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A Case of Isolated Primary Hepatic Amyloidosis Presenting as Hepatomegaly And Cholestatic Jaundice.

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ABSTRACT

Amyloidosis is a multisystem disorder. Even though liver involvement is common in amyloidosis, it is usually asymptomatic, and cholestasis and jaundice is rare. Here, we report a case of 45 years old female presenting with huge hepatomegaly and cholestatic jaundice. On evaluation, patient is diagnosed of having isolated primary hepatic amyloidosis with underlying monoclonal gammoapathy of undetermined significance (MGUS).

Introduction:
Amyloidosis is characterized by deposition of protein fibrils in the extra cellular matrix and vessel wall. It can be divided majorly into primary and secondary amyloidosis. According to the type of protein that get deposited, it may be sub-classified into major two types those associated with immunoglobulin light chain (AL) or primary and those with serum amyloid A protein (AA) or secondary.

Primary hepatic amyloidosis (PHA) is an AL type of amyloidosis of liver tissue. Liver involvement in amyloidosis is common but isolated liver involvement preceding systemic disease is rare, and whenever present is usually asymptomatic. Symptomatic hepatomegaly with cholestasis as complication is even rarer. [1]

Case report:
A 45 years old female presented with the chief complaint of fever without chills and rigors for 2 days which was associated with nausea and vomiting and mild abdominal pain. Patient did not have any history of illness other than presenting complaint and was not on any medication.

On examination patient had high grade fever, yellowish discoloration sclera and urine was dark yellow in color. On abdominal examination patient had hard hepatomegaly, liver was palpable 4 cm below subcostal margin. There was no evident splenomegaly clinically.

In laboratory investigation, Hemogram was unremarkable but liver function tests was severely altered with, total bilirubin 22.69 mg/dl, unconjugated being 11.66 mg/dl, ALT 179, AST 786, ALP 1005 IU/mL and PT-INR was 1.45 of normal control. Patient was started on tablet ursodeoxycholate (150 mg BD). On third day fever subsided, but total bilirubin kept on increasing and reached maximum on third day. Values were 40.54 being total out which 17.18 was unconjugated bilirubin, SGPT had declined over the course to 119.5 and SGOT to 408, but ALP had risen to 1170 IU/mL. Ultrasonography of liver showed hepatomegaly with no evidence of CBD obstruction. All available markers for acute hepatitis HBsAg, HAV, HEV and HCV were negative. CECT was done which showed plain hepatomegaly with no evident obstruction of intra or extrahepatic biliary radicles with no evidence of cirrhosis. ANA, AMA, ANCA all were found negative, ruling out their etiological possibilities. On 10th day of admission, total bilirubin started decreased and reached 5.54 mg/dl with decreasing ALT of 40 and AST of 62 IU/ml. But ALP was still elevated, being 1003 IU/L.

As patient stabilized, liver biopsy was planned and carried out with no complication. Histopathology showed no evidence of intrahepatic cholestasis or cirrhosis but had Congo Red positivity suggesting hepatic amyloidosis.

To rule out associated plasma cell disorders, serum protein electrophoresis was done and it showed characteristic M band (0.52g/dl). Though it was not in the range of Multiple Myeloma, it was suggestive of monoclonal gammopathy of undetermined significance (MGUS), suggestive of Primary Amyloidosis (PA) due to monoclonal immunoglobulin light chain deposition. To rule out other ailments of PA, abdominal fat pad biopsy, urine examination and 2D echo was performed and found to be normal.

Patient was planned to be started on melphalan regimen and possibility of bone-marrow transplant was considered. Patient refused for both the treatment, and took discharge but was advised regular follow up. After 3 months follow up these were the major significant investigations: Hepatomegaly persisted, ALP came down to 306, serum creatinine increased to 2.3 mg/dl, proteinuria 4+ developed, ejection fraction decreased to 40% from normal and grade II diastolic dysfunction developed, suggesting renal and cardiac extension of amyloidosis. Symptomatic treatment was started. Patient was succumbed to death after 6 months due to cardiac failure.

Discussion:
Amyloidosis is a systemic disorder involving usually multiple organs by deposition of insoluble protein fibrils. In primary hepatic amyloidosis, these proteins, i.e. light chains of immunoglobulins, get deposited in the hepatic perisinusoidal space, parenchyma, portal vessels, central vein, portal stroma and intercellular space, eventually leading to hepatomegaly, liver dysfunction, ascites, portal hypertension, liver failure, and even death.

Kyle et al. in series of primary amyloidosis reported that hepatomegaly was present in 34%, while raised ALP in 16% and jaundice in only 4% of patients. [2]

In a series by Gertz et al, patients with primary hepatic amyloidosis had only mild or absent liver function test abnormalities, usually mild ALP or AST elevations. Only 8% patients had serum bilirubin above 1.5 mg/dl and in only three patients values more than 6 mg/dl. [3]

Liver biopsy is the final definitive method of diagnosing hepatic involvement. [4]

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The mean survival of patients with primary hepatic amyloidosis was 9-12 months. The major risk factor affecting survival during the first year from diagnosis was the presence of congestive cardiac failure, followed by hepatomegaly, urinary light chains, and underlying myeloma. [5]

For primary amyloidosis, the mainstay of therapy has been chemotherapy, traditionally with melphalan and dexamethasone. But this therapy has only about a 30% response rate. High-dose chemotherapy followed by autologous peripheral blood stem cell transplantation (ASCT) has recently been deemed the treatment of choice, with a response rate from 50% to 60%. Ongoing studies also showed promising results for proteasome inhibitor bortezomib based regimens. [6]

Conclusion:

Even though a rare possibility, primary hepatic amyloidosis could be an important but fatal differential diagnosis in patients presenting with hepatomegaly and cholestatic jaundice and/or serum ALP elevation when cannot be explained by usual liver disorder. Other organs such as kidney, heart, and plasma cell and their function tests should be assessed to rule out systemic amyloidosis.

Definite diagnosis of PHA is based on histopathologic detection of amyloid in hepatic tissue by Congo Red staining. Once a diagnosis is established, definitive therapy with ASCT and chemotherapy should be started promptly. With newer treatment options and more effective chemotherapy early diagnosis may lead to improved survival and less morbidity.

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