Congenital Nephrotic Syndrome: intro and case

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Objectives:

- Review clinical features of Congenital Nephrotic syndrome
- Describe current nutrition management strategies for CNS
- Present a case study: infant/toddler with CNS
### Types of Nephrotic Syndrome

Heavy proteinuria, hypoalbuminemia, hyperlipidemia and edema…

<table>
<thead>
<tr>
<th>Congenital NS</th>
<th>Idiopathic NS</th>
</tr>
</thead>
<tbody>
<tr>
<td>first 3 months of life</td>
<td>Infantile: 4-12 months</td>
</tr>
<tr>
<td>Genetic cause</td>
<td>Childhood: after 1yr</td>
</tr>
<tr>
<td>Rare</td>
<td>Minimal Change Disease</td>
</tr>
<tr>
<td></td>
<td>FSGS</td>
</tr>
<tr>
<td></td>
<td>Membranous Nephropathy</td>
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</tbody>
</table>
CNS Types:

Most common - **Finnish Type**
- Autosomal recessive inheritance
- Occurs in 1:8000-8200 live births in Finland
  - but reported worldwide
- High incidence in Old Order Mennonites in Lancaster County, PA
- Subgroup of “Groffdale Conference” Mennonites 1:500 incidence

**Finnish Type make up:**
- 98% cases in Finnish population and
- 39-50% in non-Finnish population
CNS Types:

Non genetic causes:
- congenital syphilis
- toxoplasmosis
- viral infection

or

- by genetic defects in the structural proteins that form the glomerular filtration barriers
Structural proteins that form the glomerular filtration barriers

…..implies permeability defects in the glomerular membrane that results in this excessive protein loss.
# Etiology of CNS

## Primary CNS
- Nephrin gene mutations [NPHS1, **Finnish type of CNS** (CNF)]
- Podocin gene mutations (NPHS2)
- WT1 gene mutations (Denys-Drash, isolated CNS)
- LamB2 gene mutations (Pierson syndrome, isolated CNS)
- PLCE1 gene mutation
- LMX1B mutations (nail-patella syndrome)
- LamB3 gene mutation (Herlitz junctional epidermolysis bullosa)
- Mitochondrial myopathies
- CNS with or without brain and other malformations (no gene defect identified as yet)

## Secondary CNS
- Congenital syphilis
- Toxoplasmosis, malaria
- Cytomegalovirus, rubella, hepatitis B, HIV
- Maternal systemic lupus erythematous
- Neonatal autoantibodies against neutral endopeptidase
- Maternal steroid-chlorpheniramine treatment

Since 1998 increasing number of genetic defects have emerged: **NPHS1, PHHS2, WT1, LAMB2 or PLCE1**
Etiology of CNS

Genetic
- Congenital nephrotic syndrome of Finnish type
- Diffuse mesangial sclerosis (DMS)
  - Isolated DMS
  - Part of Denys–Drash syndrome
- Epidermolysis bullosa associated
- Steroid-resistant nephrotic syndrome
- Familial focal segmental glomerulosclerosis (FSGS)

Infectious causes
- Congenital infections including syphilis, toxoplasmosis, and HIV
- Cytomegalovirus
- HIV-associated nephropathy

Idiopathic
- Minimal change nephropathy
- Focal segmental glomerulosclerosis
- Diffuse mesangial hypercellularity
- Membranous glomerulonephritis
- Membranoproliferative GN (MPGN) (NS may predominate or with nephritic syndrome)

Others
- Lupus nephropathy
- IgA nephropathy
- Drugs
- Malignancies
- Hemolytic uremic syndrome (HUS)
Etiology of CNS

Flow diagram shows the variant analysis pathway in patients with congenital nephrotic syndrome. HIV: human immunodeficiency virus; HBV: hepatitis B virus; NEP: neutral endopeptidase; CNS: congenital nephrotic syndrome; AD: autosomal dominant; AR: autosomal recessive.

