Cardiac amyloidosis

Dr Jane Cannon
British Society For Heart Failure
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CS, Age 55

- 55 YO Caucasian female
- Height 163cm, weight 61kg, BMI 23
- Psoriatic arthritis (previously on methotrexate)
- Severe obstructive sleep apnoea (2015)
- SH:
  - Never smoked
  - 8-10 units alcohol per week
  - Works for husband’s haulage company
  - Going through marital separation
CS, Age 55

- **FH**
  - No family history of cardiac disease
  - 2 children (31 & 29 years old)

- **Medication**
  - Selenium sulphide shampoo
  - Nocturnal CPAP
  - Off DMARDs for 18 months
CS, Age 55

- **August 2016:**
  - Increasing SOB on exertion & peripheral oedema
  - Reduced exercise tolerance
  - BNP checked by GP = 232
  - Referred via heart failure diagnostic pathway

- SR 90bpm, supine BP 109/77mmHg, standing BP 114/74mmHg
- Clinically euvoalaemic with normal heart sounds
- Subtle macroglossia
Discussion point 1

Use of BNP in primary care
<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
<th>Reference Range</th>
<th>Notes</th>
</tr>
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<tbody>
<tr>
<td>Na</td>
<td>141</td>
<td>135-145</td>
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</tr>
<tr>
<td>ALT</td>
<td>60 (&lt;50U/L)</td>
<td>40-50</td>
<td></td>
</tr>
<tr>
<td>Tsat</td>
<td>22%</td>
<td>20-25</td>
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<tr>
<td>IgG</td>
<td>4.2</td>
<td>6.0-16.0</td>
<td>(6.0-16.0g/L)</td>
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<tr>
<td>K</td>
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<tr>
<td>AST</td>
<td>52 (&lt;40U/L)</td>
<td>30-40</td>
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<tr>
<td>CRP</td>
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<td>0.5-5.0</td>
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<tr>
<td>IGA</td>
<td>0.78</td>
<td>0.8-4.0</td>
<td>(0.8-4.0 G/l)</td>
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<tr>
<td>Urea</td>
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<td>3.0-7.0</td>
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<tr>
<td>Alk Phos</td>
<td>180 (30-130u/L)</td>
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<tr>
<td>ESR</td>
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<tr>
<td>IgM</td>
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<td>(0.4-2.4g/L)</td>
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<td>Creat</td>
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<tr>
<td>Alb</td>
<td>31 (35-50g/L)</td>
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<tr>
<td>Serum Ferritin</td>
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<td>K/L Ratio</td>
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<tr>
<td>Bil</td>
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<tr>
<td>Serum ACE</td>
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<td>Kappa 12.5mg/L</td>
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<td>Kappa</td>
<td>12.5</td>
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<td>Lambda</td>
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<tr>
<td>Adj Ca</td>
<td>2.49 (2.2-2.6mmol/L)</td>
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<td>CK 297 (25-200U/L)</td>
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<tr>
<td>NT-pro BNP</td>
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<tr>
<td>eGFR</td>
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<td>2.49 (2.2-2.6mmol/L)</td>
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<td>297</td>
<td>25-200</td>
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Urinalysis

- Blood +, Protein +++

- Urine protein:creatinine 487 (<30mg/mmol)
- Urine protein 7.69 (<0.2g/L)
- Urine albumin >500 (<20mg/L)
- Urine Creatinine 15.8mmol/L
- Free lambda BJP detected on urine immunofixation
Discussion point 2

CMR appearances consistent with cardiac amyloid?
Progress

- Referred to National Amyloid Centre & local haematology team

- SAP Scintigraphy:
  - No visceral amyloid deposition

- XR Skeletal survey:
  - No evidence of lytic lesions

- 6 minute walk test:
  - 635 metres with no oxygen desaturation
Fat aspirate biopsy:
- Apple green birefringence on congo red studies when viewed under high intensity cross-polarised light
- No immunospecific staining

Conclusion:
- Systemic AL (Lambda) amyloidosis with predominant cardiac involvement and probable renal involvement
Discussion point 3

Patient work-up prior to referral to National Amyloid Centre?
Progress

- Bone marrow trephine biopsy:
  - Small clonal plasma cell population, accounting for 3% of total cellularity
  - Specific stains for amyloid in BM negative
  - No evidence of co-existent myeloma

- Commenced on velcade, cyclophosphamide and dexamethasone

- Supportive treatment with acyclovir, omeprazole and co-trimoxazole

- Doxycycline as cardiac involvement

- Fluid restriction/ diuretic therapy
Progress

- Minor amyloid related peripheral neuropathy
- Mild clinical decompensation of HF with initiation of treatment
- Complete clonal response with first 3 cycles of chemotherapy
- Protein: Creatinine ratio falling with treatment
- Treatment finished May 2017 (5 cycles)
- BNP 114
**Outcome**

- Marked clinical improvement
- Ramipril 1.25mg BD, Bumetanide 1mg daily (Acyclovir 400mg BD & Co-Ttrimoxazole for further 2 months)
- Serum free light chains normal
- Mild LVSD with calculated EF 50%
- Follow up with HFLS with a view to D/C
Discussion point 4

Importance of MDT approach in patient management
AL (Light chain) Amyloidosis

- Multisystem disease which can lead to delay in diagnosis
- Most common type of amyloidosis with 500-600 new cases/yr in UK
- Cardiac involvement is leading cause of morbidity and mortality in primary light chain amyloidosis
- Light chain aggregation results in restrictive cardiomyopathy
- Chemotherapy aimed at suppressing underlying plasma cell clone
- Serial measurements of free light chains to assess response
- Reference treatment includes alkylating agent plus dexamethasone
Red flags signs/symptoms

- Nephrotic syndrome
- Autonomic neuropathy (Postural hypotension)
- Soft tissue infiltration (Macroglossia, carpal tunnel syndrome)
- Bleeding (Cutaneous e.g. Periorbital)
- Malnutrition/Cachexia
- Syncope (Poor prognostic sign)
- Multisystem disease
AL (Light chain) Amyloidosis

- Usual treatment for HF ineffective
- Diuretic is mainstay of therapy
- Prognosis depends on spectrum of organ involvement
- Cardiac involvement confers poorer prognosis
- Early diagnosis is critical
- MDT approach essential
Thank you