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CASE REPORT

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Spontaneous remission of persistent severe hematuria in an adolescent with nutcracker syndrome: seven years' observation

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Abstract
A Japanese boy aged 14 years presented with gross hematuria associated with mild proteinuria and was diagnosed as having nutcracker syndrome. Magnetic resonance angiography (MRA) revealed significant compression of the left renal vein between the aorta and the superior mesenteric artery with collaterals. A percutaneous renal biopsy on the right kidney revealed no evidence of glomerular or interstitial changes with immune deposition. He was observed closely without any intervention thereafter. Although repeat MRA performed 4 years after our first observation disclosed the development of collateral veins, severe hematuria with an intermittent exacerbation remained unchanged. During the next 2 years, the hematuria completely subsided spontaneously. Although the etiology of spontaneous remission of the disease remains speculative, his good physical development (i.e., approximately 10 cm taller than his height at the onset) may change presumptive hemodynamic factors. These clinical observations suggest that a proportion of pubertal patients with nutcracker syndrome should be treated conservatively for a relatively long time.

Key words Adolescent · Gross hematuria · Nutcracker syndrome (phenomenon) · Physical development · Spontaneous remission

Introduction

Nutcracker syndrome refers to compression of the left renal vein (LRV) between the aorta and the superior mesenteric artery (SMA), leading to LRV hypertension and the formation of renal hilar varices.[1–4] This is an unusual but well accepted cause of hematuria. The etiology of this condition has been reported to result from abnormal branching of the SMA from the aorta.[1–4] Some of the patients with the syndrome suffering from recurrent gross hematuria with flank pain have been treated with surgical procedures (i.e., nephrectomy,[2] transposition of the LRV,[2,5] autotransplantation of the left kidney,[3] intravascular stent[6]). However, patients with mild, tolerable symptoms may be treated conservatively,[1] as the development of collateral veins with time may resolve the LRV hypertension.[7] Hence, invasive treatment for nutcracker syndrome is controversial, especially in patients with a pediatric onset. To our knowledge, there have been no reports of this syndrome describing clearly how long it takes for persistent hematuria to resolve spontaneously.

We report our experience about an adolescent case of nutcracker syndrome with persistent severe hematuria. His clinical symptoms completely subsided without intervention following 6 years of observation, during which time he grew approximately 10 cm taller than his height at the onset.

Case report

A previously well Japanese boy aged 14 years was referred to Hirosaki University Hospital because of hematuria and proteinuria detected by urine screening of school-children. At presentation, the physical examination revealed a well-developed boy [i.e., height 169 cm (+1.0 SD) and weight 58 kg (+0.5 SD)] without peripheral edema or a flank mass. His blood pressure was 122/50 mmHg, and no skin or mucosal lesions were observed. Urinalysis showed dark urine of specific gravity 1.025, protein 52 mg/dl, numerous red blood cells (RBCs) per high power field, and a sterile culture. The urinary β_2-microglobulin was slight increased to 320 μg/l (normal <300 μg/l). Laboratory studies revealed the following results: leukocyte count 6700/μl with a normal hemogram; hemoglobin 12.4 g/dl; hematocrit 38.1%; plate-

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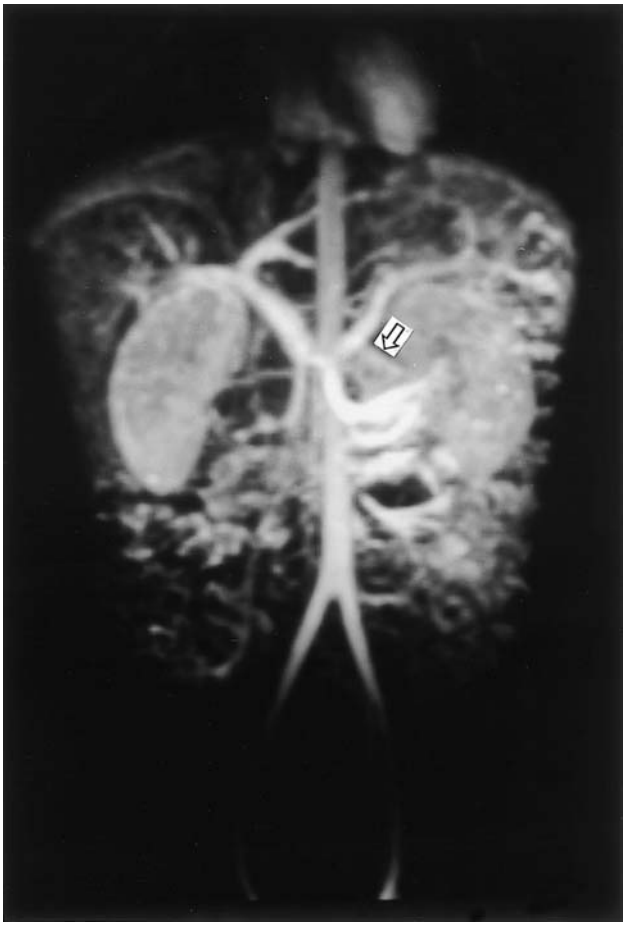

Fig. 1. Significant dilatation of the left renal vein (LRV) is visible by magnetic resonance angiography (MRA) (*arrow*). The development of collaterals from the left renal vein is not clear from this scan

