

Significant Proteinuria Caused by Posterior Nutcracker Phenomenon

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= Abstract =

Posterior nutcracker phenomenon (PNP) was found to be the cause of significant proteinuria in a 10-year-old female. PNP was documented by Doppler ultrasonography and abdominal 3D CT as a cause of her proteinuria. Despite treatment with ACE inhibitor for several months, her persistent and progressive proteinuria lead us to perform a left renal biopsy, which revealed no significant finding except for focal effacement of foot processes. We speculate that nutcracker phenomenon can induce not only orthostatic proteinuria but also significant proteinuria by focal effacement of foot processes. (**J Korean Soc Pediatr Nephrol 2010;14:84-88**)

Key Words : Nutcracker phenomenon, Retroaortic left renal vein, Foot processes effacement

Introduction

The name, Nutcracker phenomenon (NP), was given by De Schepper who described left renal vein (LRV) entrapment in 2 patients with persistent hematuria. Its possible symptoms include gross or microscopic hematuria, flank pain, orthostatic proteinuria, varicoceles, pelvic congestion, and chronic fatigue. Orthostatic proteinuria has often been reported as a presenting symptom in NP since 1991. Shintaku et al. suggested that LRV entrapment was the cause of orthostatic proteinuria in children [1]. Its exact pathogenesis is still unknown. An

underlying subclinical immune injury and an additional exaggerated hemodynamic response may be responsible [2]. But, a significant isolated proteinuria has rarely been reported as a symptom of NP in related literature search.

The posterior nutcracker, one of the rarer patterns of NP is characterized by a retroaortic position of the LRV and its compression between the aorta and spine with a reported incidence of 0.5-3.7% [3].

We report a young female who developed significant proteinuria resulting from posterior nutcracker phenomenon (PNP) with no glomerular lesions.

Case Report

A 10-year-old girl visited our unit for the evaluation of proteinuria detected incidentally

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in a mass school urine screening test. She was well-developed, and her blood pressure was 125/85 mmHg. There were no remarkable findings on history taking involving past medical history, family history, and physical examination. In the first morning void urine sample, urine albumin was negative, and urine protein to creatinine ratio was 0.36 (mg/mg) without microscopic hematuria. But, 24 hour urine collection analysis showed 546 mg of protein, 372 mg of microalbumin and 650 mg of creatinine. Laboratory tests revealed serum albumin 4.3 g/dL, BUN 17 mg/dL, creatinine 0.8 mg/dL, C3 101 mg/dL and IgA 185 mg/dL. ANA and HBsAg were negative. Renal doppler sonogram revealed retroaortic left renal vein which inner diameter in a hilar portion was 2.2 times larger than that in a proximal stenotic portion. The measured peak velocity at the retroaortic portion increased more than 150 cm/s. Unfortunately, the superior mesenteric artery angle was not measured. With the suspicion of PNP, she had been followed up 10 months under the treatment of an angiotensin-converting enzyme (ACE) inhi-

bitor. However, her proteinuria had progressed worse and worse over several months. A urine dipstick test for albuminuria of a sample of the first morning void urine showed positive (+3) continuously for several weeks, and peak proteinuria and microalbuminuria level in a 24 hour urine collection sample reached 1,500 mg and 907 mg, respectively (Fig. 1). For this reason, we performed renal biopsy. The results were as follows. In the light microscopy, the sections contained 32 glomeruli without sclerosis. There was no hypercellularity, mesangial expansion, collapsed capillaries, or tubulointerstitial atrophic changes (Fig. 2). Immunofluorescence examination showed nonspecific granular deposits of IgM with speckled pattern. By electron microscope, focal effacement of foot processes was seen, but there were no electron dense deposits or deformation of glomerular basement membrane (Fig. 3). This implied her proteinuria was caused by PNP. Subsequently, abdominal and pelvis 3D CT was undertaken in supine position to identify any change in vessels anastomosing with left renal vein. And its

