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Clinical and radiological features in four adolescents with nutcracker syndrome

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Abstract We describe four adolescents with the nutcracker syndrome. In three patients, the nutcracker syndrome was detected through mass urinary screening; the other patient was diagnosed after a sudden onset of dark urine. All patients underwent magnetic resonance angiography (MRA) for diagnosis of the nutcracker syndrome, which revealed dilatation of the left renal vein ranging between 7.4 and 13 mm at the hilar portion. A renal biopsy, perfomed in three patients, showed no remarkable abnormalities in the glomerulus or tubulointerstitial tissue. The patients complained of physical discomfort, including headache, abdominal pain, fainting, and tachycardia mimicking clinical symptoms of an orthostatic disturbance. However, no chronic systemic diseases were detected in any of the patients after repeated laboratory examinations. An orthostatic disturbance preceded diagnosis in three patients. This report indicates that the nutcracker syndrome may cause serious physical ailments that clinically mimick an orthostatic disturbance. It may be important to identify the nutcracker syndrome among children who manifest non-specific physical complaints. MRA could be a safe and reliable method for diagnosing the nutcracker syndrome.

Key words Nutcracker syndrome · Orthostatic symptoms

Introduction

Nutcracker syndrome causes left-sided renal bleeding by compressing the left renal vein (LRV) between the aorta and the superior mesenteric artery (SMA), leading to an elevation of the LRV pressure, renal hilar varices, and the development of collateral veins [1, 2]. De Schepper [1] described two patients with persistent hematuria of unknown origin who showed compression of the LRV by the aorta and the SMA in 1972. Similar patients were subsequently reported [3, 4, 5], which clarified the final clinical diagnosis of patients with long-term persistent idiopathic hematuria. These studies mainly utilized renal venography for the diagnosis. Recently, ultrasonography (US), Doppler US, computed tomography, and magnetic resonance angiography (MRA) have been developed and are routinely available for the diagnosis of nutcracker syndrome, even at an early stage [6, 7]. The typical clinical features of this syndrome are microscopic hematuria associated with or without proteinuria or a sudden onset of dark urine [8, 9]. In a recent report, orthostatic proteinuria was recognized as a urinary abnormality of this disease [10]. Some patients with the nutcracker syndrome have complained of lower abdominal pain or backpain, but serious physiological disturbance was usually lacking [8, 9]. In this paper, we describe the features of four adolescents with nutcracker syndrome who refused to go to school.

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Patient profiles

The details of the patients are summarized in Table 1. In the last 2 years, four adolescents (1 boy and 3 girls) visited our hospital because of urinary abnormalities, including microscopic and macroscopic hematuria and/or proteinuria. Of these patients, three (nos. 2,3, and 4) were detected by mass urinary screening, and the remaining patient (no. 1) showed a sudden onset of macroscopic hematuria. The age at initial discovery of the urinary abnormality was between 3 and 13 years. The magnitude of proteinuria varied from 0.2 to 0.5 g/day. No patient showed renal functional deterioration. The urinary excretion of calcium and the ratio of calcium/creatinine in urine were normal in all patients. A cystoscopic examination was carried out in three patients (nos. 1, 3, and 4), which revealed left-sided unilateral renal bleeding. The proportion of isomorphic erythrocytes in the urine, evaluated by phase-contrast microscopy, was more than 80% in all patients, indicating that the hematuria was non-glomerular in origin. Discovery of the urinary abnormalities preceded truancy in three patients (nos. 1, 3, and 4). All patients exhibited anxiety from various physiological abnormalities resembling the clinical symptoms of orthostatic disturbances listed in Table 1. Systemic chronic diseases such as ane-

Table 1 Clinical and laboratory findings of the four adolescents with nutcracker syndrome (*LRV* left renal vein, *RBC* red blood cell, *ND* not done, *MC* minimal change)

Patient no.	Age/ sex	Initial discovery/ detection of urinary abnormalities	Urinary abnormalities	Isomorphic RBC (%)	Diameter of LRV (at hilar portion)	Pressure gradient (mmHg)	Development of collateral	Renal biopsy	Clinical symptoms	Age at onset of school absence	Duration of school absence	Complicating diseases
1	15 years/F	13 years/sudden onset of dark urine	Macroscopic hematuria	90	13 mm	8	Poor	ND	Abdominal pain,headache, tachycardia	12 years	3 years	None
2	16 years/M	6 years/ school urinalysis	Microscopic hematuria + proteinuria (0.5 g/day)	80	11 mm	ND	Well	MC	Abdominal pain, headache	10 years	3 years	Allergic rhinitis
3	14 years/F	8 years/s chool urinalysis	Microscopic hematuria + proteinuria (0.5 g/day)	86	7.4 mm	3	Poor	MC	Fainting, headache	10 years	4 years	None
4	12 years/F	3 years/mass screening	Microscopic hematuria + proteinuria (0.2 g/day)	92	10.5 mm	5	Poor	MC	Abdominal pain, tachycardia	8 years	4 years	None

Fig. 1 The representative ultrasonography findings of the left renal vein (*LRV*) in the transverse plain (patient no. 1). Significant dilatation of the LRV and the compressed LRV between the aorta (*A*) and the superior mesenteric artery (*SMA*) are observed

mia, collagen diseases, cardiovascular disease, hepatic diseases, gastrointestinal ulcer, endocrinological disease, metabolic diseases, and neoplasia were excluded by repeated laboratory examinations. Two patients (nos. 1 and 4) had tachycardia (90–110 beats/min in both) even while at rest. The duration of the truancy ranged between 3 and 4 years in all patients.

