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Primary Hepatic Amyloidosis Associated with Multiple Myeloma Causing Acute Liver Failure: A Case Report

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Abstract

Primary amyloidosis is the most prevalent type of amyloidosis and is usually due to plasma cell dyscrasia. It more commonly presents with renal and cardiac involvement and, although the liver is frequently involved in primary amyloidosis, it rarely causes clinically apparent disease. The most common form of hepatic involvement is hepatomegaly and mild elevation of alkaline phosphatase. Diagnosis requires tissue biopsy that demonstrates positive staining for Congo red and treatment is ideally a combination of chemotherapy and hematopoietic cell transplantation. The prognosis of hepatic amyloidosis associated with liver failure is poor. Here, we report a fatal case of primary amyloidosis in the setting of multiple myeloma in a 54-year-old man who presented with acute liver failure.

Keywords: AL amyloidosis, primary amyloidosis, acute liver failure, multiple myeloma.

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Introduction

Amyloidosis is a systemic infiltrative disease caused by deposition of misfolded precursor protein as insoluble amyloid fibrils in many organs, leading to their dysfunction [1]. There are several major forms of amyloidosis based on the fibril precursor protein. The most common type is primary amyloidosis (AL) caused by plasma cell dyscrasia leading to the deposition of protein derived from immunoglobulin light chain fragments [2]. Hepatic involvement can be seen in up to 90% of patients with AL and clinical manifestations are usually mild. These include hepatomegaly, elevated serum alkaline phosphatase level and non-specific symptoms such as anorexia, abdominal pain, and fatigue. Portal hypertension and progressive liver failure are rare [3]. Acute liver failure has been described for AL in the setting of multiple myeloma [4–6]. Here, we report a rare, fatal case of kappa AL presenting with acute liver failure in a 54-year-old man, managed by plasmapheresis sessions and bortezomib. Initially, there was mild improvement which was followed by a rapid deterioration and development of heart failure.

Case Report

A 54-year-old man presented with a 2-month history of generalized weakness, nausea, vomiting, loss of appetite, itching and 20kg weight loss. This was associated with

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right upper quadrant fullness and epigastric pain, shortness of breath and dry cough. He also reported a history of taking multiple courses of clarithromycin over the past few months for an upper respiratory tract infection. There was no history of other medications or herbal use. On examination, he was alert and oriented, pale, with icteric sclera and skin. Elevated jugular venous pressure was present, lungs were clear to auscultation, and the precordium exam was normal. Abdominal exam was remarkable for moderate ascites and hepatomegaly. Extremities had +3 bilateral pitting lower limb edema.

The patient's liver function tests revealed a cholestatic picture with mild transaminitis, an INR of 1.76, and very low serum globulins (Table 1). His complete blood count was as follows: Hb 13 g/dL, WBC $12x10^9$/L and platelets $114x10^9$/L. Serum creatinine was elevated at 2.01 mg/dL and urinalysis revealed +1 protein. Ascitic fluid analysis revealed high serum-ascitic albumin gradient (3.3 g/dL) and an ascitic total protein of 1.7 g/dL. Viral hepatitis serology, ceruloplasmin, anti-nuclear antibody (ANA), anti-smooth muscle antibody (ASMA), and anti-mitochondrial antibody (AMA) were all negative. Ferritin was normal.

Liver ultrasound (U/S) was negative for biliary obstruction or dilatation and Doppler flow was normal. Computed tomography (CT) scan showed hepatomegaly with fatty infiltration of the liver, mild splenomegaly and pelvic ascites (Figure 1). An upper endoscopy showed no evidence of esophageal varices or portal hypertensive gastropathy. Trans-jugular liver biopsy was performed and showed extensive amyloidosis with positive Congo red stain for amyloid bodies (Figure 2). Bone marrow biopsy showed 20% malignant plasma cells (lacking CD19). His kappa to lambda ratio was 70.8. The diagnosis of primary AL amyloidosis associated with multiple myeloma was made and he was managed with multiple sessions of plasmapheresis and bortezomib (proteasome inhibitor) with mild improvement initially followed by rapid deterioration with heart and liver failure, culminating in death.

Discussion

Amyloidosis results from the extracellular deposition of fibrils composed of low molecular weight subunits of a variety of proteins that stain with Congo red. Men are affected more than women (65–70%), with a median age of presentation of 64 years [7]. Amyloidosis is classified based on the chemical composition of amyloid fibrils and their precursor protein. The two main types are AL (primary) and AA (secondary) amyloidosis. AL is associated with plasma cell dyscrasias and malignant B-cell-type lymphoproliferative malignancies and is due to the deposition of immunoglobulin κ or λ light chain fragments. AA is associated with chronic infections and inflammatory conditions and is characterized by the deposition of amyloid A fibrils. Hepatic involvement is common in both forms and can be observed in 60–90% of cases [8–10]. However, portal hypertension and acute liver failure are uncommon manifestations of AL [11–12]. Similar to our patient's presentation, Park et al. [3] published the largest cohort of patients with hepatic AL, with the most common symptoms being weight loss (72%), fatigue (60%), and abdominal pain (53%). The most common physical findings were hepatomegaly (81%) and ascites (42%). The most frequently abnormal blood test was an increased ALP level (86%), which was mostly above 500 IU/L, and proteinuria was present in 89%.

Monoclonal proteins were detected on serum protein electrophoresis in 38% and hypogammaglobulinemia was found in 28% [3].

Cases of acute liver failure complicating hepatic amyloidosis have been reported in the literature. Liver failure can be attributed to severe portal hypertension, prolonged cholestasis, and hepatic congestion [13].

