ASNIT
onlus

Associazione
Sindrome
Nefrosica

Complicanze all'esordio e a lungo termine della SN idiopatica

III
Congresso
Medici
Famiglie

Villa
Floridiana
29 ottobre
2011

NAPOLI

Giovanni Conti

UO Nefrologia e Reumatologia Pediatrica con Dialisi

Direttore C Fede

AOU Policlinico "G.Martino", Messina

Mario, 4 anni

Esordio di sindrome nefrosica all'età di 3 anni

Sindrome nefrosica cortico-dipendente:
4 recidive in coincidenza della riduzione della terapia steroidea

Terza recidiva a dicembre 2010 complicata da IRA prerenale in concomitanza a gastroenterite

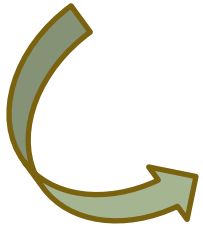
Prednisone 60 mg/mq/die con remissione nelle prime due settimane

Recidiva durante il passaggio del prednisone a gg alterni ad inizio febbraio 2011

Durante l’ultima recidiva (importante ipoalbuminemia con ascite ed edemi periferici) comparsa di dolore inizialmente in sede sacroccigea, successivamente in sede *addominale diffuso, intenso e continuo*

All’E.O. addome uniformemente globoso, notevolmente dolente alla palpazione superficiale e profonda, teso e non trattabile su tutti i quadranti, immobile con respirazione di tipo costale

Evacuazione stimolata (glicerina) nelle 6 ore prima
Da allora alvo chiuso a feci e gas



Quadro di addome acuto

Diagnosi differenziale dell'addome acuto in paziente con recidiva di sindrome nefrosica

- **Trombosi vene renali**
- **Invaginazione intestinale**
- **Peritonite**
- **Colite ischemica**
- **Pneumatosi intestinale**

Procediamo dunque ai vari approfondimenti diagnostici…

Rx addome d'urgenza:

"Si documenta mancata visualizzazione delle anse ileo-coliche, con evidenza di una marcata gastrectasia e di alcune anse digiuno-ileali sede di livelli idroaerei nel contesto"

***Prelievo ematochimico d'urgenza*:**

GB 19.400 mmc, N 87%, L 8%

GR 4.610.000 mmc, Hb 12,9 gr/dl, PLT 555.000 mmc

azotemia 52 mg/dl, creatinina 0,3 mg/dl, proteine totali 3,6 gr/dl

Ca 7,78 mg/dl, Na 132 mmol/l, K 3,6 mmol/l

PCR 1,2 mg/dl (v.n.0,5)

D-dimero 4,34 mg/l (v.n. <0,50)

Nel sospetto di una trombosi della vena renale…

Eco-color-Doppler vasi addominali:
“La vena splenica, la mesenterica superiore ed il tronco portale appaiono pervi. Entrambe le vene renali presentano regolare flussimetria alla valutazione eco color Doppler. Regolare la morfologia dello spettro arterioso dei vasi renali al campionamento delle arterie interlobari”

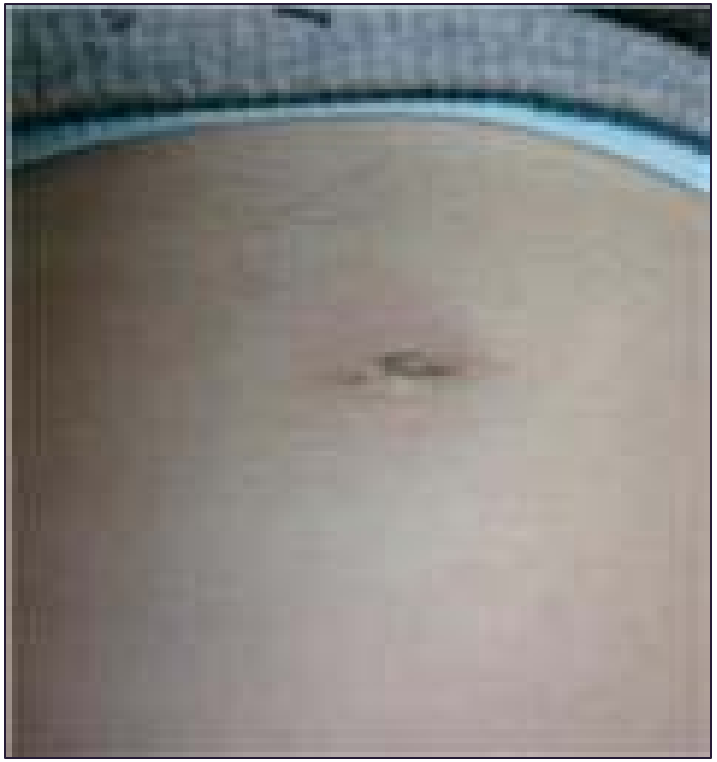
Ecografia addome:
“Presenza di abbondante versamento ascitico sopra e sottomesocolico. Le anse intestinali, disposte in sede centroaddominale, appaiono alquanto distese da aria. In tali condizioni non è possibile valutare eventuali alterazioni di parete o immagini di invaginazione”

Si tratta di invaginazione intestinale o di colite ischemica?

Consulenza chirurgica:
"In atto addome globoso, dolente alla palpazione profonda, con meteorismo diffuso. Riscontro all'Rx di marcata gastrectasia e all'ecografia di distensione intestinale, motivo per cui si pone sondino NG e si consiglia di non alimentare il bambino. Nuova rivalutazione clinica a breve termine"

Alcune ore dopo l'esordio del dolore addominale…

Comparsa di eritema ombelicale



EPICRISI

- Bambino affetto da SN cortico-dipendente, con due recidive ravvicinate (l'ultima ad alto dosaggio steroideo), importante ipoalbuminemia ed ascite

- Quadro clinico di addome acuto
(resistenza addominale, respirazione superficiale e prevalentemente costale, eritema attorno alla cicatrice ombelicale diffuso poi anche in regione sovrapubica)

-Non febbre

- Eritema cicatrice ombelicale progressivamente diffusosi in regione sovrapubica

Esami di laboratorio
Quadro di SN
Leucocitosi neutrofila
D-dimero
PCR lievemente aumentata

Esclusa la trombosi vascolare,
Poco probabile l'invaginazione intestinale

?

I dubbi

L'eritema ombelicale…
Che significato semeiologico esprime?

Kaohsiung J Med Sci. 2007 Feb;23(2):80-3.

Red umbilicus as a clinical manifestation in a 19-month-old girl with typhoid colonic perforation.

Chang YT, Lin JY.

Division of Pediatric Surgery, Department of Surgery, Kaohsiung Medical University Hospital, and Department of Surgery, Faculty of Medicine, College of Medicine, Kaohsiung Medical University, Kaohsiung, Taiwan.

Abstract

Redness of the umbilicus is usually considered to be a reliable sign of underlying gangrenous bowel or peritonitis in tiny infants but seldom among non-neonatal patients. We report a 19-month-old girl with final diagnosis of typhoid colonic perforation who initially presented with abdominal distention and umbilical erythema on arrival at our emergency department. The redness of umbilicus diminished gradually after laparotomy. Thin abdominal wall, severe intra-abdominal soiling, and polymicrobial infection accounted for the inflammatory process spreading to the skin of the umbilicus. Because of its rarity beyond the neonatal period, prompt diagnosis depends on maintaining a high index of suspicion when the abdomen is distended and suddenly tender to palpation.

Ipotesi:... PERITONITE PRIMITIVA SPONTANEA

Terapia antibiotica ev con:
- Metronidazolo (7,5 mg/kg/dose x 3 vv/die)
- Ceftazidime (100 mg/kg/die)

Terapia d'attacco della SN:
- Albumina
- Plasma
- Furosemide
-Calcio gluconato
- *Sospesi momentaneamente i boli di cortisone*

Andamento della PCR
0,10 mg/dl (all'esordio della recidiva di SN)
1,20 mg/dl (all'esordio dei sintomi addominali)
12,9 mg/dl (12 h ore dopo)

Teicoplanina: dose carico 10 mg/kg/ogni 12 ore per le prime 3 somministrazioni, poi 10 mg/kg/die

24 ore dopo: **PCR 21,10** mg/dl

Risoluzione del quadro clinico addominale dopo 48 h dalla comparsa della sintomatologia algica con progressivo miglioramento delle condizioni cliniche generali

Graduale riduzione degli indici di flogosi e della leucocitosi neutrofila:

	06/02	***07/02***	***11/02***	***12/02***
GB (mmc)	23.000	12.200	9.000	7.000
N%	82	78	60	56
L%	12	16	33	25
PCR (mg/dl)	21,1	15,3	0,20	0,10

