed a blood pressure of 82/57 mmHg and a pulse of 83 beats/min with positive orthostatic changes. Mild bibasilar crackles were noted. His abdomen was moderately distended with a fluid wave present, but no hepatosplenomegaly was noted. He displayed anasarca with significant extremity and scrotal edema, but no jaundice, telangiectasias, or other stigmata of chronic liver disease were present. Liver function tests demonstrated a total bilirubin of 1.5 mg/dL (normal value: 0.2–1.2 mg/dL), AST 111 IU/L (normal value 5–34 IU/L), ALT 51 IU/L (normal value 5–55 IU/L), and GGT 583 U/L (12–64 U/L). Alkaline phosphatase was 645 U/L (40–150 U/L). Analysis of peritoneal fluid was consistent with portal hypertension due to liver disease. Given an atypical presentation of cirrhosis with unclear etiology, a biopsy was performed and revealed amyloid deposition.

Conclusions: Liver disease can be due to various etiologies, many of which can present ambiguously. Although the most typical etiologies have been well defined, we present a case of an atypical presentation of hepatic amyloidosis discovered in a patient with ascites and without typical hepatomegaly.

MeSH Keywords: Amyloidosis • Ascites • Cirrhosis

Full-text PDF: http://www.amjcaserep.com/abstract/index/idArt/893012

Background

The diagnosis of amyloidosis dates back to 1854, when it was described by Rudolph Virchow [1]. It is the extracellular tissue deposition of abnormal proteinaceous material and can be limited to a single organ or be systemic. The most commonly involved organs are the heart and kidney [2]. It can also involve the liver, gastrointestinal tract, bone marrow, and infiltrate other tissues. Hepatic involvement most commonly presents with hepatomegaly. The most common laboratory abnormality is elevated alkaline phosphatase. Ascites is not commonly seen in hepatic amyloidosis [3].

Case Report

A 72-year-old man presented with a 2-week history of worsening abdominal, scrotal, and extremity swelling. He denied any hemoptysis or hematemesis, but did complain of melanotic stools and intermittent dizziness. He had a history of peptic ulcer disease, coronary artery disease, and congestive heart failure with an unknown ejection fraction. Over the last several weeks he noticed an increase in his abdominal girth. He had gained approximately 10 pounds during this time. While never experiencing chest pain, he did complain of exertional dyspnea.

His home medications included aspirin, atorvastatin, clopidogrel, furosemide, lansoprazole, lisinopril, and metoprolol succinate. He denied the use of any NSAIDs.

He had a 25-pack-year smoking history and drank 2–3 alcoholic drinks nightly for the past 30 years, quitting both in the last year. He reported having a screening colonoscopy 3 years prior, during which a single polyp was the only pertinent finding.

He was afebrile, with a blood pressure of 82/57 mmHg and a pulse of 83 beats/min with positive orthostatic changes. The patient was alert and orientated. Cardiopulmonary exam demonstrated mild bibasilar crackles; otherwise, no jugular venous distension, heart murmurs, or extrasystolic heart sounds were appreciated. While soft and non-tender, his abdomen was moderately distended with a fluid wave present. No hepatosplenomegaly was noted. He displayed anasarca with significant extremity and scrotal edema. His skin was without jaundice, telangiectasias, or other stigmata of chronic liver disease.

Laboratory evaluation revealed hemoglobin of 13.4 g/dL (normal value: 14.1–18.1 g/dL), MCV 88 FL (normal value: 80–97 FL), BUN 50 mg/dL (normal value: 6-20 mg/dL), and creatinine 1.2 mg/dL (normal value: 0.72–1.25 mg/dL). His albumin was 1.8 g/dL (normal value: 3.5–5 g/dL) and total protein was 4.9 g/dL (normal value: 6.4–8.3 g/dL). Liver function tests demonstrated a total bilirubin of 1.5 mg/dL (normal value: 0.2–1.2 mg/dL), AST 111 IU/L (normal value: 5–34 IU/L), ALT 51 IU/L (normal value: 5–55 IU/L), and GGT 583 U/L (normal value: 12–64 U/L). Alkaline phosphatase was 645 U/L (normal value: 40–150 U/L). Protime was 13.3 seconds (normal value: 9–12.5 seconds) and partial thromboplastin time was 26.1 seconds (normal value: 20-33 seconds). B-natriuretic peptide was 1661 (normal value: <100). A urinalysis revealed proteinuria and hematuria.

His ejection fraction was measured at 60–65% on transthoracic echocardiography, with significant left ventricular hypertrophy and abnormal left ventricular relaxation consistent with a grade 1 diastolic dysfunction without abnormalities in tissue densities. Analysis of peritoneal fluid was consistent with portal hypertension due to liver disease. The serum-to-ascites albumin gradient (SAAG) was 1.5 and total protein was 0.8 g/dL. Abdominal MRI revealed a small and nodular liver with several cysts, esophageal varices, mild splenomegaly, and significant ascites. Spot assessment of urine protein excretion was 2.5 g/dL, in the sub-nephrotic range. Esophagogastroduodenoscopy (EGD) was performed due to reported melena and declining hemoglobin. No source of bleeding was evident, only mild gastritis was present, and biopsies were taken. After autoimmune, infectious, and genetic etiologies of cirrhosis were excluded, a liver biopsy was performed and revealed amyloid deposition.

