CHRONIC KIDNEY DISEASE IN A SMALL CHILD

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Patient

- $3^{9/12}$ year old boy
- CKD patient
- Referred for further treatment of fungal peritonitis (December 2006)

(In the last month he was treated for bacterial peritonitis due to Klebsiella, and there after developed candida peritonitis-iv amphotericin B)

Patient-Past history

- Nephrotic syndrome at 5 months of age
- Renal biopsy:FSGS
- ESRD at 3 years of age → PD (CCPD)
- 3 peritonitis episodes (all with GN microorganisms)
  Hypertension (on quadruple therapy)
  Volume overload findings during peritonitis episodes
- Family history: Unremarkable

Physical examination

Weight:10 kg (<3p)

Height:85 cm (<3p) Height SDS: -7.08

BP:120/80 mmHg

HR:120/min

2/6 systolic murmur at the left sternal border

Hepatomegaly

Laboratory findings

- CBC: Hb 8.3 g/dl, Htc 24%, WBC 8900/mm^3, Plt 285000/mm^3
- Blood urea 179 mg/dl, cr 4.7 mg/dl, Na 137 mmol/L, K 6.0 mmol/L, Tot protein 6.8 g/dl, alb 4.2 g/dl, Ca 8 mg/dl, P 5.7 mg/dl, AP 440 U/L
- BGA: pH 7.34, pCO2 27.8 mmHg, HCO_3 15.2 mmol/L, Ba -10.3 mmol/L

1st problem

- Frequent peritonitis episodes (4 / 8 months)

- Fungal peritonitis

Peritonitis

- CPD → most common dialysis modality
- Peritonitis → most significant complication of CPD
  primary reason for modality change
- Frequency → children>adults
- According to NAPRTCS → an inverse relationship between the age and peritonitis rate

Chadha V, et al. Pediatr Nephrol 2010;25:425-40

NAPRTCS 2007 Annual Report

Gram (-) peritonitis

- A statistical association between young age and GN peritonitis

- According to IPPR half of the GN peritonitis episodes occured in children <5 years

- Young age
  Presence of gastrostomy
  Use of spike disconnect system

  } Predisposed to GN peritonitis

Warady BA, et al. J am Soc Nephrol 2007;118:2172-9

Zurowska A, et al. Am J Kidney Dis 2008;51:455-62

Fungal peritonitis

- In adults 2.8-15%

  pediatric population <3%

- Rare but associated with a high technique failure (50%)

- Risk factors for FP: High bacterial peritonitis rate

  Prior use of antibiotics

  Previous bacterial peritonitis with gram (-) organisms

Raaijmakers R, et al. Pediatr Nephrol 2007;22:288-93

Question 1

- How could we treat fungal peritonitis in our patient?

a. iv amphotericin B
b. ip amphotericin B
c. iv fluconazole
d. ip fluconazole
e. Immediate catheter removal

Fungal peritonitis – Treatment

- Fluconazole: First choice
  Excellent bioavailability and peritoneal penetration
  Almost always active against Candida species

- Amphotericin B should be avoided
  iv-more than 90% protein-bound, does not facilitate peritoneal passage
  ip-irritating to the peritoneum, severe abdominal pain

- Fungi colonize the surface of the catheter →
  Immediate catheter removal

Chadha V, et al. Pediatr Nephrol 2010;25:425-40

Raaijmakers R, et al. Pediatr Nephrol 2007;22:288-93

Treatment of FP in our patient

- PD catheter removal
- Antimycotic treatment for about 3 weeks
- Hemodialysis

2nd problem

- Vascular access
- Hemodialysis procedure

Vascular access in our patient

- A central venous catheter → first choice in urgent hemodialysis
- 8F cuffed hemodialysis catheter – right IJV
- 2 months later we retried PD → unsuccessful → go on with hemodialysis

Question 2

- Which one of them is the ideal vascular access in pediatric chronic hemodialysis patients ?

a. Temporary hemodialysis catheter (uncuffed)
b. Permenant hemodialysis catheter (cuffed)
c. AVF
d. AVG