Canalizzazione intestinale spontanea normalizzatasi solo dopo una settimana

Complicanze nella fase d’esordio o recidiva della sindrome nefrosica

INFEZIONI

TROMBOSI

LE COMPLICANZE INFETTIVE NELLA SN

I soggetti affetti da SN sono più ***suscettibili*** alle infezioni a causa di numerosi meccanismi patogenetici legati alla loro malattia di base:

- riduzione di Ig
- disfunzione di fattori implicati nell'attivazione del complemento (perdita dei fattori B e D del complemento) e della fagocitosi
- alterata funzione di cellule T ed in particolar modo dell'immunità cellulo-mediata
- trattamento immunosoppressivo prolungato

GERMI MAGGIORMENTE RESPONSABILI

- bambini: pneumococco
- adulti: gram negativi

VARIE LOCALIZZAZIONI

- Polmonite
- Osteomielite
- Peritonite
- Cellulite

REV. HOSP. CLÍN. FAC. MED. S. PAULO 59(5):273-278, 2004

ORIGINAL RESEARCH

INFLUENCE OF NEPHROTIC STATE ON THE INFECTIOUS PROFILE IN CHILDHOOD IDIOPATHIC NEPHROTIC SYNDROME

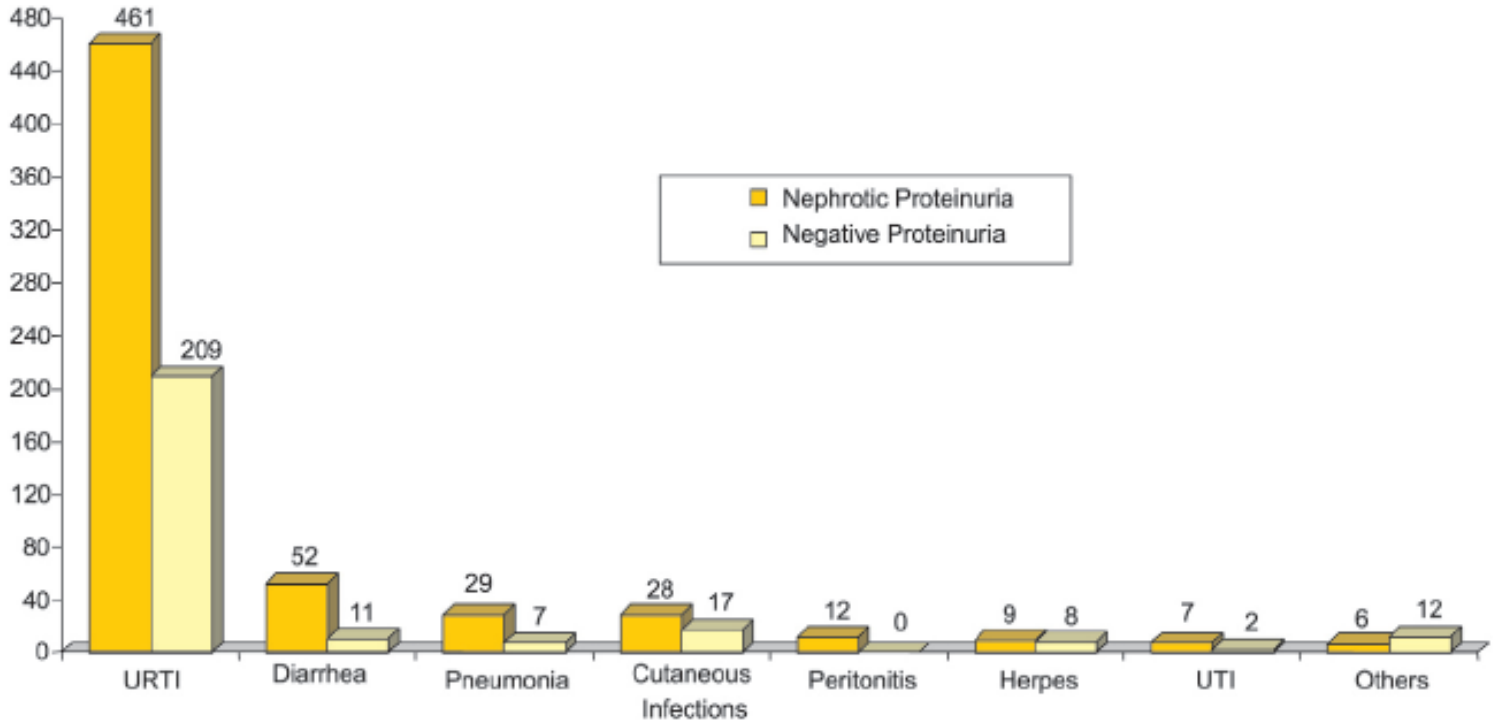


Figure 1 - Number and type of infection of 92 patients during the period with nephrotic proteinuria (604 infections/1140 months) and of the 89 patients during the period with negative proteinuria (266 infections /6822 months).

Table 1 - Characteristics of the 92 patients in relation to type of response to steroid therapy, sex, age, and period of follow-up.

	Subgroups	n	Sex	Age*	Follow-up period* (months)
Steroid-responsive Group I	Single episode IA	10	7 M /3 F	5.8 (3 yr - 12 yr)	113 (53-156)
	Infrequent relapsers IB	5	1 M / 4 F	4.2 (2 yr - 4 yr 10 m)	121 (22-180)
	Frequent relapsers IC	14	11 M / 3 F	3.9 (1 yr - 6 yr 10 m)	107 (27-166)
	Steroid-dependent ID	46	31 M / 15 F	4.9 (1 yr 4 m - 10 yr 11m)	93.1 (16-180)
Steroid-resistant Group II	17	13 M / 4 F	6.5	53.6 (1 yr 11 m - 11 yr 11 m)	(3-158)

n = number of patients; * = data given as mean and range

Table 2 - Comparison of the incidence-density of infections (number of infections/100 patients/month) during the periods with nephrotic proteinuria and with negative proteinuria.

Groups and Subgroups	Nephrotic Proteinuria	Negative Proteinuria	(z score)	(P)
I	55.26	3.81	-8.365	<.001*
IA	15.79	1.36	-1.192	.117
IB	42.86	1.61	-1.806	.035*
IC	53.40	3.44	-3.520	<.001*
ID	57.48	5.09	-6.569	<.001*
II	45.49	4.99	-3.021	.001*

* Statistic significance

Table 3 - Comparison of the number of infections/100 patients/month, during the period with nephrotic proteinuria.

Groups and Subgroups	Number of Infections/100 Patients/Month	(z score)	(P)
I X II	55.26 X 45.49	-0.731	.232
IA X IB	15.79 X 42.86	1.085	.139
IA X IC	15.79 X 53.40	2.134	.016*
IA X ID	15.79 X 57.48	3.056	.001*
IA X II	15.79 X 45.49	1.779	.038*
IB X IC	42.86 X 53.40	0.408	.342
IB X ID	42.86 X 57.48	0.628	.265
IB X II	42.86 X 45.49	0.104	.458
IC X ID	53.40 X 57.48	0.269	.394
IC X II	53.40 X 45.49	-0.440	.330
ID X II	57.48 X 45.49	-0.850	.198

Eur J Pediatr (2010) 169:73–76
DOI 10.1007/s00431-009-0989-x

ORIGINAL PAPER

Primary peritonitis in children with nephrotic syndrome: results of a 5-year multicenter study

Nermin Uncu · Mehmet Bülbül · Nurdan Yıldız · Aytul Noyan · Cemlettin Koşan · Salih Kavukçu · Salim Çalışkan · Zübeyde Gündüz · Nesrin Beşbaş · Ayfer Gür Güven

Pediatr Nephrol (2002) 17:678–682
DOI 10.1007/s00467-002-0890-6

CLINICAL NEPHROLOGY

Sangeeta R. Hingorani · Noel S. Weiss
Sandra L. Watkins

Predictors of peritonitis in children with nephrotic syndrome

Caratteristiche della peritonite nella SN in letteratura

- Spesso la peritonite primitiva avviene nei primi 2 anni della SN
- Sempre in fase di esordio o recidiva
- Più severa è l'ipoalbuminemia e maggiore è il rischio
- Spesso la paracentesi non viene effettuata per la gravità delle condizioni cliniche del bambino, ma anche per un rapporto benefici/rischi sfavorevole (mancata identificazione di germe, sovrainfezioni fungine…)
- Il germe più frequentemente responsabile è lo Streptococco pneumoniae ma sono descritti anche germi gram-negativi

Pediatr Nephrol. 1995 Aug;9(4):411.

How would you treat a 4-year-old boy with nephrotic syndrome in relapse with ascites developed peritonitis and abdominal pain?

Potter DE.

University of California, San Francisco School of Medicine, Department of Pediatrics 94143-0748, USA.

Ask the expert*

A 4-year-old boy with nephrotic syndrome in relapse with ascites developed peritonitis and abdominal pain. Paracentesis of the abdomen revealed turbid fluid with a large number of white cells, but no growth on culture in spite of there being no previous history of administration of antibiotics. What treatment would you advise?

