1st Jamaican Paediatric Nephrology Conference

Jamaica Conference Centre
Kingston Jamaica
October 4th 2014
CASE SCENARIO

- A 4 year old boy presents with a 6/7 h/o swelling around his eyes which initially improved during the course of the day.
- He was seen by his doctor who diagnosed him as having allergies and was prescribed antihistamines
- The swelling progressed to involve his entire body
- He had been passing normal volumes of urine with no discoloration
- Abdominal Swelling √ / Pain
- Haematuria
- Sore throat / skin rash / joint pains
- Previous History of Renal Disease
- Family History of Renal Disease
EXAMINATION

- Growth parameters
- Blood pressure / CCF
- Oedema / ascites / effusions
- Anaemia
- Skin – Rash, sepsis
- Infection / peritonitis
INVESTIGATIONS

**BLOOD**

- CBC, Hb, electrophoresis,
- Urea, creatinine, electrolytes,
- Total Proteins, albumin, globulin,
- Cholesterol, Triglycerides,
- C3, ASTO, ANA, VDRL, Hepatitis B surface antigen, HIV, HTLV.

**URINE**

- Dipstick,
- +/- SSA (Sulphosalicylic acid) test,
- Microscopy,
- Culture,
- Spot urine protein: creatinine (mg/mg).
**Nephrotic Syndrome - Definition**

- Oedema
- Hypoalbuminaemia < 25g/l
- Heavy Proteinuria - Nephrotic Range
  - >40mg/m²/hr
  - ≥ 50mg/kg/day
  - Spot Urine Protein/Creatinine > 2 (units mg/mg)
  - Proteinuria ≥ 2+
- +/- Hypercholesterolemia
- +/- Hypertriglycerideridemia
MCNS FEATURES

- **Age** 2-6 years
- **No**-gross haematuria (1%) or PH of nephritis
  - (microscopic haematuria -25%)
- **No**-severe hypertension / CCF
  - (may be transient mild hypertension)
- **No** secondary disease
  - e.g. skin sepsis, auto-immune, Arthritis
- **No** sickle cell disease
- **Normal** renal function tests, Hb, C3
- **Negative** serology
- **Urinalysis** – +/- hyaline casts only
EPIDEMIOLOGY - MCNS

- Incidence (literature) 2-3/100,000

- AGE
  - Peak: 2-6 years

- SEX
  - Male: Female – 2:1

- RACE
  - United Kingdom – \(\uparrow\) Incidence in Asians and Indians

- IDIOPATHIC – 90%
PATHOGENESIS IN MCNS

- T cell function abnormality
  - Susceptibility to Pneumoccocal infection
  - Occurrence in patients with Hodgkins disease

- Allergic Phenomenon
  - High incidence in Atopic Children
  - 34 -60% of NS have Atopy

- Alteration in Basement Membrane Charge
  - Albumin leak due to loss of anionic charge in the glomerular basement membrane

- Urinary albumin loss >> hypoalbuminaemia >>> oedema, intravascular volume depletion
HISTOPATHOLOGY

Normal light microscopy

Effacement of foot processes on EM
NEPHROTIC SYNDROME
TREATMENT - GENERAL
NEPHROTIC SYNDROME – GENERAL TREATMENT MCNS

Admit for first episode

Diet
- Protein – normal (not high) protein
- No added salt diet

Fluids
- Maintenance for weight
- Fluid restriction only
- if nephritic
- in renal failure

Monitor fluid balance
- accurate intake output
  - Catheterize/ weigh diapers
- Daily weights
NEPHROTIC SYNDROME – GENERAL TREATMENT MCNS

- BP measurement q 4hrly
  - Hypertension/hypotension

- Monitor Proteinuria
  - Daily urinalysis
  - SSA
  - Protein: Creatinine ratio
NEPHROTIC SYNDROME – TREATMENT MCNS

- +/- Thiazide
  - Bendrofluazide 0.1-0.2 mg/kg divided od or bd
  - Hydrochlorothiazide 1-2 mg/kg/day od or bd
- Spironolactone 3-5 mg/kg/day (divided t.i.d)
- Avoid Furosemide (unless with colloid)
  - Especially if volume depleted
NEPHROTIC SYNDROME – TREATMENT