Vascular access

- The ideal vascular access

  -delivers a flow rate adequate for the dialysis prescription

  - has a long use-life

  - has a low rate of complications (infection, stenosis, thrombosis…)

AVF best approximates this definition

Am J Kidney Dis 1997;30:150-91

Vascular access

- According to NAPRTCS in pediatric hemodialysis patients

  CVC → 78.9%

  AVF → 12.3%

  AVG → 8.5%

NAPRTCS 2006 Annual Report

- Compared with AVFS/AVGs vascular catheters have been associated with

  - significantly increased morbidity
  - 2X increase in hospitalization for any cause
  - 3X increase in vascular access complications
  - 5X increase in hospitalization as a result of infection

Fadrowski JJ, et al. Clin J Am Soc Nephrol 2006;1:987-92

(Children with AVFs/AVGs → improved urea clearance
greater Hb and serum albumin levels)

Chand DH, et al. Am J Kidney Dis 2005;45:303-8

Vascular access

- 2006 update of KDOQI included pediatric specific vascular access recommendations for the first time

  - Fistula or graft is the preferred form of vascular access

  - Circumstances in which a CVC may be acceptable
    - Lack of surgical expertise in small children
    - Too small patient size
    - Bridging HD for PD training or PD catheter removal for peritonitis
    - Expectation of expeditious kidney transplantation

Am J Kidney Dis 2006;48:274-6

SPECIAL ARTICLE

International Pediatric Fistula First Initiative: A Call to Action

Deepa H. Chand, MD, MHSA,[1] and Rudolph P. Valentini, MD[2]

The Centers for Medicare & Medicaid Services and the National Kidney Foundation-Kidney Disease Outcomes Quality Initiative have emphasized the need for increased arteriovenous fistula (AVF) use and decreased central venous catheter use. A Fistula First National Vascular Access Improvement Initiative was undertaken to achieve these targets in adult patients through change concepts and process improvement. Despite increasing numbers of children receiving hemodialysis in the United States, AVF use rates decreased during the past 10 years. Studies of children dialyzed using AVFs showed superior dialysis delivery, improved access survival, and markedly lower infection rates. The purpose of this article is to alert nephrologists to consider a fistula first in long-term pediatric hemodialysis patients. In this article, we describe the status of vascular access in the United States and worldwide in children, the importance of AVF creation, and the need for surgical expertise, including microsurgery, in this population. Additionally, we introduce the International Pediatric Fistula First Initiative, a multidisciplinary team consisting of pediatric nephrologists, vascular access surgeons, and interventional radiologists aiming to increase awareness, offer educational tools, and implement the fistula first initiative in children.

Am J Kidney Dis 51:1016-1024.