Clinical Presentation

80% of children premature (35-38 wks) fetal distress is common

Infants may have small nose and low ears

Low birthweight for gestational age / with enlarged placenta
Marked ascites by 3 months

Proteinuria accompanied by severe hypoalbuminemia (<1 g/dL)

Hematuria is uncommon

Edema is present at or shortly after birth, abdominal distention soon after birth,

Severe hypogammaglobulinemia
Clinical Presentation (cont’d)

Nutritional status and growth are poor

Highly susceptible to bacterial infections and thromboembolic complications

Hypothyroidism because of urinary losses of thyroxine-binding proteins is also common

The blood urea nitrogen and creatinine concentrations are initially normal
- Serum creatinine and urea levels are variable
- BP can be low or high depending on level of renal failure

Not immune process, does not respond to immunosuppression
Goals of Management of CNS

- Steroids and other immunosuppressive drugs do NOT bring remission
- Control edema – albumin infusions, ACE inhibitors
- Prevent complications such as infections and thromboses
- Provide *optimal nutrition to support growth and development*
- Kidney transplant often only curative treatment

Medical treatment related to nutrition:
- Albumin infusion 3-4 grams/day
- Anti-proteinuria medication (ie. Ace inhibitors)
- Anticoagulation therapy
## Implications to Losses

<table>
<thead>
<tr>
<th>Loss</th>
<th>Result</th>
<th>Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alb</td>
<td>Edema, protein malnutrition, growth issues</td>
<td>Replace Alb, Provide high energy and protein, Limit fluid and Na</td>
</tr>
<tr>
<td>Apoproteins, Plasma Lipoprotein Lipase</td>
<td>Low Alb, High FFA lead to high TG, high total and LDL chol, low HDL, arteriolar changes in infancy, Increased risk arteriosclerosis</td>
<td>Modify dietary fat into to increase ratio of MUFA:PUFA and PUFA:SFA (1.4)</td>
</tr>
<tr>
<td>Ceruloplasmin (Cu containing)</td>
<td>Cu deficiency</td>
<td>Cu supplement</td>
</tr>
<tr>
<td>Vitamin D binding protein, Vitamin D</td>
<td>Vitamin D deficiency, decrease Calcitriol production</td>
<td>Vit D2 supplements, Calcitriol if PTH increased</td>
</tr>
<tr>
<td>Antithrombin III, Plasminogen, Fibrinogen, Thromboplastin, Factors II, V, VII, VIII, X, XIII</td>
<td>Hypercoagulopathy, Thrombosis</td>
<td>Low dose aspirin + Dipyramidone if evidence of Hypercoagulation or Thrombosis</td>
</tr>
<tr>
<td>IgG, Complement Factors B, D</td>
<td>Reported increased infections</td>
<td>Prophylactic IgG</td>
</tr>
<tr>
<td>Transferrin, Transcobalamin, EPO</td>
<td>Transferrin and Transcobalamin deficiency, Non-responsive anemia</td>
<td>Transferrin replacement with blood transfusions, Increase risk of sensitization</td>
</tr>
</tbody>
</table>
More Specific Nutritional Goals

Control edema
Replace nutritional losses
Manage and correct consequences caused by multiple protein losses

Optimize nutrition and growth, achieve a weight that allows transplant.
Nutrition Rx for CNS

- Limit fluids to 100-130 ml/kg/day
- Protein: 3-4 g/kg/day
- Energy: 130 kcal/kg/day \textit{(increase as needed to promote weight gain)}
- Energy Distribution: \textit{10-14\% protein; 40-50\% fat, 40-50\% CHO’s}
- Vitamins A, D, E
- Renal vitamin \textit{(water soluble)}
- DHA/EPA supplementation due to high TG:
  - 1.25g-2.5g EPA/DHA daily
- Rapeseed oil: 10-15 ml \textit{(rapeseed, sunflower oil)}
- Calcium to DRI
- Follow magnesium and copper (Mg can be low; Cu supplementation?)
- **2 ml fish oil \textit{(to increase the ratio of monounsaturated and polyunsaturated fatty acids in the diet)}