MCNS

Indications for colloid and Furosemide

- Anasarca
- Ascites / pleural effusions embarrassing respirations
- Pre renal azotaemia and oliguria
- Abdominal pain suggesting mesenteric ischemia
- Massive oedema in areas likely to become infected or have skin breakdown e.g. scrotum
NEPHROTIC SYNDROME – TREATMENT

MCNS

Colloid and Furosemide

- 25% salt poor Albumin 1g/kg IV over 2-4 hours
  - Furosemide 1mg /kg IV half way through

- Fresh frozen plasma 20cc/kg  IV over 4 hours
  - Furosemide 1mg/kg IV half way through

- Monitor for volume overload during infusion
NEPHROTIC SYNDROME – MONITORING MCNS

► Treat infection
  ▶ Must be treated before initiating steroids
► Monitor for complications
► Patient education
  ▶ Record keeping
  ▶ Early morning urine testing – SSA, Dipstix
  ▶ Treatment plan for relapse – dose
  ▶ Treatment plan for remission – dose
TREATMENT - SPECIFIC
NEPHROTIC SYNDROME - RX MCNS SPECIFIC - PREDNISONE

ONLY children with MCNS presentation have steroids before biopsy!!
NEPHROTIC SYNDROME - TREATMENT

First presentation:

Induction of remission

- Duration of daily steroid Rx crucial in determining future outcome re: subsequent relapse frequency

Maintenance of remission
NEPHROTIC SYNDROME - DEFINITIONS

Remission
► trace / negative proteinuria (clear on SSA)
► 5 consecutive days

Relapse
► proteinuria ≥ 2+ (cloudy urine on SSA)
► For 5 consecutive days
► ≥ 2+ proteinuria with oedema
NEPHROTIC SYNDROME - DEFINITIONS

• Frequent relapses:
  • > 2 relapses within first six months or > 4 within a year

• Steroid dependency:
  • 2 consecutive relapses during corticosteroid treatment or within 14 days after its cessation
NEPHROTIC SYNDROME - DEFINITIONS

➢ Steroid resistance:
  ▶ Failure to remit
    ▶ despite 4 weeks of high dose daily steroid therapy

➢ Other definition
  ▶ despite 8 weeks of high dose steroid therapy
  ▶ Includes 4 weeks daily and 4 weeks alternate days
OUR NEW PROTOCOL
Advantage of longer steroid Rx of initial presentation in reducing relapse rate

- Prednisone / Prednisolone
- 60mg/m2 or 2 mg/kg/day (max 80mg)
- Single or divided doses

- Daily for six weeks (vs. 4 weeks in initial protocol)
OUR NEW PROTOCOL
FIRST PRESENTATION - MAINTENANCE

- Prednisone / Prednisolone

- 40mg/m2 or 2 mg/kg (max 80mg)

- Single alternate day dose for six weeks (vs. 4 weeks)

- Then taper slowly over the next 2-5 months
  (usually 3 months)
# FIRST PRESENTATION

<table>
<thead>
<tr>
<th></th>
<th>KDIGO 2012</th>
<th>OLD JA PROTOCOL</th>
<th>NEW JA PROTOCOL</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>INDUCTION PREDNISONE</strong></td>
<td>60mg/m2/day 2mg/kg/day</td>
<td>60mg/m2/day 2mg/kg/day</td>
<td>60mg/m2/day 2mg/kg/day</td>
</tr>
<tr>
<td></td>
<td>4-6 weeks</td>
<td>4 weeks</td>
<td>6 weeks</td>
</tr>
<tr>
<td><strong>MAINTENANCE</strong></td>
<td>40mg/m2 1.5mg/kg alt day</td>
<td>40mg/m2 2mg/kg alt day</td>
<td>40mg/m2 2mg/kg alt day</td>
</tr>
<tr>
<td></td>
<td>Tapering each week over 2-5 mo</td>
<td>4 weeks Then taper Over 2-5 mo</td>
<td>6 Weeks Then taper Over 2-5 mo</td>
</tr>
</tbody>
</table>
OUR NEW PROTOCOL RELAPSES - INDUCTION

Prednisone / Prednisolone

- 2mg/kg/day (or 60mg/m²/day) - max 80mg
- od or divided bd or t.i.d
- Until Remission
  - (urine trace or negative for protein for
  - 5 consecutive days)
OUR NEW PROTOCOL
RELAPSES – MAINTENANCE

