Test Your Knowledge: Dysproteinemic Kidney Diseases

A recent Core Curriculum by Hogan et al published in AJKD reviews the pathogenesis, diagnosis, and treatment of dysproteinemic kidney diseases. Test your knowledge on this topic with the quiz below.

1. A 73-year-old female with a past medical history of IDDM T2, hypertension, and hyperlipidemia presented to the hospital with 1 month of neck and shoulder pain with associated paresthesia and weakness in the fingertips. The pain radiates down both arms. There is no history of recent fall or trauma. Current medications include: lantus 20 units QD, lisinopril 20 mg QD, and atorvastatin 40mg QD. She was also taking ibuprofen 600 mg 3-4 times daily for 3 weeks for the pain with no significant relief. Initial laboratory tests show a serum creatinine 1.48 mg/dL, calcium 14.1 mg/dL, and elevated protein gap of 6.2. The remainder of her chemistry panel is normal. In the ED, CT of the cervical spine disclosed a pathologic C7 fracture. In this setting of renal insufficiency, hypercalcemia, elevated protein gap and pathologic fracture, which combination of screening tests for plasma cell dyscrasias is most sensitive?
   A. UPEP and SPEP
   B. SPEP, Serum IFE, and Serum FLC assay
   C. UPEP, SPEP, and Serum IFE
   D. UPEP, SPEP, and Serum FLC Assay

2. The following screening tests were done. Serum IFE revealed a monoclonal IgG kappa protein, and serum FLC assay measured the kappa at 16.8, lambda at 1.56, and a kappa/lambda ratio of 10.77. Multiple IV boluses of normal saline were given and the serum calcium normalized. However, the serum Cr continued to worsen despite the improvement in calcium, and progressed to 2.5 mg/dL. The patient underwent anterior cervical corpectomy of C7 with arthrodesis fusion with structural allograft from iliac crest for C6-T1. Specimens were sent to pathology from the bone fragment which revealed plasmacytoma. If a kidney biopsy was to be performed in this patient what would be the most common expected finding?
   A. Hypereosinophilic PAS negative fractured casts within the tubules
   B. Nodular mesangial sclerosis and tubular basement membrane thickening
   C. Endocapillary and membranoproliferative glomerulonephritis with granular staining for IgG heavy chain
   D. Noncongophillic, polychromatophilic, PAS positive intracapillary deposits
3. Type I cryoglobulinemia is diagnosed by the presence of monoclonal immunoglobulins that precipitate at colder temperatures. The primary disease that is associated with type 1 cryoglobulins are plasma cell dyscrasias such as multiple myeloma, Waldenstrom's macroglobulinemia, and lymphoplasmacytic lymphoma. As these proteins precipitate, they can damage surrounding tissues in the skin, nervous system, and kidney. Where does precipitation primarily occur in cryoglobulinemic kidney disease?

   A. Proximal tubules
   B. Distal tubules
   C. Glomerular capillaries
   D. Bowman’s space

4. Which of the following is associated with improved mortality benefit in patients with AL amyloidosis?

   A. Amyloid deposits within the tubules and vasculature
   B. Reduction of serum FLC to normal
   C. Absence of clonal plasma cells on bone marrow biopsy
   D. < 5% plasma cells on bone marrow biopsy

5. Which of the following findings on electron microscopy best describes the pattern of light chain deposition disease?

   A. Dense intramembranous “sausage-shaped” deposits
   B. Punctate, powdery electron dense deposits
   C. Random nonbranching fibrils
   D. Parallel, hollow microtubules

6. Which of the following dysproteinemic kidney diseases is associated with low-grade proteinuria, metabolic acidosis, hypokalemia, hypophosphatemia, hypouricemia, and normoglycemic glycosuria?

   A. Light chain cast nephropathy
   B. Light chain deposition disease
   C. Light chain proximal tubulopathy
   D. Light chain amyloidosis

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To view this Core Curriculum (FREE), please visit [AJKD.org](http://www.ajkd.org).

**Title:** [Dysproteinemia and the Kidney: Core Curriculum 2019](http://www.ajkd.org)

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Answers to Test Your Knowledge: Dysproteinemic Kidney Diseases

1. B. SPEP, Serum IFE, and Serum FLC assay

SPEP is inexpensive and widely available, with an 88% sensitivity for detecting a monoclonal gammopathy in patients with multiple myeloma. UPEP can increase the detection rate when added to SPEP but has a low sensitivity by itself. Adding serum IFE to SPEP increases sensitivity to 94%, and also identifies the type of monoclonal protein. However, it is not quantitative like the serum FLC, which not only increases the sensitivity to nearly 100% but also quantifies the amount of light chain production. See Table 1 (©NKF) below:

