#### Approaches to Nephrotic Syndrome

Chia-shi Wang, MD Emory University School of Medicine Children's Healthcare of Atlanta

### Objectives

- Recognize the presenting symptoms of nephrotic syndrome
- Describe the disease course and complications of nephrotic syndrome
- Describe nephrotic syndrome management strategies



Incidence: 2-7/100,000 children Prevalence: 16/100,000 children One hospitalization → \$26,500 (HCUP-KID)

National inpatient charges in 2 years  $\rightarrow$  \$259 million (HCUP-KID)

FSGS is the common diagnosis among pediatric dialysis patients (NAPRTCS 2014)

**3**<sup>rd</sup> most common diagnosis among pediatric transplant recipients (NAPRTCS 2014)



#### Mechanism of Disease



http://emedicine.medscape.com/article/244631-overview#a3

#### \*alteration in glomerular filtration barrier leads to the loss of protein

# Etiology

#### • Primary/idiopathic

- Minimal change disease
- Focal segmental glomerulosclerosis
- Secondary
  - Infections: HIV, hepatitis C
  - Autoimmune diseases: lupus
- Genetic/Syndromic
  - Finnish-type congenital nephrotic syndrome

#### Childhood Idiopathic Nephrotic Syndrome

• Minimal change disease (MCD)

• Focal segmental glomerulosclerosis (FSGS)



http://library.med.utah.edu/WebPath/jpeg2/RENAL102.jpg



#### Presentation



# • At 23 months-old: 2 weeks of swelling in eyes, scrotum, and legs

- Initially diagnosed with allergies
- In the ED:
  - Diffuse swelling
  - Normal blood pressure, normal Cr
  - 3+ protein on UA, UPCR = 27mg/mg
  - Albumin 1.6, Hgb elevated



http://nephcure.org/connect/patient-stories/pediatricstories/pediatric-stories-h-m/

#### Caleb

- Started on prednisolone at 2mg/kg
- Remission achieved within 2 weeks (steroid-sensitive)
- Likely minimal change disease

#### Caleb

- Relapses within 2 weeks every time prednisolone weaned off
- Remained on prednisolone for 4 years, resulting in hypertension, obesity, and poor growth
- Mycophenolate mofetil started 5/2014. Off steroids 7/2014. No relapses since.

#### Minimal Change Disease

- Approximately 80% of children with nephrotic syndrome
- Peak age: 2-3 years
- Male:Female = 2:1
- Normal BP and creatinine
- Most respond to steroid therapy, good prognosis for long term renal function
- 60% are steroid dependent or frequently relapsing
  - 2<sup>nd</sup>-line therapy required for maintenance and steroid avoidance



#### Jeremy

- Presented at age 4 with swelling
- Responded to steroids but was steroid dependent
- Biopsy showed minimal change disease

#### Jeremy

- Numerous hospitalizations for severe edema
- Bacterial peritonitis at age 6
- Bilateral pulmonary emboli and infarcts, DVTs at age 17

#### Jeremy

- Unable to wean off steroids from age 4 to 17
- Tried on mycophenolate mofetil, IV methylprednisolone, and tacrolimus without disease control
- Tacrolimus resulted in hyperglycemic hyperosmotic syndrome (glucose >900)
- Had decreased pulmonary function and pulmonary hypertension
- Cyclosporine started in 12/2012, weaned off steroids 9/2013, no relapses 12/2012.

