Childhood Nephrotic Syndrome

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Introduction

Let's get started!

What kind of patients are we talking about anyway?

Nephrotic Syndrome Children over the age of 1 year

- Edema
- Urine Protein:Creatinine ratio (uPCR) $>= 2000$mg/g
- Urine Protein > 300mg/dL
- Dipstick Urine protein 3+
- Hypoalbuminemia ($<= 2.5$mg/L)

What is missing from the case definition?

Important resources to know

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- KDIGO - Kidney Disease: Improving Global Outcomes (www.kdigo.org/home/glomerulonephritis-gn)

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- Lower incidence of steroid sensitive nephrotic syndrome in African children
- Increased incidence (all types) in Asians (up to 6 times increase in some studies)

Steroid Sensitive Nephrotic Syndrome

Xiao Ma - The case

Xiao Ma is a 3YO Asian male who presented to his local doc 3 days ago with puffy eyes. The local doc gave cholorpheniramine and sent him home. He comes back today with extension of the swelling to the feet and legs.

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- What is the most important predictor of outcome in Xiao Ma's case?

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- Follow up dose of 1.5mg/kg alternate days and tapered over 2 - 5 months

Why so long?

Hodson, et.al. did some meta-analysis of RCTs using steroid therapy regimens.

Objective	Result	Stats stuff
3 vs. 2 months	30% relapse reduction	RR 0.7 (0.58-.84)
6 vs. 3 months	reduction in 12-24m relapse	RR 0.57 (0.45-0.71)

Relapse Therapy - The Return of Xiao Ma

Poor Xiao Ma got a cold. It has been 5 months since his original episode but now he has three plus protein in his urine by mom's home albustix. She calls the office for advice.

- What are you going to tell her?

Approach to Relapse Therapy in Childhood Nephrotic Syndrome

Relapse uPCR >= 2000mg/g (200mg/mmol)
3+ protein on dipstick for 3 consecutive days

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- After initial therapy give 1.5mg/kg every other day for 4 weeks minimum

On ward!

Frequent Relapse/Steroid Dependent Therapy

Xiao Li

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- What therapy can you offer this family?

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4+ relapses within a 12 month period

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4+ relapses within a 12 month period

Steroid dependence 2 consecutive relapses during corticosteroid therapy or within 14 days of ceasing therapy

Steroid side effects

Figure: Cushing Syndrome

Steroid side effects

- Obesity

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- Hypertension

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- Impaired linear growth

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- Etc. (skin changes, behavior changes . . .)

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- Hematuria at presentation

Approach to therapy - Steroids

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- Daily prednisone at lowest dose possible for SD patients
- Consider daily prednisone during times of URI or other infection in kids with FR or SD disease who are already on alternate day therapy

Approach to therapy - Steroid sparing agents

Corticosteroid sparing agents

1. Alkylating Agents (cyclosporing/chlorambucil)

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2. Calcinurin inhibitors (cyclosporine/tacrolimus)
3. Mycophenolate mofetil
4. Rituximab

Alkylating Agents

Cyclophosphamide (Cytoxan)

- 2mg/kg/day for 8-12 weeks

Chlorambucil

Others: Levamisole, Mizoribine, Azothioprine

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Chlorambucil

- 0.1-0.2mg/kg/day for 8 weeks

Others: Levamisole, Mizoribine, Azothioprine

Calcineurin inhibitors

Cyclosporine

- 4-5mg/kg/d divided bid

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- 0.1mg/kg/d divided bid
- Monitor troughs (5-10ng/mL, 6-12nmol/l)

Calcineurin inhibitors

Cyclosporine side effects

Side Effect	Prevalance
Hypertension	5-10%
Renal dysfunction	5-10%
Tubulointerstitial lesions	30-40% of patients after 12 months
Hypertrichosis	70%
Gum hypertrophy	30%

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Caveats

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- no levels needed

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Mycophenolate mofetil

Hogg, et. al. study

- Prospective study design

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- 24 kids stayed in remission (75%)
- 12 kids relapse free for 6 months post-treatment
- 8 of the 12 relapse free for up to 30 months follow up

Lesser established therapies

Coming attractions: Clinicaltrials.gov

Cyclophosphamide Versus Mycophenolate Mofetil for the Treatment of Steroid-dependent Nephrotic Syndrome in Children (NEPHROMYCY)

This study is ongoing, but not recruiting participants.

