Letter to the Editor

Hepatic amyloidosis

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Immunoglobulin light chain amyloidosis presenting as Budd-Chiari syndrome

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Dear Editor,

Immunoglobulin light chain (AL) amyloidosis is the most prevalent type of systemic amyloidosis. It is characterized by deposits of unfolded proteins in various organs, such as the kidneys, liver, and intestines, and can lead to organ dysfunction and death.[1] The incidence of AL amyloidosis may be as much as 12 cases per million individuals per year.[2] The kidneys are the most commonly affected organ, followed by the heart, liver, and gastrointestinal tract.[1] Patients with hepatic involvement are usually asymptomatic. The most common symptoms are involuntary weight loss (71%), followed by fatigue (60%) and abdominal pain (53%).[1–3] Hepatomegaly is the most common physical examination finding (81%), and ascites has been observed in 42% of patients.[3] Hepatic involvement is a poor prognostic factor, with a median survival around 8.5 months.[4–6] Presently described is a rare case of aggressive AL amyloidosis with liver involvement presenting as Budd-Chiari syndrome.

Case Report

A 69-year-old female patient presented at an outpatient clinic in August 2020 with fatigue, loss of appetite, and right upper quadrant abdominal pain. Her medical history included a previous cholecystectomy. A physical examination revealed hepatomegaly. The findings of laboratory tests performed at the time of presentation indicated a white blood cell (WBC) count of 13.0x10^6/L. In addition, results of a serum aspartate aminotransferase (AST) level of 49 IU/L (normal range: 0–35 IU/L), alkaline phosphatase (ALP) level of 405 IU/L (normal range 35–110 IU/L), gamma glutamyl transferase (GGT) level of 663 U/L (normal range: 7–50 IU/L), total bilirubin level of 1.7 mg/dL (normal range: 0.3–1 mg/dL), and albumin level of 2.7 g/dL (normal range: 3.5–5.5 g/dL) were noted. The results of serological studies for viral hepatitis, an autoimmune panel, and a metabolic panel were all normal. Her D-dimer level was high: 5321 ng/mL (normal range: <250 ng/mL). The antithrombin-III and protein C activity level was 43% (normal range: 70–125%) and 51% (normal range: 70–140%), respectively. Abdominal ultrasonography (US) revealed hepatomegaly and a diffuse increase in parenchyma heterogenicity. Doppler US suggested no flow in the right hepatic vein. Magnetic resonance imaging (MRI) also showed hepatomegaly, a heterogenic liver parenchyma, and no contrast filling in the right hepatic vein, consistent with right hepatic vein occlusion. Anticoagulant therapy with low-molecular-weight heparin was initiated. She was followed-up in the outpatient clinic.

She presented at the outpatient clinic in September with fatigue, dyspnea, and abdominal distension. Ascites and peripheral edema were present. Her total bilirubin level had increased to 5.5 mg/dL, and the albumin level had decreased. A bone marrow biopsy was performed due to an increased WBC count. A cardiologist diagnosed her with diastolic myocardial dysfunction, and diuretic treatment was implemented.

Progressive fatigue and abdominal distension were observed in October. Epigastric tenderness, hepatosplenomegaly, and substantial ascites were noted. Blood test results indicated a WBC count of 22.8x10^6/L, and a neutrophil value of 16.1x10^6/L, a hemoglobin value of 10.9 g/dL, and a platelet count of 449x10^9/L. Her serum ALP level was 261 IU/L, the GGT was 91 IU/L, the total bilirubin was 3.1 mg/dL, the direct bilirubin was 1.8mg/dL, and the albumin level was 2.7 g/dL. Her international normalized ratio was 1.5. Genetic analysis revealed a heterozygosity mutation of the methylenetetrahydrofolate reductase gene (MTHFR C677T). MRI showed hepatosplenomegaly, advanced heterogeneity in the liver parenchyma, narrowing and irregular hepatic veins (especially the right hepatic vein), and considerable ascites, as illustrated in Figure 1a. The hepatic venous pressure gradient (HVPG) was measured. Hemodynamic examination demonstrated a right atrium pressure of 6 mmHg, a free hepatic venous (HV) pressure of 10 mmHg, and a wedged HV pressure of 25 mmHg. The HVPG was 15 mmHg. A transjugular liver biopsy was also performed. The results revealed diffuse hepatocyte plate atrophy with the deposition of pale amorphous, homogenous extracellular material in the space of Disse, shown in Figure 1b. Deposits were also seen in the walls of arteries and veins, and in the portal connective tissue. The deposits produced apple-green birefringence under polarized light using Congo red stain and were consistent with amyloid structures. Am-

