

Proteinuria in a Child with Bilateral Vesicoureteral Reflux and Dysplastic Kidneys

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Abstract

Key words:

Vesicoureteral reflux; dysplastic kidneys; orthostatic proteinuria; SDS-PAGE; stress tolerance test.

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Vesicoureteral reflux associated with congenital dysplastic kidneys is still an important etiological factor in children with chronic renal failure. Proteinuria in a child with reflux and scarring is an unfavorable prognostic parameter preceding the functional renal deterioration. Although there are no controlled studies in children angiotensin converting enzyme inhibitors have been used in those with proteinuria or hypertension to slow down progression of the disease. Herein we present a female child with bilateral reflux and significant proteinuria. Stress tolerance test and analysis of urinary proteins with SDS-PAGE electrophoresis disclosed typical orthostatic proteinuria. Therefore children with reflux and congenital/acquired scarring should have regular quantitative and qualitative evaluation of proteinuria to avoid unnecessary treatment in those with typical orthostatic pattern.

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Introduction

Vesicoureteral reflux is the most common congenital anomaly of the kidney and urinary tract. In association with congenital kidney dysplasia and urinary tract infection there is permanent damage of the kidney tissue (1, 2) and it represents still an important etiological factor in children with chronic renal failure (3-8). Proteinuria in a child with reflux and scarring is an unfavorable prognostic parameter preceding the functional renal deterioration (1, 7, 8). Therefore quantification and continuous monitoring of proteinuria in children with reflux and scarring is mandatory in order to implement early appropriate therapeutic measures to retard the progression of the disease. In this paper we describe a 10 year old female with vesicoureteral reflux and dysplastic kidneys, whose proteinuria was characterized by SDS-PAGE electrophoresis and stress tolerance test.

Case report

A 6 year old female was referred to the University Children's Hospital Skopje for investigation after a urinary tract infection. Her past medical history was characterized by frequent febrile episodes which had been treated with antibiotics. Urinalysis and urine culture had not been performed. On referral to the Children's Hospital the girl appeared healthy and her growth was within referent limits for the age and sex. Her physical examination did not reveal any abnormality. The blood pressure was 105/70 mmHg. An ultrasound scan was performed and showed small left kidney. There was no dilation of the pelvicalyceal system. The bladder appeared with regular contour and normal thickness of the walls (3.6 mm). After voiding there was 45 ml of the residual urine. Further investigation included Tc99-DMSA scan and direct radionuclide cystography. Cortical scintigraphy dis-

closed small and scarred left kidney with relative uptake of the radionuclide at 29%, compared with 71% on the right side (Figure 1). On cystography bilateral reflux grade III was detected. The girl was prescribed regular low dose chemoprophylaxis (nitrofurantoin 1 mg/kg every evening). She had been followed for one year and then was lost for follow up.

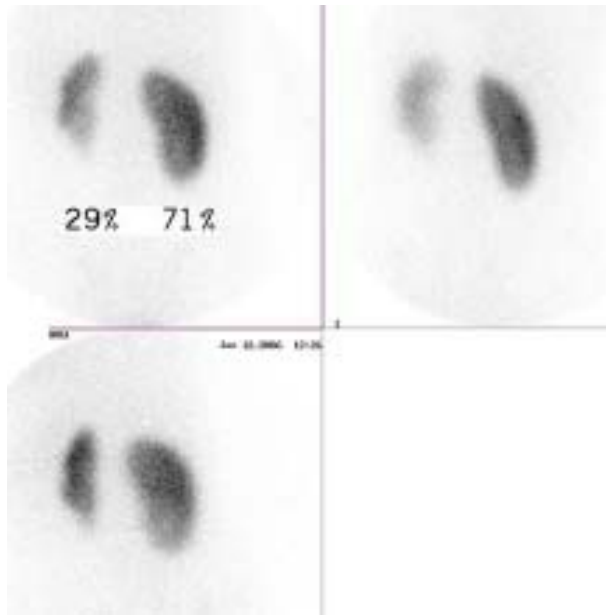


Figure 1: Cortical scintigraphy with Tc99-DMSA.

At the age of 10 she was referred again to the Children's Hospital because of proteinuria. Her creatinine was 55 micromol/l with calculated GFR at 106 ml/min/1.73 m² according to Schwartz formula (9). Daily urinary excretion of protein was moderately increased at 0.786 g (normal <0.15). The appearance of proteinuria in a child with reflux and scarring was very suggestive for disease progression, thus before administration of angiotensin converting enzyme (ACE) inhibitor we indicated analysis of urinary proteins with sodium dodecyl sulphate polyacrylamide gel electrophoresis (SDS-PAGE) after stress tolerance test. Briefly urinary excretion of total protein was 17 mg/l and 30 mg/l during the rest (Figure 2, lane 1 and 5 respectively) what was within referent values (<45 mg/l). During normal physical activity it increased to 580 mg/l and 360 mg/l (Figure 2, lane 2 and 4 respectively). At maximal physical activity proteinuria peaked up to 1440 mg/l (Figure 2, lane 5). Analysis of the electropherograms at the lanes 2, 3 and 4 revealed presence of a clear shaped 28KD fraction (apolipoprotein A1) which strongly suggested the functional type of proteinuria. On all electroferograms bands corresponding to low molecular weight proteins (B2-microglobulin,

alfa-1 microglobulin, retinol binding protein) were not identified.

