

# Amyloidosis presenting as acute liver failure: a case report

Raj Parikh\* and Christine S. Tsai

\*Correspondence: [raj\\_parikh@rush.edu](mailto:raj_parikh@rush.edu)



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Department of Internal Medicine, Rush University Medical Center, Chicago, IL, USA.

## Abstract

**Introduction:** Amyloidosis has two principle types: multiple myeloma-associated (AL) and amyloid-associated amyloidosis (AA). Both types can be local or systemic and can often involve the liver. Hepatic amyloidosis carries a poor prognosis, but commonly presents with a more gradual time course of evolving hepatomegaly and elevated serum alkaline phosphatase. This casereport involves an unusual presentation of hepatic amyloidosis with acute liver decompensation resulting in death.

**Case presentation:** A 76 year old man presented with complaints of progressive weakness and anorexia resulting in weight loss. He was initially found to have laboratory abnormalities notable for cholestasis and a mild transaminitis. On exam, the patient was cachectic with scleral icterus, jaundice, and abdominal distention. Liver ultrasound with doppler imaging was significant for increased echogenicity of the liver and ascites. The patient underwent transjugular liver biopsy, which demonstrated hepatic amyloid. Additional testing revealed a diagnosis of amyloidosis secondary to multiple myeloma. On day 5 of the patient's admission, cholestasis and transaminitis acutely worsened, with eventual peaking of aspartate aminotransferase to 3362 u/l, alanine aminotransferase to 1439 u/l, and total bilirubin to 18.8 mg/d. Further work-up for this acute decompensation, including imaging and laboratory tests, did not reveal any triggering events such as portal vein thrombosis or intra-abdominal bleeding from recent liver biopsy. Additionally, cardiovascular compromise, infectious etiologies, and toxins were ruled out. Unfortunately, the patient was not a candidate for chemotherapy given his acute hepatic decompensation and subsequent encephalopathy on day 8 of admission. The patient was started on Lactulose and N-acetylcysteine, though his mental status continued to worsen and the patient died on day 10 of admission from multi-organ compromise secondary to acute liver failure.

**Conclusion:** Amyloidosis resulting in acute hepatic failure has previously been reported but remains quite rare. Clinicians must consider infiltrative diseases, such as multiple myeloma and amyloidosis, when patients present with an extended prodromal illness paired with unexplained, worsening hepatic dysfunction. Likewise, physicians should be aware that patients who present with hepatic amyloid secondary to multiple myeloma are at high risk for rapid clinical deterioration.

**Keywords:** Amyloidosis, acute liver failure, multiple myeloma, ascites, biopsy, encephalopathy

## Introduction

Amyloidosis has two principle types: multiple myeloma (MM)-associated and amyloid-associated amyloidosis (AA). Amyloids are characterized as proteins that fold into insoluble deposits in organs and tissues, causing significant disruption of normal function. Meanwhile, MM is defined as a malignancy of white blood cells. In specific, plasma cells, which are responsible for producing antibodies, are malfunctioning in MM. Typically, these cells will aggregate in the bone marrow and also disrupt production of normal blood cells. MM often involves significant

kidney injury, which is a result of paraprotein production. Bone lesions and high calcium levels are also common findings in the disease as well.

Both AL and AA can present with involvement of the liver. Hepatic amyloidosis most commonly presents with hepatomegaly (81%) and elevated serum alkaline phosphatase (86%) though pancreatic infiltration has been seen as well [1-6]. In MM, plasma cell infiltration of the liver can be seen in up to 45% of patients [9,10]. However, the development of acute liver failure is rare in patients with AL. In fact, the incidence of acute

liver failure in patients with any infiltrating malignancy, such as MM, is less than 1% [7]. Here, we report an unusual case of hepatic amyloidosis presenting as acute liver decompensation resulting in death.

### Case presentation

A 76 year old man presented to a community hospital with a six month history of progressive weakness and anorexia resulting in weight loss. The patient had a past medical history significant for a left pontine stroke one year prior to presentation and had since been on atorvastatin and clopidogrel. At the onset of the patient's symptoms of weakness and anorexia, laboratory results were significant for an alkaline phosphatase (ALP) of 300 u/l. At that time, the atorvastatin was discontinued. The patient's symptoms of fatigue and weight loss persisted and he eventually developed abdominal distention, prompting the patient to seek further care. On admission to the hospital, his laboratory results were notable for ALP 948 u/l, total bilirubin 3.8 mg/dl, aspartate aminotransferase (AST) 150 u/l, and alanine aminotransferase (ALT) 130 u/l.

