Minimal Change Disease

Jai Radhakrishnan, MD, MS, MRCP, FACC, FASN
Question 1

- A 42 year old WF develops edema and is found on renal biopsy to have MCD. Which would be an unusual clinical finding in this patient at time of biopsy?

1) Urine Micro: 5-10 rbc/HPF
2) Urine Protein 1.5 g / 24 hours
3) BP 150/88 mm Hg
4) Serum creatinine 1.6 mg/dl
## MCD in Adults: Clinical Features at Presentation

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>45 years (19-68)</td>
</tr>
<tr>
<td>Serum Creatinine</td>
<td>1.39 mg/dL (0.5-6.1)</td>
</tr>
<tr>
<td>Serum Albumin</td>
<td>2.21 g/dL (0.6-4.3)</td>
</tr>
<tr>
<td>Serum Cholesterol</td>
<td>421 mg/dL (227-799)</td>
</tr>
<tr>
<td>Urine Protein</td>
<td>9.9 g/d (2.5-26)</td>
</tr>
<tr>
<td>Microscopic Hematuria</td>
<td>29 %</td>
</tr>
<tr>
<td>ARF at presentation</td>
<td>18 %</td>
</tr>
<tr>
<td>Hypertension</td>
<td>43 %</td>
</tr>
</tbody>
</table>

Spontaneous remission in MCD?

- Mean starting dose: 26mg/day
- At 1 year: 11mg/day

Fig. 2.—Group A patients (minimal change). Proportion of patients with proteinuria of more than 1 g./24 hours expressed as a percentage of those alive and in the trial (numbers of patients in trial after two years in parentheses).

Steroid Sensitive NS: from childhood to adulthood

- 102 children with SSNS followed to adults
  43 % at least one relapse as adults
- By multivariate analysis, only number of relapses during childhood was predictive of adulthood relapses ($P < 0.0058$
- 44% with side effects
  - Osteoporosis 63%
  - Weight gain 19%
  - Short stature 16%

By multivariate analysis, only number of relapses during childhood was predictive of adulthood relapses ($P < 0.0058$
Treatment of Minimal Change Disease

- Corticosteroids
- Alkylating agents
- Calcineurin inhibitors
- Mycophenolate
- Mizoribine
- Rituximab
- Levamisole
### Adult Minimal Change Disease
Response to Steroids 125mg qod x 2 months

#### Minimal Change—Population

<table>
<thead>
<tr>
<th></th>
<th>n</th>
<th>Age</th>
<th>Initial Proteinuria</th>
<th>Disease Duration</th>
<th>Follow-up “Blind”</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prednisone</td>
<td>14</td>
<td>29 yr</td>
<td>9.8 g/d</td>
<td>2 mo</td>
<td>60 mo</td>
<td>69 mo</td>
</tr>
<tr>
<td>Control</td>
<td>14</td>
<td>32 yr</td>
<td>9.8 g/d</td>
<td>2 mo</td>
<td>50 mo</td>
<td>85 mo</td>
</tr>
</tbody>
</table>

#### Risk Ratio

<table>
<thead>
<tr>
<th>Prednisone</th>
<th>Placebo</th>
<th>Risk Ratio  M-H,Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>5/14</td>
<td>2/14</td>
<td>2.50 [0.58, 10.80]</td>
</tr>
</tbody>
</table>

Fig 1. The proportion of study patients continuing to have 1 kg or more proteinuria during follow-up. Months of follow-up are indicated on the horizontal axis. C = those who received placebo, T = patients who received prednisone treatment.
Adult Minimal Change Disease
Time to Remission on Steroids

TIME TO REMISSION

Adult MCD – Relapse Free Survival

RELAPSE FREE SURVIVAL

Treatment of Frequent Relapser/Steroid Dependent MCD: Alkylating agents vs. corticosteroids in CHILDREN

Treatment of Frequent Relapser/Steroid Dependent MCD: Alkylating agents vs. corticosteroids in CHILDREN

- Cyclophosphamide
  - Relapse at 6-12 M (RR 0.44, 95% CI 0.26 to 0.73)

- Chlorambucil
  - Relapse at 6-12 M (RR 0.15, 95% CI 0.02 to 0.95)

- Chlorambucil vs. cyclophosphamide 2 Years (RR 1.31, 95% CI 0.80 to 2.13).

- IV vs. oral cyclophosphamide 1 Year (RR 0.99, 95% CI 0.76 to 1.29).

Treatment of Frequent Relapser/Steroid Dependent MCD: Other agents in CHILDREN

- **Cyclosporin vs. cyclophosphamide**
  - (RR 1.07, 95% CI 0.48 to 2.35)

- **Cyclosporine vs. chlorambucil**
  - (RR 0.82, 95% CI 0.44 to 1.53)

- **Levamisole**
  - (RR 0.43, 95% CI 0.27 to 0.68) was more effective than steroids alone but the effects were not sustained once treatment was stopped.

- **Mycophenolate mofetil vs. cyclosporin** (RR 5.00, 95% CI 0.68 to 36.66) but CI were large.

- **Mizoribine** and **azathioprine** were no more effective than placebo or prednisone alone in maintaining remission.

