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Amyloidosis may be associated with chronic hepatitis and cirrhosis of liver: A case report

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Abstract
Introduction: *Amyloid is a protein mucopolysaccharide structure. It appears as a hyaline homogenous, acellular substance. In liver, it may get deposited in blood vessels, sinusoids, bile ductules and liver parenchyma. Current patient was a female, aged 43 years. Microscopic examination of liver showed massive deposition of amyloid in perisinusoidal region. Sinusoidal dilatation, ballooning and atrophy of hepatocytes were also seen. At several places, hepatocytes had disappeared and were replaced by amyloid. In addition, dense lymphocytic infiltration was seen in portal tract. Thick bands of fibrosis were also seen.*

Case report : *Patient was a female aged 43 years. Liver was firm, rubbery and waxy. Patient had mild hepatomegaly. Microscopically, at several places hydropic swelling of hepatocytes was seen. Excessive necrosis and lymphocytic infiltration, suggestive of chronic hepatitis were also seen. In addition, thick bands of fibrosis suggesting cirrhosis of liver were seen. Massive amyloid deposition was seen in liver parenchyma. Compression atrophy of hepatocytes and sinusoidal dilatation were also seen.*

Conclusion: *Present case relates to deposition of amyloid in liver parenchyma. In addition, ballooning of hepatocytes, hepatocyte necrosis and lymphocytic infiltration were seen. Thick bands of fibrosis extending from central vein to periphery of portal tract were also seen. The patient was finally diagnosed as a case of hepatic amyloidosis associated with chronic hepatitis and cirrhosis.*

Keywords: *Congo red positive Amyloid deposition, chronic hepatitis, massive hepatic fibrosis*

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I. Introduction

Virchow first coined the word 'amyloid' meaning starch-like. However, later it was identified as a protein[1]. Thirty-six different proteins have been isolated from amyloid (amyloidogenic proteins). Determination of protein subtype may be useful in the treatment of a patient with amyloidosis. Amyloid is a fibrillar protein-mucopolysaccharide structure. Amyloid is defined as extracellular deposition of amorphous hyaline homogenous eosinophilic fibrils. Several patterns of amyloid deposition have been reported, e. g. vascular type. Another pattern may be sinusoidal type. In addition, amyloid may get deposited in intrahepatic biliary ductules[2]. Amyloid is rubbery, firm in consistency. Either amyloid may get deposited focally without much clinical features or it may involve whole of the liver and produce severe pathophysiological alterations. Amyloid gives green staining with double refraction when Congo red-stained sections are seen by polarized light[3]. Moreover, Kupffer cells may phagocytose amyloid. Stimulated monocytes may secrete interleukin-1 (IL-1) and serum amyloid associated protein (SAA), a major constituent of amyloid[4]. Additionally, marked dysfunction of B-cells may be associated with synthesis of amyloid and later its deposition in liver.

Another component of amyloid (P component) has been identified. Though P component may resemble with C reactive protein (CRP), yet it does not behave as classical acute phase protein[4]. Extensive enlargement of liver has been described in amyloidosis. Rarely, liver may weigh upto~9000gm[2]. Further, liver involvement appears to be a sign of advanced amyloidosis[5]. Perisinusoidal amyloidosis with atrophic hepatocyte trabeculae have also been reported[3]. Levine reported a high incidence of ascites in 21% patients[6]. However, many cases of ascites were due to congestive heart failure, not due to portal hypertension[7]. Asymptomatic hepatomegaly is the most frequent physical finding in 60% of patients. Only 10 cases of primary portal hypertension have been reported upto 1984[7]. Isolated hepatic amyloidosis has been rarely described[8]. Moreover, liver parenchymal involvement may be found in AL and vascular type in AA amyloid[9].

II. Case Report:

A 43 year-old female had non-tender liver. Liver was palpable 2 cm below right subcostal margin. Liver was firm, rubbery in consistency. Serum bilirubin and transaminases were not raised. Left lobe of liver was biopsied and histopathological examination was done. The patient did not complain of symptoms related with other organs. In addition, she did not had any gross finding, suggestive of pathology in any other organ except liver. Grossly, two linear greyish white biopsy pieces together measuring1.2x1x1 cms were received. Microscopic examination of liver showed ballooning of hepatocytes and fibrocollageneous bands extending from central vein to periphery of portal triad. Proliferated biliary ductules, necrosis and lymphocytic infiltration were seen (figure 1). Sinusoidal dilatation was also seen. The deposits were located within the space of Disse with displacement of Kupffer cells towards the centre of sinusoids. The hepatocytes showed atrophic changes adjacent to sinusoidal deposits. At few places, bile duct hyperplasia was also observed. Pink staining of amyloid was seen in haematoxylin and eosin-stained sections. Congo red also stained amyloid pink. Additionally, Masson's trichrome stained collagen blue (figure 2). Anti-AA antibody failed to stain amyloid. Prognosis for hepatic amyloidosis is serious; the patient may survive for two to five years. The patient was treated with Colchicine alone because no specific cause for amyloidosis could be ascertained.