Identification of nutcracker syndrome by imaging techniques

US was performed on all patients. The representative findings of the LRV in the transverse plain are shown in Fig. 1 (patient no. 1). The diameter of the hilar portion of the LRV ranged from 7.5 to 13 mm, as shown in Table 1. Significant dilatation of the LRV in the hilar portion was identified in three patients (nos. 1, 2, and 4), while a compressed LRV between the aorta and the SMA was recognized in all patients.

MRA (patients 1, 2, and 4) or LRV venography (patients 1, 3, and 4) was carried out for a definite diagnosis of the nutcracker syndrome. The LRV was visualized by infusing gadolinium during the MRA examination. Figure 2 shows the dilated LRV observed in patient 1 (A), 2 (B), and 4 (C) by MRA. A significant dilatation of the LRV was observed in all patients. An imaging defect of the LRV portion was observed in patient 3. Collateral veins from the LRV were well developed in patient 2, while they were poor in patients 1 and 4. Fig. 3 shows the renal venography findings of the LRV in patients 1 (A) and 2 (B). In these patients, the development of side branches from the LRV was poor, but the ascending lumbar vein or gonadal vein were visible as the backflow veins in both patients. In patient 3, compression of the LRV portion diverging from the inferior vena cava (IVC) and the post-stenotic dilatation were detected by renal venography (not shown). The pressure gradient between the LRV and the IVC was measured in the three patients during renal venography. The results were 8 mmHg (no. 1), 3 mmHg (no. 3), and 5 mmHg (no. 4).

Renal biopsy

A renal biopsy was carried out in three patients (nos. 2, 3, and 4). There were no remarkable glomerular or interstitial injuries in any of the patients (data not shown). No deposition of immunoglobulins or complement components was observed in any part of the renal tissues.

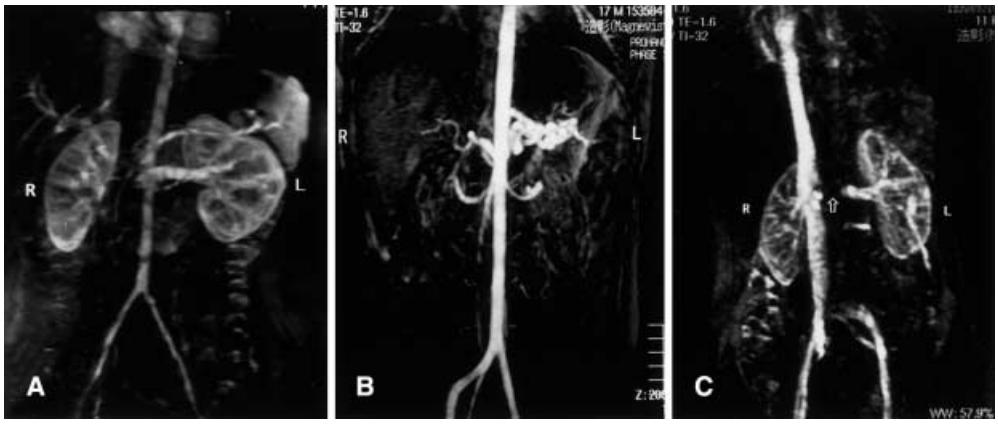

Fig. 2A–C Identification of the nutcracker syndrome by magnetic resonance angiography (MRA). The dilatation of the LRV is shown in all patients examined, and an imaging defect at the portal region of the LRV (*arrow*) is visible in patient no. 4 (**C**). The development of collateral veins from the LRV was observed only in patient no. 2 (**B**)