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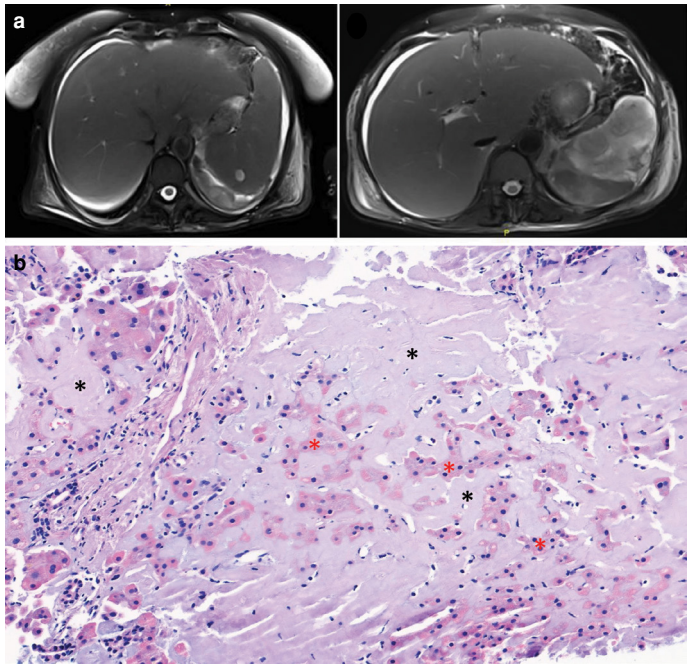

Figure 1. (a) Magnetic resonance images of hepatosplenomegaly, advanced heterogeneity in the liver parenchyma, narrowing and irregular hepatic veins (especially the right hepatic vein), and considerable ascites, and **(b)** liver biopsy result illustrating diffuse hepatocyte plate atrophy with the deposition of pale amorphous, homogenous extracellular material in the space of Disse.

yloid typing with immunohistochemistry indicated non-AA amyloidosis. Further typing was performed using mass spectrometry-based proteomics, and amyloid protein identification using a liquid chromatography-mass spectrometry test identified a peptide profile consistent with AL kappa amyloid deposition. The bone marrow biopsy also revealed a proliferation of plasma cells (10%) in aggregates that were kappa monotypic. Evidence of a monoclonal plasma cell proliferative disorder was further supported by the presence of an abnormal monoclonal serum protein.

AL amyloidosis with liver involvement was diagnosed, and bortezomib plus dexamethasone combination therapy was initiated. After the second course of therapy, the patient was admitted to the hospital for fatigue. She was diagnosed with septic shock due to a urinary tract infection. Antibiotic treatment, volume replacement, and vasopressor therapy were used; however, the patient died 10 days after hospitalization.

Discussion

Since the clinical symptoms of AL amyloidosis are vague and nonspecific, unfortunately, many cases are underdiagnosed. Early diagnosis and treatment are crucial, but can be difficult. Fatigue, peripheral edema, non-diabetic nephrotic range proteinuria, unexplained dyspnea on exertion, weight loss, progressive neuropathy, orthostatic hypotension, and hepatosplenomegaly suggest the need to evaluate for amyloidosis. Initial management depends on whether the patient is eligible for treatment with high-dose melphalan followed by autologous hematopoietic cell transplantation. If not, bortezomib-based chemotherapy is administered to most patients with AL amyloidosis. Treatment is generally ineffective if the total light chain load in organs such as the liver and heart is high, as in our case. Therapies for AL amyloidosis have been demonstrated to improve survival and quality of life,[7] but in our case, unfortunately, we had the opportunity to provide only 2 courses of therapy.

Physicians need to be aware of clinical presentations that may be AL amyloidosis to avoid misdiagnosis. AL amyloidosis should be considered in patients with a multisystem disorder. Early diagnosis allows for effective therapy to improve organ function.

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References

1. Obici L, Perfetti V, Palladini G, Moratti R, Merlini G. Clinical aspects of systemic amyloid diseases. Biochim Biophys Acta 2005;1753(1):11-22. [CrossRef]
2. Gertz MA, Dispenzieri A. Systemic amyloidosis recognition, prognosis, and therapy. A systematic review. JAMA 2020;324(1):79-89. [CrossRef]
3. Park MA, Mueller PS, Kyle RA, Larson DR, Plevak MF, Gertz MA. Primary (AL) hepatic amyloidosis: clinical features and natural history in 98 patients. Medicine (Baltimore) 2003;82(5):291-298. [CrossRef]
4. Gertz MA, Kyle RA. Hepatic amyloidosis (primary [AL], immunoglobulin light chain): the natural history in 80 patients. Am J Med 1988;85(1):73-80.
5. Ryšavá R. AL amyloidosis: advances in diagnostics and treatment. Nephrol Dial Transplant 2019;34(9):1460-1466. [CrossRef]
6. Rowe K, Pankow J, Nehme F, Salyers W. Gastrointestinal amyloidosis: review of the literature. Cureus 2017;9(5):e1228. [CrossRef]
7. Lamm W, Willenbacher W, Lang A, Zojer N, Müldür E, Ludwig H, et al. Efficacy of the combination of bortezomib and dexamethasone in systemic AL amyloidosis. Ann Hematol 2011;90(2):201-206. [CrossRef]