Hepatic amyloidosis: a cause of rapidly progressive jaundice

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DESCRIPTION
An 83-year-old man presented with an acute history of weight loss and jaundice. He had a history of type 2 diabetes mellitus and hypertension. He consumed 30 units of alcohol per week.

The patient was cachectic and jaundiced with non-tender hepatomegaly and no evidence of chronic liver disease. There was evidence of hypoalbuninaemia (albumin 25 g/L, reference 34–51 g/L), hyperbilirubinaemia (bilirubin 188 μmol/L, reference <22 μmol/L) and a raised alkaline phosphatase (629 IU/L, reference 35–105 IU/L). Full blood count, coagulation tests and the remaining liver function tests were normal. An estimated Glomerular filtration rate (eGFR) was 71 mL/min/1.73 m². Autoantibodies and immunoglobulins were normal. Hepatitis viral serology was negative. Serum light chain measurements revealed kappa chain concentration of 13.3 (reference 3.3–19.4 mg/L) and lambda chain concentration of 28.5 (reference 5.7–26.6 mg/L) with a ratio of 0.47 (reference 0.26–1.75). A CT abdomen revealed hepatomegaly and ascites. He subsequently had a liver biopsy (figures 1–3). The histology from the liver biopsy demonstrates hepatic amyloid with extensive deposition of extracellular hyaline material (figure 1A,B). Staining with Congo red shows characteristic salmon pink amorphous material (figure 2). Lambda staining shows diffuse positivity confirming AL-type amyloidosis (figure 3). A bone marrow biopsy revealed no evidence of bone marrow plasmacytosis or amyloid deposition.

Three weeks later, liver function deteriorated (bilirubin 349 μmol/L, alkaline phosphatase 1072 IU/L). Additionally, there was progressive kidney injury (eGFR 39 mL/min/1.73 m²) with evidence of microalbuminuria (albumin:creatinine ratio 3.1 mg/mmol) presumed secondary to renal amyloid involvement.

Amyloidosis involves a complex pathway of extracellular protein deposition and poses significant diagnostic and treatment challenges. The most common subtype is primary/amyloid-light chain (AL) amyloidosis due to haematological disorders, commonly clonal plasma cell disorders. Secondary/ Amyloid A (AA) amyloidosis due to chronic inflammation, infection or malignancy has become less common in recent years due to advancement in treatment for these conditions. Transthyretin (ATTR) amyloidosis is now the second most common subtype in the UK and includes wild-type ATTR (previously known as systemic senile amyloidosis) and hereditary ATTR.1

The deposition of protein in the gastrointestinal tract mostly occurs in the small bowel and liver. Hepatic deposition is not an uncommon consequence of amyloidosis, with one autopsy study identifying 70% of patients with primary amyloidosis having liver involvement.2 However clinical manifestations of hepatic amyloidosis are rare. A review of 98 patients with hepatic amyloidosis concluded that weight loss, hepatomegaly and elevated alkaline phosphatase levels should warrant consideration of primary amyloidosis. A hyperbilirubinaemia was a poor prognostic factor with a median survival of 1 month in patients with a level over 34 μmol/L. If considered, systemic amyloidosis can be diagnosed

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Figure 1 Hepatic amyloid deposition.

Figure 2 Hepatic amyloid deposition (Congo red stain).

Figure 3 Hepatic amyloid deposition (lambda stain).
Images in...

Regression of the disease is slow and clinical improvement is often not apparent until 6–12 months after completion of chemotherapy. In view of progressive liver and renal involvement, aggressive treatment for this patient was deemed inappropriate due to a poor prognosis (estimated less than 6 weeks). He received best supportive care and died 3 months after admission.

Learning points

► In systemic amyloidosis, deposition of protein occurs in a variety of tissues, yet it is the degree of organ impairment inflicted by protein deposition that is clinically relevant. Clinical manifestations of hepatic amyloidosis are rare and it is type-dependent.
► Hyperbilirubinaemia is a poor prognostic factor in hepatic amyloidosis.
► Liver biopsy can lead to a definite diagnosis of hepatic amyloidosis. However, it is not a requirement and should be initially discouraged due to risk of bleeding, unless alternative diagnosis is considered. A rectal biopsy or subcutaneous fat biopsy carries a high yield in establishing a diagnosis and should be considered to remove the need for unnecessary organ biopsies.

REFERENCES