

Primary hepatic amyloidosis: A Case Report

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Abstract

Primary amyloidosis is a rare disease characterized by the deposition of amyloid protein in many organs. We report a case of a 68-year-old man who had biopsy-proven liver involvement, and describe his clinical presentation and abdominal contrast-enhanced computed tomographic findings, which was investigated in few studies. We also discuss diagnostic criteria of organ involvement and treatment approach of AL amyloidosis.

INTRODUCTION

Primary systemic amyloidosis AL is an uncommon disease characterized by the extracellular deposition of insoluble fibrils derived from immunoglobulin light chains. Widespread deposition of amyloid fibrils causes multisystem organ dysfunction. The heart, kidney, and peripheral nerves are most commonly affected by primary systemic amyloidosis. The liver is also a common site of amyloid deposition. The clinical manifestations are often and nonspecific and diagnosis of primary systemic amyloidosis may be overlooked.

We report a case of 68-year-old man who had biopsy-proven liver involvement, and describe his clinical presentation and contrast-enhanced computed tomographic findings, which was investigated in few studies^{1,2}.

CASE REPORT

In November 2005, a 68-year old man presented with mild right epigastric pain and abdominal fullness for 2 months was admitted to our department. He also had anorexia, pedal edema, and fatigue. On admission his blood pressure was 120/80 mmHg, heart rate was 75 beats/min, and temperature was 37°C. The physical examination showed the liver to be firm and enlarged accompanied by pedal edema, the spleen was not palpable.

On admission, laboratory data were as follows: red blood cell count, 5.3×10^9 cells/L; hemoglobin, 96 g/L; platelet count, 127×10^9 cells/L; serum urea, 8.2 mmol/L; serum creatinine, 98 μ mol/L;

Liver tests produced the following results: total bilirubin, 20

μ mol/L; conjugated bilirubin, 11 μ mol/L; aspartate aminotransferase, 46 U/L; alanine aminotransferase, 75 U/L; lactate dehydrogenase, 209 U/L; alkaline phosphatase, 396 U/L; γ -glutamyl transpeptidase (GT), 310 U/L; Cholesterol, 3.2 mmol/L; prothrombin time, 17.8 s; partial thromboplastin time, 48.9 s; total protein, 65 g/L; and albumin, 31 g/L. Hepatitis B surface antigen and antihepatitis C virus antibodies were absent, as were antinuclear, antimitochondrial, and anti-smooth muscle antibodies, and tumor markers.

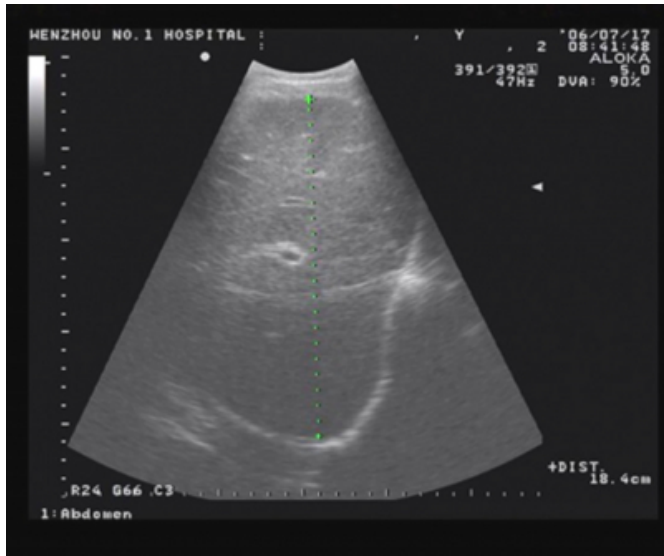
Urinalysis showed 2.24g of proteinuria every 24 h. Serum and urinary immunoelectrophoreses showed increase of monoclonal light-chain. In the serum, the immunoglobulin light-chain concentration was 239 g/L (normal, 0–18.5) and the immunoglobulin κ light-chain concentration was 184 g/L (normal, 0–50). And in the urine, the immunoglobulin light-chain concentration was 17.2 g/L (normal, 6.29–13.5) and the immunoglobulin κ light-chain concentration was 10.5 g/L (normal, 3.13–7.23).

