中文題目：原發性類澱粉沉著症導致急性肝衰竭

英文題目：Acute hepatic failure secondary to primary amyloidosis

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Background:

Amyloidosis is a group of diseases characterized by deposition of amyloid fibrils in extracellular matrix of organs, which can result in end-organ dysfunction. Amyloidosis related hepatic failure was rarely reported. The diagnostic difficulty relates to lack of specific imaging and laboratory tests [1]. Biopsy is the gold standard. Early diagnosis is necessary for timely management.

Method:

We report a case with primary liver amyloidosis with presentation of rapidly progressive hepatic failure.

Result:

A 66-year-old female with hypertension and mitral regurgitation presented to regional hospital with bilateral legs edema for 2 months and bleeding diathesis for 1 month. Laboratory exam revealed creatinine 1.02 mg/dL(0.5-1.2 mg/dL), albumin 2.4 g/dL(3.8-5.3 g/dL), international normalized ratio(INR) 2.24(0.9-1.2), total bilirubin(TBIL) 1.5 mg/dL(<1.3 mg/dL), aspartate aminotransferase 28 IU/L(8-38 IU/L), alanine transaminase 11 IU/L(4-44 IU/L), alkaline phosphatase 712 IU/L (104-338 IU/L). Normocytic anemia (hemoglobin 7 g/dL, >11.1g/dL) was related to gastric ulcer bleeding according esophagogastroduodenoscopy. However, rapidly progress jaundice with elevated total bilirubin from 1.5 mg/dL to 15 mg/dL within 1 week, accompanied with hepatic encephalopathy (ammonia level 257 ug/dL(<82 ug/dL)) at the same time. Computed tomography demonstrated hepatosplenomegaly without biliary tract dilatation nor hepatic mass (Fig.1).

The patient was referred to medical center, where an extensive workup were negative, include viral serologies (HAV, HBV, HCV, HEV, CMV, HSV, EBV), autoimmune, metabolic studies. Drug-induced liver injury was unlikely based on history taking. INR remained greater than 2 despite daily fresh frozen plasma transfusion and elevated TBIL from 15 mg/dL to 37.8 mg/dL within 6 days. We started liver transplantation preparation and performed 7 times of plasma exchange since day 7. Liver biopsy was done after 6 times of plasma exchange for correction of coagulopathy. The pathology demonstrated extensive amorphous eosinophilic deposition in sinusoids and the hepatocytes was replaced with cholestasis. Congo red stain showed apple-green

birefringence under polarized light (Fig.2). These findings were consistent with amyloid light-chain (AL) amyloidosis. In order to stage the amyloidosis, echocardiogram only showed grade I diastolic dysfunction and moderate mitral regurgitation. Bone marrow biopsy showed focal amyloid substance deposition. Immunohistochemical study for CD138, kappa and lambda light chain showed no evidence of myeloma(Fig.3). No characteristic amyloid fibrils deposition in skin was found. Regrettably, serum and urine immunoelectrophoresis and free light-chain assay were performed after plasma exchange, which revealed no apparent monoclonal gammopathy.

Unfortunately, she was intubated for acute respiratory distress syndrome secondary to plasma exchange induced transfusion related acute lung injury. She continued to be managed with mechanical ventilation, hemofiltration, vasopressor and broad-spectrum antibiotics. The patient was not considered to be a suitable candidate for liver transplant because of multiple organ failure and progressive amyloidosis related hepatic failure. She was treated with bortezomib and dexamethasone on day 23. Finally, the patient died after one month period of jaundice.

Discussion

AL amyloidosis is a rare disorder caused by extracellular deposition of immunoglobulin light chains. The prevalence of AL amyloidosis increased from 15.5 cases per million in 2007 to 40.5 in 2015 in the United States, while the incidence ranged from 9.7 to 14.0 cases per million person-years with no significant increase [2]. Clinical features depend on organs involved. About three quarter of the patients had involvement of two or more organs [3]. Liver is also a common site of amyloid deposition. In 1 autopsy series, 70% of the patients with primary systemic amyloidosis had liver involvement [4]. The presentation of hepatic amyloidosis is usually subclinical or with mild elevation of liver enzymes, but liver failure has rarely been reported. In 1 case series of 98 patients and 3 case reports demonstrated that hepatic amyloidosis usual presented as weight loss, elevated alkaline phosphatase, proteinuria and mild anemia [5-8].

High-dose melphalan followed by autologous stem cell transplantation has been shown to be effective in treating AL amyloidosis, although only a few patients are eligible. Alternatively, bortezomib-based regimen has shown promising activity [9]. Ryosuke Nakano et al. have reported a case of systemic AL amyloidosis progressed to liver failure undergoing liver transplant followed by bortezomib-dexamethasone chemotherapy was successfully treated [10].

Conclusion

Amyloidosis should always be considered in elderly patient with infiltrative liver pattern and multiple organ involvement, and liver biopsy must be performed. Transjugular liver biopsy is a safer alternative to percutaneous liver biopsy if coagulopathy and ascites are consideration [11]. All patients with a systemic amyloid syndrome require therapy to prevent deposition of amyloid in other organs and prevent progressive organ failure. Liver transplant combined chemotherapy may represent a potential salvage treatment option for hepatic AL amyloidosis with liver failure.