Treatment of Frequent Relapser/Steroid Dependent MCD: Mycophenolate mofetil vs. cyclosporine in CHILDREN

- 12 pts MMF vs. 12 CsA
- 12 months of therapy
- Side effects with CsA
  - GFR drop -14ml/min
  - Hypertrichosis
  - Gingival hyperplasia
- Side effects with MMF
  - Fatigue

Treatment of Frequent Relapser/Steroid Dependent MCD: Mycophenolate mofetil + steroids in CHILDREN

- N = 33  
  6 pts were steroid-dependent
- Pre-Entry Relapses  > 4 per year
- 28-week course of MMF (600mg/m^2) + 16-week tapering course of alternate day prednisone (starting at 1 mg/kg QOD)
- 24 pts stayed in remission during therapy
- Post-Treatment Phase
  - Relapse rate: 1 every 2 M->1 every 14.7 M
  - 8 stayed in remission, 16 relapsed
- Serious adverse events in 2 pts (leucopenia, HZV)

Adult SRNS-MCD:
*Tacrolimus (TAC) vs IV-Cyclophosphamide (IVCP)*

- Prospective case-matched trial in Steroid-Resistant MCD
- **TAC + pred vs. pulse IV-CP x 12 months**
- **Follow-up 23.7 ± 10.7 months**

<table>
<thead>
<tr>
<th></th>
<th>TAC</th>
<th>IVCP</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>11</td>
<td>13</td>
<td></td>
</tr>
<tr>
<td>CR/PR (6mo)</td>
<td>91%</td>
<td>77%</td>
<td>NS</td>
</tr>
<tr>
<td>Time to Rem (d)</td>
<td>32</td>
<td>60</td>
<td>0.031</td>
</tr>
<tr>
<td>Relapse</td>
<td>50%</td>
<td>40%</td>
<td>NS</td>
</tr>
</tbody>
</table>

Li et al, ASN 08, PO-1976
Tacrolimus as a steroid-sparing agent for adults with steroid-dependent minimal change nephrotic syndrome

Xiaoyu Li, Heng Li, Jianghua Chen, Qiang He, Rong Lv, Weiqin Lin, Qun Li, Xuelin He, Lihui Qu and Wang Suya

Intravenous CYC (750 mg/m²)
- TAC 4-8ng/ml
- Prednisone 0.5mg/kg/d

Relapse:
- CYC = 40%
- TAC = 50%

N=26
Rituximab for Severe Steroid- or Cyclosporine-Dependent Nephrotic Syndrome

- N=22, age 14 yrs
- 11 years of NS
- 1-3 immunosuppressive drugs (7 pts CYA toxicity)
- CR: 3/7 nephrotic pts
- 19 pts: ≥ 1 drugs withdrawn
- Relapses in 3 pts - B cells increased
- A.E.: Mild
  - 1 pt with PCP

Guigonis V. Pediatr Nephrol 23:1269–1279
IgM or Clq
IgM Nephropathy

- IF: Mesangial deposits of IgM ± Complement
- Rebiopsy: FSGS in 5/11

- Steroid response:
  - Sensitive 13%
  - Dependent 60%
  - Resistant 27%

C1Q Nephropathy

- Definition:
  - Focal mesangial proliferation +/- sclerosis
  - Mesangial EDD
  - IF prominent C1Q

- 2% Bxs, 2.5 % NS Bxs

- Young AA (5:1), M (2:1)

- Present with proteinuria or NS

- Most steroid dependent or resistant (21/34 w/o response)

- Renal survival 84 % at 3 yrs

Features of C1q Nephropathy

- Dominant or co-dominant C1q IF, mesangial EDD, absence SLE.
- 0.2% of 9000 Bx 1994-02 CUMC
- 74%AA 74%F age 24yo
- Present: NS 50%, Nprot 79%, nl GFR 72%
- 17 FSGS, 2 MCD

12/16 follow immunoRx: 1 complete 6 part remit
2 FSGS ESRD over 7 yrs. Predictors int fibros. + tub atrophy

Clq N MCD/FSGS spectrum, not always bad prognosis.

A 72-year old male has been diagnosed with Minimal Change Disease. Which features of this patient’s clinical history and biopsy findings would increase the likelihood of him developing **acute renal failure** as a complication of his minimal change disease?

1. His age (72)
2. Underlying arteriosclerosis
3. Severe proteinuria (18 grams/day)
4. Hypertension
5. All of the above
## Adult MCD with ARF

<table>
<thead>
<tr>
<th></th>
<th>No ARF S Cr&lt;1.5 mg/dl</th>
<th>ARF S Cr&gt;2.0 mg/dl</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>50</td>
<td>21</td>
</tr>
<tr>
<td>Serum creatinine</td>
<td>1.0 ± 0.2</td>
<td>5.5 ± 3.3*</td>
</tr>
<tr>
<td>Age</td>
<td>40 ± 16</td>
<td>60 ± 16*</td>
</tr>
<tr>
<td>BP</td>
<td>138 /85</td>
<td>158/89</td>
</tr>
<tr>
<td>Serum albumin (g/dl)</td>
<td>2.7 ± 1.0</td>
<td>2.1 ± 0.8**</td>
</tr>
<tr>
<td>Proteinuria (g/24h)</td>
<td>7.9 ± 5.6</td>
<td>13.5 ± 9.4*</td>
</tr>
<tr>
<td>Arteriosclerosis (0-4 scale)</td>
<td>0.7 ± 0.9</td>
<td>1.7 ± 1.4*</td>
</tr>
</tbody>
</table>

All patients recovered