The ECG on admission revealed left anterior bundle branch block and low ECG voltages 0.5mV mean ORS in limb leads I, II, III, aVL and aVF. Echocardiogram showed hypertrophy of left ventricular wall and an interventricular septum thickness of 12cm normal, 8 -10

Ultrasound examination of the upper abdomen showed a diffusely enlarged liver with heterogeneous echogenicity and no definitive evidence of focal lesions Fig. 1

Figure 1

Figure 1: Ultrasonogram shows diffuse hepatomegaly with heterogeneous decreased attenuation



Abdominal enhanced-contrast CT scans revealed presence of a markedly acute left lobe hepatic margin and asymmetric hepatomegaly of triangular shape with an apex at the falciform ligament and heterogeneous attenuation, splenomegaly with diffuse hypoperfusion Fig. 2, 3, 4, 5

Figure 2

Figure 2: Pre-contrast CT scan showed asymmetric and triangular hepatomegaly with the apex at the falciform ligament black arrow, mild atrophic change of the lateral border of both hepatic lobes white arrow, splenomegaly with diffuse low density.

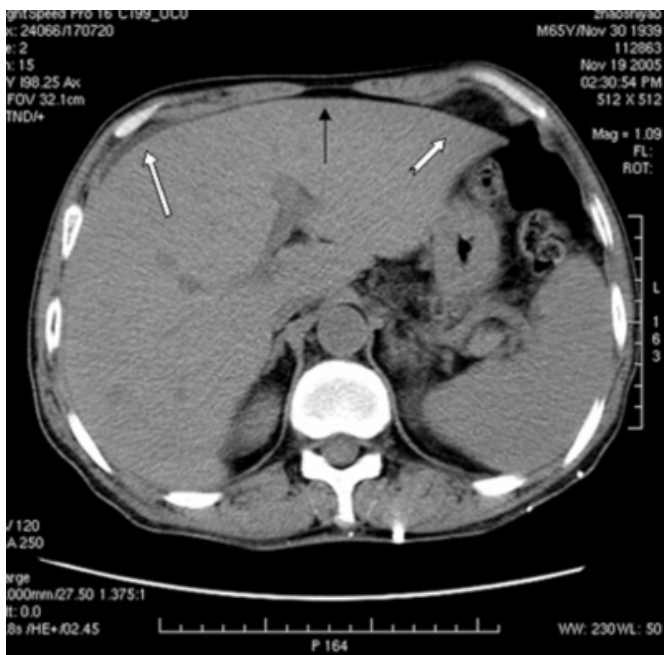


Figure 3

Figure 3: Arterial phases CT scan shows the lack of parenchymal enhancement in the liver and spleen

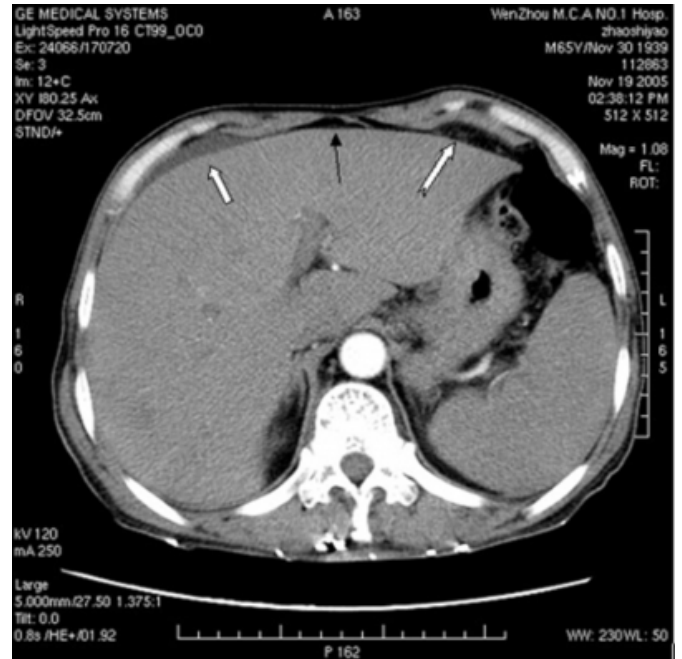


Figure 4

Figure 4: Portal phases CT scan shows heterogeneous enhancement in the liver and spleen