<table>
<thead>
<tr>
<th></th>
<th>Multiple Myeloma</th>
<th>Smoldering Multiple Myeloma</th>
<th>AL Amyloidosis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SPEP</strong></td>
<td>87.6%</td>
<td>94.2%</td>
<td>65.9%</td>
</tr>
<tr>
<td><strong>Serum IFE</strong></td>
<td>94.4%</td>
<td>98.4%</td>
<td>73.6%</td>
</tr>
<tr>
<td><strong>Serum FLC assay</strong></td>
<td>96.8%</td>
<td>81.2%</td>
<td>88.3%</td>
</tr>
<tr>
<td><strong>SPEP and serum FLC</strong></td>
<td>100%</td>
<td>99.5%</td>
<td>94.2%</td>
</tr>
<tr>
<td><strong>SPEP, serum IFE, and serum FLC assay</strong></td>
<td>100%</td>
<td>100%</td>
<td>97.1%</td>
</tr>
</tbody>
</table>

*Note: Based on information in Katzmann et al (Screening panels for detection of monoclonal gammopathies. *Clin Chem.* 2009;55(8):1517-1522).* 

Abbreviations: FLC, free light chain; IFE, immunofixation; SPEP, serum protein electrophoresis.

2. A. Hypereosinophilic PAS negative fractured casts within the tubules

The most common cause for decreased GFR in patients with multiple myeloma is light chain cast nephropathy. Cast nephropathy is the result of monoclonal FLCs binding and precipitating with the Tamm-Horsfall protein in the distal nephron. Typically, patients do not have nephrotic syndrome, as the disease primarily affects the tubules. The remaining choices suggest diseases like amyloid or light chain deposition disease, which tend to cause more glomerular damage and subsequent proteinuria, which this patient does not have. See Panels A-B from Figure 1 (©NKF):
3. C. Glomerular capillaries

Cryoglobulins are mostly found in the glomerular capillaries, which show on microscopy as intracapillary “cryoplugs”. The patients often also exhibit an endocapillary MPGN pattern of injury.

4. B. Reduction of serum FLC to normal

A complete hematologic response to AL amyloid is reduction of the serum FLC to normal, along with negative SPEP, UPEP, serum and urine IFE. A partial response is defined by a decrease in FLC by > 50%. See Box 2 (©NKF) below:

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**Hematologic Response Criteria for AL Amyloidosis**

- **Complete response**
  - Negative SPEP, sIFE, UPEP, uIFE, and normal sFLC ratio
- **Very good partial response**
  - dFLC < 40 mg/L
- **Partial response**
  - Decrease in dFLC by >50% (in patients with baseline dFLC > 50 mg/L)
- **No response**
  - Improvement in paraprotein levels but less than partial response
- **Progression**
  - From complete response: any detectable monoclonal protein or abnormal sFLC ratio (involved light chain must be at least double the normal range)
  - From partial response: 50% increase in serum monoclonal protein to >5 g/dL or 5% increase in urine monoclonal protein to >200 mg/d
  - At any time: sFLC increase of 50% to >100 mg/L


Abbreviations: dFLC, difference in free light chains (involved minus uninvolved light chain in serum); sFLC, serum free light chain; sIFE, serum immunofixation; SPEP, serum protein electrophoresis; uIFE, urine immunofixation; UPEP, urine protein electrophoresis.
5. **B. Punctate, powdery electron dense deposits**

   This is the characteristic finding of light chain deposition disease. On light microscopy, patients will have nodular mesangial sclerosis, and on IF there is linear staining that restricts to the monoclonal protein (typically kappa, in 80% of patients with light chain deposition disease). The presence of random nonbranching fibrils suggests amyloidosis, and parallel, hollow microtubules that are larger in diameter are diagnostic of immunotactoid glomerulopathy. See Figure 2 (©NKF):

6. **C. Light chain proximal tubulopathy**

   LCPT is rare, accounting for just 5% of kidney biopsies in patients with monoclonal gammopathy. The abnormal light chain clone is reabsorbed in the proximal tubule via the megalin/cubulin receptor by clathrin-mediated endocytosis. Once internalized, the light chain can cause damage to the lysosomes, resulting in generalized proximal tubule dysfunction (Fanconi syndrome). These patients manifest with hypokalemia, hypophosphatemia, hypouricemia, normoglycemic glycosuria, and aminoaciduria. Patients without all of these features may have partial Fanconi syndrome.

- Quiz prepared by Angela Pauline Calimag @CalimagPauline (PGY-1, Internal Medicine, UIC/Advocate Christ Medical Center), and Edgar Lerma, AJKDBlog Contributor. Follow him @edgarylernamd.