### **Complications of Nephrotic Syndrome**

- Infections
  - Cellulitis
  - Bacterial peritonitis
- Blood clots
- Acute kidney injury
- Cardiovascular disease?
  - Chronic hyperlipidemia
  - Steroid toxicity
- Bone health
  - Vitamin D deficiency
  - Steroid toxicity

### **Medical Therapy**

- Steroids
  - Initial course: 2mg/kg/day x 6 weeks, 1.5mg/kg qod x 6 weeks
  - Relapse: 2mg/kg/day until remission, taper over 4 weeks
  - Maintenance: variable dose to sustain remission
- Second-line (corticosteroid-sparing) agents
  - Alkylating agents: cyclophosphamide, chlorambucil
  - Calcineurin inhibitors: tacrolimus, cyclosporine
  - Mycophenolate mofetil
  - Others: rituximab, ACTH

### **Complications of Therapy**

- Steroids
  - Hypertension
  - Poor linear growth
  - Obesity
  - Immunosuppression
  - Adrenal insufficiency
  - Cosmetic changes: cushingoid facies, buffalo hump, straie, acne
- Second-line agents
  - Immunosuppression
  - − Tacrolimus and cyclosporine → renal toxicity



http://emedicine.medscape.com/article/921086-clinical



- Presented at 3 years old with swelling
- Normal blood pressure, fairly mild swelling
- Started on prednisolone



- Swelling quickly worsened despite steroids and low salt diet
- Within 1 month, developed septic shock with multiorgan failure
- Seizures from hypertension



- Repeatedly hospitalized for edema
- Managed with home albumin and lasix infusion
- Developed blood clot from indwelling line
- Reached ESRD in 6 months
- Bilateral nephrectomies at 7 months



- Transplanted Jan. 2015 (age 4)
- Immediate FSGS recurrence
  - Aggressive immunosuppressive agents
  - Plasmapheresis daily > 1 month
  - Now on weekly plasmapheresis
  - HD x 3 weeks



- Medications: IV methylprednisolone, mycophenolate mofetil, tacrolimus, cyclosporin, rituximab
- Albumin/lasix
- Lovenox
- Hemodialysis
- Plasmapheresis
- Nephrectomies
- Transplant



Biopsy Result?

FSGS

#### Focal Segmental Glomerulosclerosis

- Approximately 10% of children with idiopathic nephrotic syndrome
- Only 20% are steroid-sensitive
- Increased risk of hypertension and renal insufficiency
- 50-70% progress to ESRD in 10 years
- Disease recurs in 25% of transplanted patients

#### **FSGS** Recurrence

- Most common kidney disease to recur after transplant
  - Higher rates of ATN
  - Higher rates of delayed graft function
  - 5y graft loss 30-50%
- Circulating factor?
- Management
  - Plasmapheresis: remission rate 60-80%
  - Medications: cyclosporin, cyclophosphamide, rituximab, ACEI/ARB

### **Complications of Nephrotic Syndrome**

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#### **Psychosocial Impact**

#### Psychosocial Impact

- Higher anxiety, depression, and aggression while taking high dose steroids
- Active disease associated with higher measures of anxiety, pain interference, fatigue, and mobility
- Active disease associated poorer social functioning
- Steroid dependence and use of cytotoxic agent associated with poorer QoL and psychosocial adjustment
- Decreased QoL in caregivers of children with nephrotic syndrome

# Caring for Our Children

- Partnership between family and providers
  - Education
    - Chronic condition
    - Drug usage and side effects
    - Relapse and complications
  - Communication
    - Early detection of relapses and complications
  - Support
    - Emotion
    - Social

### Multidisciplinary Team Care

- Nurses
  - Home monitoring education
  - Communication
- Dietician
  - Low sodium diet
  - Low calorie diet
  - Growth monitoring
- Social worker/case manager
  - Insurance, financial hardship
  - Missed school and work
  - Adherence to medical management
- Child Life specialists
- Pharmacists

#### What patients want to tell us:

*"I believe people should pay close attention to nephrotic syndrome because it's missed a lot in children."* 

"Nephrotic syndrome is serious and comes on quick."

"Being in and out of the hospital is no fun and missing school all the time sucks."

"The worst thing is the stress on me and my family. It has led me to depression."

"Use me as an example for the future, so kids won't have to go through what I went through."



### Thank you!

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• Lisa Palm, RN

• Larry Greenbaum, MD, PhD

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