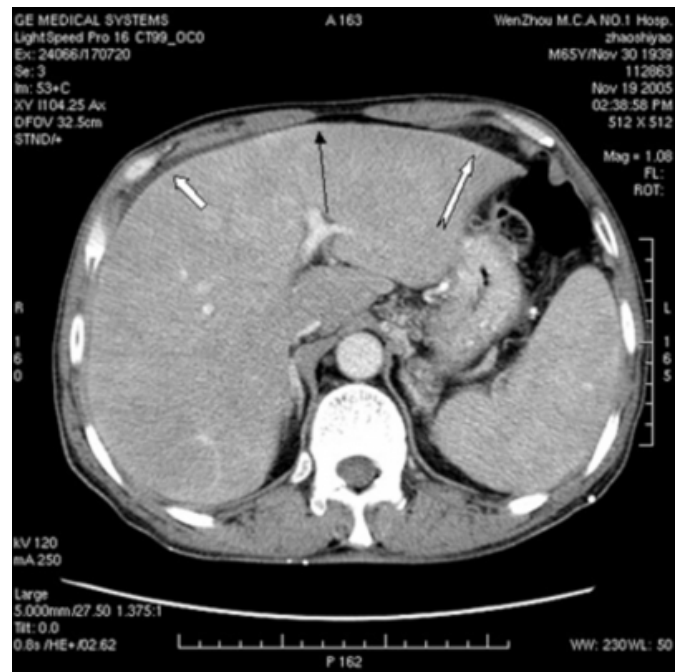
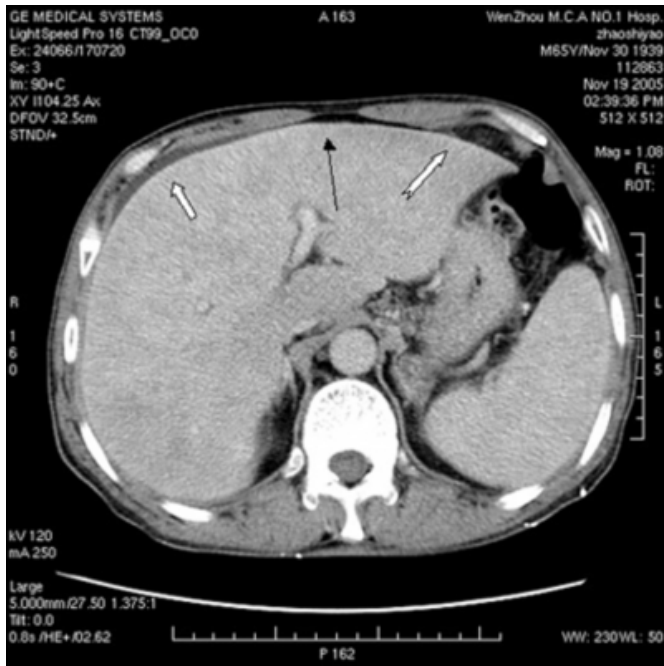


Figure 5

Figure 5: Delayed phase CT scan shows heterogeneous enhancement and diffuse hypoperfusion in the liver and spleen



Hepatic needle biopsy specimen revealed an irregular expanded portal triad infiltrated with an amorphous eosinophilic material that stained with Congo red. Amyloid deposit along the sinusoidal wall and marked atrophy of the liver cell cord were observed (Fig. 6, 7). Bone marrow aspirate showed a small increase in the percentage of plasma cells (8%). These examinations confirmed the diagnosis of AL, which was classified as primary systemic AL.

Figure 6

Figure 6: Amorphous amyloid deposit filling up the sinusoids and causing compression atrophy of the liver parenchyma (hematoxylin and eosin stain, original magnification $\times 100$)

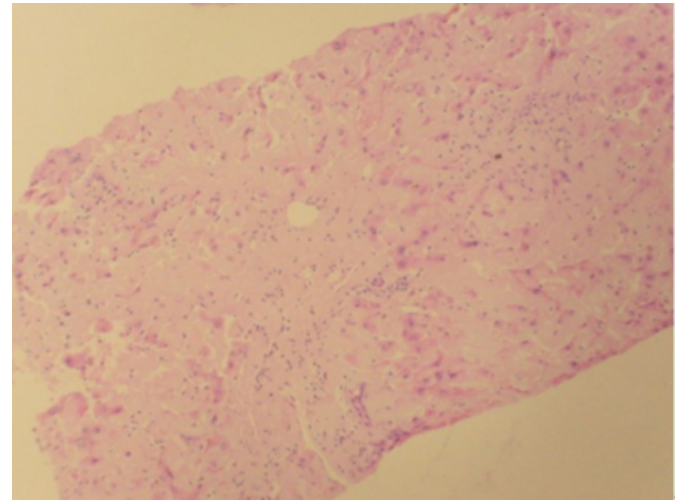
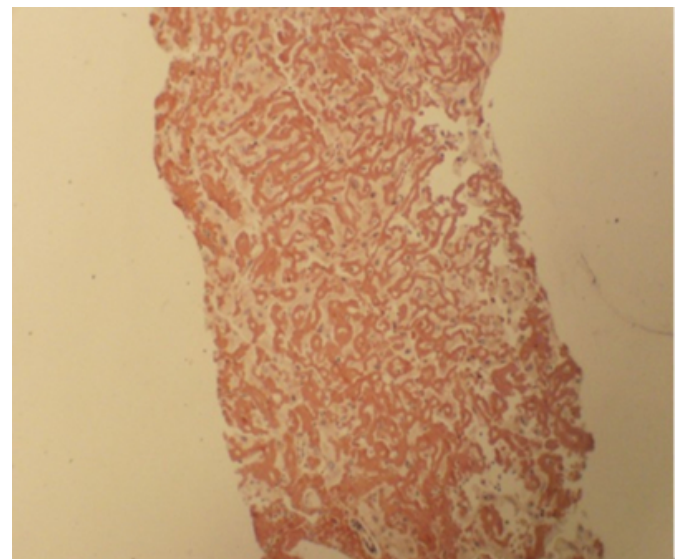