Key words: Nephrotic syndrome – Ascites – Peritonitis – Treatment

A third-generation cephalosporin for 10–14 days. In two large series of children with nephrotic syndrome and documented peritonitis, only 43% [1] and 54% [2] had positive peritoneal fluid cultures, although an additional 18% and 29%, respectively, had positive blood cultures. Of the bacteria cultured, the pneumococcus predominated, 77% and 60% respectively, whereas other streptococcal species accounted for 13% and 5%, respectively, and Gram-negative rods, mostly *Escherichia coli*, accounted for 9% and 35%, respectively. *Haemophilus influenza* has been an uncommon pathogen.

The combination of penicillin and an aminoglycoside has been the recommended therapy for children with nephrotic syndrome and culture-negative peritonitis. A third-generation cephalosporin is effective against virtually all of the organisms implicated in nephrotic syndrome-associated peritonitis, however, and has the advantage of monotherapy. The emergence of penicillin-resistant strains of pneumococci also makes a third-generation cephalosporin an attractive choice, although pneumococcal resistance to cephalosporins as well as penicillin has recently been reported [3].

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San Francisco, CA 94143-0748, USA

References

1. Gorensek MJ, Lebel MH, Nelson JD (1988) Peritonitis in children with nephrotic syndrome. Pediatrics 81: 849–856
2. Krensky AM, Ingelfinger JR, Grupe WE (1982) Peritonitis in childhood nephrotic syndrome. Am J Dis Child 136: 732–736
3. Leggiadro RL (1994) Penicillin- and cephalosporin-resistant *Streptococcus pneumoniae*: an emerging microbial threat. Pediatrics 93: 500–503

Penicillina ed aminoglicoside

Oppure Cefalosporina di terza generazione

E’ possibile prevenerire le infezioni ed in particolar modo la peritonite primitiva in bambini con SN?

Eur J Pediatr (2010) 169:73–76
DOI 10.1007/s00431-009-0989-x

ORIGINAL PAPER

Primary peritonitis in children with nephrotic syndrome: results of a 5-year multicenter study

Nermin Uncu · Mehmet Bülbül · Nurdan Yıldız · Aytul Noyan · Cemlettin Koşan · Salih Kavukçu · Salim Çalışkan · Zübeyde Gündüz · Nesrin Beşbaş · Ayfer Gür Güven

Although chemoprophylaxis with penicillin is shown to reduce the incidence of pneumococcal infections in children with sickle cell disease, there are no controlled trials on the use of penicillin prophylaxis in children with NS [15]. Penicillin prophylaxis has been used sporadically in nephrotic children, and peritonitis was reported in children both with and without penicillin prophylaxis. In our series, none of the peritonitis cases received penicillin prophylaxis.

dependent, steroid-resistant, or frequent relapsers. We suggest that it makes possible sense to administer a polyvalent vaccine to children switching to either steroid-dependent, steroid-resistant, or frequently relapsing forms of NS within 2 years after the beginning of the disease.

Prevention of Pneumococcal Disease Among Infants and Children — Use of 13-Valent Pneumococcal Conjugate Vaccine and 23-Valent Pneumococcal Polysaccharide Vaccine

Recommendations of the Advisory Committee on Immunization Practices (ACIP)

TABLE 2. Underlying medical conditions that are indications for pneumococcal vaccination among children, by risk group

Risk group	Condition
Immunocompetent children	Chronic heart disease*
	Chronic lung disease†
	Diabetes mellitus
	Cerebrospinal fluid leaks
	Cochlear implant
Children with functional or anatomic asplenia	Sickle cell disease and other hemoglobinopathies Congenital or acquired asplenia, or splenic dysfunction
Children with immunocompromising conditions	HIV infection
	Chronic renal failure and nephrotic syndrome
	Diseases associated with treatment with immunosuppressive drugs or radiation therapy, including malignant neoplasms, leukemias, lymphomas and Hodgkin disease; or solid organ transplantation
	Congenital immunodeficiency§

Pediatr Nephrol (2010) 25:1773–1774
DOI 10.1007/s00467-010-1492-3

LETTER TO THE EDITORS

Polysaccharide pneumococcal vaccination of nephrotic children at disease onset–long-term data

Bilal Aoun · Hala Wannous · Christine Azéma · Tim Ulinski

- **La terapia con immunosoppressori non influenza la risposta anticorpale a 12 e 36 mesi**
- **I pazienti con SNFR presentano livelli anticorpali più bassi, ma in maniera non significativa**
- **Nessuna infezione pneumococcica invasiva era osservata**
- **Tendenza all'aumento del titolo anticorpale tra 1 e 36 mesi**

S Afr Med J. 1993 Apr;83(4):253-6.

Abdominal complications in black and Indian children with nephrotic syndrome.

Adhikari M, Coovadia HM.

Department of Paediatrics and Child Health, University of Natal, Durban.

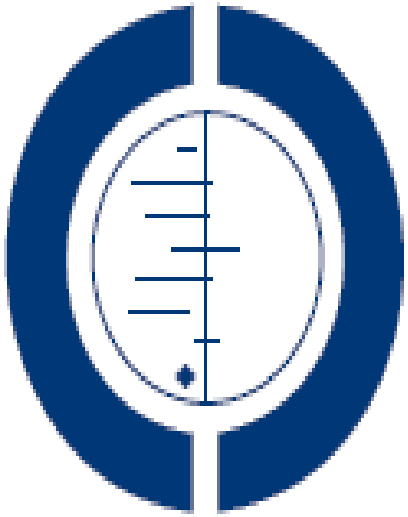
Abstract

Abdominal complications were detected and investigated in 19 (10%) of 191 children with nephrotic syndrome who experienced 35 episodes of these complications. Fourteen children were Indian with steroid-responsive nephrotic syndrome, and 5 were black, of whom 4 had membranous nephropathy and 1 focal proliferative nephritis. All had clinical features of peritonitis and hypovolaemia was frequently present. Eleven of the 35 episodes were culture-proven peritonitis (5 due to Pneumococcus, 6 due to Gram-negative bacteria) and in 24 the cultures were negative. Hypovolaemia occurred in 6 of the former group and 5 of the latter. The occurrence of these episodes bore no temporal relationship to steroid and cyclophosphamide treatment. Sixty-nine per cent of the complications appeared within the first 3 years of onset of the nephrotic syndrome and 8 of 19 patients experienced multiple episodes. In this study, hypovolaemia always occurred in the context of clinically detected peritonitis and not as a separate complication, suggesting infection together with fluid and protein losses as likely pathogenetic mechanisms.

3 pazienti sviluppavano peritonite dopo vaccinazione anti-pneumococcica

PLAIN LANGUAGE SUMMARY

No strong evidence for any interventions for preventing infection in nephrotic syndrome



Trattamenti studiati

- Immunoglobuline e.v.
- timosina
- erba medicinale cinese
- antibiotico profilassi

This is a reprint of a Cochrane review, prepared and maintained by The Cochrane Collaboration and published in *The Cochrane Library* 2009, Issue 2

http://www.thecochranelibrary.com

Complicanze nella fase d’esordio o recidiva della sindrome nefrosica

INFEZIONI

TROMBOSI

Arq Neuropsiquiatr 2003;61(4):1026-1029

CEREBRAL SINOVENOUS THROMBOSIS IN A NEPHROTIC CHILD

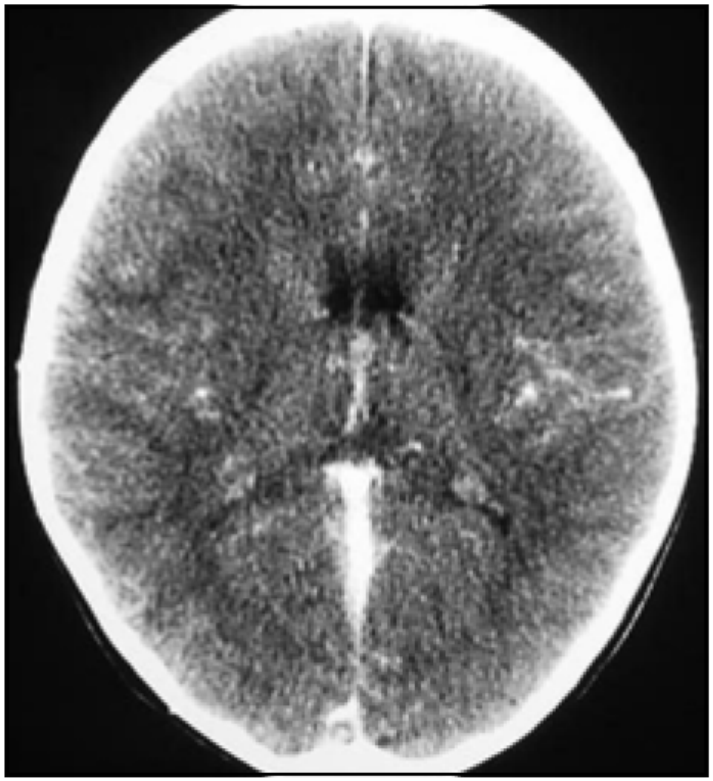


Fig 1 Axial contrast-enhanced cranial CT shows a filling defect in the region of the venous confluence (the empty delta sign) associated with a dilated straight sinus.

