Clinical Case Report

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Primarily isolated hepatic involvement of amyloidosis

A case report and overview

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Abstract

Background: Amyloidosis is particularly difficult to diagnose because the signs and symptoms are subtle. Additionally, there are no specific imaging or laboratory tests, except histopathology. Although it is considered to be a systemic disorder, a small portion of cases may be localized.

Introduction of the case: A 54-year-old man presented with nonspecific symptoms (jaundice and back pruritus). Biochemical tests showed a high level of bilirubin and elevated serum tumor markers (CA19–9 and CA125). Routine imaging showed hepatomegaly without heterogeneous enhancement. Liver biopsy confirmed the diagnosis of hepatic amyloidosis. No cardiac or renal involvement was found. The patient accepted treatment involving oral chemotherapy.

Conclusion: A rare and unique presentation of hepatic amyloidosis was highlighted in this case.

Abbreviations: AL = amyloid light-chain, ALP = alkaline phosphatase, CT = computed tomography, GTT = glutamyl transpeptidase, MR = magnetic resonance, MRCP = magnetic resonance cholangiopancreatography.

Keywords: hepatomegaly, jaundice, liver, primary amyloidosis

1. Introduction

Amyloidoses are a group of disorders that primarily consist of 3 forms, namely primary amyloidosis, secondary amyloidosis, and familial amyloidosis. Amyloidosis is characterized by the deposition of abnormal proteins undergoing a conformational change to form insoluble β-sheet protofilaments.[1] The difficulty associated with diagnosing amyloidosis relates to the lack of specific imaging or laboratory tests,[2] which poses a great challenge for clinicians. Biopsy is the gold standard in the diagnosis of amyloidosis. Cases of amyloidosis that are primarily localized in the liver rarely have been reported. Here, we report a case involving a patient with primary hepatic amyloidosis who presented with liver dysfunction.

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LY and HS equally contributed to this study.

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2. Case report

A 54-year-old man was admitted to our hospital for gradual jaundice and weight loss over 2 months. His vital signs were stable and afebrile. On physical examination, his skin and sclera were mildly jaundiced, with scratch marks on his arms and back. An enlarged liver was palpitated 3 fingerbreadths in the right hypochondriac region. The spleen was not palpable. Biochemical tests showed a high level of both total and direct bilirubin (97.8 μmol/L and 82.6 μmol/L, respectively). Serum alkaline phosphatase (ALP) (374 μ/L) and gamma glutamyl transpeptidase levels (γ-GTT) (319 μ/L) were also elevated (listed in Table 1). Computed tomography (CT) and magnetic resonance (MR) imaging showed hepatomegaly with no suspicious nodules (Fig. 1). To determine whether there were blockages in the bile ducts, magnetic resonance cholangiopancreatography (MRCP) was used and showed hepatomegaly with cholecystitis. He then was treated with ursodeoxycholic acid capsules and compound ammonium glycyrrhetate single S and ademetionine for a week. However, he developed epigastric pain and had no improvement in the biochemical tests. After consent was obtained from the patient, ultrasonography-guided liver biopsy was utilized. The liver biopsy demonstrated a massive amount of amyloid deposition along the sinusoids (Fig. 2C–G).

Since the patient was found to have amyloid deposition in his liver, we had to conduct other tests to determine whether it was localized or systemic. Echocardiographic and renal function tests, bone marrow aspiration, serum-free light chain test, and skin biopsy (from multiple sites) were performed. Histopathological evaluation showed positive staining with Congo red and characteristic "apple-green" birefringence on polarized microscopy. All these results indicated primary hepatic amyloidosis, and the skin biopsy was positive for lambda light chains (Fig. 2A, B, H), whereas cardiac and

Table 1

Patient's laboratory results on admission.