Discussion

On presentation, there were multiple etiologies for his anasarca and ascites: decompensated heart failure, cirrhosis, and hypoalbuminemia due to malabsorption or nephrotic syndrome. End-stage liver disease was a likely culprit based on exam, and was later confirmed with diagnostic paracentesis and abdominal imaging. The serum-ascites albumin gradient (SAAG) greater than 1.1 g/dL indicated portal hypertension as the etiology of his ascites. Additionally, the ascites total protein less than 2.5 g/dL decreased the likelihood of cardiac ascites [4,5]. The etiology of his end-stage liver disease was unclear following routine laboratory and radiological evaluation. Although he endorsed chronic daily alcohol use, which could have explained his presentation of advanced liver disease, his elevated alkaline phosphatase at 645 U/L and sub-nephrotic range proteinuria was incongruent with end-stage liver disease and prompted further evaluation with liver biopsy.

Alkaline phosphatase elevation can originate from bone or liver. When it is combined with an elevation of liver enzymes or bilirubin it is suggestive of a hepatic cause. In end-stage liver disease, alkaline phosphatase levels are not typically elevated. Elevation in alkaline phosphatase can be extahepatic or intrahepatic. Extrahepatic causes include malignancies, chronic pancreatitis, choledocholithiasis, or primary sclerosing

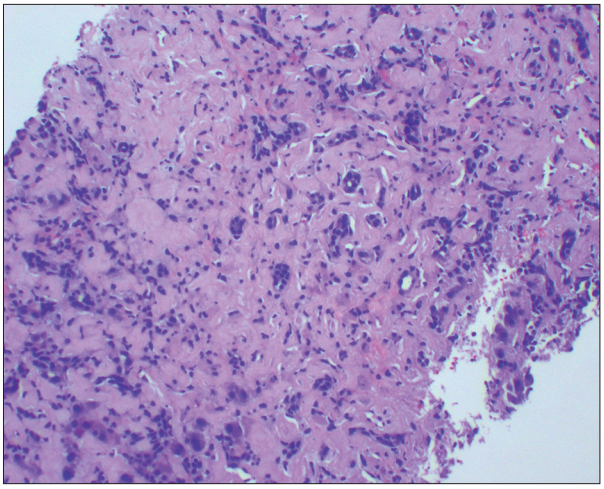

Figure 1. Liver biopsy demonstrating hepatic parenchymal changes consistent with cirrhosis.

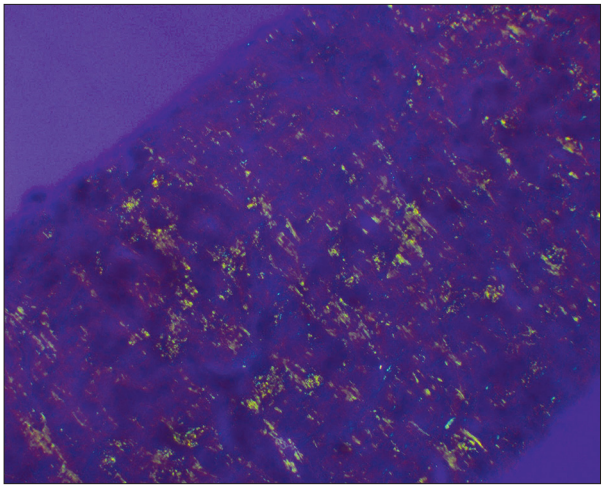

Figure 2. Congo red staining indicating apple-green birefringence.

cholangitis [6]. Intrahepatic causes include viral and alcoholic hepatitis, drug toxicities, primary biliary cirrhosis, or infiltrative diseases like sarcoidosis and amyloidosis [6,7]. Some of the conditions that cause an elevated alkaline phosphatase can lead to cirrhosis: infiltrative diseases, primary biliary cirrhosis, and chronic obstruction [6].

Our patient's radiologic studies did not show any signs of obstruction or common bile duct dilation. Autoimmune work-up, including ANA and anti-mitochondrial antibody, were negative. Random gastric biopsies performed to identify the source of melena revealed amyloid deposition within the lamina propria. His subsequent liver biopsy confirmed the same: near total replacement of hepatic parenchyma with amyloid deposition (Figures 1 and 2). A subsequent bone marrow biopsy showed normocellular (30%) marrow with relative erythroid hyperplasia with Congo red positive staining. This confirmed the diagnosis of systemic AL amyloidosis.

Our patient had systemic amyloidosis involving several organs: the liver, gastrointestinal tract, and kidneys. Hepatic amyloidosis typically does not cause symptoms of liver disease [8]. One of the most common manifestations, hepatomegaly, is found in at least 80% of the patients [9]. Other manifestations noted have been weight loss, proteinuria, edema, and ascites. Laboratory abnormalities are unusual with liver involvement; elevated alkaline phosphatase is the most common, present in approximately 86% of patients [9]. Elevation in AST, ALT, and bilirubin is rarely seen, most commonly in patients presenting with hepatomegaly [9].

Due to the patient's poor performance status, Hematology recommended melphalan with high-dose dexamethasone. Unfortunately, hepatic amyloidosis combined with involvement of other organs like the heart or kidney is associated with a poorer prognosis, and, after a prolonged hospitalization complicated by worsening renal failure, our patient subsequently died [8].

Conclusions

The evaluation for the underlying etiology of ascites and cirrhosis is typically predictable. Our case highlights an atypical presentation of systemic amyloidosis. This diagnosis was untangled from the clinical clues of proteinuria and alkaline phosphatase elevation, suggesting an accompanying diagnosis.

Conflicts of interest statement

There are no conflicts of interest among the authors of this case report.

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