CASE REPORT

Vasotropic light-chain amyloidosis and ischaemic cholangiopathy

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SUMMARY

A 75-year-old woman was incidentally found to have deranged liver function tests (LFTs). She was well, apart from 2 years of dyspnoea. Investigations had revealed atrial fibrillation and a right pleural effusion, without identified aetiology. On examination, the only finding was a palpable liver edge. Initial blood and ultrasound screening suggested no cause. The patient underwent liver biopsy. Microscopy showed κ -immunoglobulin light chains deposited exclusively in portal tracts, within blood vessel and bile duct walls. This pattern, although unusual, raised the possibility of κ -light chain disease. Serum electrophoresis was normal, as were serum immunoglobulin values. Serum concentrations of κ -light chains were elevated and microscopy of aspirated bone marrow found light-chain deposits with 10% plasmacytosis. Serum amyloid P (SAP) scintigraphy demonstrated splenic uptake. Myeloma, κ -light chain, with light-chain amyloidosis was diagnosed. The patient has responded well to cyclophosphamide, bortezomib and dexamethasone chemotherapy, and her LFTs are now nearly normal.

BACKGROUND

This rare case highlights an unusual but important clinicopathological presentation of light-chain amyloidosis (AL). It acts as a reminder of the varied clinical manifestations, particularly gastrointestinal, that AL amyloidosis can exhibit. AL can mimic other more common conditions and should be considered in all disorders with multiorgan involvement. In addition, in our patient, serum protein electrophoresis was normal, as in 50% of cases; serum electrophoresis should not be used in screening when AL is suspected.

This case was also interesting histopathologically. Ours is only the second patient, of whom we know, with AL in the liver involving only portal tracts and lacking perisinusoidal deposits.

CASE PRESENTATION

A 75-year-old woman was referred to hepatology clinic with abnormal liver function tests (LFTs). She had no symptoms of liver disease (abdominal pain or swelling; jaundice). Her main concern was of shortness of breath (SOB), which was most noticeable during walks with her local rambling club. Investigations into this 2 years previously had found her to be in atrial fibrillation (AF), and she was started on warfarin and bisoprolol. The bisoprolol exacerbated the SOB so it was substituted for with digoxin, which showed mild improvement in the dyspnoea.

The patient's only other medical history was of a moderate right-sided pleural effusion identified 6 months previously and drained via videoassisted thoracoscopy. This resulted in improvement, but not resolution, of the SOB. Fluid analysis and histopathological study of a pleural biopsy specimen showed no evidence of infection or malignancy.

On presentation, the patient was taking warfarin and digoxin 62.5 μ g, along with senna and lactulose as required. She denied over the counter medication use. She was not high risk for viral hepatitis and there was no relevant family history. She had a less than five pack year smoking history, stopping in 1966, and drank a minimal amount of alcohol. Examination found no jaundice or stigmata of chronic liver disease; smooth, non-tender hepatomegaly was present with a span of 16 cm in the midclavicular line.

INVESTIGATIONS

Full blood count and coagulation screen were normal, as were urea and electrolyte values. LFTs were elevated showing a predominantly cholestatic picture: bilirubin 25 μ mol/L (expected 0–21 μ mol/L), alanine transaminase (ALT) 87 IU/L (4–45 IU/L), alkaline phosphatase (ALP) 266 IU/L (35–129 IU/L) and γ -glutamyl transferase (GGT) 696 μ U/L (4–60 IU/L). Looking back, her LFTs had been marginally elevated at the time of her pleural effusion drainage: ALT 59 IU/L and ALP 166 IU/L. A comprehensive chronic liver disease screen, including tumour markers, suggested no aetiology of hepatobiliary disease. An abdominal ultrasound, including the intra- and extrahepatic bile ducts, was normal apart from two small gallstones within the gallbladder.

As the cause of the derangement in her LFTs was unclear, the patient underwent liver biopsy. Microscopy found amorphous, pale eosinophilic material entrapping and infiltrating vessels and bile ducts (right of star: [figure 1](#); H&E, original magnification $\times 100$) with thickened small-arteriolar walls (star; [figure 2](#); H&E, original magnification $\times 200$). In both images, ductular reaction is apparent at the portal-tract margin (arrow), with oedema and mixed inflammation. Deposits along the sinusoidal margins within the lobule are lacking. Apple-green birefringence on polarised-light microscopy was faint or ambiguous in Congo red-stained sections. Immunostaining found κ -immunoglobulin, but not λ -immunoglobulin light chains within the deposits. These findings, together with elevated serum ALP

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Figure 1 Amorphous, pale eosinophilic material entraps and infiltrates vessels and, to the right of the star, bile ducts (H&E, original magnification $\times 100$).

and GGT activity, suggested ischaemic cholangiopathy due to κ -light chain deposition disease.