Laboratory measurements	Value on admission (normal range)
WBC ($\times 10^9$/L)	10.6 (3.5–9.5)
Hemoglobin (g/L)	121 (130–175)
Platelet ($\times 10^9$/L)	442 (125–350)
TBIL (μmol/L)	97.8 (3.4–17.1)
DBIL (μmol/L)	82.6 (0–10.0)
IBIL (μmol/L)	15.2 (0–12.2)
TP (g/L)	53.5 (65.0–85.0)
Albumin (g/L)	32.2 (40.0–55.0)
ASAT (U/L)	53 (0–38)
ALP (U/L)	374 (45–125)
gGT (U/L)	319 (10–60)
LDH (U/L)	279 (90–250)

ALP = alkaline phosphatase, ASAT = aspartate aminotransferase, DBIL = direct bilirubin, gGT = gamma glutamyl transpeptidase, IBIL = indirect bilirubin, LDH = lactate dehydrogenase, TBIL = total bilirubin, TP = total protein, WBC = white blood cell.

Table 2

Bilirubin and aminotransferase level in serum.

Time	TBIL (μmol/L)	ASAT (U/L)
On admission	97.8	53
5 days	139.4	50
10 days	151.7	51
28 days	227	74

ASAT = aspartate aminotransferase, TBIL = total bilirubin.

renal function were normal. Serum bilirubin and amino transaminases levels measured at admission and afterward are listed in Table 2.

The patient refused to take melphalan or undergo stem cell transplant; therefore, we provided him with supportive therapies. No obvious improvement in liver function was observed. Subsequently, he was discharged from the hospital and continued to take oral chemotherapy (thalidomide 100 mg/d and prednisone 20 mg/w).

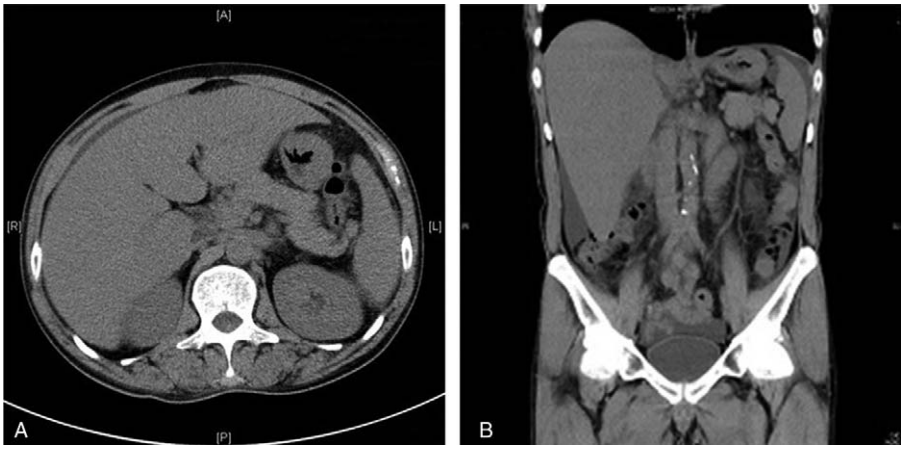

Figure 1. CT and MRI images of the abdomen showed an enlarged liver and no filament. CT = computed tomography, MRI = magnetic resonance imaging.