Vascular access in our patient

- 6 months later - Catheter infection with S. aureus – revision

- 9 months later (September 2007)-left brachiocephalic fistula

  HD from fistula at December 2007

  AVF - Used for 20 months without any problem

Hemodialysis procedure

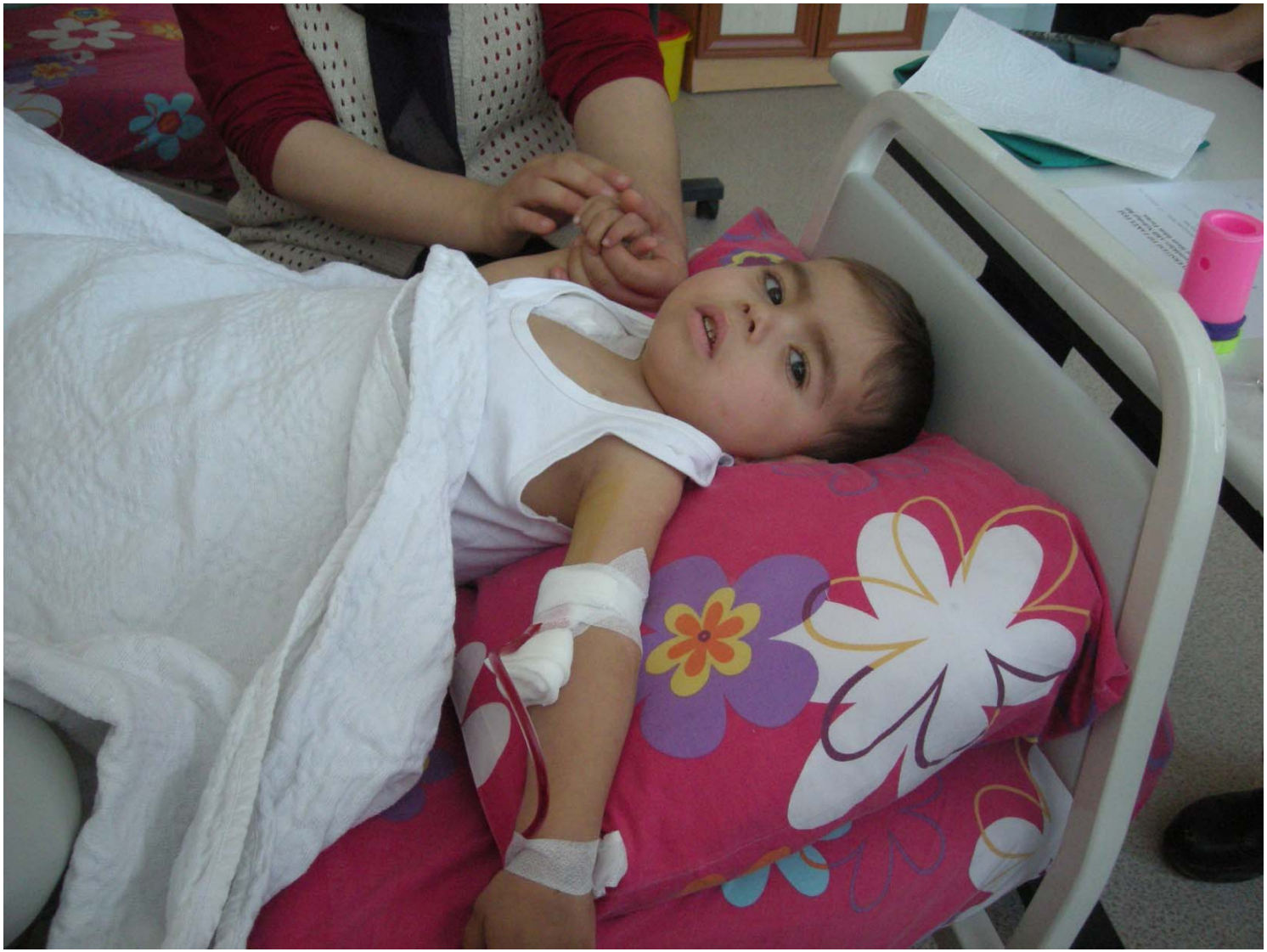
- In infants → associated with significant morbidity and mortality
- Technical difficulties (need for smaller dialysis lines,coagulation, bleeding..)
- Hemodynamic instability
- Environmental adaptation
- Anemia, HT, inadequate fluid removal, impaired growth
- Recurrent hospitalizations

Kovalski Y, et al. Pediatr Nephrol 2007;22:2105-2110

Hemodialysis procedure in our patient

- Machine with a volumetric ultrafiltration control
- Blood lines for babies/small infants were not available in our country
- The total extracorporeal blood volume should be less than 10% of patient total blood volume

System priming with blood, albumin and saline was applied at the beginning of dialysis sessions



3rd problem

- Severe hypertension
- Volume overload

3rd problem

- HT was detected with the diagnosis of FSGS
- Intensified during PD period

  Enalapril, amlodipine, propranolol and doxazosin
- Became more severe with the start of hemodiaysis (UO=0)
- Repeated attacks of severe hypertension, volume overload and pulmonary edema (frequent hospitalizations)

HT in pediatric HD patients

- Present in 79% of US pediatric HD patients

  87% of patients in the first 6 months of HD

  uncontrolled in 74% of treated patients

  Chavers BM, et al. Clin J Am Soc Nephrol 2009;1363-9

- 73% of children weighing less than 15 kg – treated with HD had stage 2 HT

  Kovalski Y, et al. Pediatr Nephrol 2007;22:2105-2110

Pathophysiology of HT in HD patients

- Volume overload
- Activation of RAAS
- Increased sympathetic nervous system activity
- Endothelial cell dysfunction, oxidative stress
- Hyperparathyroidism
- Erythropoiesis-stimulating agents (dose dependent)