Prednisone / Prednisolone

- 2mg/kg/day (OR 40mg/m²/day) - max 80mg
- Single alternate day dose
- For six (6) weeks
- Then taper and discontinue over 2-5 months
OUR NEW PROTOCOL
FR/ SS/ SD NEPHROTIC SYNDROME

► Slower taper > 3 - 5 months

► If not steroid toxic maintain on the lowest dose of daily or alternate day steroids that can maintain remission

► Consider addition of steroid sparing drugs

► REFER To Paediatric Nephrologist
<table>
<thead>
<tr>
<th></th>
<th>KDIGO 2012</th>
<th>OLD JA PROTOCOL</th>
<th>NEW JA PROTOCOL</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Induction</strong></td>
<td>60mg/m2/day 2mg/kg/day</td>
<td>60mg/m2/day 2mg/kg/day</td>
<td>60mg/m2/day 2mg/kg/day</td>
</tr>
<tr>
<td></td>
<td>Till remission</td>
<td>Till remission</td>
<td>Till remission</td>
</tr>
<tr>
<td><strong>Maintenance</strong></td>
<td>40mg/m2 1.5mg/kg alt day</td>
<td>40mg/m2 2mg/kg alt day</td>
<td>40mg/m2 2mg/kg alt day</td>
</tr>
<tr>
<td></td>
<td>Taper over &gt;3months</td>
<td>4 weeks Then slower Taper &gt; 3 mo</td>
<td>6 weeks Then slower Taper &gt; 3 mo</td>
</tr>
<tr>
<td></td>
<td>Minimum daily or alt day dose</td>
<td>Minimum alt Day dose *</td>
<td>Minimum alt Day dose *</td>
</tr>
<tr>
<td></td>
<td>Daily if infection*</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
NEPHROTIC SYNDROME – STEROID SPARING AGENTS

- Steroid toxicity – SD, FR - SSNS
- Alkylating agents:
  - Cyclophosphamide
  - Chlorambucil
- Levamisole
- Calcineurin inhibitors
  - Cyclosporin**, Tacrolimus
- Mycophenolate mofetil
- Rituximab
COMPLICATIONS
MCNS - COMPLICATIONS

Infection

- Urinary losses: Immunoglobulin, Properdin, Factor B
- Abnormal cell mediated immune function
- Immunosuppressives
- Oedema/Ascites – Potential Culture media
- Spontaneous bacterial peritonitis – S. pneumoniae,
NEPHROTIC SYNDROME COMPLICATIONS

Thromboembolic Events

Thrombosis – arterial / venous

▶ Hypercoagulability
  ▶ ↑ Prothrombotic Factors (Fibrinogen, Throbocytosis, Clotting Factors)
  ▶ ↓ Fibrinolytic Factors (Urinary Losses of Antithrombin III, protein S & C)

▶ Prevention:
  ▶ Close attention to fluid balance
    ▶ Replace extrarenal losses e.g. diarrhoea and vomiting
  ▶ Avoid dehydration especially with
  ▶ Diuretics
  ▶ Remission induced diuresis
  ▶ Encourage Mobilisation
OUTPATIENT MANAGEMENT
NEPHROTIC SYNDROME – MONITORING

- Daily urinalysis
- Dipstix or SSA (Sulphosalicylic acid)
- First morning urine (avoid orthostatic proteinuria)
NEPHROTIC SYNDROME – ADVICE

- No live virus vaccines when
  - on Prednisone and for 3 months after its cessation
  - on alkylating agents

- Pneumococcal vaccine
- Letter to school
- VZIG for varicella infection on steroids
INDICATIONS FOR RENAL BIOPSY - REFER

- Non MCNS presentation – nephritic presentation
- Steroid resistance
- Renal failure
- Positive serology
- Sickle cell disease
- Secondary nephrotic syndrome
- Older child
- Frequent relapser / steroid dependent
POINTS TO REMEMBER

- Refer atypical patients at diagnosis
- Avoiding dehydration helps prevent complications
  - Acute kidney injury
  - Thromboses
- Accurate fluid balance
- Educate and communicate with parents
- Outpatient home urine testing reduces admissions for relapses
THANKS FOR YOUR ATTENTION.