CASE 3

AN UNUSUAL CASE OF NEPHROTIC SYNDROME

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Case history

• 34 year old gentleman
• Nephrotic range proteinuria 1 year ago
• Treated with steroids and endoxan for a short duration.
• Renal functions been gradually and steadily deteriorating.
• No h/o diabetes mellitus/ hypertension.
• Physical examination revealed moderately built man, uremic with dry skin. BP- 150/90mmHg. USS : Bulky kidneys with preserved CMD ,
• No organomegaly.
Investigations

- Hb – 7gm TC- 9100./cmm
- Urine sugar- Trace, Urine Albumin +++,
- Microscopy: Pus Cells – 8-10/ HPF, RBC0-1/ HPF, Epithelial cells – OCC/ HPF
- S.creatinine – 7.5mg/dl
- 24hr urine volume : 1750mg/dl
- 24hr urine protein : 5040mg
Investigations

- Urine Bence jones protein - Negative
- Serum electrophoresis: Normal electrophoretic pattern with reduced albumin (14-11-.06). No abnormal band
- Bone marrow – No plasmacytosis
- Renal biopsy done
H&Ex100
Congo red x400
• **Special stain**: Nodules are negative for congo red stain, Nonpolarising

• **Immunofluorescence studies**: The glomeruli are negative for IgG, IgA, IgM, C3 and C1q.

• **Immunohistochemistry**

• Nodules in glomeruli showed kappa light chain restriction
**Diagnosis:**
Renal Biopsy: **LIGHT CHAIN DEPOSITION DISEASE**

**FOLLOW UP**

Started of hemodialysis, proteinuria persisted, repeat bone marrow evaluation on 22/1/07 (after 2 months of initial biopsy) showed 42% plasma cells with kappa light chain restriction
Algorithm for evaluation of organized deposits in kidney

CONGO RED STAIN

Positive
- Amyloid

Negative
- Non-amyloid

Immunofluorescence

+ve
- Ig derived
  - Cryoglobulinemia
    - CLL
    - Mixed essential
    - Multiple myeloma
  - Monoclonal gammopathy
    - Benign
    - CLL
    - LCDD
    - Multiple myeloma

-ve
- Non-Ig derived eg DM
  - SLE
  - Immunotactoid glomerulopathy
### Special stains in nodular glomerular lesions

<table>
<thead>
<tr>
<th>LESIONS</th>
<th>PAS</th>
<th>PAS/JONES</th>
<th>MASSON Trichrome</th>
<th>CONGO RED</th>
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<tbody>
<tr>
<td>IMMUNOTACTOID</td>
<td>+++</td>
<td>Neg</td>
<td>Blue</td>
<td>Neg</td>
</tr>
<tr>
<td>DM</td>
<td>+++</td>
<td>Black</td>
<td>Blue</td>
<td>Neg</td>
</tr>
<tr>
<td>LIGHT/HEAVY CHAIN</td>
<td>++</td>
<td>Neg</td>
<td>Blue</td>
<td>Neg</td>
</tr>
<tr>
<td>AMYLOID</td>
<td>Neg</td>
<td>Neg</td>
<td>Blue</td>
<td>++++</td>
</tr>
<tr>
<td>FIBRONECTIN</td>
<td>++</td>
<td>Neg</td>
<td>Red</td>
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</tr>
<tr>
<td>COLLAGEN</td>
<td>Neg</td>
<td>Neg</td>
<td>Blue</td>
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LCDD

- Light chain deposition disease (LCDD) is the deposition of monoclonal, amorphous, noncongophilic light chains in multiple organs that do not exhibit a fibrillar structure when examined ultrastructurally.
LCDD-BIOLOGY OF DISEASE

- Uncommon complication of multiple myeloma / other plasma cell dyscrasias
- Occurs in 5% of cases of myeloma.
- 1/3rd of patients do not fulfill the diagnostic criteria of myeloma at the time of diagnosis.
- Kappa to lambda ratio is approximately 4:1.
- In 1976, Randall et al recognized LCDD as an infiltration of light chains involving multiple organs.
- Renal disease usually dominates
- Deposition found in the heart, liver, lungs, endocrine glands, skin and other organs.
CLINICAL FEATURES

• Mean age – 57 yrs
• M/F ratio of 4:1
• Many patients have heavy proteinurias +/- haematuria.
• Proteinuria is usually non-selective.
• Progressive renal failure
• Prognosis of patients with LCDD is generally poor
• Death - attributed to cardiac disease, heart failure, or infectious complications.
Discussion

Glomerulopathic LCs have been reported to play pivotal roles in the pathogenesis of LC-mediated glomerulopathies. Interaction of these LCs with mesangial cells initiates a receptor-mediated process which then controls downstream events. Based on the type and degree of structurally abnormal LC, processes such as endocytosis, activation of growth factors and cytokines, and mesangial matrix alterations are regulated. Two distinct glomerulopathies have been described with different pathogeneses. However, damage to the glomerulus is a sequel shared by both (AL-amyloidosis and LCDD), which if left uncontrolled eventually results in renal failure.

Upon incubation of mesangial cells with glomerulopathic LCs, c-fos changes its normal cytoplasmic location to a nuclear location. c-fos, through the action of PDGF-β, controls cell proliferation and is also responsible for cell surface changes (ruffling) and rounding-up of mesangial cells. PDGF-β is activated in both conditions (AL-amyloidosis and LCDD). TGF-β is increased in LCDD and decreased in AL-amyloidosis.
Treatment

High-dosage chemotherapy with blood stem cell transplantation (LCDD and overt myeloma)

Conventional chemotherapy including high-dosage dexamethasone (older than 70 yr)

As in AL-amyloidosis, monitoring of LC production should rely on free LC assay, particularly in patients without a blood and urine monoclonal component

Kidney transplantation should not be an option for patients with LCDD unless measures have been taken to reduce LC production

Future pathophysiology-driven therapeutic directions include

1. Blocking of LC binding to mesangial receptors,
2. Use of TGF- antagonists,
3. Inhibitors of LC-induced signaling pathways.

References


5. Hepstinstall’s Pathology of kidney 6th ed (lippincot-Raven)