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Editorial

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Nutcracker syndrome in pediatrics: a rare entity?

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See "Effect of renal Doppler ultrasound on the detection of nutcracker syndrome in children presenting orthostatic proteinuria" by Hwang et al. on page 74, Vol. 28, No. 2, 2024

Left renal vein (LRV) entrapment between abdominal aorta and superior mesenteric artery (SMA) was first termed as "nutcracker phenomenon (NCP)" by De Schepper in 1972 [1]. Nutcracker syndrome (NCS) refers to NCP accompanied by clinical findings, including hematuria, proteinuria, left flank pain, gonadal varicocele, orthostatic hypotension, and renal dysfunction [2]. Most children with NCS are asymptomatic and diagnosed incidentally during a diagnostic workup for hematuria and/or proteinuria. Although NCP/NCS is recognized as a rare condition, a recent study has reported that NCP/NCS is much more common than previously thought [2]. In addition, NCP/NCS has been described to coexist with various glomerular diseases in the literature [3-5]. Reduction in retroperitoneal and mesenteric adipose tissues and left kidney ptosis with stretching of the LRV over the abdominal aorta have been suggested as underlying mechanisms for the development of NCS [6,7].

The diagnosis of NCS is challenging due to the lack of consensus on diagnostic criteria. Doppler ultrasonography (US) is the first-line modality for evaluating NCS since both anatomical and physiological features of LRV can be obtained without radiation exposure. An LRV hilar-to-aortomesenteric (AM) diameter ratio >4–5:1 on computed tomography (CT), magnetic resonance imaging, and Doppler US suggests the presence of NCS [6]. On Doppler US, the peak velocity (PV) ratio (AM to hilar) of LRV >4–5:1 implies the diagnosis of NCS [6]. A "beak" sign with abrupt narrowing of the LRV between aorta and SMA in the axial plane and a decreased aorta-to-SMA angle <35° in sagittal dimension on CT or magnetic resonance imaging also suggest NCS [6]. While venography with measurement of pressure gradient between the LRV and inferior vena cava is considered a gold-standard method for diagnosing NCS, it may not be needed if Doppler US and CT are properly used in patients with suspicious NCS [2]. Meanwhile, elevation in renal venous pressure and venous congestion of kidney may cause various symptoms of NCS [8]. While micro- or macroscopic hematuria has been reported as the most common finding of NCS, proteinuria has been recently shown to be one of the significant features in children with NCS [6]. Generally, elevated LRV pressure causes rupture of thin-walled septum between varices and the collecting system, contributing to non-glomerular hematuria in NCS. However, the mechanism of NCS-related proteinuria has not been clarified yet. It has been suggested that proteinuria is related to venous hypertension within the nephron, inducing the subclinical immune cascade in the vascular endothelium and the release of angiotensin II and norepinephrine upon standing [7]. This hypothesis is in line with the finding that the NCS is one of the most important causes of orthostatic proteinuria [9]. Gulleroglu et al. [9] have investigated the diagnostic utility of the AM angle between upright and supine positions on Doppler US in the presence of orthostatic proteinuria for the diagnosis

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of NCS. Instead of ratios for PVs and diameters of hilar and AM segments of LRV, the use of a decrease in the ratio of AM angle between upright and supine positions has been found to be more helpful for the diagnosis of NCS in thirty-nine pediatric patients with isolated orthostatic proteinuria.

