Localized solitary left renal vein thrombus complicating nutcracker syndrome: a case report and review of the literature

Takashi Nakashima¹ · Yuki Sahashi¹ · Hiromitsu Kanamori¹ · Yasushi Ohno² · Hiroyuki Okura¹

Received: 12 January 2020 / Accepted: 13 March 2020 / Published online: 3 April 2020
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Abstract

Nutcracker syndrome (NCS) refers to compression of the left renal vein (LRV) between the abdominal aorta and the superior mesenteric artery (SMA). The clinical presentation of NCS includes hematuria, abdominal and left flank pain, gonadal varices, and varicocele formation. Theoretically, thrombosis can occur in the LRV in patients with NCS. However, an isolated solitary left renal vein thrombus (LRVT) complicating NCS is rare. In addition, the clinical features of an LRVT complicating NCS remain unclear. We describe a 43-year-old woman presenting with an asymptomatic LRVT complicating NCS. She was referred to our hospital for investigation of dysfunctional uterine bleeding, and detailed examination revealed endometrial cancer. Computed tomography angiography (CTA) and Doppler ultrasonography revealed compression of the LRV between the aorta and the SMA, as well as an LRVT. CTA performed 4 months after the administration of an anticoagulant showed complete disappearance of the LRVT. We have also included a review of published reports describing LRVT complicating NCS and discussed the clinical features of such a presentation.

Keywords Case report · Left renal vein · Nutcracker syndrome · Renal vein thrombus · Review

Introduction

Nutcracker syndrome (NCS) refers to compression of the left renal vein (LRV) between the abdominal aorta and the superior mesenteric artery (SMA). The clinical presentation of NCS includes left flank pain, hematuria, lower extremity and gonadal varices, varicocele, ovarian vein syndrome, and pelvic congestion syndrome. Patients may also present with anemia secondary to significant hematuria [1–4].

Venous thrombosis is a common clinical condition and may occasionally cause life-threatening events such as pulmonary embolism. Thrombosis localized in the renal vein is a fairly unusual site for venous thrombosis [5]. Theoretically, LRV thrombosis can occur in patients with NCS because stenosis predisposes to stagnation of blood flow in the LRV, with consequent thrombosis. However, a localized isolated left renal vein thrombus (LRVT) complicating NCS is rare.

Notably, the clinical features of an LRVT associated with NCS remains unclear. We described a 43-year-old woman presenting with an asymptomatic LRVT complicating NCS. We have also reviewed the published literature describing an LRVT associated with NCS and discussed the clinical features of such a presentation.

Case report

A 43-year-old woman with dysfunctional uterine bleeding was referred to the gynecology department at our hospital. She reported an unremarkable medical and family history. She denied any physical complaints such as abdominal or back pain. Physical examination revealed she was 1.57 m tall and weighed 51 kg with a low body mass index (BMI) of 20.0 kg/m². Detailed examination revealed findings of endometrial cancer (Fig. 1). Computed tomography angiography (CTA) performed during the course of evaluation for endometrial cancer revealed compression of the LRV between the aorta and the SMA with an LRVT (Fig. 2a). Doppler ultrasonography (USG) also revealed compression of the LRV between the abdominal aorta and the SMA, as well as an LRVT. The SMA angle (the angle between the aorta and the SMA), the diameter

✉ Takashi Nakashima
takashin727jw@yahoo.co.jp

¹ Department of Cardiology, Graduate School of Medicine, Gifu University, 1-1 Yanagido, Gifu 501-1194, Japan

² Department of Respiriology, Graduate School of Medicine, Gifu University, 1-1 Yanagido, Gifu 501-1194, Japan