The diagnosis of AL is made by tissue biopsy that demonstrates positive staining for Congo red. In addition, a combination of serum and urine protein electrophoresis followed by immunofixation is required to determine whether a monoclonal population of plasma cells is present. Treatment includes chemotherapy and autologous hematopoietic cell transplantation (HCT) for patients who are eligible, and for those who are ineligible treatment is a combination of bortezomib (a proteasome inhibitor that targets amyloid-produced plasma cells and myeloma cells), chemotherapy, daratumumab (if available) and dexamethasone [14–5]. The use of chemotherapy was contraindicated in our patient due to associated liver failure and he was ineligible for HCT, so we combined bortezomib with dexamethasone. The role of liver transplantation is not well established in AL [16].

The prognosis of hepatic amyloidosis with concomitant portal hypertension and/or liver failure is poor, with a median survival of 8.5 months. Factors predicting survival include the presence of heart failure, hyperbilirubinemia, and thrombocytosis [3].

Conclusion

Hepatic AL amyloidosis with acute liver failure is a rare presentation and associated with poor prognosis. Earlier recognition and diagnosis of this disease could lead to improved prognosis.

Acknowledgments

None

Table 1. The patient's liver function tests

Test	On admission	2 weeks later	2 months later
AST (IU/L)	30	125	131
ALT (IU/L)	95	44	57
ALP (IU/L)	855	791	86
GGT (IU/L)	255	179	59
Protein (g/dL)	4.9	5.2	5.1
Albumin (g/dL)	2.7	2.61	4.3
Total bilirubin (mg/dL)	4.3	17.66	21.7
Direct bilirubin (mg/dL)	5.7	14.23	14.8
INR	1.76	1.69	3.02

AST, aspartate aminotransferase; ALT, alanine transaminase; ALP, alkaline phosphatase; GGT, **gamma-glutamyl** transferase; INR, international normalized ratio.

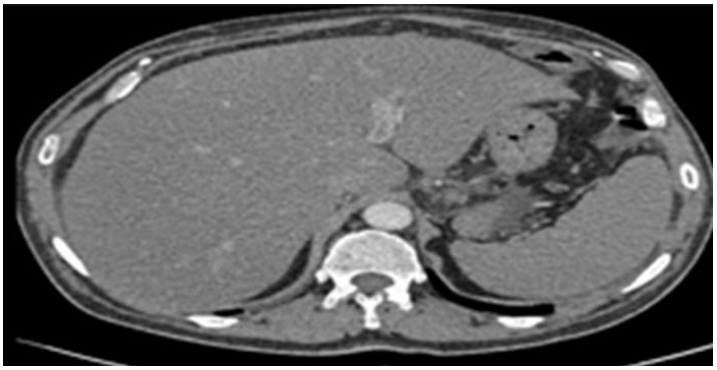

Figure 1: Abdominal CT scan showing hepatosplenomegaly

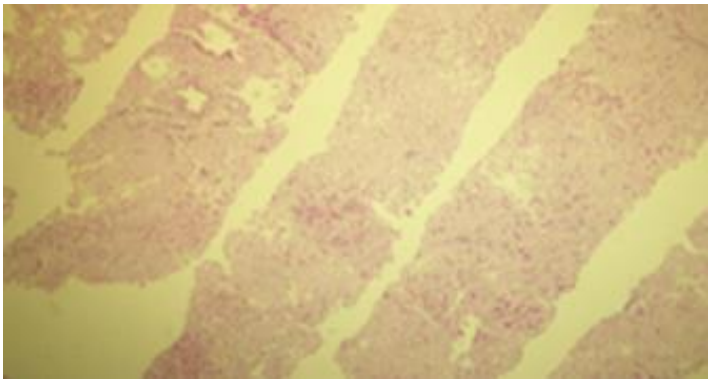

Figure 2: Liver biopsy with positive Congo red stain for amyloid bodies

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تقرير حالة عن الداء النشواني الأولي الكبدي المصاحب لورم نقوي متعدد مؤدي لفشل كبدي حاد

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الملخص

يعد الداء النشواني الأولي من أكثر أنواع الأمراض شيوعًا؛ والذي ينجم –عادة– عن خلل في الخلايا البلازمية، وعادة ما يؤدي هذا المرض لظهور أعراض نتيجة تأثر القلب والكلى بترسب البروتينات النشوانية فيها، وبالرغم من أن الكبد –أيضًا– يُعدُّ من الأعضاء الشائع تأثرها بهذا المرض، إلا أنه نادرًا ما يُظهِرُ أعراضًا واضحة. ومن أكثر أعراض إصابة الكبد بالداء النشواني شيوعًا، هو تضخم في الكبد وارتفاع بسيط في نسبة أنزيم الفوسفاتيز القلوي، ويتم التشخيص عن طريق أخذ خزعة من الأنسجة المصابة، وإظهار تَصَبُّغِها بصبغة أحمر الكونغو، ويتم معالجة هذا الداء بإعطاء علاج كيماوي، وزراعة الخلايا الجذعية، وفي حال حصول فشل في وظائف الكبد فإن فرصة النجاة تكون سيئة. وفي هذا التقرير نقدم حالة لمريض يبلغ من العمر (55) عامًا كان مصابًا بالداء النشواني الأولي المرافق لورم نقوي متعدد، وظهرت عليه أعراض فشل في وظائف الكبد مما أدى إلى وفاته.

الكلمات الدالة: الداء النشواني الأولي، فشل الكبد الحاد، ورم نقوي متعدد.