In the previous issue of *Childhood Kidney Diseases*, Hwang et al. [10] evaluated the correlation between orthostatic proteinuria and PV ratio in pediatric patients with NCS. In their study, the PV ratio between AM and hilar portion of LRV in the orthostatic proteinuria group was higher than that in the group without orthostatic proteinuria. A positive correlation between the proteinuria ratio (the urine protein-to-creatinine ratio of the afternoon urine sample/that of the morning urine sample) and the PV ratio was also found. The authors have suggested that a greater LRV compression in patients with NCS can result in congestion of renal blood flow, which affects orthostatic proteinuria. These findings seem to be compatible with those of a recent study by Akdemir et al [6]. In a total of 123 patients with NCS, the diameter and PV ratios between the two portions of LRV were greater while SMA angles were lesser in the upright than in the supine position, indicating a more apparent compression of the LRV in the upright position [6]. Although not all NCS patients have orthostatic proteinuria and vice versa, higher LRV compression in the upright position in patients with NCS may lead to greater proteinuria in the upright position associated with a higher PV or diameter ratio of LRV and a lower AM angle. However, Hwang's research [10] has some limitations. Firstly, they were unable to determine the association between orthostatic proteinuria and the PV ratio of LRV in patients without NCS. Since patients without NCS were not enrolled in their study, their results cannot be generalized or used in all patients with orthostatic proteinuria. Furthermore, the mechanism of NCS-related proteinuria would not be explained in the absence of orthostatic proteinuria. Secondly, the correlation of proteinuria in upright or supine position with the PV ratio of LRV in upright or supine position was not directly evaluated in Hwang's study [10]. While the proteinuria ratio calculated by dividing the urine protein-to-creatinine ratio of the afternoon urine sample by that of the morning urine sample was positively correlated with the PV ratio of LRV, a direct association between proteinuria in upright or supine position and PV ratio of LRV would be more helpful for understanding mechanisms of NCS-related proteinuria. Lastly, as suggested by other studies [6,9], comparison of Doppler US findings in both supine and upright positions might strengthen the validity of the conclusion of Hwang's evaluation [10]. These aspects should be taken into account when interpreting results of their study. Despite these limitations, their study revealed a possible association between the severity of LRV entrapment and orthostatic proteinuria in pediatric patients with NCS.

To solve challenging issues of diagnosing NCS in patients with proteinuria and/or hematuria, numerous puzzle pieces need to be filled. Mechanisms of NCP-related proteinuria and/or hematuria also should be clarified and the co-existence of NCS with other kidney diseases should be evaluated, especially in patients with atypical presentation or courses that cannot be explained by only the presence of NCS [3-6]. Given that there is no clear consensus on management or course of the NCS, especially in children, studies that determine long-term prognosis of NCS are needed urgently.

Conflicts of interest

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References

1. de Schepper A. "Nutcracker" phenomenon of the renal vein andvenous pathology of the left kidney. J Belge Radiol 1972;55:507-11.
2. Yoon T, Kim SH, Kang E, Kim S. Nutcracker phenomenon and syndrome may be more prevalent than previously thought. Korean J Radiol 2022;23:1112-4.
3. Wang F, Zhu H, Bao S, Qi H, Xu L, Liu X, et al. Associations of left renal vein entrapment with IgA nephropathy and Henoch-Schönlein purpura nephritis. Ren Fail 2022;44:1519-27.
4. Hirakawa Y, Miura R, Sasaki Y, Yoshida Y, Mimura I, Katsura M, et al. Nutcracker syndrome with the superimposition of thin basement membrane syndrome. Intern Med 2019;58:411-4.
5. Ma Z, Liu X, Ning Y, Shao J, Liu W, He X. Nutcracker phenomenon in

combination with glomerular nephritis in isolated hematuria patients. Int Urol Nephrol 2013;45:809-16.
6. Akdemir I, Mekik Akar E, Yılmaz S, Cakar N, Fitoz S, Ozcakar ZB. Nutcracker syndrome in pediatrics: initial findings and long-term follow-up results. Pediatr Nephrol 2024;39:799-806.
7. Kolber MK, Cui Z, Chen CK, Habibollahi P, Kalva SP. Nutcracker syndrome: diagnosis and therapy. Cardiovasc Diagn Ther 2021;11:1140-9.
8. Meyer J, Rother U, Stehr M, Meyer A. Nutcracker syndrome in children: appearance, diagnostics, and treatment: a systematic review. J Pediatr Surg 2022;57:716-22.
9. Gulleroglu NB, Gulleroglu K, Uslu N, Baskin E. Left renal vein entrapment in postural proteinuria: the diagnostic utility of the aortomesenteric angle. Eur J Pediatr 2022;181:3339-43.
10. Hwang EJ, Kim JH, Lee MJ, Yoon H, Shin JI, Lee KH. Effect of renal Doppler ultrasound on the detection of nutcracker syndrome in children presenting orthostatic proteinuria. Child Kidney Dis 2024;28:74-9.

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