Case Report

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# A Case of Secondary Hypertension Associated with the Nutcracker Phenomenon

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A 25-year-old Korean woman was referred for uncontrolled hypertension. Laboratory examination revealed increased plasma renin activity and microscopic hematuria. Computed tomography demonstrated compression of the left renal vein (LRV) between the aorta and superior mesenteric artery; however, both renal arteries were intact and there was no adrenal mass. Renal vein catheterization showed external compression with a pressure gradient of up to 8 mm Hg between the LRV and the inferior vena cava. Plasma renin activity in the LRV was almost five times higher than that in the right renal vein. In this patient, renin-dependent hypertension was caused by renal congestion due to LRV obstruction. **(Korean Circ J 2014;44(6):434-436)**

**KEY WORDS:** Renal nutcracker phenomenon; Hypertension.

## Introduction

The common causes of renin-dependent secondary hypertension are renovascular hypertension or renin-secreting adrenal tumor that induces renin hypersecretion. Renovascular hypertension refers to the rise in arterial pressure attributable to reduced perfusion of the kidney. Most often, this is from main renal arterial obstruction from either atherosclerotic occlusion or fibromuscular dysplasia.[1)] However, renal venous obstruction seldom causes renin-dependent systemic hypertension. Nutcracker syndrome (NCS) is also known as left renal vein (LRV) entrapment syndrome, and is characterized by the compression of the LRV between the superior mesenteric artery (SMA) and the abdominal aorta.[2)] The common manifestations of NCS are left flank and abdominal pain, with or without unilateral macroscopic or microscopic haematuria.[3)] However, very rarely, NCS causes secondary hypertension due to renin hypersecretion. We report the first case of a Korean female patient who was diagnosed with renin-dependent systemic hypertension due to NCS in the absence of a renin-secreting tumor or renal artery stenosis.

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## Case

A 25-year-old Korean woman was referred by a general physician with a 7-month history of uncontrolled hypertension. Her past medical and family histories were otherwise non-contributory. On admission, she was 165 cm tall and weighed 53 kg. Physical examination was unremarkable except for high blood pressure of 182/115 mm Hg. Urinalysis revealed microscopic hematuria and minimal proteinuria. Laboratory examination results were within normal limits, except for an increase in plasma renin activity (>20 ng/mL/hr, normal range: supine, 0.5–1.9 ng/mL/hr; erect, 1.9–6.0 ng/mL/hr), plasma aldosterone (668.21 pg/mL, normal range: supine, 10–105 pg/mL; erect, 34–273 pg/mL) and angiotensin II (90 pg/mL, normal range: 9–47 pg/mL). Electrocardiogram showed sinus rhythm with left ventricular hypertrophy (LVH), which was confirmed as mild LVH on echocardiography. Abdominal computed tomography demonstrated compression of the LRV between the aorta and SMA with pelvic congestion syndrome (Fig. 1). An adrenal tumor was not detected, and both renal arteries were intact. Renal scintigraphic findings using technetium-99m diethylenetriaminepentaacetic acid,

with and without captopril challenge, were normal. Selective renal venography demonstrated stenosis of the LRV at the level of the aorta, with dilatation of the left ovarian vein and multiple collateral veins with contrast filling the pelvic cavity (Fig. 2). The pressure gradient between the LRV and the inferior vena cava was 8 mm Hg (normal <3 mm Hg). Plasma renin activity in the LRV was almost five times higher than that in the right renal vein (5.88 ng/mL/hr vs. 1.17 ng/mL/hr). Hypertension did not respond to calcium channel antagonist and beta adrenergic blocker, but, the blood pressure decreased to 110/65 mm Hg after administration of angiotensin receptor blocker, candesartan (16 mg/d). The patient has not suffered from hypertension for more than 2 years with the use of this medication.

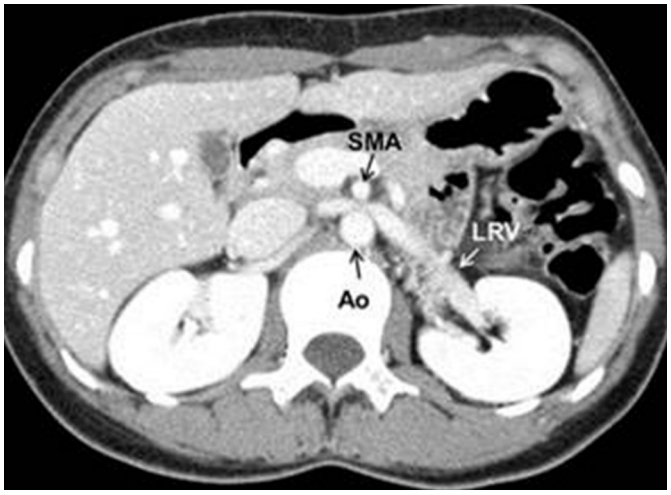


**Fig. 1.** An computed tomography image. Contrast-enhanced computed tomography demonstrating compression of the left renal vein between the aorta (Ao) and superior mesenteric artery (SMA) with dilatation of the distal part of the left renal vein (LRV).