Fig. 1 CTA (A) and MRI images showing endometrial cancer (arrows). A mass of 40 mm in diameter is observed in the uterine body. CTA computed tomography angiography, MRI magnetic resonance imaging

of the stenotic portion, and the diameter of the dilated portion were 25°, 1.1 mm, and 9.9 mm, respectively (Fig. 2b, c). Urinalysis revealed macroscopic hematuria. During detailed medical interview, she revealed a long-term history of intermittent macroscopic hematuria, but denied known medical history of coagulopathy. CTA and USG did not detect renal tumor or hydronephrosis. She denied a history of surgical therapy, trauma, recent immobilization secondary to long-distance travel, and/or the use of oral contraceptives. She was not pregnant. Transthoracic echocardiography did not indicate any finding suspicious for pulmonary embolism. Therefore, she was diagnosed with an LRVV complicating NCS. Warfarin was administered 4.5 mg daily for anticoagulation, and the prothrombin time-international normalized ratio was targeted ranging from 2.0 to 3.0. Four months after the initiation warfarin, CTA and USG showed complete disappearance of the LRVV (Fig. 2d); therefore, warfarin was discontinued. Repeat CTA performed 3 months later showed no recurrence of the LRVV.

Semiradical hysterectomy with bilateral adnexectomy, para-aortic and pelvic lymphadenectomy, subsequent chemotherapy with paclitaxel and carboplatin was performed for endometrial cancer.

Discussion

Localized thrombosis in the renal vein is relatively unusual. Although Asghar et al. [5] reviewed the clinical features of a renal vein thrombosis and its etiologies, NCS had not been described as a cause of LRVV in their review.

Updated current diagnostic criteria/guidelines for the management of NCS mention an LRVV originating as a complication of NCS [4]. However, these guidelines refer to reports in the literature describing patients with NCS who underwent surgical or endovascular procedures such as stenting, in whom the LRVV was observed as a post-stenting or postoperative complication [6–9]. Therefore, the clinical features of an isolated localized LRVV complicating NCS are not available in the literature [4]. The clinical relationship between NCS and an LRVV has not been investigated, and the clinical features of this condition remain unclear.

To our knowledge, Cakir et al. first reported an isolated LRVV associated with NCS in 1995. A review of the literature reveals that since 1995, three reports have described an isolated LRVV complicating NCS [10–12]. Reed et al. reported two cases of an LRVV associated with NCS; however, in these two cases, the LRVV was incidentally detected during an LRV transposition procedure performed in patients with NCS [6]. Preoperative imaging did not reveal any evidence of the LRVV in these cases. Therefore, these two cases are not included in the present review of the literature.

Table 1 shows the clinical features of the aforementioned three cases and the present case showing a solitary localized LRVV associated with NCS. These patients were relatively young (32.5 ± 8.7 years old). Three patients were women, which concurs the previous study showing a slightly higher prevalence of NCS in women [13]. BMI values were available in two cases and these were relatively low. All three cases except the present patient presented with symptoms including abdominal or left flank pain. Three cases showed macroscopic and/or microscopic hematuria. Case 3 showed

Fig. 2 **a** CTA image of the abdomen and pelvis showing an LRV and compression of the LRV between the Ao and the SMA. **b** USG image showing the diameter of the stenotic portion is 1.1 mm, and compression of the LRV between the Ao and the SMA can be visualized. **c** USG image showing the diameter of the dilated portion is

9.9 mm. The thrombus is visualized in the LRV. **d** CTA scan obtained 4 months after warfarin administration showing complete disappearance of the LRV. *Ao* abdominal aorta, *LRVT* left renal vein thrombus, *SMA* superior mesenteric artery, *USG* Doppler ultrasonography

an anemia. These presentations commonly occur in patients with NCS or LRV [1, 2, 4, 5]; therefore, we could not conclude that these symptoms characterize an LRV associated with NCS.

All four patients did not develop deep vein thrombosis at any site other than the LRV. Compression of the LRV with stagnation of the blood flow in the vessel predisposes to LRV thrombosis. Notably, hypercoagulability additionally predisposes to LRV thrombosis. Furthermore, the diagnosis of NCS is occasionally delayed because some cases of the NCS do not have any specific symptomatic presentation; therefore, chronic blood congestion in the LRV can trigger LRV thrombosis. Membranous glomerulonephritis (an immune-mediated disease) diagnosed in case 1, the use of oral contraceptive by the patient described in case 2, and the endometrial cancer in the present case contributed to a hypercoagulable state that predisposed to LRV thrombosis.