Ma diverse possono essere le sedi arteriose e venose

80% venose arti inferiori

20% vena cava inf e renali

Trombosi vena renale: complicanza più frequente

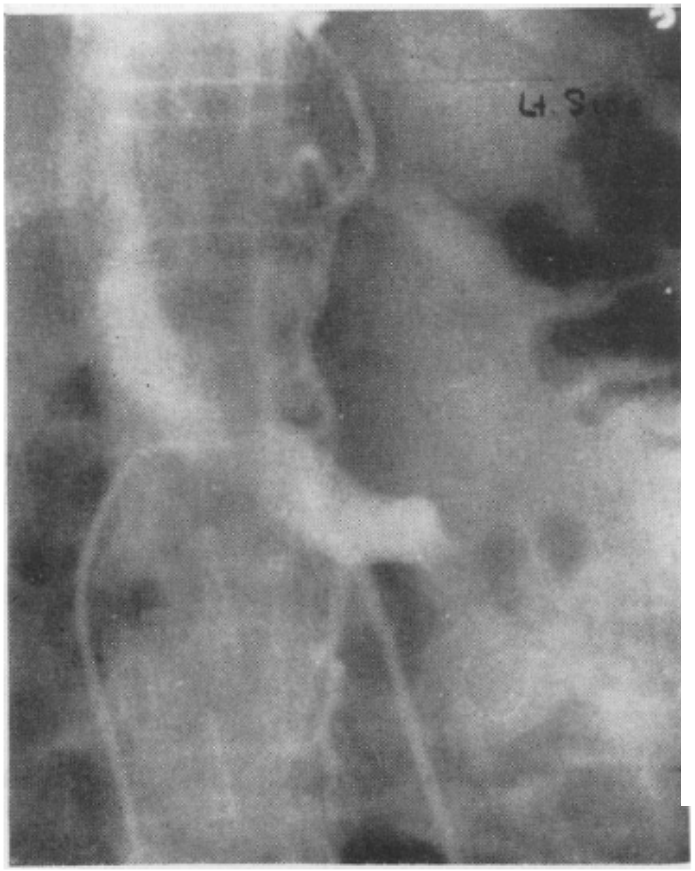


FIG. 1. Contrast study of the left renal vein showing obstruction by a thrombus and extensive collaterals. Catheter tip is seen proximal to the thrombus.

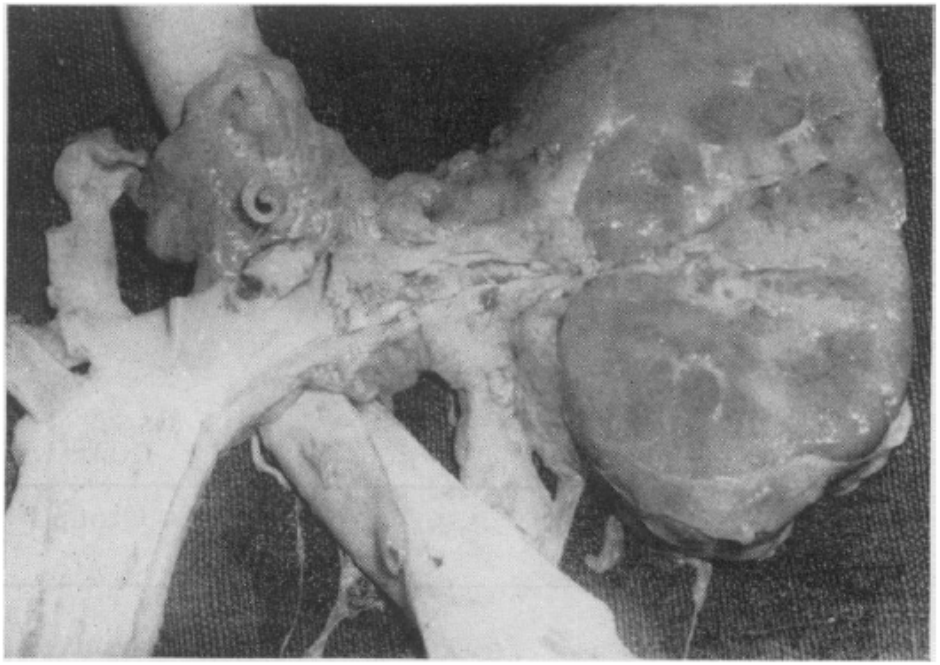


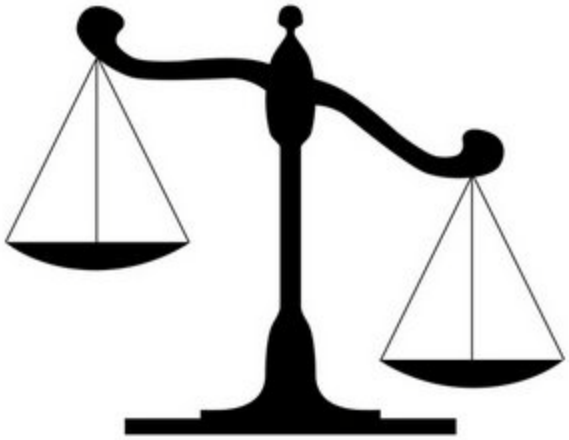
FIG. 2. Photograph showing thrombosed renal vein with collaterals as seen in a post-mortem specimen.

Spesso correlata all'entità della proteinuria;

più frequente nella GN membranosa (40% dei casi)

PATOGENESI DELLE TROMBOSI NELLA SINDROME NEFROSICA

Fattori anticoagulanti



Fattori Pro-trombotici

- Ipercolesterolemia ed ipertrigliceridemia
- Aumento di piastrine e fibrinogeno
- Aumento di fattori della coagulazione (V, VII, VIII, X, XIII)
- Accelerata formazione di tromboplastina
- Plasminogeno ed antitrombina III ridotti
- Aumento di trombossano A2

FATTORI PREDISPONENTI ALLA TROMBOSI IN CORSO DI SINDROME NEFROSICA

- **IPOALBUMINEMIA**
- **IPOVOLEMIA**
- **EVENTUALE ABUSO DI DIURETICI**

Epidemiology and Risk Factors for Thromboembolic Complications of Childhood Nephrotic Syndrome: A Midwest Pediatric Nephrology Consortium (MWPNC) Study

Table I. Patient demographics

Category	Total	Non-TE patients	TE patients
Number of patients	326	296	30
Sex, male, n (%)	168 (52%)	156 (53%)	12 (40%)
Age at NS diagnosis, years, median (range)*	6.5 (0-20.7)	6.2 (0-20.7)	13.8 (1-20.3)
Age ≥ 12 years at NS diagnosis, n (%)†	99 (30%)	80 (27%)	19 (63%)
Age at TE diagnosis, years, median (range)			15.2 (1-21.6)
Race, n (%)			
African-American	68 (21%)	60 (20%)	8 (27%)
Caucasian	224 (69%)	204 (69%)	20 (67%)
Other	34 (10%)	32 (11%)	2 (7%)
NS category, n (%)*			
Primary NS	244 (75%)	228 (77%)	16 (53%)
Secondary NS	82 (25%)	68 (23%)	14 (47%)
Follow-up time, years, median (range)	3.7 (0-20.8)	3.7 (0-20.8)	3.7 (0.3-14)
Peak uPr:Cr, median (range)*	10.0 (2.1-307.7)	9.8 (2.1-307.7)	14.2 (3.9-294.7)
Serum albumin nadir, median (range)	1.9 (0.6-3)	1.9 (0.6-3)	1.8 (1-2.7)
Previous history of TE, n (%)†	5 (2%)	1 (0.3%)	4 (13%)
Membranous histology, n (%)*,‡	32 (10%)	24 (8%)	8 (27%)

9.2%

6.5%

J Thromb Thrombolysis. 2010 Oct;30(3):281-5.

Relationship between proteinuria and venous thromboembolism.

Kato S, Chernyavsky S, Tokita JE, Shimada YJ, Homel P, Rosen H, Winchester JF.