Liver ultrasound (without duplex imaging) was normal. Markers for Hepatitis B, Hepatitis C, Hepatitis E, and Hepatitis A were negative. Further work-up including CA 19-9, antinuclear antibody, anti-smooth muscle antibody, anti-mitochondrial Ab, cytomegalovirus titer, and Epstein barr virus titers were normal. Magnetic resonance cholangiopancreatography (MRCP) was normal as well. A diagnostic paracentesis was performed, with labs reported normal except for an ascitic albumin of 0.3 g/dl. The patient was discharged with a diagnosis of presumed drug-induced liver injury. After discharge, the patient developed recurrent ascites and within the following week, sought a second opinion at a tertiary hospital. Upon admission there, initial laboratory abnormalities included creatinine 1.32 mg/dL, total bilirubin 6.9 mg/dl, AST 134 u/l, ALT 68 u/l, ALP 1026 u/l, internationalized normalized ratio (INR) 1.26, and platelet count 271,000. On exam, the patient was cachectic and jaundiced, with scleral icterus and abdominal distention. Liver ultrasound with doppler imaging was significant for increased echogenicity of the liver with residual ascites present. On day 4 of the admission, a transjugular liver biopsy was performed, which was significant for massive amyloid deposition in the liver; the deposits were positive for amyloid birefringence and generic amyloid protein P (Figures 1 and 2). Additionally, lambda light chain restriction was noted within the amyloid as well. These findings, as well as laboratory results significant for elevated immunoglobulin (Ig) A, decreased IgG and IgM, renal disease, significant, elevated beta-microglobulin, and urine protein electrophoresis showing monoclonal IgA lambda, suggested a diagnosis of hepatic amyloid secondary to MM.

The liver biopsy also identified elevated portal pressures and therefore, the patient underwent an esophagogastroduodenoscopy (EGD), demonstrating esophageal varices, which were banded, and gastric erythema. Biopsies from the EGD were significant focal amyloid deposits. Transthoracic

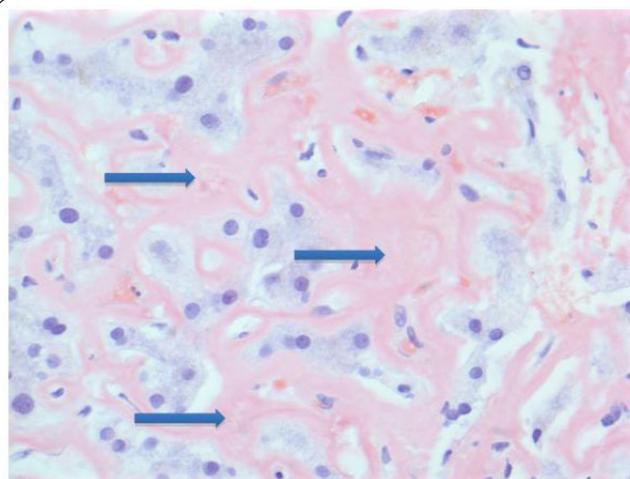


Figure 1. Congo red staining of liver tissue. Arrows depict amyloid deposition.

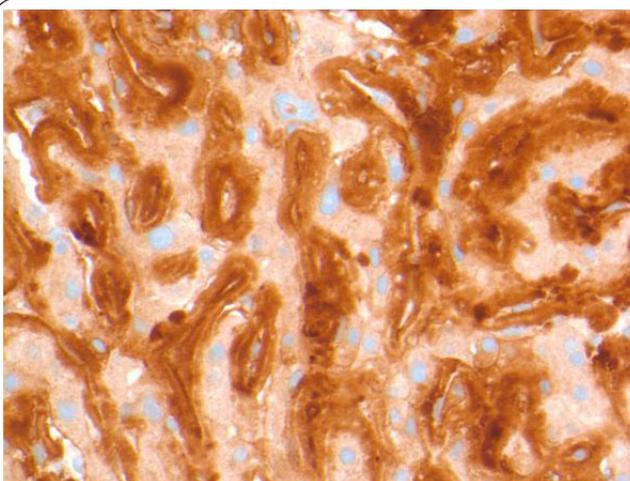


Figure 2. Amyloid deposition seen in liver tissue.

echocardiogram (TTE) was suspicious for cardiac amyloid given the sparkly appearance of the myocardium and biventricular hypertrophy. On day 5 of the hospitalization, the patient's disease acutely worsened with AST increasing from 98 to 1043 u/l and ALT increasing from 48 to 436 u/l; transaminases eventually peaked to AST 3362 u/l, ALT 1439 u/l, and total bilirubin 18.8 mg/dl. Work-up during this development of acute liver failure remained nondiagnostic as imaging and laboratory tests were not suggestive of triggering factors such as portal vein thrombosis or intra-abdominal bleeding as a complication of the recent liver biopsy. Additionally, cardiovascular compromise, infectious etiologies, and toxins were ruled out. Unfortunately, given the acute hepatic decompensation including development of encephalopathy on day 8 of admission, the patient was not a candidate for chemotherapy. The patient was started on Lactulose and N-acetylcysteine (NAC) though his mental

status continued to worsen. patient died on day 10 of the admission from multi-organ compromise secondary to acute liver failure.