Figure 7

Figure 7: Amorphous eosinophilic material that stains with Congo red infiltrating the sinusoid and marked atrophy of the liver cell cord and vascular wall (original magnification $\times 100$)



DISCUSSION

Primary amyloidosis often involves the liver. Hepatomegaly and weight loss are the most common clinical manifestations in patients with hepatic amyloidosis³. Previous study had reported that 27% of patients with primary systemic amyloidosis present with hepatomegaly⁴, and that 81% of patients with primary amyloidosis with liver involvement have hepatomegaly while jaundice and portal hypertension

are rare ³. About 86% patients had elevated serum alkaline phosphatase levels ³, our patient presented with nonspecific symptoms, such as epigastric pain and abdominal fullness with high serum alkaline phosphatase level.

The ultrasonographic findings is non-specific, which includes heterogeneous echogenicity on ultrasonography, diffuse or focal regions of decreased parenchymal attenuation ⁵. While as to abdominal contrast-enhanced CT scan, in previous preliminary studies ^{2,5}, it was believed that presence of a markedly acute left lobe hepatic margin and asymmetric hepatomegaly of triangular shape with an apex at the falciform ligament and heterogeneous attenuation were characteristic features of hepatic amyloidosis, which may help to differentiate amyloidosis from other infiltrative diseases. Splenic involvement is common in amyloidosis, but splenomegaly was seen in only 10% of patients ³. The clinical manifestations of splenic involvement are infrequent but include pain, infarction, rupture and hyposplenism. Previous study noted that the CT findings of splenic amyloidosis include splenomegaly, calcification, and the lack of contrast enhancement⁵. Recently, Mainenti et al proposed that CT pattern of diffuse splenic hypoperfusion with or without splenomegaly could be used as a sign of systemic amyloidosis ⁶. Similar findings of CT scan but only no calcification in liver and spleen are observed in our patient.

Apart from live and spleen, the heart, and kidney are also most commonly affected by primary systemic amyloidosis. Congestive heart failure with predominant diastolic dysfunction and nephritic syndrome were most common clinical manifestations for cardiac and renal amyloidosis respectively. The presence of low voltage on ECG all limb leads less than 5 mm in height is a clue to cardiac involvement by amyloid ⁷. After obtaining biopsy proof of amyloid at an alternate site such as subcutaneous fat, noninvasive diagnostic criteria of amyloid-related organ involvement in AL amyloidosis has been proposed at 10th International Symposium on Amyloid and Amyloidosis ⁸. These including: Kidney: proteinuria 0.5g/24h, predominantly albumin. Heart: mean wall thickness 12mm, no other cardiac cause on echocardiogram. Liver: Total liver span 15cm in the absence of heart failure or alkaline phosphatase 1.5 times institutional upper limit of normal. According to above criterias, liver, spleen, heart, kidney were considered involved in our patient.

Diagnosis of amyloidosis mainly relies on tissue

confirmation by biopsy of affected organ. Diffuse infiltration of liver and spleen with amyloid materials will increase fragility of texture, and spontaneous rupture and massive hemorrhage may occur. ² So hepatic needle biopsy should be performed carefully in order to avoid possibility of serious complication. And alternative sites such as abdominal fat aspirate and rectal and labial salivary gland biopsies with a total sensitive of 80% have been recommended ⁹.

For primary amyloidosis, the mainstay of therapy has been chemotherapy, traditionally with melphalan and prednisone. But this therapy has only about a 30% response rate ¹⁰. 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% ⁴. However, ASCT is associated to a relatively high treatment related mortality 13% to 14% ⁴. Patients with primary systemic amyloidosis who have biopsy-proven liver involvement (primary hepatic amyloidosis) have poor prognoses, the median survival of patients has been reported as 8.5 months ³.

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