Disclosure Information

I hereby declare that I have had business or personal interests in the following industrial enterprises since 1 September 2016:

<table>
<thead>
<tr>
<th>Name of the enterprise / Nature of the interest</th>
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<tr>
<td>Enterprise</td>
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<td>Nothing to declare</td>
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Minimal change disease (MCD) related new electron microscopy findings in a patient on Levothyroxine sodium (LT) for hypothyroidism: A case report

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What to cover?

• Minimal change disease (MCD)
• Levothyroxine sodium (LT)
• Our case
  – History
  – Presentation
  – Investigations
  – Histopathology
    • Light microscopy (LM)
    • Immunofluorescence (IF)
    • Electron microscopy (EM)
MCD

- Nephrotic syndrome (common)
- Massive proteinuria and hypoalbuminemia
- No histological (LM/IF) evidence of immune-mediated damage in the glomeruli.
- Oedema and hypercholesterolemia.
- Genetic effect vs immunological disturbance

# Common GN diagnosis by Age

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Children</th>
<th>Adults</th>
<th>65-79 years old</th>
<th>80-91 years old</th>
</tr>
</thead>
<tbody>
<tr>
<td>MCD</td>
<td>58%</td>
<td>26%</td>
<td>20%</td>
<td>46%</td>
</tr>
<tr>
<td>FSGS</td>
<td>36%</td>
<td>39%</td>
<td>39%</td>
<td>36%</td>
</tr>
<tr>
<td>Mem. GN</td>
<td>6%</td>
<td>35%</td>
<td>41%</td>
<td>15%</td>
</tr>
</tbody>
</table>

MCD

• The pathogenesis is related to abnormal cytokines
• Affect glomerular permeability and do not promote sclerogenic mechanisms.
• MCD is associated with:
  – drug-induced hypersensitivity reactions,
  – bee stings,
  – Hodgkin’s disease, and other venom exposure, implicating immune dysfunction as an initiating factor.
• MCD respond well to steroids, unlike FSGS.

MCD

- LM (H&E and special stains) – unremarkable
- IF – negative for reactants
- EM – extensive podocyte foot effacement and podocyte microvilli
Levothyroxine sodium (LT)

- LT: synthetic T4 hormone, biologically similar to that secreted naturally by the thyroid gland.
- Absorbed by the small intestine (jejunum and ileum).
- Bioavailability around 70 - 80% in euthyroid individuals.

Levothyroxine sodium (LT)

- Metabolism runs through multiple reactions, main reaction involves deiodination of T4 to form the inactive reverse T3 (rT3) and T3, occur in liver followed by other organs such as kidneys.
- Elimination is primarily by the kidneys followed by the gut.

Levothyroxine sodium (LT)

• Conclusion: since the kidneys play major role in the peripheral metabolism of T4 to T3, metabolism of LT can be affected in patients with renal insufficiency and can lead to accumulation of toxins which would cause further harm.

38F

• PMHx
  – Primary hypothyroidism → LT
  – Learning difficulties since birth
  – Atrial septal defect requiring surgical intervention
  – Adrenal insufficiency and type2 DM secondary to steroids treatment
6/12 Dizziness & nystagmus

Primary Hypothyroidism

Commenced on Levothyroxine sodium

Bilateral leg & sacral oedema concurrent with LT
Urine Dip:
- High Protein (7g)

Blood tests:
- High protein (55)
- Low albumin (24)

¿NS
Further Tests

- Urinary Protein 17g
- P/C ANCA - negative
- US kidneys - Normal
- IgA & IgG – Normal
- IgM – 5.43g/l (↑)
- C3 – 2.03g/l (↑)
- C4 – Normal
- Urine functions – Normal
Histopathology! --- LM

H&E

- 10 glomeruli with moderate mesangial matrix expansion and mild mesangial hypercellularity
- Capillary walls appear unremarkable
- No crescent formation or segmental sclerosis

PAS & Silver stains

- Mild fine fibrillar mesangial accentuation
- Otherwise, normal peripheral profiles
Histopathology! --- LM
Histopathology! --- LM
Histopathology! --- LM

Differential Diagnosis
- MCD
- FSGS
- MPGN pattern
Histopathology! --- Immunofluorescence

renal
medullary
tissue only
Histopathology! --- EM
Histopathology! --- EM
Histopathology! --- EM
Histopathology! --- EM
Histopathology! --- EM
Histopathology! --- EM
Histopathology! --- EM
Histopathology! --- EM
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Histopathology! --- EM

- EM showed protrusion of a mass of filamentous actin in the base of the podocyte epithelial cell cytoplasm into the glomerular basement membrane and mesangial matrix.
- The inclusions are surrounded by a cluster of rounded profiles.
Conclusion

• Diagnosis – MCD with unusual protrusion of a mass of filamentous actin in the base of the podocyte epithelial cell cytoplasm into the glomerular basement membrane and mesangial matrix -- ? Related to Levothyroxine.

• Treated with Steroids with excellent response
Thank You For Listening

ANY QUESTIONS?