

# ***Giant hepatomegaly and portal hypertension in an elderly patient with primary liver amyloidosis: an uncommon clinical occurrence***

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**Abstract.** – Primary systemic amyloidosis (AL) is an uncommon disease characterized by the extracellular deposition of a protein with a beta-fibrillar structure, consisting of monoclonal immunoglobulin light chains,  $\lambda$  or  $\kappa$  (ratio of  $\lambda$  to  $\kappa$ , 3:1).

In systemic amyloidosis liver involvement is frequent but it rarely has clinical importance. The massive and localized liver deposition of amyloid, characterized by marked hepatomegaly and portal hypertension without hepato-cellular failure and by a severe prognosis, without systemic involvement, is less frequent.

The authors describe an unusual case of primary hepatic amyloidosis with giant hepatomegaly, intrahepatic cholestasis, portal hypertension and splenomegaly, occurred in an elderly patient.

**Key Words:**

Amyloidosis, Giant hepatomegaly, Portal hypertension, Elderly.

A ApoA1, Gelsolin, Fibrinogen A $\alpha$  and Lysozyme<sup>1,2</sup>.

Local deposition of amyloid without systemic involvement is an uncommon type of primary amyloidosis and it is also called “amyloid pseudo-tumor” or “amyloidoma”. Liver involvement in systemic amyloidosis is frequent but it rarely assumes clinical importance. The authors describe a rare case of primary liver amyloidosis (AL) with giant hepatomegaly and portal hypertension observed in an elderly patient, and confirmed by histological examination.

## ***Cinical case – Description***

The patient was a white man, 71-years old, who had been well until the age of 70 when he began suffering from asthenia, early satiety, weight loss and abdominal distension. At the physical examination anterior abdominal wall were dilated; liver edge was palpable 20 cm below the right costal margin while the spleen was appreciable 10 cm below the left costal margin. Neither ascites nor peripheral oedema were detected. Moreover the patient did not present symptoms or signs referable to heart failure, renal insufficiency and peripheral neuropathy.

Biochemical tests were normal a part from a remarkable rise in serum alkaline phosphatase (1728 U/L, range: 39-117 U/L) and in serum  $\gamma$ GT (341 U/L, range: 10-50 U/L), and from a decrease of serum albumin (2.2 g/dl); moreover a monoclonal band in the  $\gamma$ -zone of the serum protein electrophoretic pattern was present. The urinalysis revealed proteinuria, that included Bence-Jones proteins, and

## ***Introduction***

Amyloidosis is characterized by the extracellular deposition of pathologic insoluble fibrillar proteins in organs and tissues. The classification of amyloidosis is based on the nature of the precursor proteins that form the fibril deposits. Amyloid fibrils in primary amyloidosis and amyloidosis associated with multiple myeloma are fragments of immunoglobulin light chains (AL amyloidosis). In the secondary amyloidosis or reactive amyloidosis, associated with chronic infection or inflammation, the precursor proteins are the SAA acute phase proteins (AA form), while in familial amyloidosis the precursor proteins are transthyretin (ATTR form), or

immunofixation showed that the monoclonal component was IgG $\lambda$ .

Ultrasonographic examination and computed tomography showed a giant hepatomegaly without focal lesions, splenomegaly, and very mild ascites (Figure 1); the portal vein diameter was enlarged (20 mm  $\varnothing$ ).

At that point the severity of the clinical features associated with normal values of the liver function tests and high levels of serum alkaline phosphatase strongly suggested an interstitial liver disease without hepatocellular failure. Our suspect was confirmed by the histological examination of a fine-needle liver biopsy specimen.

Histological examination revealed massive deposits of amorphous, homogeneous, metachromatic material in the interstitial tissue. When stained with Congo-red this material was pink in normal light (Figure 2) and showed typical apple-green birefringence in polarized light, that proved its amyloid nature. It was resistant to potassium permanganate pretreatment, indicating it to be of the

AL type<sup>3</sup>. Laboratory and instrumental examinations were performed to differentiate primary from myeloma-associated amyloidosis. Histological examination of rectal and gastric biopsies did not reveal amyloid deposition in the interstitial tissue. Because of these findings and the absence of other significant parenchymal alterations a diagnosis of primary liver amyloidosis was performed.