Department of Medicine, Beth Israel Medical Center, University Hospital and Manhattan Campus for the Albert Einstein College of Medicine, First Avenue at 16th Street, New York, NY 10003, USA. shkato@chpnet.org

Abstract

Nephrotic syndrome is known to cause venous thromboembolism (VTE) due to urine loss of antithrombin III and activation of the coagulation system. We hypothesized that the degree of proteinuria may predict the development of VTE. This was a retrospective case-controlled study of in-patients urban academic teaching hospital from April, 2007 to March, 2009 and who had undergone an imaging study for VTE. All radiology reports (N = 1,647) for CT angiography of chest and Doppler sonogram of extremities were reviewed. The following data were collected: race/ethnicity, degree of proteinuria on urinalysis, serum protein and albumin levels, risk factors for VTE and renal function. The study population consisted of 284 patients with VTE and 280 age/sex matched controls. Relative to those who did not have proteinuria, patients who tested positive for protein had a 3.4-fold increased risk of VTE (odds ratio (OR) 3.4, 95% confidence interval [2.4, 5.0]). The association was unchanged when adjusted for other risk factors. Patients with proteinuria may have an increased risk of venous thromboembolism.

CONCLUSIONI:

- I livelli di proteinuria rappresentano il parametro maggiormente correlato al rischio di trombosi
- La terapia si basa sull'uso di alte dosi di eparina da mettere in relazione ai bassi livelli di ATII
- La profilassi con anticoagulanti orali è efficace nella prevenzione di recidive della trombosi

PREVENZIONE DELLA TROMBOSI IN CORSO DI SINDROME NEFROSICA

- **Rapida correzione dell'emoconcentrazione**
- **Mobilizzazione**
- **Acido acetilsalicilico (3-5 mg/kg/die) se:**
  - **Albumina <1 g/dl**
  - **Fibrinogeno > 600 mg/dl**
  - **ATIII < 70%**
  - **Piastrine > 1.000.000/mmc**

Pediatr Nephrol (2005) 20:1818–1820
DOI 10.1007/s00467-005-2050-2

BRIEF REPORT

Koichi Asai · Shin-ichiro Tanaka · Noriko Tanaka ·
Kumi Tsumura · Fumihide Kato · Kiyoshi Kikuchi

Intussusception of the small bowel associated with nephrotic syndrome

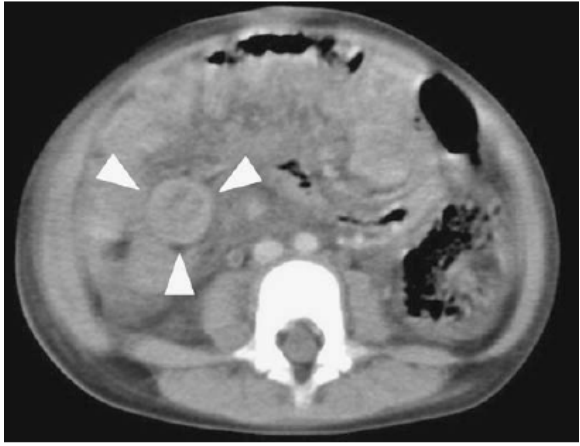


Table 1 Details of the patients with nephrosis-associated intussusception (MCNS minimal change nephrotic syndrome, *NS* nephrotic syndrome)

Patient [reference]	1 [3]	2 [4]	3 [5]		4 [6]	Present case
Age	19 years	6 months	4 years		5 years	2 years
Gender	Male	Female	Female		Male	Male
Nephrotic syndrome						
Episode	1st	1st	1st		2nd	1st
-	Steroid-resistant	Drash syndrome	-		-	-
Renal histopathology	MCNS	diffuse mesanigial sclerosis	MCNS		IgM nephropathy	Not performed
Duration between the onset of recent NS episode and intussusception	35 days	1 day	14 days	18 days	14 days	21 days
Intussusception						
Symptoms						
Abdominal pain	+	+	+	+	+	+
Palpable abdominal mass	-	-	-	-	-	-
Vomiting	-	+	+	-	+	-
Bloody stool	+	+	-	-	+	-
Portion	Ileo-colic	Ileo-colic	Ileo-colic	Jejuno-Ileal	Ileo-colic	Ileo-ileal
Treatment	Not done (autopsy detected)	Laparotomy	Both laparotomy		Laparotomy	Air enema reduction

Da non sottovalutare anche l'ipotesi di una *colite ischemica*, documentata in soggetti che hanno eseguito boli di MPDN

Pediatr Nephrol. 2008 Apr;23(4):655-7. Epub 2007 Nov 24.

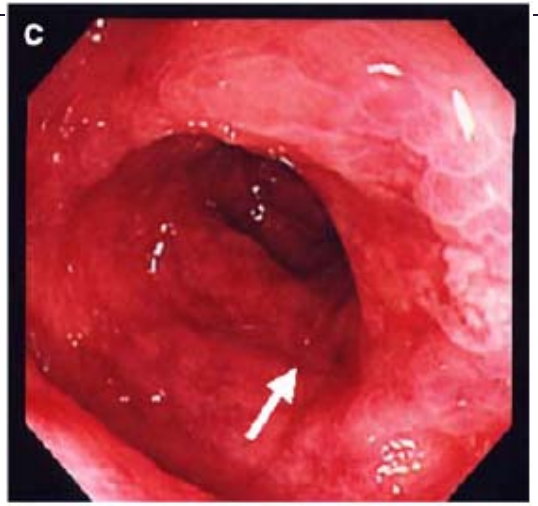
Ischemic colitis as a complication in a patient with steroid-dependent nephrotic syndrome.

Yanagisawa A, Namai Y, Sekine T, Igarashi T.

Department of Pediatrics, Ohta Nishinouchi Hospital, Fukushima, Japan.

Abstract

We report the case of a 16-year-old male patient with steroid-dependent nephrotic syndrome who developed ischemic colitis. He was diagnosed as having nephrotic syndrome at 10 years of age and had been administered steroid, cyclosporine A, and mizoribine for 7 years. He presented with severe abdominal pain 5 days after intravenous methylprednisolone pulse therapy; thereafter, massive bloody diarrhea developed. Abdominal ultrasonography and computed tomography revealed a marked thickening of the wall of the transverse colon. Colonoscopy confirmed the diagnosis of ischemic colitis. This is the first report of the development of ischemic colitis in a pediatric patient with nephrotic syndrome.



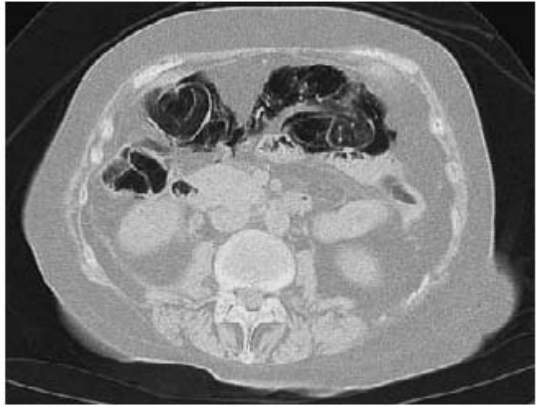


Figure 2. **Transverse section of abdominal CT.**
Massive air in the intestinal wall caused narrowing of the lumen.

INTERNAL MEDICINE

□ CASE REPORT □

Fulminant Pneumatosis Intestinalis in a Patient with Diabetes Mellitus and Minimal Change Nephrotic Syndrome

Yoshitaka Maeda, Naoto Inaba, Makoto Aoyagi, Eiichiro Kanda and Tatsuo Shiigai

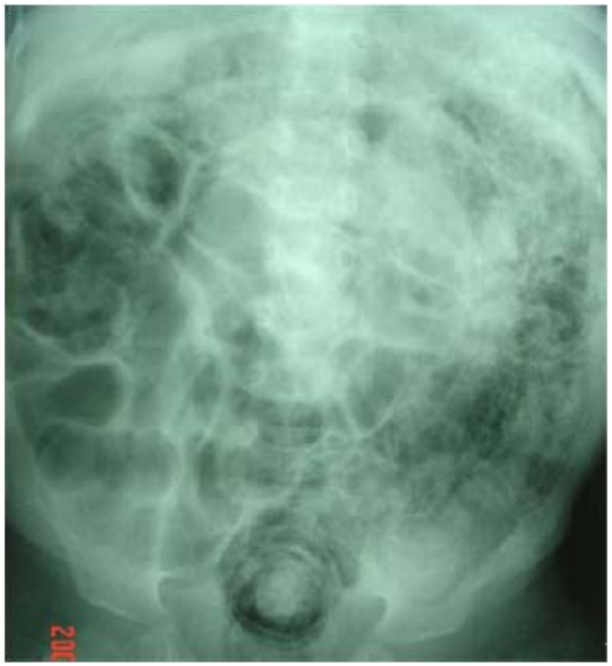
da non lasciare a terzi

Pediatr Nephrol (2010) 25:1563–1566
DOI 10.1007/s00467-010-1478-1

BRIEF REPORT

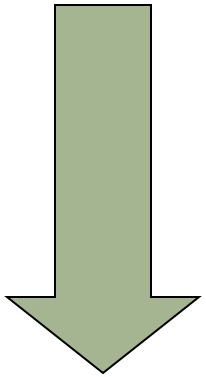
Pneumatosis intestinalis in a child with nephrotic syndrome and norovirus gastroenteritis

