Non-Hodgkin's lymphoma causing light-chain (AL) amyloidosis

Introduction

Light chain amyloidosis (previously termed 'primary' and now 'AL' amyloidosis) is the most commonly diagnosed form of amyloid in the UK. The amyloid fibrils are derived from monoclonal immunoglobulin light chains, produced by a plasma cell dyscrasia. Light chain amyloidosis will complicate between 10 and 15% of cases of multiple myeloma. Light chain (AL) amyloidosis may rarely develop in association with other haematological malignancies, including Waldenstrom's macroglobulinaemia, monoclonal gammopathies of unknown significance and lymphoma (Gertz et al, 1993). This article describes a case of non-Hodgkin's lymphoma that resulted in light chain (AL) amyloid deposition and severe renal impairment.

Discussion

This article describes the somewhat unusual association of non-Hodgkin's lymphoma with AL amyloidosis, resulting in severe renal dysfunction. Six similar cases, characterized by visceral amyloid deposits and, in common with this case, no cardiac involvement, have been reported (Cohen et al, 2004). The most frequent association is with lymphoplasmacytic lymphoma, which comprises around 1% of all cases of non-Hodgkin's lymphoma.

A series described 10 patients with multi-organ involvement, of predominantly lymphoplasmacytic lymphoma, with systemic AL amyloid deposition, including cardiac involvement (Telio et al, 2010). On occasions, extensive AL amyloid may be localized to lymph nodes containing lymphoma (Simmonds et al, 1997). The current patient exhibited an IgM gammopathy with a high kappa:lambda light chain ratio, similar to previous reports in AL amyloid associated with non-Hodgkin's lymphoma (Cohen et al, 2004; Simmonds et al, 1997), whereas in AL amyloid complicating plasma cell dyscrasias a lambda light chain bias predominates.

The relationship of non-Hodgkin's lymphoma with amyloidosis is uncommon and the phenotype varied. In addition to light chain amyloid, patients with non-Hodgkin's lymphoma may rarely develop AA (previously termed secondary) amyloidosis (Zhu et al, 2004; Piskin et al, 2008). The mechanism is presumably through serum amyloid A protein being produced in response to the chronic inflammatory stimulus of lymphoma. An unexplained excess of non-Hodgkin's lymphoma has also been described in Swedish

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CASE REPORT

A 64-year-old man presented with an 18-month history of easy bruising and excessive bleeding following a tooth extraction. Examination was unremarkable. Blood tests revealed mild anaemia (haemoglobin 105 g/litre), normal leucocytes, platelet count and clotting. Renal function was normal (creatinine 102 umol/litre). Abdominal ultrasound demonstrated an enlarged spleen (17 cm). Computed tomography of the chest, abdomen and pelvis confirmed splenomegaly, but otherwise normal viscera with small lymph nodes identified in both the mediastinum and both hilar regions of the lungs. Hepatitis B and C, anti-nuclear factor and glomerular basement membrane antibodies were negative.

Serum electrophoresis showed an IgM paraprotein with kappa light-chain restriction and immune paresis. Bone marrow biopsy showed diffuse infiltration with small lymphoid cells amounting to around 80% of the bone marrow and expressing CD20 (*Figure 1*). Plasma cells amounted for 3–4% of the sample, expressing CD138 and showing kappa light-chain restriction. These features were consistent with a low-grade B-cell non-Hodgkin's lymphoma with plasmacytic differentiation, of likely marginal zone type.

Over the following 18 months the patient's renal function deteriorated with a creatinine of 550 umol/litre (normal 60–125 umol/litre), urea 27.8 nmol/litre (normal 2.5–7.8 nmol/litre) and marked proteinuria of 2.1 g/litre. Renal biopsy confirmed AL amyloid (kappa type). An electrocardiogram exhibited normal voltage amplitude and an echocardiogram showed no obvious features of amyloid deposition. Serum amyloid P scintigraphy indicated amyloid deposition, predominantly in the kidneys but also in the liver, spleen and bone marrow.

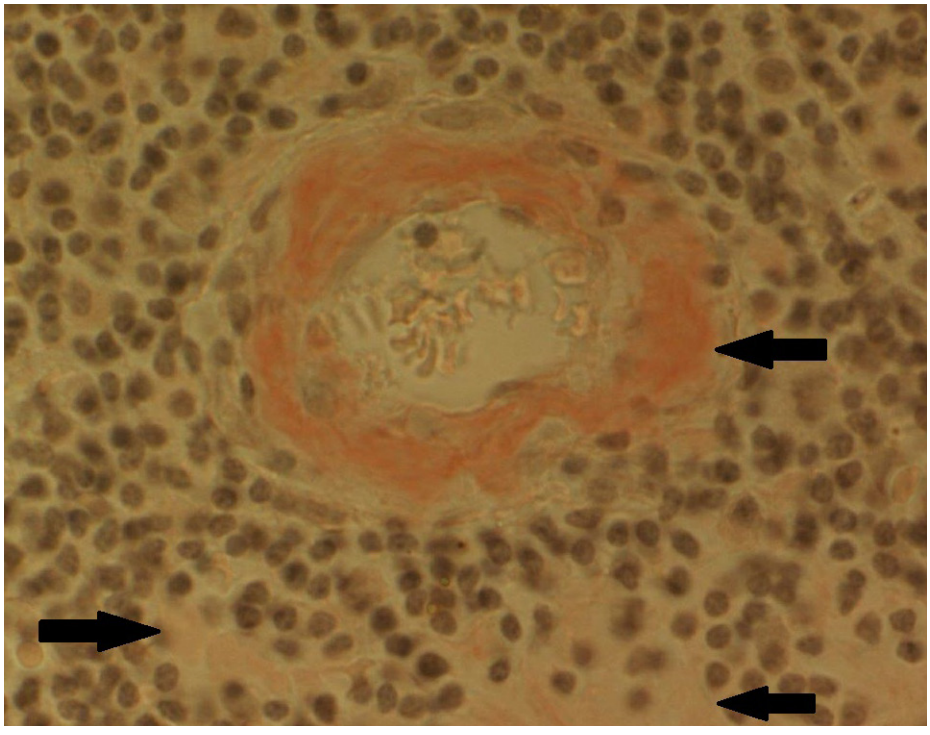
Chemotherapy was started using a combination of rituximab (a monoclonal anti-CD20 antibody active against B-cell malignancies), bortezomib (a proteosome inhibitor to address the supply of amyloid precursor (light chain) proteins) and dexamethasone to give a synergistic therapeutic effect on both the lymphoid and plasma cell lines. In accordance with guidelines on commencing monoclonal antibody therapy (rituximab), the patient was confirmed as being human immunodeficiency virus negative.

The patient responded well with a recent bone marrow trephine showing a scanty background of CD138 plasma cells. There remains abundant amyloid but no significant CD20 lymphocytes or evidence of a residual B-cell lymphoma.

LEARNING POINTS

- Light chain (AL) amyloidosis usually complicates a plasma cell dyscrasia of bone marrow.
- Light chain (AL) amyloidosis is a recognized complication of multiple myeloma.
- Light chain (AL) amyloidosis has occasionally been described in association with non-Hodgkin's lymphoma.

Figure 1. Bone marrow biopsy (x80 magnification) showing diffuse infiltration with small lymphoid cells and abundant amyloid deposition (stained with Congo red) in a perivascular and intercellular distribution (black arrows).



patients with a particular familial form of amyloidosis, caused through deposition of a variant molecule of transthyretin (Hemminki et al, 2013). **BJHM**

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