Further Medical Management

- Unilateral nephrectomy:
  - to reduce protein loses and decrease frequency of albumin infusions, postpone transplant to an older age

- Bilateral nephrectomy and start PD:
  - stay at home

- Early pre-emptive transplant
BCCH Clinical Experience
Presentation

CM:
- NPHS1 gene mutation
- Presented 50 days after birth (adm wt 4.3 kg)
- Bilateral lower limb swelling
- Poor feeding (100-150 ml in 24 hrs)
- Loose stools, 1 episode of bloody stool (?CMP allergy)
- Dry weight close to birth weight (3.77 kg)
- TID albumin and lasix
CM:

Labs:
- Hgb 12.4 g/dL (124 g/L)
- Na 130 mEq/L
- K 2.5 mEq/L
- Cl 109 mEq/L
- HCO3 12 mEq/L
- Urea 8.12 mg/dL (2.9 mmol/L)
- Crt 48.5 mg/dL (37 mmol/L)
- Ca 5.32 mg/dL (1.33 mmol/L)
- Phos 5.11 mg/dL (1.65 mmol/L)
- Alb 1.1 g/dL (11 g/L)
Nutrition Therapy and Course

Based on weight of 4.3 kg

- Fluid 110-130 ml/kg/day = 475-560 ml
- Calories 130 kcal/kg/day = 560 kcal
- Protein 4g/kg = 17.2 g/day

- Feeds:
  - Nutramigen® 22 kcal/oz then titrated up to 27 kcal/oz
  - G-tube placed

- Ongoing issues:
  - feed intolerance, bloody stools and frequent vomiting

- Social issues:
  - complicated.....apprehended from parents

- Initial hospitalization 6 months with unilateral nephrectomy @ 5mos.
  released to care of foster mom (ex-pediatric nurse)
Ongoing Nutrition Issues

- Growth
- Persistent vomiting
- **Phosphorus management
Nutrition Therapy and Course cont’d

- Issues with elevated phos …..Nutramigen®
- At ~11 months, after testing - for occult blood “-”,…….. Suplena® added to Nutramigen®
- 32 kcal/oz
- Continued on 3x per week albumin and Lasix
- ++time spent travelling for outpatient appointments
- CKD progressing
Nutrition Therapy and Course cont’d

- Started on Renvela to control phos
- Cu, Zn and Se low on oral supplements - IV infusion of Micro +6™ Pediatric (1ml in 50 ml IV over 3 hours)

- Severe oral aversion – referred to / assessed by swallowing team.
- At ~30 mos. started GH
- At ~32 mos. started peritoneal dialysis
Ongoing Course / Issues

- ESRD
- Peritoneal Dialysis
- Unilateral nephrectomy @ 6 mos
- Urine output 100-150 ml/day with ongoing proteinuria
- Sensory hearing loss
- Hypothyroidism
- Episode of necrotizing myositis
- Episode of pseudomonas peritonitis
- Oral aversion
- Selective mutism
Fast forward.....

.........5 yr old, smart as a whip and entering Kindergarten!!
Current TFI
800 ml/24 hr

Current Nutrition Rx:
- 237 ml Nova Source Renal 2.0
- 33 scoops Nephea Kid powder
- Water to 550 ml

Formula provides: 118 kcal/kg, 3.1 g pro/kg, 0.7 mmol/kg K, 264 mg phos

In addition:
- 60 ml of HBTFrecipe
- 250 ml oral fluid intake
- Takes no solid food by mouth
## Current formula / feed rx

<table>
<thead>
<tr>
<th>Name:</th>
<th>CM</th>
<th>Age:</th>
<th>4-8 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>MRN:</td>
<td></td>
<td>Sex:</td>
<td>Female</td>
</tr>
<tr>
<td>Date:</td>
<td>1-Jan-19</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Formula Order:
- Novasource + Nepheal Kid with water to 550ml Plus 60 ml HBTF