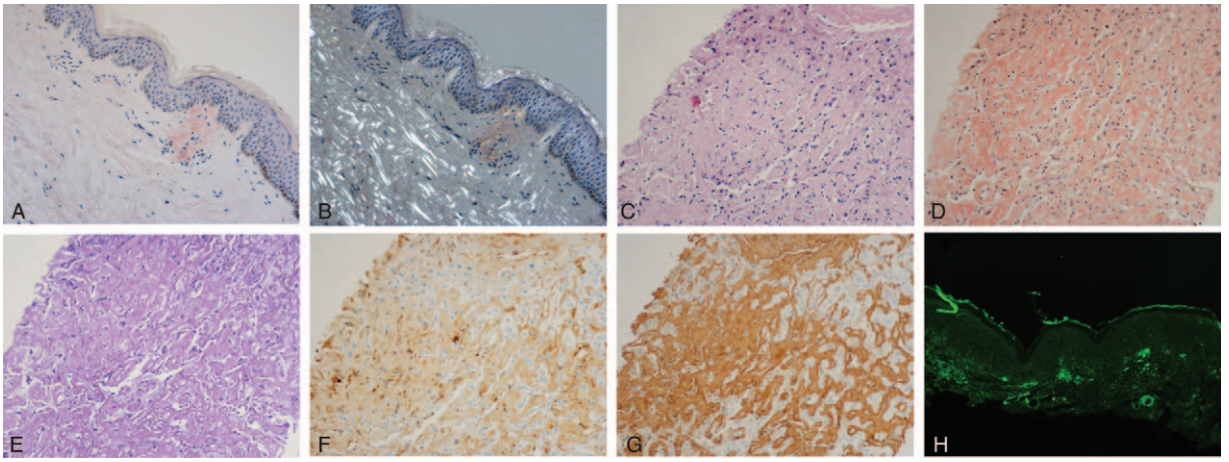

Figure 2. (A) A biopsy specimen from the skin, photomicrograph (H&E stain) showed collagen-type extracellular material, (B) characteristic "apple-green" birefringence on polarized light microscopy, which is consistent with amyloidosis, (C) biopsy specimen from the liver tissue, photomicrograph (H&E stain) showed collagen-type extracellular material, (D) Congo red stain demonstrated characteristic staining, (E) methyl violet stain revealed strong affinity for the material, (F) immunostaining with antibodies to kappa light chains was negative, (G) immunostaining with antibodies to lambda light chains was positive, (H) the biopsy specimen from the skin, immunofluorescence with antibodies to lambda light chains was positive. Immunofluorescence with antibodies to kappa light chains was negative (not shown). H&E stains = hematoxylin and eosin stains.

3. Discussion

Immunoglobulin light chain amyloidosis is a clonal plasma cell disorder in which amyloid fibrils that are derived from immunoglobulin light chains are deposited in organs and tissues. The prognosis is often poor if fibril deposits build up in vital organs such as cardiac muscles. With no treatment, the median survival time is 2 years.[3] As reported, a patient with primary amyloidosis presented symptoms that were similar to those of Crohn's disease, delaying accurate diagnosis.[4] Therefore, early and precise diagnosis is urgently needed. Since the presenting symptoms tend to mimic those of other diseases, physicians should suspect amyloidosis in any patient with generalized fatigue, weight loss, skin lesions, paresthesias, nondiabetic nephrotic syndrome, and hepatomegaly.[5–6] Symptoms may vary according to the organs and tissues involved. The gastrointestinal system, especially the colon, is the most frequently involved system.[1]

Amyloidosis is usually considered to be systemic, but 10% to 20% of cases can be localized.[7] Here, we reported a case in which a patient presented with jaundice and altered liver function tests. At first, the elevated serum tumor markers and enlarged liver suggested liver cancer or carcinoma of the gall bladder. However, imaging results did not support cancer. Since the patient was allergic to iodine, contrast-enhanced CT was forbidden. Elevated tumor markers in association with amyloidosis rarely are described in the literature. Serum immunofixation electrophoresis provided a clue that primary amyloidosis was the correct diagnosis. Thus, a subsequent liver biopsy was performed.

The diagnosis of amyloidosis requires 2 components: a generic and a type-specific diagnosis. Invasive organ biopsy is not always necessary, as fat pad aspiration, in particular, is even more sensitive (72%) than bone marrow biopsy in diagnosing amyloidosis.[8] However, if a fat pad aspiration fails to demonstrate amyloidosis, then biopsies of involved organs should be considered.[9] Currently, mass spectrometry-based proteomics have emerged as a new technique to classify systemic amyloidosis and analyze serum transthyretin in patients with potentially amyloidogenic mutations.[10,11] Serum-free light