## Discussion

Renin-dependent hypertension is the most common cause of secondary hypertension induced by renin hypersecretion. In most of the cases, renin-dependent hypertension is caused due to a renin-secreting adrenal tumor or renal artery stenosis. In this patient, LRV compression due to the nutcracker phenomenon caused renin-dependent hypertension, in the absence of an adrenal tumor and renal artery stenosis. LRV entrapment syndrome, characterized by the compression of the LRV between the SMA and the abdominal aorta was first described in 1950.[2] Chait et al.[4] described the abdominal aorta and the SMA as the two arms of a 'nutcracker' that can potentially compress the LRV. This description prompted the Belgian physician De Schepper to name this phenomenon as the NCS.[5]

The NCS is a very rare condition, and hence, there is no data about its actual prevalence or incidence. According to the recently published data including case reports and small case series, this disorder occurs in the 3rd or 4th decade of life, and has a predilection for women.[6]

Common clinical manifestations of the NCS are hematuria, pain, pelvic varicosities, and varicocele formation.[3] The pathophysiology of NCS is not fully understood. There are some theories that explain why compression of the LRV by the SMA occurs only in a few patients, and why LRV hypertension causes hematuria and pain. One of the theories suggest that posterior renal ptosis with stretching of the LRV over the aorta may be a contributing factor,[7] and the other theory suggests that abnormal branching of the SMA from the aorta contributes to the development of NCS.[8] However, very rarely, NCS causes secondary hypertension due to renin hypersecretion.

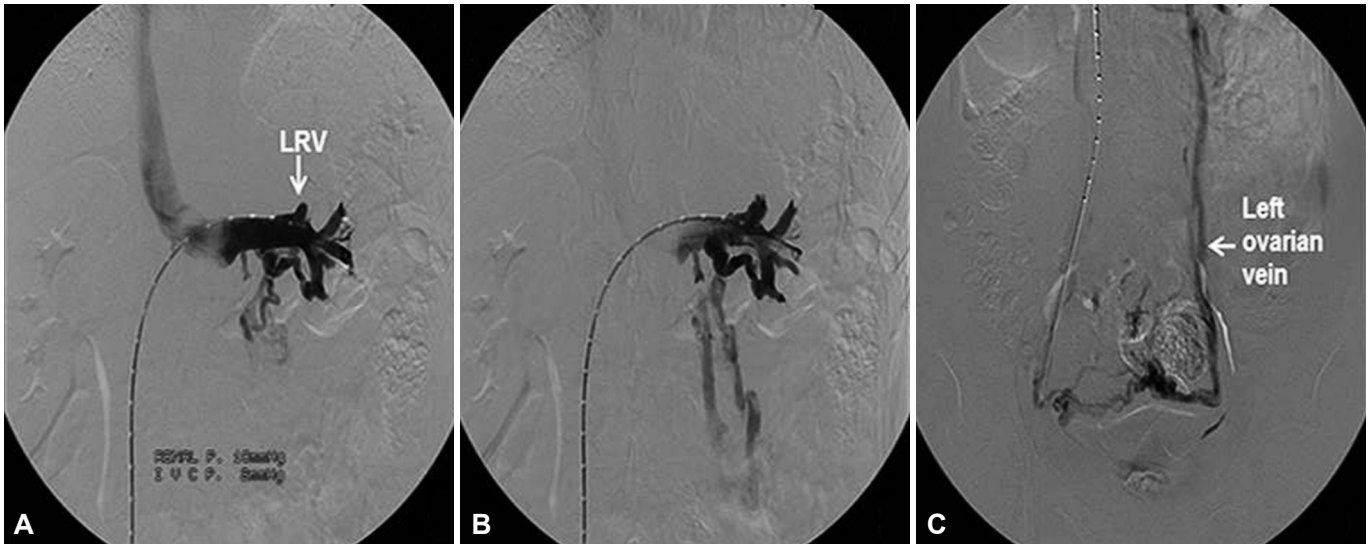


**Fig. 2.** Venography of the left renal vein. A: left renal vein (LRV) showing poststenotic dilatation. B: perirenal and periureteral collateral veins. C: anomalous reflux of ovarian vein and varices of ovarian plexus (arrow). The pressure gradient between the left renal vein and the inferior vena cava was 8 mm Hg (normal <3 mm Hg) and plasma renin activity in the LRV was almost five times higher than that in the right renal vein (5.88 ng/mL/hr vs. 1.17 ng/mL/hr).