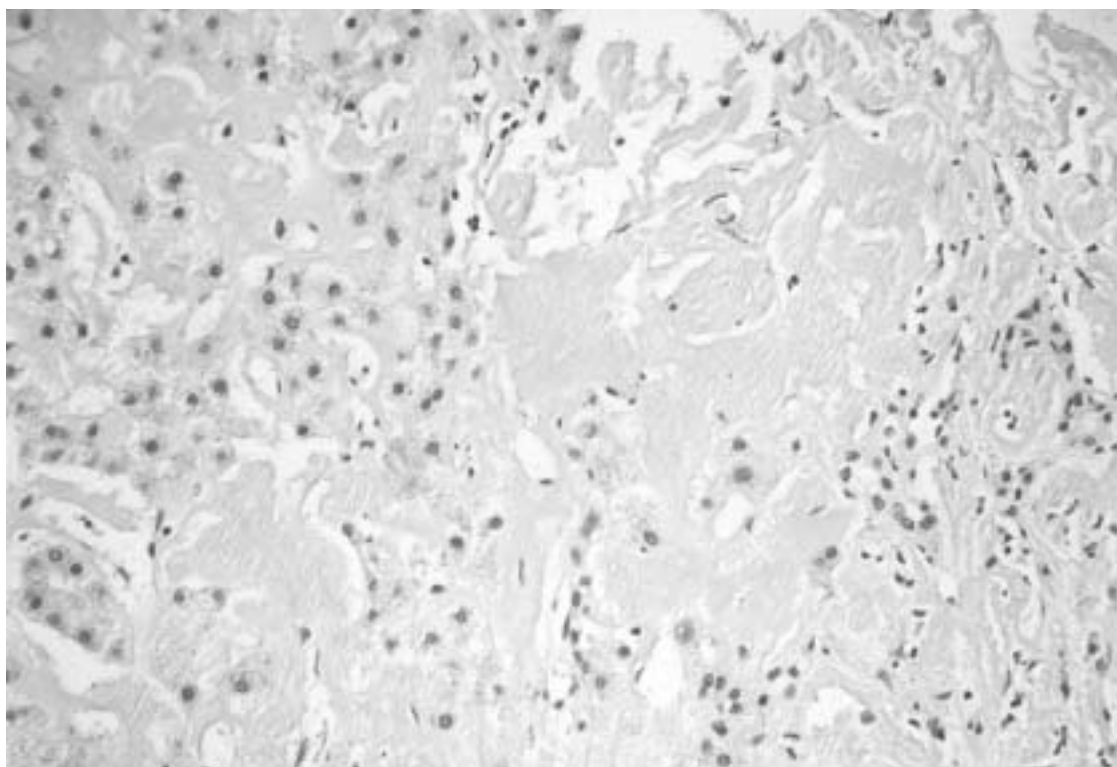
Because of the progressive worsening of the disease the patient could not receive therapy with melphalan and prednisone, that has been demonstrated to be the most active treatment for primary systemic amyloidosis<sup>4</sup>. Three months after the diagnosis the patient died because of a severe renal insufficiency. The autopsy was not performed.

### Discussion

The diagnosis of primary AL amyloidosis often occurs in 60-years or older male patients<sup>5,6</sup>. In AL amyloidosis the amyloid fib-



**Figure 1.** Abdomen computed tomography. The computed tomography showed a giant hepatomegaly without focal lesions and splenomegaly.



**Figure 2.** Histological section of the liver. Congo red positivity for interstitial amyloid. (Congo red  $\times 180$ ).

rils are typically deposited in numerous organs including heart, kidney and liver. Localized AL amyloidosis without systemic involvement is uncommon; isolated deposits of amyloid in a single organ are known as “amyloidoma” or amyloid pseudo-tumor. In the clinical case described there was only liver deposition of amyloid fibrils, in fact the biopsy specimens from gastric and rectal mucosa did not reveal amyloid deposition. Hepatomegaly is frequent in patient with AL amyloidosis<sup>7</sup> but clinical dominant liver disease is rare<sup>8</sup>. Moreover the hepatic amyloidosis is an unusual cause of ascites and portal hypertension<sup>9</sup>. Splenomegaly is rare in AL amyloidosis, occurring in about 5 percent of all cases. This paper describes a case of clinically dominant liver amyloidosis with giant hepatomegaly, portal hypertension and splenomegaly, that were confirmed by computed tomography.

In our patient we suspected an infiltrative disease of the liver because of the giant hepatomegaly and the increase of the serum alkaline phosphatase level with normal values of the liver function tests. Our hypothesis was confirmed by the liver biopsy examination

that revealed amyloid deposition in the perisinusoidal space and in portal tracts.

Hepatomegaly, portal hypertension and marked increase in alkaline phosphatase levels are associated with a poor prognosis<sup>10</sup>. The most frequent causes of death in patients with hepatic amyloidosis and portal hypertension are haemorrhage and renal failure<sup>11</sup>.

Our patient died three months after the diagnosis because of a severe renal failure.

Recently few similar cases of primary liver amyloidosis with atypical clinical features have been reported in the English literature<sup>12-18</sup>.

The dramatic and unusual clinical picture and the progressive worsening of the disease did not allow the patient to receive therapy with melphalan and prednisone but only support treatment.

Our conclusive message is that in patients with clinical symptoms of fatigue, early satiety, weight loss and marked abdominal distension, associated with hepatomegaly and increase in serum alkaline phosphatase and normal values of liver function tests, an infiltrative liver disease should be suspected and amyloidosis in particular. For an accurate diagnosis a liver biopsy should be performed,

also in elderly patients, because the diagnosis is rarely made until signs or symptoms referable to a single organ<sup>19</sup>. In case of an unexplained intrahepatic cholestasis or portal hypertension the possibility of amyloidosis should be always considered.

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