Winnie K. Y. Chan · Kwok Wai Lee · Tsz Wo Fan



Avviene dopo prolungato trattamento immunosoppressivo, ma più frequentemente in fase da remissione, con sovrainfezione da E.coli, e colpisce spesso pazienti con stipsi o affetti da gastroenteriti

Complicanze nel decorso della sindrome nefrosica



FARMACI

Inibitori Calcineurina

Corticosteroidi

Agenti alchilanti

CORTISONE IN ETA'PEDIATRICA

I bambini e gli adolescenti tendono a metabolizzare il farmaco più rapidamente e perciò necessitano di dosaggi più elevati

TOSSICITA' STEROIDE

- **l'aspetto cushingoide**
- **osteoporosi** → **Densitometria ogni 12 mesi**
- **obesità**
- **bassa statura** → **Misura con statimetro ogni 6 mesi**
- **diabete mellito**
- **cataratta** → **Visita oculistica con L.F. una volta l'anno**
- **aumentato rischio di infezioni**
- **ipertensione**
- **disturbi psichici**
- **rischio di aterosclerosi prematuramente**

Questione aperta:

Bambini con sindrome nefrosica sottoposti

a lunghi e/o continui cicli di terapia steroidea presentano

una **ridotta velocità di crescita staturale e densità ossea?**

ALTI DOSAGGI DI STEROIDI

Calcio
Assorbimento intestino ⇩
Urine ⇧

⇩ secrezione e pulsatilità del GH

Alterazione IGF-I
Inibizione IGFBP

⇩ Osteoblastogenesi
⇧ Apoptosi osteoblasti

⇩ Crescita staturale

⇩ Densità ossea

Pediatr Nephrol (2003) 18:783–788
DOI 10.1007/s00467-003-1176-3

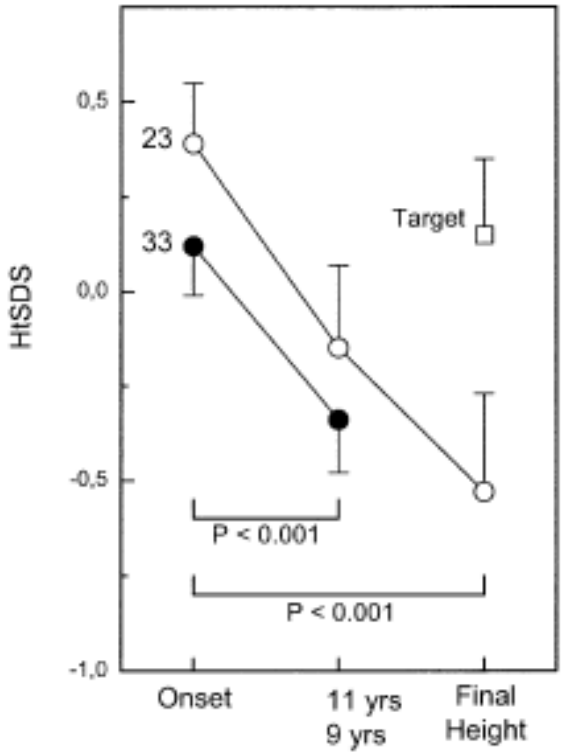
ORIGINAL ARTICLE

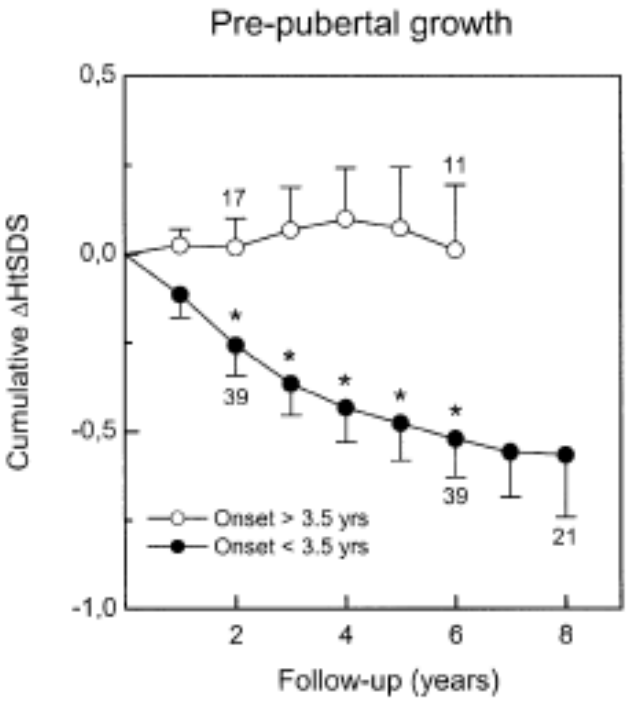
Francesco Emma · Antonella Sesto
Gianfranco Rizzoni

Long-term linear growth of children with severe steroid-responsive nephrotic syndrome

42 SN steroido-dipendente

14 SN frequenti recidive





Long-Term, High-Dose Glucocorticoids and Bone Mineral Content in Childhood Glucocorticoid-Sensitive Nephrotic Syndrome

Mary B. Leonard, M.D., M.S.C.E., Harold I. Feldman, M.D., M.S.C.E., Justine Shults, Ph.D., Babette S. Zemel, Ph.D., Bethany J. Foster, M.D., M.S.C.E., and Virginia A. Stallings, M.D.

N Engl J Med 2004;351:868-75.

Il trattamento con cortisone ad alti dosaggi, ma a giorni alterni, durante il periodo di crescita, non sembra determinare deficit significativi nel contenuto minerale osseo valutato con densitometria della colonna verticale

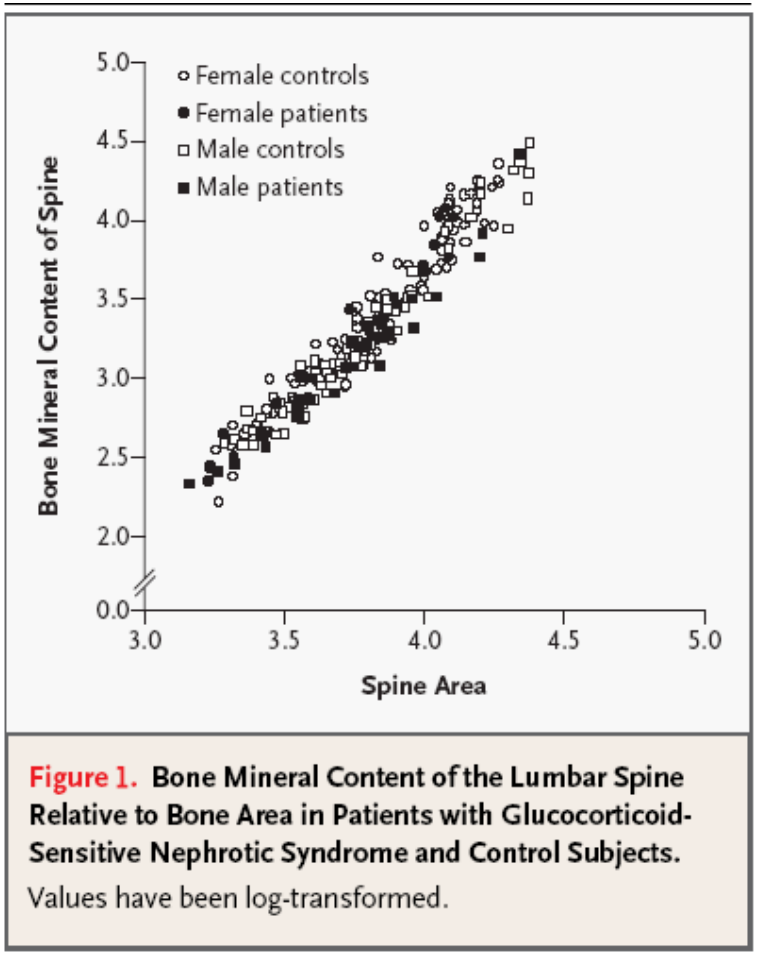


Figure 1. Bone Mineral Content of the Lumbar Spine Relative to Bone Area in Patients with Glucocorticoid-Sensitive Nephrotic Syndrome and Control Subjects.
Values have been log-transformed.