III. Discussion:

Most important feature of this report was collection of excessive amount of amyloid in liver parenchyma. Amyloid is known to deposit in Kupffer cells to start with. Later, it gets deposited in space of Disse and in perisinusoidal region. Deposition of amyloid may lead to hepatomegaly as seen in the current case. Another feature of the current case was atrophy of hepatocytes. Compression of hepatocytes by amyloid might have resulted in atrophy followed by cell death through autophagy and apoptosis. Severe lymphocytic infiltration was also seen, suggesting cell death by necrosis. Subsequently, necrosed tissue was replaced by thick bands of fibrosis.

As symptoms and signs related with pathology of other organs were not detected, it was presumed that the liver alone was diseased. It appeared that the patient had primary amyloidosis with formation of AL subtype of amyloid. Amyloidosis might be suspected when an enlarged smooth, non-tender liver was detected[10]. Another important feature of this report was the detection of hydropic swelling/or ballooning of hepatocytes. As a result of injury to bi-lipid layer, excess fluid enters in hepatocytes. ATP might not be adequate to expell the excess of water from the hepatocytes, resulting in ballooning of cells. In addition, perisinusoidal deposition of amyloid as well as massive fibrosis might have contributed to portal hypertension (portal vein pressure >30 cm saline), ascitis and cirrhosis. However, palmer erythema, gynecomastia and testicular atrophy were not seen in most of the cases of hepatic amyloidosis[6]**.** Hypoalbuminemia and mild rise in serum alkaline phosphatase had been reported in hepatic amyloidosis[11]. However, current case did not had elevated serum alkaline phosphatase. In the present case, diagnosis of amyloidosis was confirmed by Congo red staining alone. However, subtyping of amyloid by laser capture micro-dissection and mass spectrometry (LCM-MS) was not done. LCM-MS has been shown to identify the amyloid subtype[12]. Further, local production of acute phase protein, e.g. SAA has been shown to inhibit *in vitro* entry of HCV in liver cells[13]**.** Presence of chronic inflammation in the current case might have augmented local amyloid deposition. In a recent study at Mayo clinic, 62% of hepatic amyloidosis cases had amyloid light chain (AL). Other amyloid subtypes were leukocyte chemotactic factor (ALECT 2) in 25% cases, 7% cases had Apolipoprotein A ApoA1), 4% cases had serum amyloid A (AA) and 2% cases had transthyretin (ATTR). Patterns of amyloidosis in liver might be sinusoidal, globular, arteriolar and /or capsular or portal subtype. Further, ALECT 2 might be second frequently diagnosed hepatic amyloid subtype[14]. Occasionally, rupture of liver might occur due to amyloidosis[15]. Prognosis of generalized amyloidosis might be serious; the patient may survive for two to five years.

IV. Conclusion:

Present case was related to massive amyloid deposition in liver parenchyma. Atrophy of hepatic trabeculae and sinusoidal dilatation were seen. Necrosis and lymphocytic infiltration, suggestive of chronic hepatitis were seen. In addition, thick bands of fibrosis were also seen. Findings were suggestive of amyloidosis in association with chronic hepatitis and cirrhosis of liver.