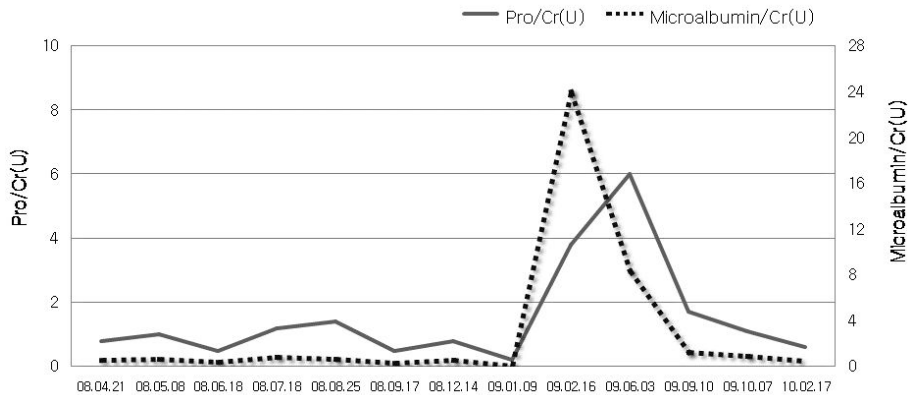


Fig. 1. The changes of urine protein and microalbumin to creatinine ratio over time.



Fig. 2. Light microscopy shows a normal glomerulus with no tubulointerstitial change (PAS, ×400).

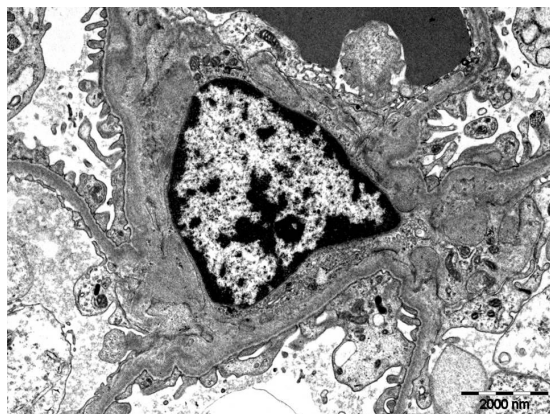


Fig. 3. Electron microscopy shows focal effacement of foot processes with no electron dense deposit.

result was that there was a small simple renal cyst on upper pole in left kidney and retroaortic left renal vein with dilated LRV in hilar portion (Fig. 4). The ratio of pre- to post-compressed vascular diameter was 4.6. Her plasma renin activity was slightly increased to 11.3 ng/ml/hour, and aldosterone level was normal. At the present time, after 2 years have passed since her proteinuria was detected, her proteinuria improved than before (Fig. 2). She has still taken a ACE inhibitor and remains normotensive

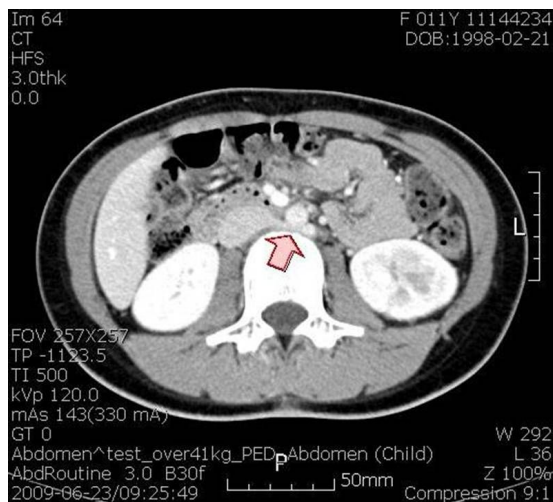


Fig. 4. Abdominal CT in the spine position reveals a compressed retroaortic left renal vein (arrow) between the aorta and the lumbar spine.

without any other symptoms besides anxiety of her parents.