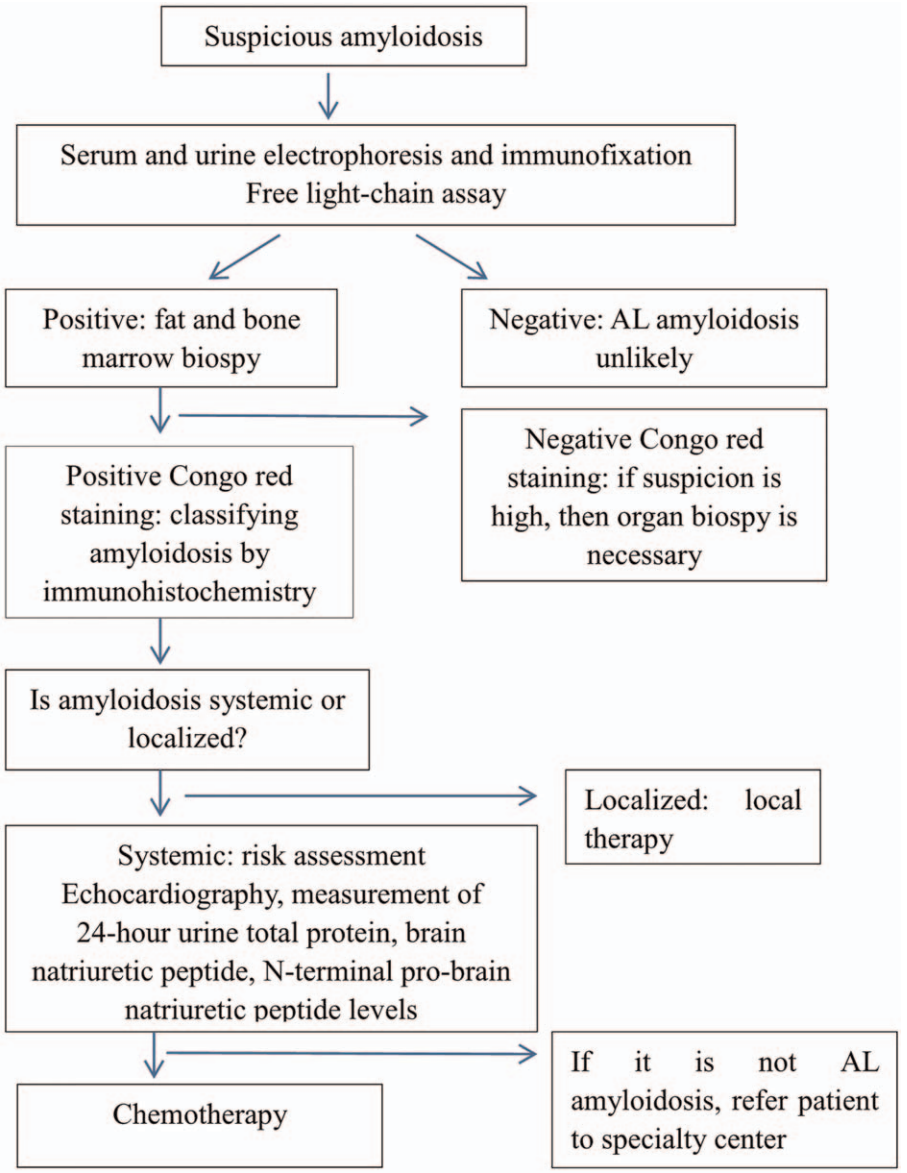

Figure 3. Algorithm for diagnosing patients with suspected amyloidosis.

chains, protein immunofixation, MR elastographic, shear-wave elastography, and other examinations support the diagnosis of amyloidosis, but they are not sufficient to define it.[1,9,12] A proposed strategy for evaluating a patient with suspected amyloidosis can be seen in Fig. 3.

Treatment for amyloidosis depends on the type of amyloidogenic protein. For amyloid light-chain (AL) amyloidosis, chemotherapy is the mainstay treatment. It has been reported that melphalan and prednisone are superior to colchicine in 2 randomized phase III studies.[13–14] Melphalan in combination with dexamethasone is highly effective in treating AL amyloidosis with minimal toxicity.[15] Autologous stem cell transplantation is a reasonable primary option, but only 20% of patients meet the requirements.[5] Researchers have explored new drugs (thalidomide, lenalidomide, pomalidomide, and bortezomib) to treat AL amyloidosis in combination with dexamethasone or melphalan and dexamethasone or dexamethasone and cyclophosphamide.[16–20] Melphalan combined with dexamethasone is still considered to be the standard treatment for nontransplant candidates. However, more data are required on treatment options in association with the pathophysiology of the amyloid formation that is generated.

Amyloidosis is uncommon, and its prognosis is poor, especially when irreversible organ damage occurs. Thus, the most urgent requirement is an early and accurate diagnosis of the disease. Clinicians should be aware of all the possible signs and initiate an effective treatment as early as possible. This case represents a standard diagnostic process of primary hepatic amyloidosis.

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