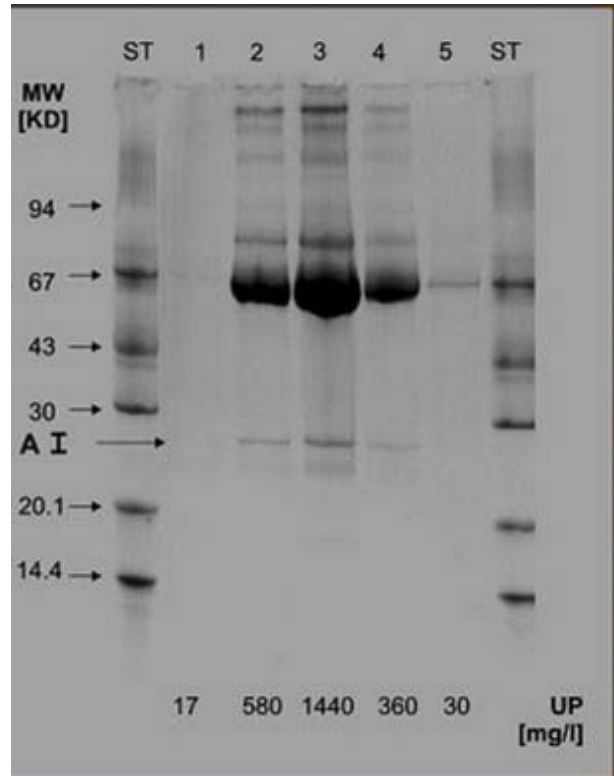


Figure 2: Electropherograms during the stress test, ST-standard, lane 1 and 5 at rest, lane 2 and 4 at ordinary physical activity, lane 5 at maximal physical activity, MW-molecular weight, KD-kilodalton, AI-apolipoprotein A1.

After obtaining the result of the SDS-PAGE and stress test, Doppler ultrasound study of the left renal vessels was performed for clarification of the orthostatic origin of the proteinuria, but nutcracker phenomenon was not detected.

Discussion

Vesicoureteral reflux associated with congenital dysplastic kidneys is still an important etiological factor in children with chronic renal failure. Proteinuria is a negative predictive sign indicating progressive renal disease and decrease in GFR. Administration of ACE inhibitors may retard progression of the disease in adults (1), although it has not yet been proven in children. The current practice is to prescribe ACE inhibitors to those children who have significant proteinuria and/or hypertension. Therefore it is crucial to identify proteinuria even in the microproteinuric range and to monitor continuously those patients. Our patient presented with late diagnosed vesicoureteral

reflux and already evident renal scarring. Since the patient was lost to follow up and did not adhere to regular hemoprophyllaxis, demonstration of significant proteinuria alerted us to the possibility of disease progression. Therefore we seriously considered administration of ACE inhibitor as an appropriate therapeutic measure. Before prescription of ACE inhibitor we wanted to characterize the type of proteinuria. We performed stress tolerance test and analysis of urinary proteins with SDS-PAGE which demonstrated clear orthostatic pattern. It is well known that patients with proteinuria due to organic renal disease may manifest orthostatism during lordotic position but at basal conditions they excrete significant amount of proteins. Contrary, our patient had normal urinary protein excretion during the rest that was in concert with functional origin of her proteinuria.

We have previously demonstrated that stress tolerance test with SDS-PAGE analysis of urinary proteins was very accurate for diagnosis of functional proteinuria and differentiation into orthostatic and exercise (sport) proteinuria (10, 11). In the latter type there is huge excretion of urinary proteins only after strenuous physical exercise - at rest and during ordinary physical activity urinary protein excretion is within normal range.

There is increasing number of reports which point to the nutcracker phenomenon as a possible cause of orthostatic proteinuria (12, 13) but we did not prove this phenomenon in our patient. Yet in a significant number of children and adolescents the etiology of orthostatic proteinuria is unknown. Concerning the long term prognosis there is general consensus that this is benign condition which spontaneously resolves usually after the puberty.

In conclusion, our patient presented with vesicoureteral reflux/kidney dysplasia and proteinuria which had typical orthostatic pattern. Presently there is no indication for ACE inhibitor. Since the progression of her nephropathy is unpredictable, stress tolerance test with SDS-PAGE is very accurate and noninvasive method for follow up of our patient.

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