Van Buren PN, Inrig JK. Pediatr Nephrol DOI 10.1007/s00467-011-1775-3

Treatment of HT in our patient

- Try to estimate optimum dry weight ????
- Try to limit interdialytic salt ingestion-strict fluid restriction ????
- Treatment with antihypertensives

  Enalapril 0.6 mg/kg/day

  Amlodipine 0.6 mg/kg/day

  Propranolol 4 mg/kg/day

  Doxazosin 2mg/day

  Losartan 50 mg/day

  Nifedipine 4X (0.3 mg/kg/dose)

- Hemodialysis every other day (December 2007)

  Everyday when necessary

- Bilateral nephrectomy (January 2009)

4th problem

- Anemia

- Hb ≈ 7-8 g/dl (December 2006-August 2007)

  We had to give repeated erythrocyte transfusions (1 transfusion/month))

Anemia

- Inadequate EPO usage (low dose and skipped doses due to severe HT)
- Iron deficiency
- Folate and vit B12 deficiencies
- Frequent blood sampling
- Blood losses during hemodialysis
- GI bleeding
- Oxidative inflammation
- Hyperphosphatemia , hyperparathyroidism
- Protein calorie malnutrition
- Drugs-angiotensin-converting enzyme inhibitors
- Infections
- Inadequate dialysis