<table>
<thead>
<tr>
<th></th>
<th>kcal</th>
<th>g</th>
<th>g</th>
<th>mL</th>
<th>mmol</th>
<th>mmol</th>
<th>mg</th>
<th>mg</th>
<th>mg</th>
<th>mg</th>
<th>IU</th>
<th>IU</th>
</tr>
</thead>
<tbody>
<tr>
<td>NovaSource® Renal</td>
<td>2.37</td>
<td>474</td>
<td>21.6</td>
<td>24</td>
<td>44</td>
<td>172</td>
<td>9.8</td>
<td>5.8</td>
<td>200</td>
<td>198</td>
<td>46.9</td>
<td>4.3</td>
</tr>
<tr>
<td>Nepheal Kid Powder/g (4.5 g/scoop)</td>
<td>33.0</td>
<td>148.5</td>
<td>725</td>
<td>9.7</td>
<td>36</td>
<td>89</td>
<td>11.9</td>
<td>0.7</td>
<td>223</td>
<td>39</td>
<td>52.0</td>
<td>5.2</td>
</tr>
</tbody>
</table>

### Additional Nutrition

<table>
<thead>
<tr>
<th></th>
<th>Vol</th>
<th>Kcal</th>
<th>g</th>
<th>Fat</th>
<th>Cho</th>
<th>Water</th>
<th>Na</th>
<th>K</th>
<th>Ca</th>
<th>P04</th>
<th>Mg</th>
<th>Mg</th>
<th>mg</th>
<th>mg</th>
<th>IRon</th>
<th>Vit A</th>
<th>Vit D</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBTF Intake</td>
<td>0.60</td>
<td>103</td>
<td>1.9</td>
<td>5</td>
<td>12</td>
<td>24</td>
<td>0.6</td>
<td>1.0</td>
<td>36</td>
<td>27</td>
<td>3.0</td>
<td>0.3</td>
<td>37</td>
<td>8</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Nutritional Intake

- Weight (kg): 10.8
- Total Volume (mL): 610
- Kcal/mL: 2.13
- ml/kg: 56

### Total Intake

- % Kcals: 1302 33 64 145 196 22 8 459 264 102 10 1243 697
- Intake/kg: 121 3.07 6.0 13.4 18 2.1 0.7 42 24 9.4 0.9 115 65

### Recommended Intake: KDOQI

- 1.35 ≤2000 ≤400

### Recommended Intake: DRI/AI

- 1112 0.95 1000 500 1333 600

### Upper Limit

- 2500 3000

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**HBTF Recipe** *(makes 650 ml):

- 6 oz pear (or other low potassium fruit)
- 3 Tbsp oil
- 1.5 Tbsp sugar
- 1 cup cooked pasta
- 1 oz chicken (or other meat)
- 9 scoops Nepheal Kid
- 4 oz veg (low potassium)
- 300 ml Almond milk (not Blue Diamond)
(1/2 scoop Beneprotein if not added to formula)

Water up to 650 ml
Current Meds

Calcitriol
EPO
Iron
Levothyroxine
KCl
Renal vitamin
NaCl
Vitamin D
Growth Hormone ??....
Growth Chart - Height

Height

Weight
At 5 years.......  
- Graduated preschool  
- Started Kindergarten in the fall  
- Currently listed for transplant
Other CNS ..... NPHS1

Height

Weight
Feed Order:
280 ml Homo Milk + 35 scoops Nephea Kid Powder + 100 ml Pedalyte liquid with sterile water UP TO 600 mls.

Formula Instructions:
1. Pour 280 ml Homo Milk into a container.
2. Mix in 35 scoops of Nephea Kid powder.
3. Add 100 ml of Pedalyte.
4. Add sterile water UP TO 600 ml.
5. Stir/shake well.
Other CNS ..... WT1 mutation

Height

Weight
Feed Order:
237 ml Novasource Renal (1 tetra) + 32 scoops (144 g) Nephea Kid powder with water to a total volume of 600 ml.

Formula Instructions:
1. Measure 237 ml (1 tetra) of Novasource Renal into a container
2. Add in 32 scoops Nephea Kid powder (use the scoop in the Nephea Kid can)
3. Add water to 600 ml
4. Stir/shake well
References