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Legends to Figures

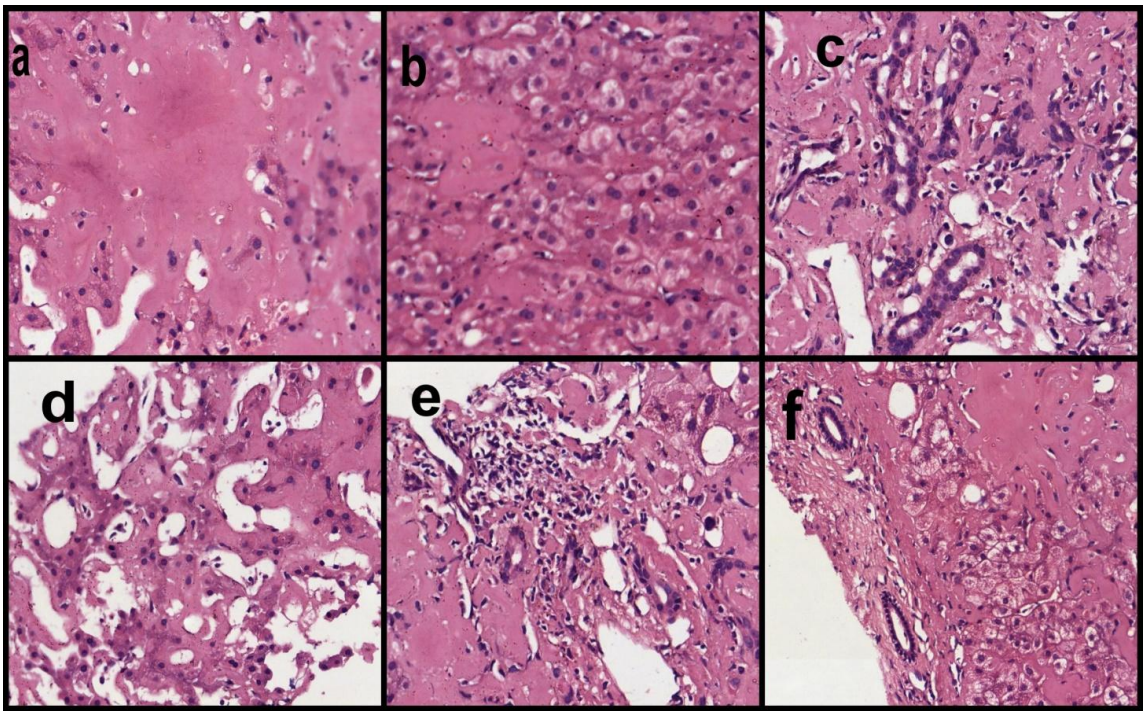
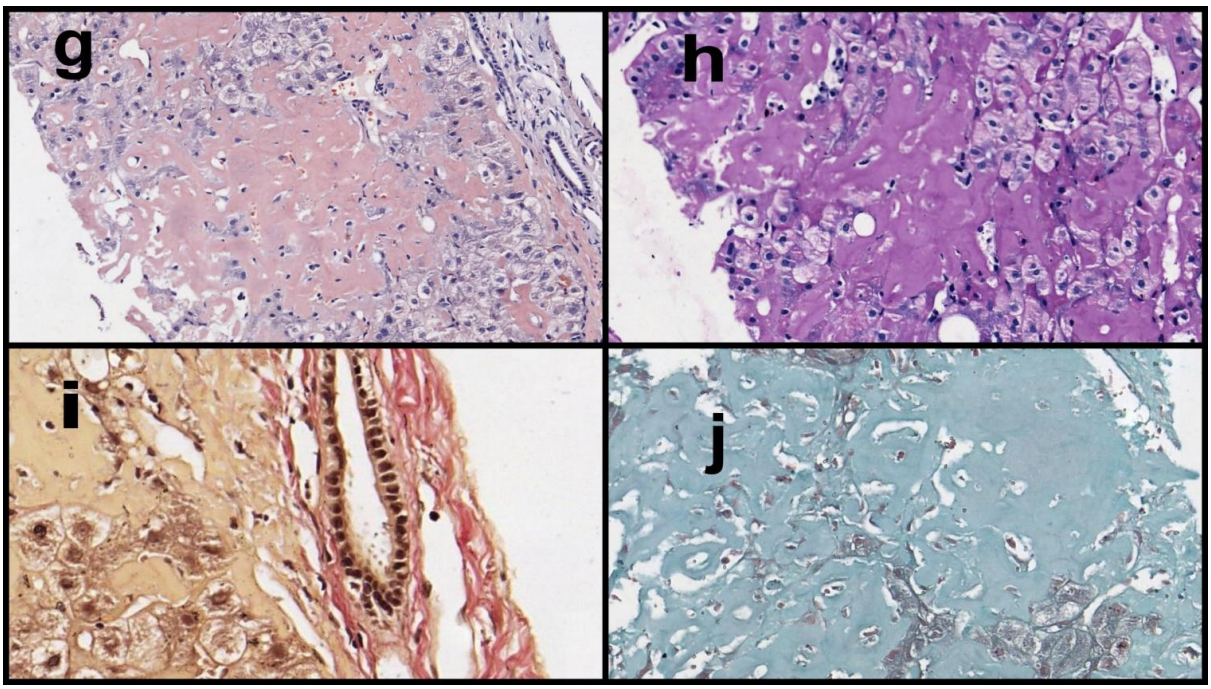


Fig.1 (a) Photomicrograph shows hyaline homogenous eosinophilic amyloid deposit in liver parenchyma (HE×400). **(b)** shows ballooned hepatocytes (HE×600). **(c)** shows biliary ductular hyperplasia in portal tract (HE×400). **(d)** shows dilated sinusoids and atrophic hepatocytes. **(e)** shows necrosis of hepatocytes and lymphocytic infiltration. Several biliary ductules were also seen (HE×200). **(f)** shows portal tract with fibrosis along with few biliary ductules and ballooned hepatocytes.



Tab/Fig.2 (g) Amyloid showing salmon pink staining (Congo red ×200). **(h)** shows amyloid and ballooned hepatocytes (PAS stain×200). **(i)** Portal tract showing a biliary ductule, collagen fibers and ballooning of hepatocytes (Van Gieson×400). **(j)** Masson's trichrome stained collagen blue (×100).

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