Discussion

Left renal vein anomalies are classified into four types according to their appearance. Type I is retroaortic left renal vein joining the inferior vena cava (IVC) in the orthotopic position. Type II is retroaortic left renal vein joining the IVC at level L4–L5. Type III is circumaortic or collar left renal vein. Type IV is retroaortic left renal vein joining the left common iliac vein [4]. Karaman et al.[4] reported that the frequency of urological symptoms was higher in type II and IV compared to the other types. But, this case belongs to type I because retroaortic left renal vein joined the IVC at level L2–L3.

Ultrastructurally, we believe that focal effacement of foot processes ultimately results in her proteinuria although it is doubtful whether

hemodynamic effect of retroaortic left renal vein by itself, unlike anterior NP, could cause focal effacement of foot processes or not. In our opinion, it is possible that prolonged hemodynamic changes in the glomeruli resulting from PNP can induce glomerular epithelial cell damages directly or indirectly through unknown complex processes like interruption of translational signaling pathway at nephrin-podocin-CD2AP complex. Furthermore, it is known that damaged podocytes themselves can increase glomerular permeability, inducing proteinuria [5].

The final diagnosis of NP is established by selective venography and venous pressure measurement between the LRV and IVC. An elevated pressure gradient of >3 mmHg between the LRV and the IVC can be used as a valid criterion to diagnose the NP. But, this procedure is invasive, time-consuming, and not indicated if there are no severe symptoms. Doppler ultrasonography can be used as the second non-invasive diagnostic test in patients with suspected NP. Zhang et al. [6] noted that the standards for the ultrasound diagnosis of the disease as follows: (a) the flow velocity of stenosis of the LRV in the supine position, which is more than 100 cm/s, (b) the inner diameter ratio between the renal hilum and stenosis of the LRV in the supine position is >3 and is >5 after the patients has stood for 15 minutes. The sensitivity and specificity of color Doppler ultrasonography for diagnosing the nutcracker syndrome has been reported as 78% and 100%, respectively. Contrast CT or MRI should be the next diagnostic step to visualize vascular diameters of the left renal vein and its tributa-

ries, aortomesenteric space abnormalities and collateral circulation. Apart from CT or MRI, selective renin estimation may be helpful for establishing the diagnosis of NP.

In conclusion, nutcracker syndrome as a cause of hematuria or proteinuria is not uncommon by virtue of developing diagnostic techniques. And most of patients with nutcracker syndrome have a benign clinical course. Its management is conservative and to reassure their parents. Therefore diagnostic confirmation using invasive tools are not usually indicated unless there are no severe symptoms. Further study is necessary to clarify the mechanism of proteinuria and proteinuria-linked surgical indications in NP.

요 약

호두까기 증후군으로 인해 발생한 다량의 단백뇨

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호두까기 증후군으로 인한 기립성 단백뇨의 보고는 적지 않다. 하지만, 아직 정확한 기전이 알려져 있지 않다. 본 증례와 같이 호두까기 증후군으로 인하여 아침 첫 소변에서도 단백뇨가 나오고, 하루 1 g 이상의 단백뇨가 지속적으로 나올 수 있다는 보고는 아직 없다. 또한, 대동맥뒤 왼쪽 콩팥정맥의 경우에 단백뇨가 많이 나올 수 있다는 보고도 아직 찾을 수 없었다. 본 증례에서 단백뇨의 원인이 뒤 호두까기 증후군이라는 직접적인 증거는 없지만, 다른 단백뇨의 원인을 찾을 수 없었다. 만일 뒤 호두까기 증후군으로 인해 다량의 단백뇨를 유발할 수 있다는 것이 사실이라면, 좌측 신정맥에서 발생하는 강력한 혈역학적인 변화 자체가 직-간접적으로 사구체 상피세포의 손

상을 유발시켰음을 암시하는 것으로 사료된다.

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