Bamgbola O. Pediatr Nephrol DOI 10.1007/soo467-011-1839-4

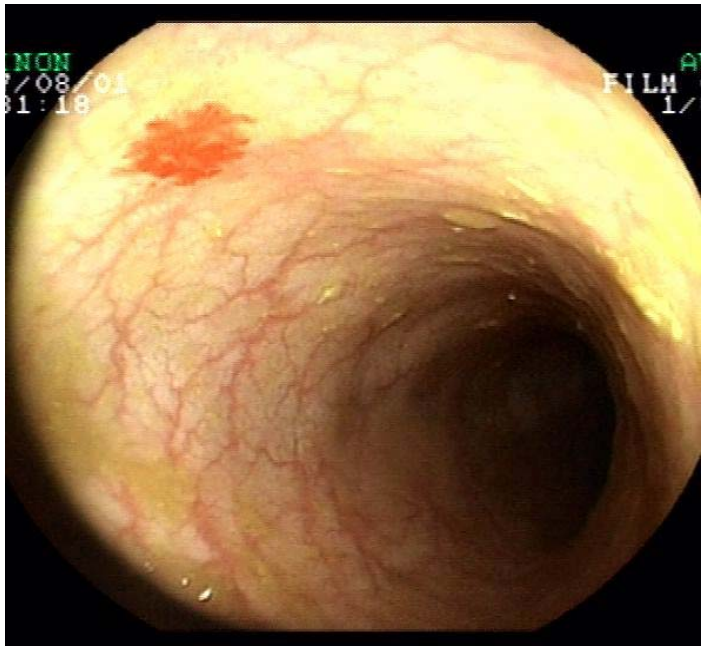
Unexpected cause of anemia

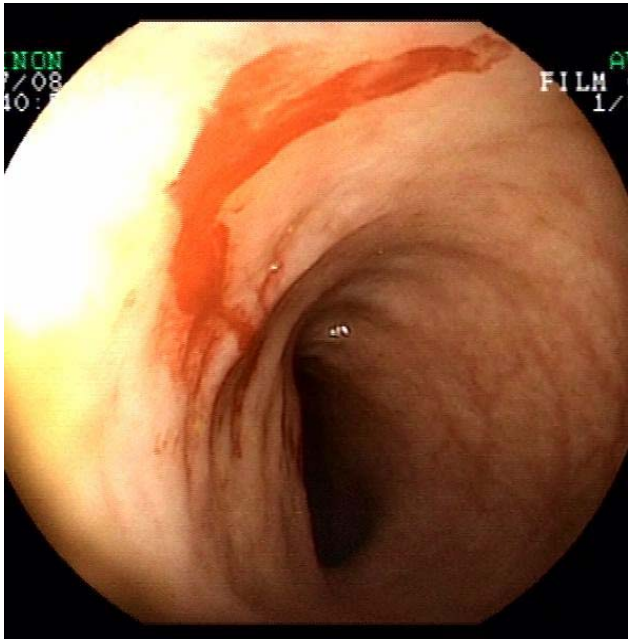
- August 2007 → Admission with massive hematochezia
- Hb:6.7 g/dl, Htc: 20%, MCV: 78 fl, PLT: 320.000 /mm^3
- Massive bleeding continued throughout the day
  (16 bloody stools/12 hours)
- Multiple blood transfusions were given (5X)
- Abd USG: Dilated colonic segments
  Lower GI endoscopy: not optimal
  Meckel scintigraphy: Normal

