Nephrotic syndrome

minimal change disease vs. IgA nephropathy

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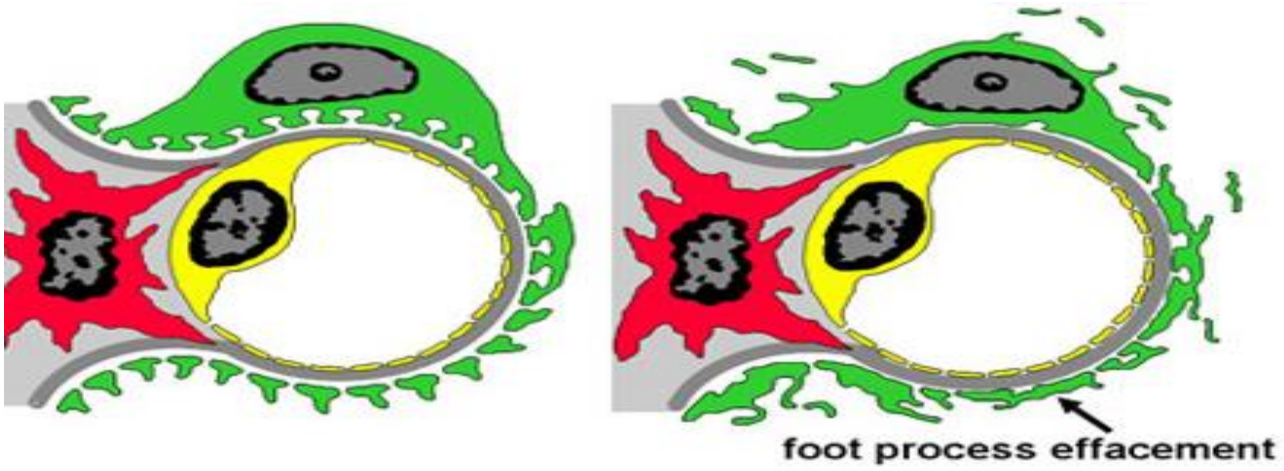


The Case

- 29 year old man diagnosed with nephrotic syndrome 2 weeks ago and complaining now about Lt.flank pain with swelling and the worsening of edema.
- Physical examination positive for anasarca.
- Renal biopsy (performed 2weeks ago) suspect for MCD with the a DD of IgA nephropathy
- Treated with steroids, statins, ACEI, aspirin.

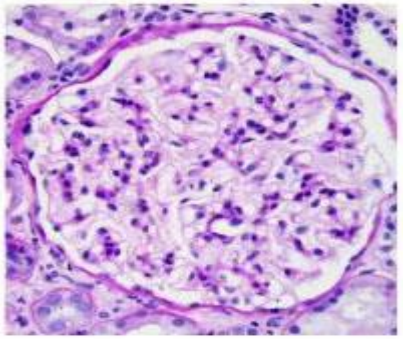
Minimal change disease (Nil lesion)

- 70-90% of nephrotic syndromes in childhood → only 10-15% in adults

- Clinically:
  - Nephrotic syndrome + acellular urinary sediment
  - Less common:
    - Hypertension (30% in children, 50% in adults)
    - Microscopic hematuria (20% in children, 33% in adults)
    - Atopy or allergic symptoms (40% in children, 30% in adults)
    - Decreased renal function (<5% in children, 30% in adults)

    - ARF usually d/t intrarenal edema (nephrosarca).
    - In children- *selective proteinuria*.

Renal biopsy



- ✓LM: no obvious glomerular lesion
- ✓DIF: negative for deposits (occasionally small amounts of IgM in the mesangium)
- ✓EM: effacement of the foot process

- In children - only nonresponders are biopsied

Complete remission

<0.2 mg/24 h of proteinuria - after a single course of prednisone

- Up to 30% of children - spontaneous remission
- But all children today are treated with steroids

- 90- 95% of children after 8 weeks of steroid therapy
- 80–85% of adults, but only after a *longer course of 20–24 weeks.*

Relapse

- ***Steroid dependant***
- ***Frequent relapsaes*** (≥2 relapse in 6m)

- In 70–75% of children after the first remission
- Early relapse → multiple subsequent relapses.
- Less after puberty

- Increased risk following rapid tapering of steroids in all groups.
- In adults relapses are ***less common*** but are ***more resistant*** to subsequent therapy.

Treatment

- ***Prednisone*** is first-line therapy

- Other immunosuppressive drugs (cyclophosphamide, chlorambucil, and mycophenolate mofetil) if
  - frequent relapsers
  - steroid-dependent
  - steroid-resistant patients

- Cyclosporine can induce remission, but relapse is common when cyclosporine is withdrawn

Biologic treatment

- **Tacrolimus [prograf, FK-506]-**(calineurin inh.)
  - after 24w of therapy 82.4% had complete or partial remission (CR rate 64.7%)
  - tacrolimus combined with prednisone showed a rapid effect (5.6w, 8w for PR or CR respectively)
  - Resistance to therapy usually with FSGS
  - 40% relapse in MCD patients
  - Relapse in most patients during tapering or cessation
  - (Chinese population, small size, only one center)

- *Li et al, American journal of kidney diseases, vol 54, July 2009, pp51-58*

Biologic treatment cont.

- **Rituximab [mabtera]-** anti CD20
  - 20 years old patient with severe steroid dependant MCD after treatment with steroids, MMF, cyclosporine, and tacrolimus.
  - After two doses with a 2 week interval , MMF was stopped and within 2w Tacrolimus and prednisone were tapered.
  - 4m after treatment: partial remission (proteinuria 0.9 g/D) with only 7.5 mg/D prednisone without relapse.

    - Hofstra et al, Nephrology Dialysis Transplantation, 22(7), 2007; pp 2100-2102

Biologic treatment cont.

- 40 year-old-female with MCD treated with high dose prednisone, attempts to taper failed and then attempt to reduce steroids with MMF with lack of response.

- Treatment with retuximab + MMF and prednisone→ rapid tapering of prednisone to 5 mg/day over 1m, prolonged and complete response

    - Yang et al, Nephrology Dialysis Transplantation, 23(1), 2008; pp:377-380

Poor prognosis

- Acute renal failure
- Steroid resistance

IgA nephropathy
(Berger's disease)

- Most common glomerulonephritis worldwide
- male preponderance
- Peak incidence: second and third decades
- Rarely - familial clustering
- geographic differences

Diagnosis

Episodic hematuria
with
IgA mesangial deposits
(usually IgA1)

- Mesangial hypercellularity
- IgM, IgG, C3, or immunoglobulin light chains may be codistributed with IgA

- **Renal biopsy is necessary to make the diagnosis**

Clinically

- Two most common presentations are :
  - Recurrent episodes of macroscopic hematuria during or immediately following an mucosal infection
  - Asymptomatic microscopic hematuria (most often seen in adults).
- Between episodes- normal urinalysis
- In children usually benign – in adults slowly progressive
- Nephrotic syndrome in 5% attributable to a concomitant minimal change nephropathy in early stages and mesangial sclerosis and crescentic GN in advanced stages.

Prognosis

- Usually benign disease

  (progression to renal failure in 25–30% over 20–25 years; and 5–30% of patients →complete remission)

- Risk factors for the loss of renal function:
  - hypertension
  - Proteinuria
  - absence of episodes of macroscopic hematuria
  - male age
  - older age of onset
  - more severe changes on renal biopsy

Treatment

- No agreement

- Usually ACE inhibitors in patients with proteinuria or declining renal function
- RPGN → steroids, cytotoxic agents, and plasmapheresis


THE END!