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Although cases of patients having NCS have been described regularly, most of these patients had the aforementioned symptoms, and they did not have systemic hypertension associated with renin hypersecretion. To the best of our knowledge, only one case of renin-dependent hypertension associated with NCS has been reported so far. This case was of a 23-year-old Japanese lady who had hypertension with elevated renin secretion due to the nutcracker phenomenon.[9] The patient underwent endovascular stent placement for the nutcracker phenomenon, although her blood pressure decreased to 100/60 mm Hg with the use of an angiotensin II receptor blocker. Although the mechanism of secondary hypertension induced by LRV compression is not obvious, the probable mechanism has been described below. In animal models, elevation in renal venous pressure increases renal interstitial pressure and renin secretion.[10-12] Some articles have suggested that increased renal pressures (venous and interstitial) reduce glomerular filtration, affect the intrarenal blood flow, and induce the release of renin.[10] With decreased glomerular filtration, there is reduction in sodium delivery to the macula densa, which stimulates renin secretion from the juxtaglomerular cells. In patients in whom alteration of renal interstitial pressure increased the plasma renin activity, renoparenchymal or excretory tract disorders have been reported.[12] Thus, LRV hypertension may have induced renin secretion in this patient.

The management options for NCS range from observation to nephrectomy, depending on the severity of symptoms. Conservative treatment has been proposed in patients with mild hematuria, while surgery such as nephrectomy, nephropexy, renocaval reimplantation or auto-transplantation is indicated in patients with massive hematuria and severe pain. However, based on the available data, LRV transposition seems to be the most common surgical intervention for the NCS. Long-term results of this surgical procedure show a high rate of improvement of symptoms.[6] Currently, external and internal stenting procedures performed either via the minimally invasive or endovascular approach are promising treatment options. Since the first case was reported in 1996,[13] some of the patients have shown a successful outcome of vein stenting. Although large-scale clinical trials for treatment with stents have not been performed, a few case series showed good results in the long-term follow-up data. Sixty-one patients with NCS were treated with endovascular stents, and they were observed for a median period of 66 months. Most of the patients experienced amelioration of their symptoms and improvement in findings of ultrasound except for 2 patients; their symptoms were unchanged.[14] Based on these outcomes, we can consider an interventional or operational strategy in our patient if she wants to get pregnant or if she does not respond to the medications.

In conclusion, renal vein obstruction could be considered as one of the causes of renin-dependent secondary hypertension although renal vein obstruction in association with NCS is very rare. In this patient, laboratory examination results showed increased plasma renin activity in the LRV and blood pressure was reduced by an angiotensin II receptor blocker. Based on these findings, we attributed the renin-dependent hypertension to the nutcracker phenomenon.

## References


1. Textor SC, Lerman L. Renovascular hypertension and ischemic nephropathy. *Am J Hypertens* 2010;23:1159-69.
2. El-Sadr AR, Mina E. Anatomical and surgical aspects in the operative management of varicocele. *Urol Cutaneous Rev* 1950;54:257-62.
3. Ahmed K, Sampath R, Khan MS. Current trends in the diagnosis and management of renal nutcracker syndrome: a review. *Eur J Vasc Endovasc Surg* 2006;31:410-6.
4. Chait A, Matasar KW, Fabian CE, Mellins HZ. Vascular impressions on the ureters. *Am J Roentgenol Radium Ther Nucl Med* 1971;111:729-49.
5. Shaper KR, Jackson JE, Williams G. The nutcracker syndrome: an uncommon cause of haematuria. *Br J Urol* 1994;74:144-6.
6. Venkatachalam S, Bumpus K, Kapadia SR, Gray B, Lyden S, Shishehbor MH. The nutcracker syndrome. *Ann Vasc Surg* 2011;25:1154-64.
7. Wendel RG, Crawford ED, Hehman KN. The "nutcracker" phenomenon: an unusual cause for renal varicosities with hematuria. *J Urol* 1980;123:761-3.
8. Hohenfellner M, Steinbach F, Schultz-Lampel D, et al. The nutcracker syndrome: new aspects of pathophysiology, diagnosis and treatment. *J Urol* 1991;146:685-8.
9. Hosotani Y, Kiyomoto H, Fujioka H, Takahashi N, Kohno M. The nutcracker phenomenon accompanied by renin-dependent hypertension. *Am J Med* 2003;114:617-8.
10. Doty JM, Saggi BH, Sugerman HJ, et al. Effect of increased renal venous pressure on renal function. *J Trauma* 1999;47:1000-3.
11. Burnett JC Jr, Knox FG. Renal interstitial pressure and sodium excretion during renal vein constriction. *Am J Physiol* 1980;238:F279-82.
12. Armanini D, Fallo F, Opocher G, Boscaro M, Scaroni C, Mantero F. Peripheral and renal vein plasma renin activity in hypertensive urological patients. *Br J Urol* 1982;54:348-53.
13. Neste MG, Narasimham DL, Belcher KK. Endovascular stent placement as a treatment for renal venous hypertension. *J Vasc Interv Radiol* 1996;7:859-61.
14. Chen S, Zhang H, Shi H, Tian L, Jin W, Li M. Endovascular stenting for treatment of Nutcracker syndrome: report of 61 cases with long-term followup. *J Urol* 2011;186:570-5.