Angiodysplasia

- Octreotide therapy → bleeding ceased at the third hour of infusion

- Colonoscopy: Multiple angiodysplastic lesions in the descending colon





Angiodysplasia

- Argon plasma coagulation

- No gross bleeding after the procedure

  Need to blood transfusions significantly decreased

  Anemia improved

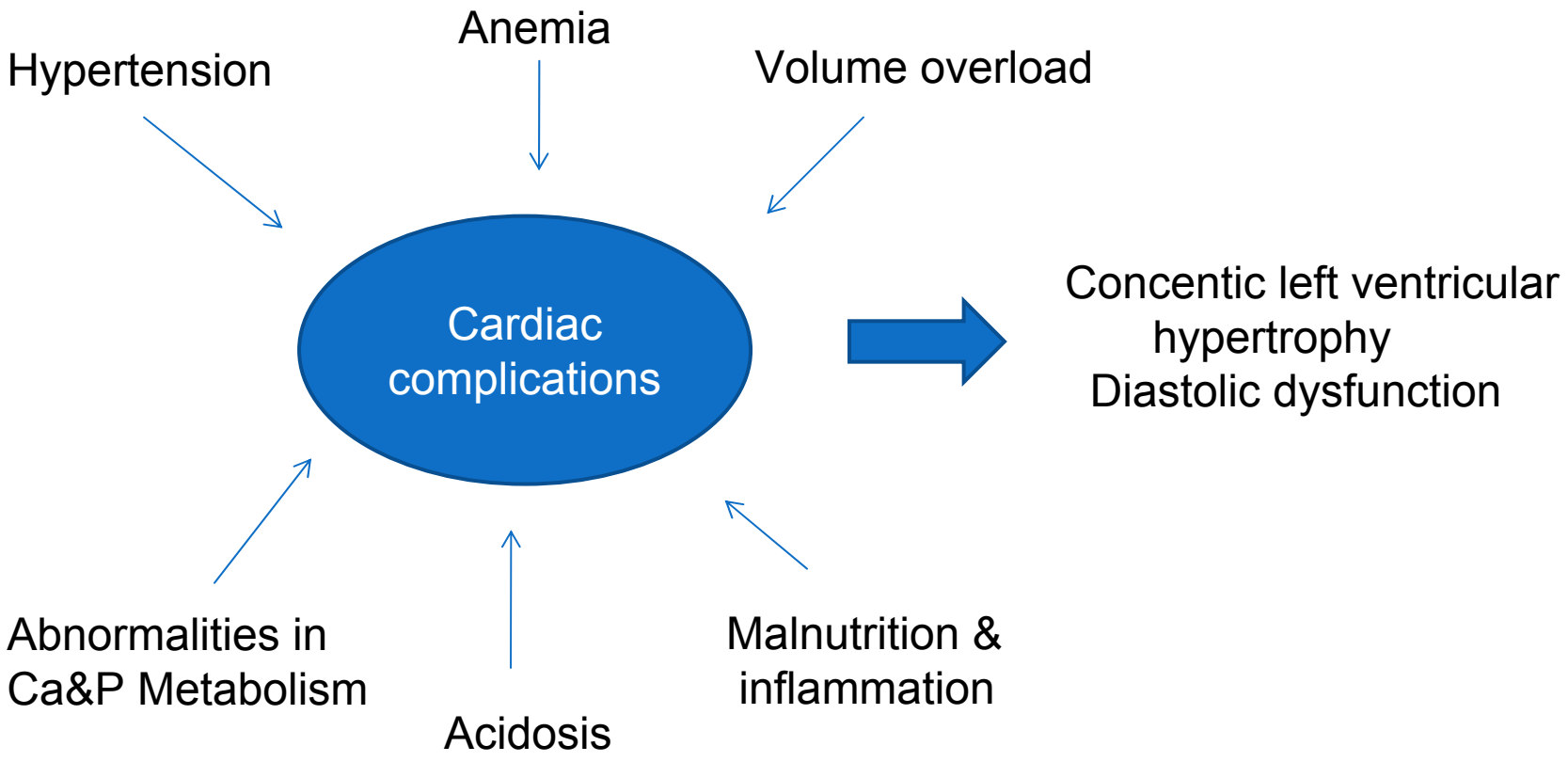
Angiodysplasia

- Common cause of GI bleeding among adults with CRF (19-47%)
- Not reported previously in pediatric CRF patients
- Characterized by dilatation, distortion or thinning of blood vessels of the mucosa
- Octreotide and APC therapy → useful for arresting bleeding and prevention of recurrent bleeding

Poralla T. Nephrol Dial Transplat 1998;13:2188-91

Karagiannis S, et al. World J Gastroenterol 2006;12:5182-5

5th problem


Hypertension
Anemia
Volume overload
Cardiac complications
Concentic left ventricular hypertrophy
Diastolic dysfunction
Abnormalities in Ca&P Metabolism
Acidosis
Malnutrition & inflammation

Management strategies

Avoidance of long term dialysis therapy

Successful renal transplantation

(eliminates uremia-related risk factors, increases predicted life expectancy)

6th problem

- Primary diagnosis → FSGS (podocin, WT1 mutations were -)

Question 3

- What could be our 6th problem related with transplantation ?

6th problem

- Recurrence after transplantation→ in 30-50% of the patients

  Risk factors: age >6 years at disease onset

  absence of hereditary forms

  short time interval between disease onset and ESRD (<3 years)

  history of a relapse in an earlier transplant

  mesangial hypercellularity with few sclerotic glomeruli on the original biopsy

- Graft loss → 20-50%

Living donor transplantation ????

Ulinkski T. Curr Opin Organ Transplant 2010;15:628-32
Vinai M, et al.Pediatr Transplantation 2010;14:314-25

Transplantation

- At 6 yrs of age → Deceased donor transplantation (May 2009)

- At the time of transplantation

  Weight:13 kg → (+3 kg)

  Height: 92 cm → (+7cm)

  } In the past 30 months

- Disease recurrence

  Other complications

  } ø

Last visit (May 2011)

- No complaints

- On tripple immunosupression (Tak+MMF+str)

  Enapril 0.22 mg/kg/day

  Propranolol 1.8 mg/kg/day

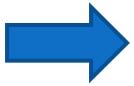
  Doxazosin 2mg/day

- PE: Weight: 22 kg (10-25 p)

  Height: 117 cm (3-10 p)

  Height SDS:-1.69

  BP: 110/60 mmHg



(+9 kg)

(+25 cm)

After transplantation, within 2 years

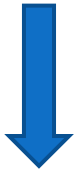
Last visit (May 2011)

- CBC: Hb 12.7 g/dl, Htc 37.8 %, WBC 7300/mm^3, Plt 345000/mm^3
- Blood urea 11 mg/dl, Cr 0.34 mg/dl
- CrCl: 125 ml/min/1.73 m^2
- Urinalysis: Protein (-)
- Echocardiography: Concentic left ventricular hypertrophy

  LVMI: 44.9 $g/m^{2.7}$

Conclusion

It is hard to treat small children with CKD



Nephrologists have many treatment options to solve different problems encountered in these patients