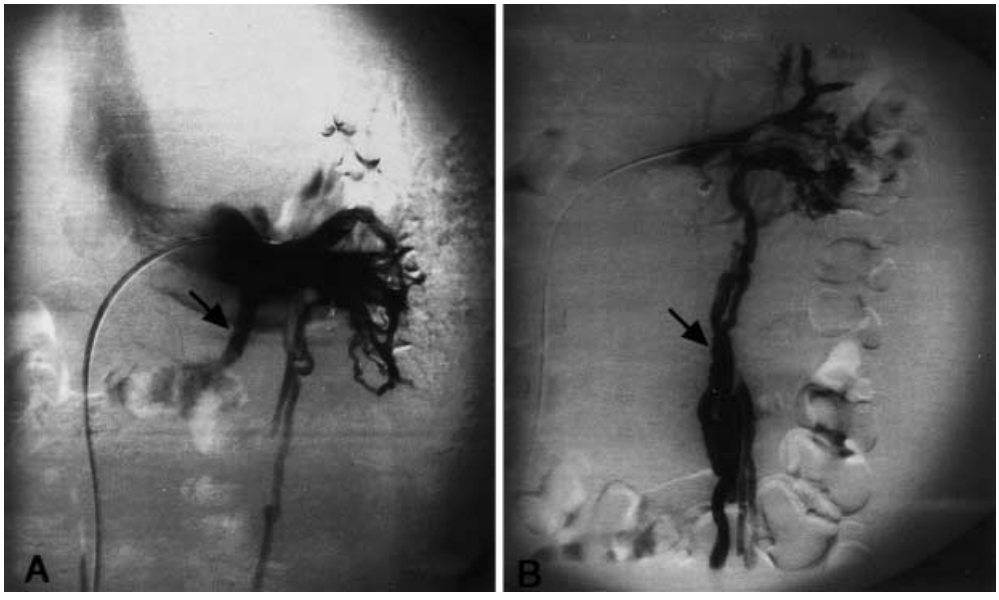

Fig. 3 Examination of the LRV in patient no. 1 (**A**) and patient no. 4 (**B**) by LRV venography. The compression of the main renal vein, and renal hilar varices, and the reflux into the gonadal vein (**A**, *arrow*) and/or ascending lumbar vein (**B**, *arrow*) are visible in both patients, but the collaterals are poorly developed

Clinical course

Despite the continuous pharmacotherapy for the orthostatic hypotension, all patients complained of various non-specific physical disturbances and persistent urinary abnormalities. They also continued to refuse to go to school.

Discussion

The nutcracker syndrome has been defined as a non-glomerular hematuria caused by compression of the LRV between the aorta and the SMA associated with periureteric varicosities [1, 2, 11]. This illness shows left-sided renal bleeding. An increased pressure in the LRV causes a rupture of the thin-walled septum, which separates the veins from the collecting system in the renal fornix [9]. Recent advances in imaging techniques, combined with erythrocyte morphological studies of urine, have led to early detection of this syndrome among patients showing idiopathic persistent hematuria [6, 7, 11]. This disease has been diagnosed using venographic imaging, which measures the pressure gradient between the LRV and the IVC, or intra-arterial digital substraction angiography [8, 12, 13]. Since these examinations are relatively invasive, a less-invasive method for diagnosing this syndrome is desirable. In this study, we utilized MRA to identify the nutcracker syndrome. MRA appears to be a safe and reliable method for diagnosing nutcracker syndrome.

The nutcracker syndrome is usually diagnosed following the discovery of microscopic hematuria and/or proteinuria during mass urinary screening, or a sudden onset of macroscopic hematuria [8, 9]. Some cases may have orthostatic proteinuria [10]. Three of our four patients had hematuria detected via mass urinary screening. The other visited us due to a sudden onset of macroscopic hematuria. Serious physical disturbances are usually lacking, except for minor lower abdominal and/or back pain, in most patients with this disease [8, 9, 14]. A recent report revealed that some patients with this syndrome fainted after standing or taking a bath, or suffered from motion sickness, loss of appetite, and gastrointestinal pain mimicking the symptoms of an orthostatic disturbance [15]. All of our patients also showed symptoms of an orthostatic disturbance. Furthermore, tachycardia

was noted in two patients (nos. 1 and 4) even at rest. A decreased venous blood flow back to the heart, due to congestion of blood in the LRV, may have caused the tachycardia or palpitations in these patients. The relationships between our patients and their parents, teachers, and friends were good. Therefore, psychological disorders were ruled out. Thus, the main reason for their refusal to attend school appears to be the non-specific physical disturbance related to the nutcracker phenomenon.

The resection of a pre-aortic fibrous tissue, a renocaval venous reimplantation, and placement of a synthetic wedge into the bifurcation of the SMA were effective procedures in improving the congestion of the LRV blood flow, which resulted in a complete resolution of the hematuria within several months [16]. An autotransplant convalescence or an artificial bypass from the LRV to the IVC was suggested for patients showing massive hematuria associated with abdominal pain [6]. In our patients, a surgical procedure may be needed for improving symptoms as well as urinary findings. We are cautious about recommending surgical treatment for our patients for the following reasons: surgery is not an established treatment for the nutcracker syndrome, and, according to the development of collateral veins from the LRV, their physical symptoms and truancy may resolve without intervention. However, if their physical ailments and truancy worsen, some treatment, including surgery, should be considered. Our findings provide evidence that the nutcracker syndrome causes serious physical discomfort, resulting in school absence.

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