F29 Nigerian

Developed proteinuria during 1\textsuperscript{st} trimester of pregnancy, nephrotic range (peak uPCR just under 400mg/mmol)

Increasing creatinine during pregnancy from about 130 umol/L to about 200 umol/L

Previous medical history

- Steroid-responsive arthralgias for several years
- Pancreatitis 2010 \textit{cause}
- Stomach ulcer May 2014
- Treatment for malaria on several occasions whilst in Nigeria
- Asthma on inhalers

ANA +

dsDNA +

C3/C4 normal

No skin rash, no fever, no cytopenias, no neurology
Protein:creatinine ratio, urine

Creatinine level, blood

Aza/Pred  Delivery  Biopsy  09/12/2016
A Sample for immunofluorescence – no glomeruli
Immunofluorescence on paraffin-embedded tissue after protease digestion
kappa
lambda
Å Anti-PLA2R: negative
Membranous glomerulonephritis with kappa light chain restriction
Moderate TIF; marked glomerular scarring (26/37 global, 2/37 segmental)

The immunohistochemical restriction for kappa light chains is unusual. Although the patient is young, please exclude a paraprotein. However, this is more likely to represent membranous-like glomerulopathy with masked IgG kappa deposits (C Larsen et al KI 2014), an entity which can be seen in young patients with autoimmune disease such as lupus.
Elevated titre of IgG kappa, but no monoclonality
Serum free light chain ratio kappa: lambda = 1.32 (normal)
Bone marrow biopsy
  Polytypic plasma cells, 4%

Post pregnancy: Rituximab x2 in January with good B cell depletion
Differential diagnosis

- Proliferative glomerulonephritis with monoclonal immunoglobulin deposits (Nasr 2004, Nasr 2009)
- Monoclonal membranous glomerulonephritis (Komatsuda 2008, Guiard 2011)
- Membranous-like glomerulopathy with masked IgG kappa deposits (Larsen 2014)
Membranous-like glomerulopathy with masked IgG kappa deposits

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• 14 cases of ~11,000 (2 years) – 0.13%
• All ethnicities, mainly young females, 65% vague autoimmune phenomena
• Proteinuria
• Hep B, Hep C, HIV negative; no recent infection; ASO negative
• Serum & urine protein electrophoresis negative for paraprotein
• C3, C4 normal
• Histology – membranous pattern with mesangial deposits (12/14) and occasional “humps”
• Conventional IF - C3 only
• IF on paraffin after protease - IgG kappa
  — “Masked IgG kappa”
<table>
<thead>
<tr>
<th>Dx (n)</th>
<th>Clinical</th>
<th>IF frozen</th>
<th>IF paraffin after pronase</th>
</tr>
</thead>
<tbody>
<tr>
<td>PGNMID (19)</td>
<td>Mean age (range)</td>
<td>67.3 (29-84)</td>
<td>IgG kappa or lambda</td>
</tr>
<tr>
<td></td>
<td>&lt;40 (n; %)</td>
<td>2 (11)*</td>
<td>18 (95)</td>
</tr>
<tr>
<td></td>
<td>Autoim (n; %)</td>
<td>1 (5)*</td>
<td>5 (26)</td>
</tr>
<tr>
<td>MonoMG (9)</td>
<td>Endo (n; %)</td>
<td>69.2 (48-87)</td>
<td>IgG κ (n; %)</td>
</tr>
<tr>
<td></td>
<td>Extra (n; %)</td>
<td>0 (0)*</td>
<td>3 (16)</td>
</tr>
<tr>
<td></td>
<td>Subendo (n; %)</td>
<td>8 (62)</td>
<td>0 (0)*</td>
</tr>
<tr>
<td>MGMTID (14)</td>
<td>Pronase required (n; %)</td>
<td>25.7 (15-49)</td>
<td>8 (62)</td>
</tr>
<tr>
<td></td>
<td>13 (93)</td>
<td>0 (0)*</td>
<td>4 (31)</td>
</tr>
<tr>
<td></td>
<td>Subepi (n; %)</td>
<td>1 (5)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

Abbreviations: Autoim, autoimmune disease features; Dx, diagnosis; Endo, endocapillary proliferation; Extra, extracapillary proliferation; IF, immunofluorescence; LM, light microscopy; MGMTID, membranous-like glomerulopathy with masked IgG κ deposits; MonoMG, monoclonal membranous glomerulopathy with staining on routine immunofluorescence; PGNMID, proliferative glomerulonephritis with monoclonal IgG deposits; Subendo, subendothelial; Subepi, subepithelial.

*P<0.001.

Larsen 2014

Our case

????????

IgG kappa

IgG kappa
Association with paraprotein and haematological malignancies

- Monoclonal membranous (Guiard 2011)
  - Paraprotein 3/14
  - CLL in 4/14, MM in 1/14

- MGMID (Larsen 2014)
  - Paraprotein 0/11 tested (of 14)

- PGMID, MPGN pattern
  - Paraprotein – 30%
  - 1/35 (Nasr 2009; MM), 4/12 (Guiard 2011; NHLx3, MMx1)
Probably a form of autoimmune glomerular disease
Differential diagnosis MGMID

- Conventional membranous GN (kappa/lambda not performed)
- C3 GN/post-infectious
Immunofluorescence on paraffin after protease for kappa and lambda light chains

- When no frozen sample available (salvage)
- Light chain tubulopathy
- C3 glomerulopathy in adults
  - (see also Larsen et al. Kidney International (2015) 88, 867–873 – MPGN)
- Consider in cases where IF and EM findings do not match up

Messias et al. Mod Path 2015
Thanks to Prof Liz Lightstone
<table>
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<th><strong>IgG subtypes</strong></th>
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<tr>
<td>PGNMID (Nasr 2009)</td>
<td>Predominantly IgG3 (some IgG1 or IgG2) Mostly kappa</td>
</tr>
<tr>
<td>MonoMG (Guiard 2011)</td>
<td>MPGN predominantly IgG3 (80%), 7/8 kappa Membranous Predominantly IgG1 (64%), kappa or lambda</td>
</tr>
<tr>
<td>MGMID</td>
<td>Authors claim cannot be done on paraffin after pronase</td>
</tr>
<tr>
<td><strong>Our case</strong></td>
<td>????????</td>
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