Casistica studiata

- **26 bambini con SN corticosensibile (ISKDC)**
- **età media: 6.9 ± 2.5 anni**
- **sesso: 19M/7F**
- **follow-up: 38.5 ± 8 mesi**

Trattamento

Prednisone 60 mg/mq/die per 4 settimane progressivamente ridotto per una durata complessiva all'esordio di 4 mesi e mezzo

26 bambini con SN corticosensibile

16 con SN infrequenti recidive (SNIR)

10 con SN frequenti recidive (SNFR) o corticodipendente (SNCD)

Materiali e Metodi

Ogni 3 mesi:

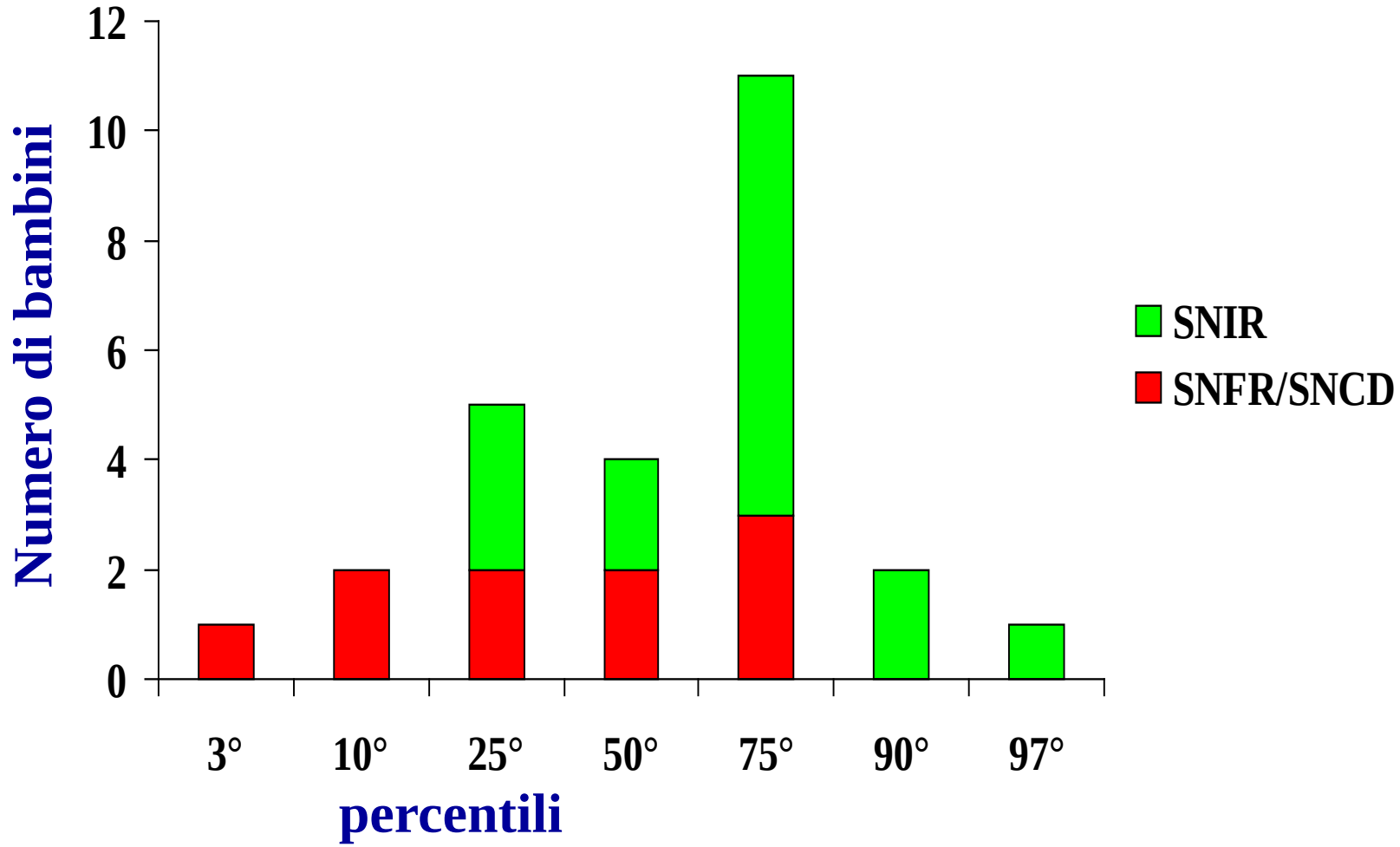
- **statura**
- **velocità di crescita staturale**

Ogni 6 mesi:

- **parametri ematochimici (Ca, P, ALP, PTH)**
- **Calciuria/Creatininuria**
- **densitometria ossea a livello del calcagno, con apparecchio ad ultrasuoni (Osteospace – Medi Link)**

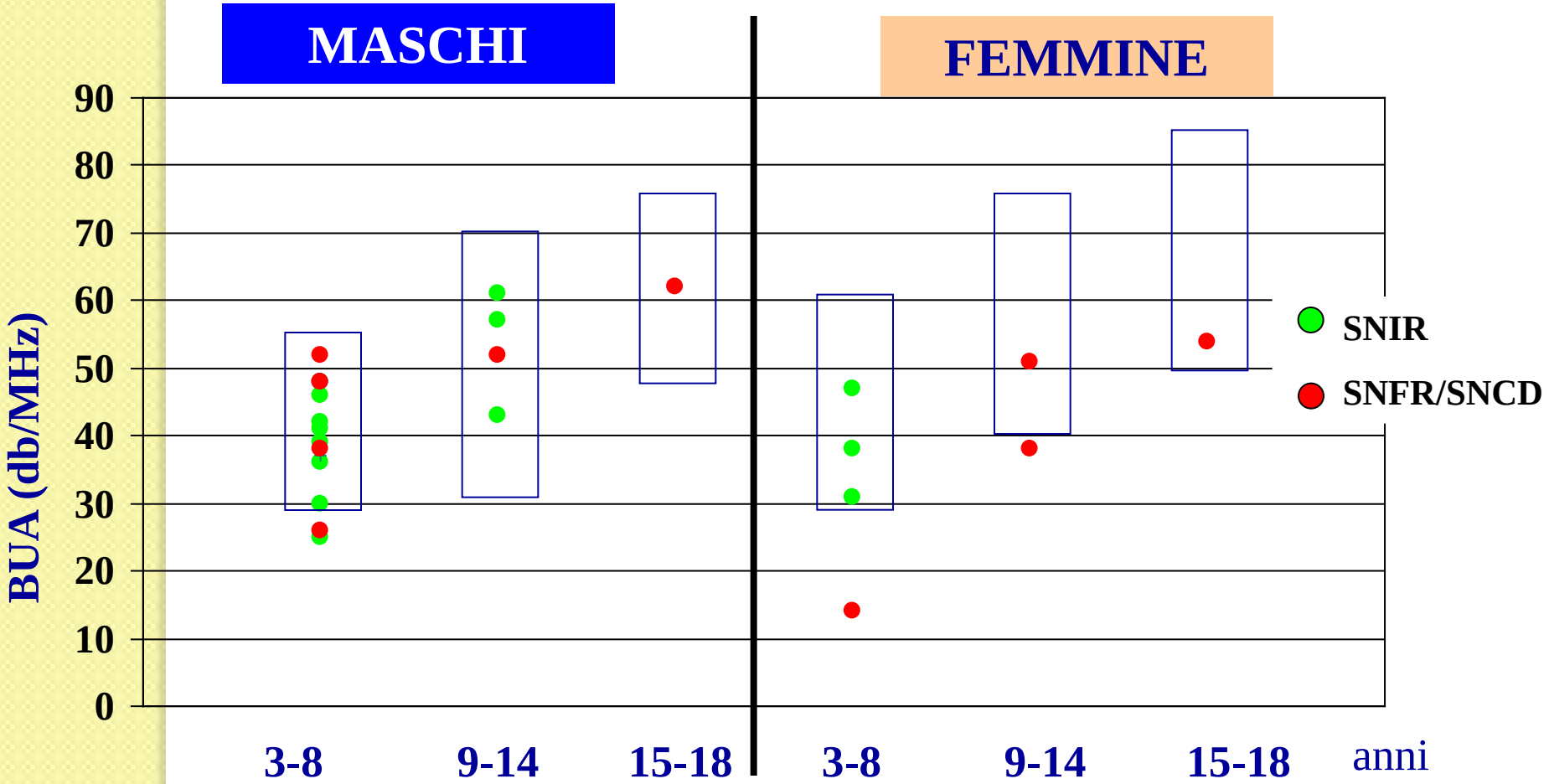
(Calcif Tissue Int. 2000; 67:19-23) (Eur J Pediatr. 2003; 162: 776-780)

Valutazione della statura in percentili in bambini affetti da sindrome nefrosica ad infrequenti recidive (SNIR) e a frequenti recidive (SNFR) o cortico-dipendenti (SNCD)



UO Nefrologia e Reumatologia Pediatrica con Dialisi- Messina

Valutazione della densità ossea in densitometria eseguita a livello del calcagno in bambini affetti da sindrome nefrosica ad infrequenti recidive (SNIR) e a frequenti recidive (SNFR) o cortico-dipendenti (SNCD).