A MR cholangiopancreatogram, obtained to look for evidence of cholangiopathy or cholangitis, was normal, as were serum immunoglobulin values and serum protein electrophoresis.

On referral to the haematology clinic, serum-free immunoglobulin light chains values were abnormal with κ -light chains elevated at 420 mg/L (3.3–19.4 mg/L) and a κ : λ ratio of 40.4 (0.26–1.65). Microscopy of an aspirated specimen of bone marrow found light chain deposits with 10% plasmacytosis. At the National Amyloid Centre, the diagnosis of κ -light chain myeloma was assigned.

Re-evaluation of the pleural biopsy specimen showed material avid for Congo red that on polarised-light microscopy exhibited apple-green birefringence. A serum amyloid P (SAP) scintigram showed a small whole body amyloid load with uptake in the spleen, confirming a diagnosis of AL amyloidosis with pleura, spleen and liver involvement.

TREATMENT

This patient went on to receive cyclophosphamide, bortezomib and dexamethasone chemotherapy for the amyloidosis.

OUTCOME AND FOLLOW-UP

Seven cycles of chemotherapy have now been completed and the patient has responded well with κ -light chains improving to 102 mg/L. LFTs have reduced to near normal: bilirubin

Figure 2 Thickened small-arteriolar walls (star), liver (H&E, original magnification $\times 200$).

21 μ mol/L, ALT 34 IU/L and ALP 232 IU/L. She is awaiting a repeat SAP scan.

Symptomatically, this patient's SOB has improved and, along with continuing to work part time, she is enjoying long walks. The chemotherapy has resulted in an altered sensation in the left side of her forehead, which is improving now the cycle has finished. As her κ -light chain values are stable, she is to be monitored rather than to receive further chemotherapy.

DISCUSSION

Amyloidosis is characterised by extracellular deposition of misfolded proteins. This progressively causes organ damage. The most common type is immunoglobulin AL amyloidosis, previously known as 'primary' amyloid. Ten to fifteen per cent of patients have myeloma at diagnosis. Serum protein electrophoresis is a standard first-line investigation but is normal in approximately 50% of cases.¹ Abnormal serum-free light chain values, however, are found in nearly 100% of cases. Further investigations include a bone marrow biopsy, skeletal survey, SAP scanning and evaluation for cardiac involvement.

Clinical presentation is varied, but 70% of patients at initial presentation have renal involvement, 60% with evidence of cardiomyopathy (a marker of poor prognosis) and 15–20% with peripheral or autonomic neuropathy.¹ Gastrointestinal manifestations include dilation and atony of the oesophagus, which can mimic achalasia; gastroparesis and gastric ulceration; small bowel polyps; and colonic narrowing and pseudo-obstruction.² These can present with a wide range of clinical symptoms that may imitate other disorders, such as inflammatory bowel disease.

Liver involvement is frequent (62–90% of patients), but hepatobiliary disease as the presenting complaint, or of clinical importance, is unusual.² Smooth hepatomegaly and mildly elevated serum ALP values are the most common manifestations, while cholestasis is rare (<5% of patients).³

At liver biopsy in AL, amyloid deposits in the space of Disse are usually demonstrable, with hepatocyte atrophy. On comparison of histopathological findings in the liver between 25 AL and 13 secondary-amyloid specimens, while vascular involvement was present in 68% of AL patients, all also had parenchymal infiltrates.⁴ A review of AL presenting as jaundice found that perisinusoidal deposition predominated, with vascular involvement in 14 of 25 instances.³

In our patient, who was anicteric despite LFTs suggesting cholestasis, light chain deposits involved only portal tracts (principally arterial vessels), an exceptional pattern; the lobule was unremarkable. We know of only one similar patient.⁵ Our report underscores that AL may manifest, albeit rarely, as ischaemic cholangiopathy without parenchymal infiltrative disease.

Learning points

- ▶ Light-chain (AL) amyloidosis can manifest with numerous gastrointestinal symptoms, although hepatobiliary disease as a presenting feature is uncommon.
- ▶ Serum protein electrophoresis is normal in 50% of AL amyloidosis cases.
- ▶ Rarely, histology of the liver in AL amyloidosis demonstrates light chain deposition in the walls of portal tract structures rather than perisinusoidally.

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