Sponsor:
Assistance Publique - Hôpitaux de Paris

Information provided by (Responsible Party):
Assistance Publique - Hôpitaux de Paris

ClinicalTrials.gov Identifier:
NCT01092962

First received: February 26, 2010
Last updated: September 2, 2013
Last verified: August 2013
History of Changes

- Compare efficacy of MMF vs. cyclophosphamide therapies

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History of Changes

- Compare efficacy of MMF vs. cyclophosphamide therapies
- Looking forward to results in September, 2014

Lesser established therapies

Rituximab

- Anti-CD20 monoclonal

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- Some studies with great results (anecdotal data of 80% remission rate)
- Ravani, et.al. showed significant reduction in relapse rate at 3 months a small, open label RCT

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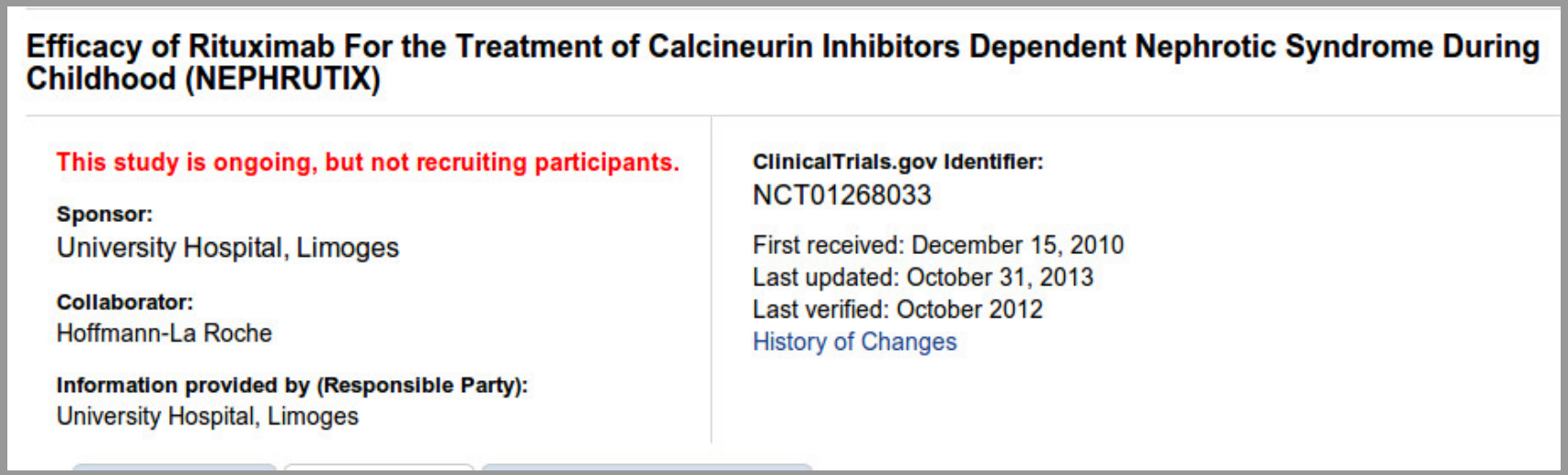

Efficacy of Rituximab For the Treatment of Calcineurin Inhibitors Dependent Nephrotic Syndrome During Childhood (NEPHRUTIX)

This study is ongoing, but not recruiting participants.

Sponsor:
University Hospital, Limoges

Collaborator:
Hoffmann-La Roche

Information provided by (Responsible Party):
University Hospital, Limoges

ClinicalTrials.gov Identifier:
NCT01268033

First received: December 15, 2010
Last updated: October 31, 2013
Last verified: October 2012
History of Changes

- Look at use of rituximab in the CNI "dependent" patients

Renal Biopsy

Renal biopsy can be helpful in evaluating prognosis, do a biopsy for

- late failure to respond to steroids following initial response

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- late failure to respond to steroids following initial response
- high index of suspicion of different underlying pathology
- decreasing renal function in child on CNI therapy

Immunizations

Steroid Resistant Nephrotic Syndrome