Non abbiamo trovato correlazioni significative tra i parametri valutati ed il dosaggio steroideo complessivo o il numero di recidive

	SNIR	SNFR/SNCD
Statura <25°perc	0/16	3/10
Densità ossea -2DS	1/16	3/10
Velocità di crescita -2DS	0/16	1/10

Nephrol Dial Transplant (2005) 20: 1598–1603
doi:10.1093/ndt/gfh809
Advance Access publication 14 June 2005

Original Article

Nephrology
Dialysis
Transplantation

Longitudinal follow-up of bone mineral density in children with nephrotic syndrome and the role of calcium and vitamin D supplements

Sanjeev Gulati[1], Raj K. Sharma[2], Kiran Gulati[3], Uttam Singh[4] and Arvind Srivastava[5]

Table 1. Comparison of biochemical and radiological values in the study group ($n=88$) before and after calcium and vitamin D supplements

	Baseline	Follow-up	*P*-value
Serum Ca (mEq/l)	8.5±0.10	8.7±0.07	0.007
Serum P (mEq/l)	4.8±0.09	4.7±0.08	0.416
Serum alkaline phosphatase (IU/ml)	317±18	270±9.0	0.002
BMD whole body (g/cm^2)	0.799±0.010	0.830±0.010	0.000
BMD mid spine (lateral)	0.526±0.011	0.546±0.010	0.054
BMD spine AP (g/cm^2)	0.561±0.013	0.607±0.013	0.000
% z score	81.6±12.3	83.6±1.4	0.05

Data are the mean±SEM.

Studio prospettico:

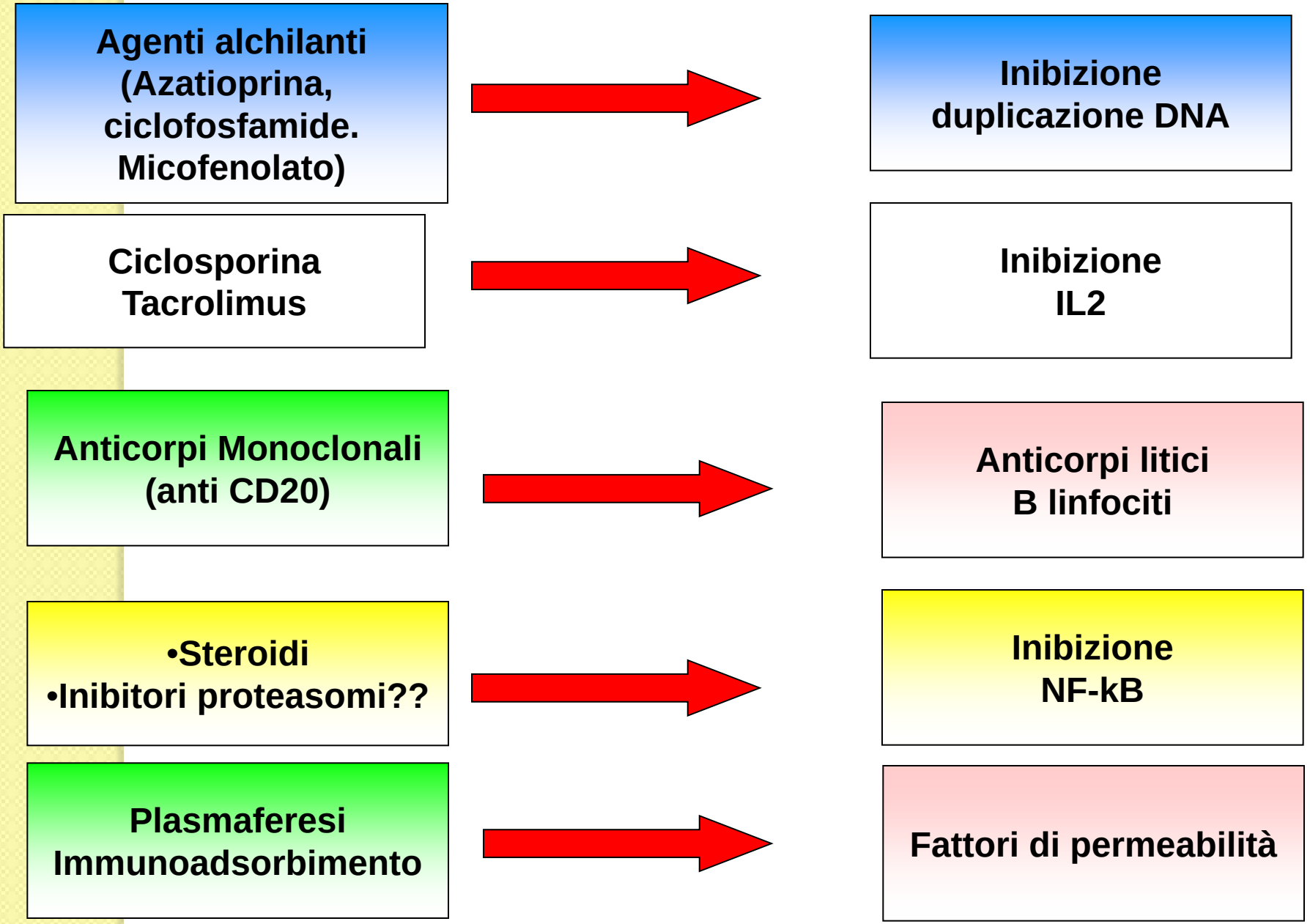
100 bambini, trattati con PDN.

Dall'esordio in supplemento di

-Calcio 500 mg/die

- Vit D3 200 U/die

Trattamenti alternativi nella sindrome nefrosica



Non-corticosteroid treatment for nephrotic syndrome in children (Review)

Table 03. Adverse effects during treatment of steroid sensitive nephrotic syndrome

Adverse event	CPA trials	CPA events/ patients	CPA (95% CI)	CHL trials	CHL events/ patients	CHL (95% CI)	CSA trials	CSA events/ patients	CSA (95% CI)
Infections	7	2/203	1% (0.1-3.5%)	5	3/97		3% (0.6-8.8%)		
Leucopenia < 5000 mm3	6	57/176	32% (26-39%)	4	14/76	18% (10-29%)			
Medication ceased due to leucopenia	6	17/132	9% (6-15%)	3	3/52	6% (1.2-15%)			
Thrombocytopenia	4	3/143	2% (0.4-5.7%)	4	8/86	9% (4.1-18%)			
Hair loss	4	26/188	14% (9-19%)	4	3/86	3% (0.7-10%)			
Cystitis	4	7/188	4% (1.5-7.5%)	4	0/86	0% (0-4.2%)			
Gum hypertrophy							2	13/56	28% (33-60%)
Hirsutism							2	19/56	34% (22-48%)
Hypertension							2	2/56	4% (0.4-12%)
Elevated creatinine level							2	5/56	9% (3-20%)

Pediatr Nephrol (2008) 23:1269–1279
DOI 10.1007/s00467-008-0814-1

ORIGINAL ARTICLE

Rituximab treatment for severe steroid- or cyclosporine-dependent nephrotic syndrome: a multicentric series of 22 cases

Vincent Guigonis · Aymeric Dallocchio · Véronique Baudouin · Maud Dehennault · Caroline Hachon-Le Camus · Mickael Afanetti · Jaap Groothoff · Brigitte Llanas · Patrick Niaudet · Hubert Nivet · Natacha Raynaud · Sophie Taque · Pierre Ronco · François Bouissou

Pediatr Nephrol (2008) 23:3–7
DOI 10.1007/s00467-007-0596-x

EDITORIAL COMMENTARY

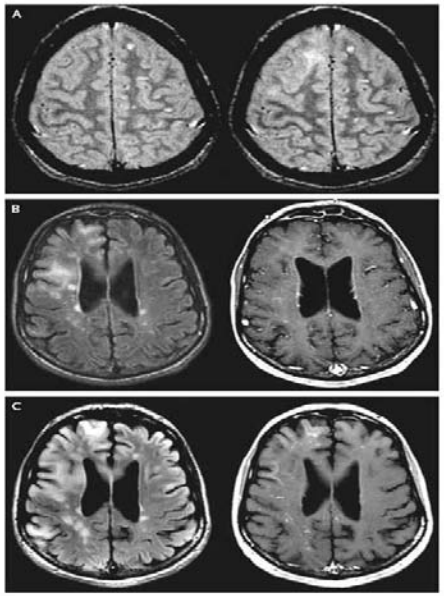
Rituximab: is replacement of cyclophosphamide and calcineurin inhibitors in steroid-dependent nephrotic syndrome possible?

Jörg Dötsch · Dirk. E. Müller-Wiefel · Markus J. Kemper

Rituximab utilizzato in > 500.000 soggetti

Tossicità, effetti colaterali:

- **2 casi di leucoenecefalite in LES trattati con multiterapia , incluso Rituximab**
- **Reazioni allergiche,**



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Nefrologia Pediatrica

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