## Discussion

Amyloidosis and MM resulting in hepatic failure has previously been reported but remains quite rare [7,8]. Only a few case reports in the past few years have been able to successfully touch on the rarity of our patient's presentation of acute liver failure in the face of newly diagnosed amyloidosis and MM [12-15]. More importantly, these cases have highlighted the rapid decline associated with acute liver failure in these patients. However, even without the complication of liver failure, patients with hepatic amyloid deposition secondary to systemic AL carry a poor prognosis. One study, consisting of 130 patients, demonstrated that 5-year survival decreased from 72% to 43% when liver involvement of amyloid was noted [16]. Elevated bilirubin and cardiac involvement are also predictors of poor prognosis, both of which are pertinent to our case as well [17].

In our case, the patient did not exhibit the common signs and symptoms of MM, which would have prompted an earlier diagnosis. Similarly, a study of 98 patients with hepatic dysfunction showed that a diagnosis of plasma cell dyscrasia, such as MM or AL, was only considered in 26% of patients at time of presentation [1]. Markers such as elevated CRP, decreased albumin, and increased formation of the globular form of amyloidosis are currently being studied as predictors of hepatic involvement in AL patients [18,19]. Moreover, treatment of MM patients with significant hepatic dysfunction is challenging because most chemotherapy agents cannot be delivered in the setting of acute liver failure due to liver toxicity, as was a limitation in our patient's case.

Another consideration in our case was the timing of acute liver failure development during the patient's hospital admission. The onset of acute liver failure began the day following the patient undergoing transjugular liver biopsy. While this may have been coincidental, complications from the procedure causing acute liver failure were considered. A higher incidence of bleeding following liver biopsy in hepatic amyloidosis has been documented in the past [1]. Large controlled trials have yet to evaluate the connection between liver biopsy and amyloidosis though a small case series in the 1960s did mention the potential risk for bleeding [22]. In fact, recent research has emphasized the increased risk of bleeding from liver biopsy in patients with amyloid deposition though the transjugular approach has decreased such risks when compared to the percutaneous method [23,24]. Additionally, portal hypertension in the setting of hepatic amyloidosis can lead to severe complications, including subcapsular hematoma and spontaneous rupture of the liver [25,26]. While the above possibilities were thoroughly considered as the source of our patient's decompensation, the work-up during the transition to acute liver failure remained unrevealing.

## Conclusions

Clinicians must consider infiltrative diseases, such as MM and amyloidosis, when patients present with an extended prodromal illness paired with unexplained, worsening hepatic dysfunction. Additionally, patients who present with AL are at high risk for rapid clinical deterioration. To optimize the approach in managing future cases of liver involvement in amyloidosis and MM, a standardized diagnostic and therapeutic plan needs to be formulated so to avoid the development of acute liver failure.

## Practice points

1. Infiltrative diseases, such as multiple myeloma and amyloidosis, are important to consider when patient's present with non-specific symptoms and abnormal liver function tests.
2. Amyloidosis often presents in association with multiple myeloma, which is commonly referred to as primary amyloidosis.
3. The most common presentation of hepatic amyloidosis involves hepatomegaly, generalized fatigue, and labs suggestive of cholestatic hepatitis.
4. In the setting of acute liver failure, etiologies such as toxins and cardiovascular compromise must be ruled out.
5. Complications of transjugular liver biopsy include intra abdominal bleeding, which can result in acute liver failure and systemic decompensation in patients.
6. Hepatic involvement in patients with amyloidosis or multiple myeloma is often an indicator of poor prognosis.
7. Multiple myeloma is often diagnosed only after the diagnosis of amyloidosis has been established.
8. Treating patients with multiple myeloma and hepatic involvement is high risk given the significant liver toxicity caused by several chemotherapy options.

## Competing interests

The authors declare that they have no competing interests.

## Authors' contributions

| Authors' contributions             | RP | CST |
|------------------------------------|----|-----|
| Research concept and design        | ✓  | ✓   |
| Collection and/or assembly of data | ✓  | ✓   |
| Data analysis and interpretation   | ✓  | ✓   |
| Writing the article                | ✓  | ✓   |
| Critical revision of the article   | ✓  | ✓   |
| Final approval of article          | ✓  | ✓   |
| Statistical analysis               | ✓  | ✓   |

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