NCS is diagnosed based on imaging studies including CTA, magnetic resonance imaging, and USG that show

compression of the LRV. Reportedly, NCS was diagnosed by USG with a relatively high sensitivity and specificity in 40% in patients presenting with cryptogenic hematuria [14, 15]. However, regarding detecting the localized LRV thrombosis, CTA has a high sensitivity and specificity [16]. The LRV was detected by CTA in all four cases. The LRV was also detected by USG in two cases. The findings of the USG were not available in other two cases. Therefore, CTA is a preferred imaging modality to diagnose thrombosis and NCS and can identify the etiopathogenic factors, as well as establish the differential diagnosis simultaneously [16].

Management of an LRV associated with NCS involves treatment of the thrombus to prevent embolic events such as pulmonary embolism and treatment of the cause of the LRV and NCS. Pulmonary embolism did not occur in any of the four aforementioned patients. All four patients received anticoagulation therapy, and disappearance of the LRV was confirmed in three patients. Notably, treatment of NCS is controversial. Close follow-up and

Table 1 Clinical features of cases of nutcracker syndrome complicated by a left renal vein thrombus (including the present case) reported in the literature

Case	Reporter	Published date (year)	Age (years old)	Sex	BMI (m ² /kg)	Symptoms	Anemia
1	Cakir et al. [10]	1995	36	Man	NA	Abdominal pain and left flank tenderness	–
2	Mahmood et al. [11]	2013	27	Woman	NA	Left flank pain	–
3	Mallat et al. [12]	2013	24	Woman	17.2	Left flank pain and left lumbar pain	+
4	Nakashima et al.	Present case	43	Woman	20.3	Asymptomatic	–
Case	Hematuria		Embolism	Diagnostic imaging tools	Possible contributing factor	Treatment	Disappearance of thrombus
	Macroscopic	Microscopic					
1	–	+	–	CTA and USG	Membranous glomerulonephritis	Anticoagulation	Confirmed
2	–	–	–	CTA	Use of oral contraceptive	Anticoagulation	NA
3	+	+	–	CTA	None	Anticoagulation	Confirmed
4	–	+	–	CTA and USG	Cancer	Anticoagulation	Confirmed

BMI body mass index, *CTA* computed tomography angiography, *NA* not available, *USG* Doppler ultrasonography

surgical therapy involving intra- or extravascular stenting, transposition of the LRV, and/or SMA, laparoscopy, and nephropexy to reduce LRV hypertension are proposed as possible treatment options for NCS [3, 15–20]. Invasive therapeutic options are considered only in patients with severe and/or persistent symptoms such as sustained severe pain, hematuria-causing anemia, renal failure, and in patient's refractory to conservative treatment [3, 15–20]. Transposition of the LRV had been proposed to treat the patient described in case 3 owing to severely symptomatic NCS complicated with an LRV. However, the operation was deferred because the patients were newly married [12].

The number of LRV complicating NCS is very small in this review because localized solitary formation of thrombus in the LRV as a clinical presentation of NCS is rare. However, to the best of our knowledge, this is the first review of the literature describing the clinical feature of the solitary LRV complicating NCS. We consider that LRV should be mentioned as a clinical presentation of NCS. Patients with NCS are perhaps at a higher risk of venous thrombosis because of the anatomical/structural variation (compression of the LRV secondary to the NCS) and consequently altered hemodynamics. Notably, a hypercoagulable state induced by cancer, immune-mediated disease, and/or the usage of oral contraceptives is an additional trigger for thrombosis in patients with NCS. Future studies should investigate the association between NCS and an LRV, the optimal therapies, the necessity of permanent anticoagulation, the role of

surgical and endovascular therapies, and the post-treatment outcomes.

Compliance with ethical standards

Conflict of interest The authors have no funding sources or conflicts of interest to disclose.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee at which the studies were conducted and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

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