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Figures and figure legends

Figure 1

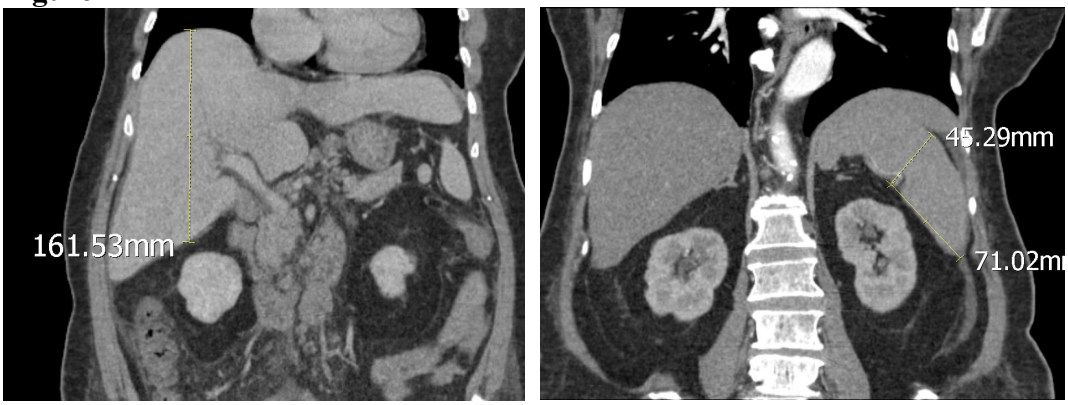

Fig.1 Hepatosplenomegaly in a patient with acute hepatic failure
Computed tomography showed enlarged liver and spleen without biliary tract dilatation.

Figure 2

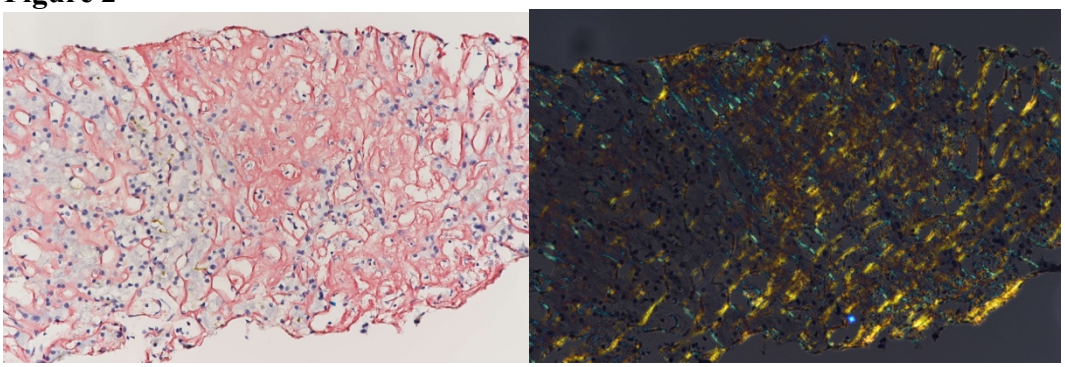

Fig.2 Biopsy specimen from the liver tissue, hematoxylin and eosin stain showed extensive amorphous eosinophilic deposition in sinusoids with atrophy of hepatocytes.
(A) Congo red stain demonstrated orange-red deposits of amyloid, (B) characteristic "apple-green" birefringence on polarized light microscopy.

Figure 3

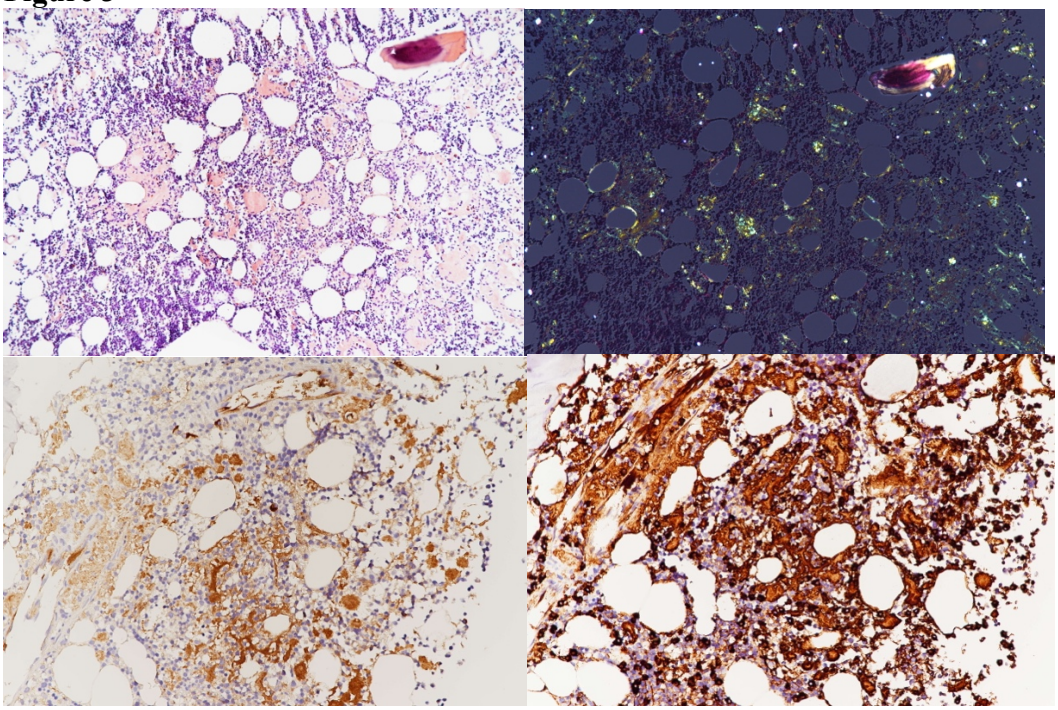

Fig.3 Biopsy specimen from the bone marrow, hematoxylin and eosin stain showed a normocellular marrow with focal amyloid deposition

(A) amyloid deposition with Congo red staining, (B) “apple-green” birefringence on polarized light microscopy, immunostaining to (C) kappa and (D) lambda light chains were both positive.