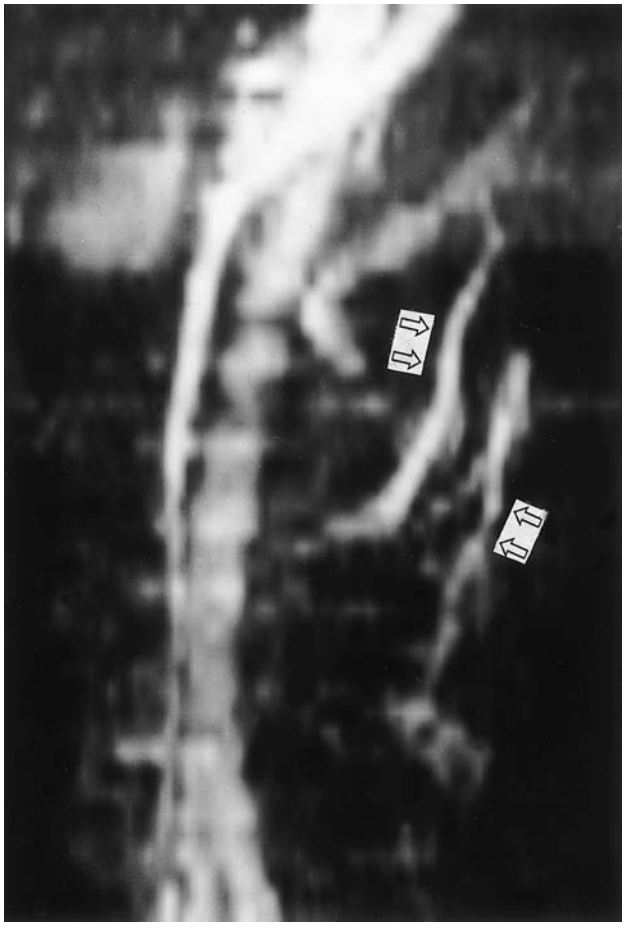

Fig. 2. Development of periureteral collateral veins (*arrows*) from the LRV with reflux into the gonadal vein, ascending lumbar vein, or both are clearly visible by repeat MRA

lets 189000/μl; serum total protein 6.9 g/dl; albumin 4.4 g/dl; total cholesterol 115 mg/dl; urea nitrogen 14 mg/dl; creatinine 0.8 mg/dl; sodium 143 mEq/l; potassium 4.2 mEq/l; chloride 107 mEq/l; and C-reactive protein 0.1 mg/dl. Immunological studies revealed the following results: immunoglobulin G (IgG) 811 mg/dl; IgA 78 mg/dl; IgM 89 mg/dl; C3 80 mg/dl (normal 70–130 mg/dl); antistreptolysin O 34 U/ml (normal 0–210 U/ml); and antinuclear antibody <1:20. The creatinine clearance was 134.0 ml/min/1.43 m^2. A total of 60% of RBCs were isomorphic according to a morphologic study of urinary RBCs.

The diameter of the hilar portion of the LRV measured by ultrasonography was 7.2 mm with compression between the aorta and the SMA. Intravenous pyelography and abdominal computed tomography (CT) disclosed no definite evidence of renal or urinary tract abnormalities that would cause renal bleeding. Magnetic resonance angiography (MRA) for a differential diagnosis of the nutcracker syndrome[7–9] disclosed significant dilatation of the LRV with the development of collaterals and the ascending lumbar vein as the back-flow vein (Fig. 1). Because of its invasive nature, angiography to measure the pressure gradient between the LRV and the inferior vena cava (IVC) and urethrocystoscopy were not performed.

In a search for underlying glomerulonephritis, percutaneous renal biopsy was performed on the right kidney. There were no remarkable glomerular or interstitial changes, and there was no evidence of immune deposition or thin basement membrane disease. Thus, the diagnosis was probable nutcracker syndrome.

The patient was observed conservatively thereafter. Although repeat MRA performed 4 years after our first observation disclosed the development of collaterals (Fig. 2), the severe hematuria with intermittent exacerbations remained unchanged. Despite the syndrome, he did not complain of any disabilities, and he grew well; that is, he was approximately 10 cm taller than he was at the onset. During the next 2 years the urine abnormalities completely subsided spontaneously. At present, 7 years after our first observation, he is free from urinary abnormalities. Because of the complete remission, no further MRA was carried out.

Discussion

Idiopathic persistent hematuria with intermittent exacerbations is a common clinical hallmark of glomerulonephritis,

whereas nutcracker syndrome has been reported to be an important cause of nonglomerular hematuria.[1–4] Although the precise mechanism of hematuria due to the syndrome remains unclear, it has been presumed that compression of the LRV results in LRV hypertension, leading to the development of collaterals with intrarenal and perirenal varicosities, which can cause hematuria if the thin-walled septum separating the veins from the collecting system ruptures.[9] Because of recent advances in imaging techniques,[7–9] early detection of the syndrome has been reported.[7] However, to our knowledge, a diagnostic criteria of nutcracker syndrome has not been definitively established as a cause of left-sided hematuria.[1–4,7–9]

Our patient was detected by mass urinary screening for school children because of the sudden onset of gross hematuria. Despite an intensive search for its cause by CT, MRA, and renal biopsy, no remarkable findings were observed except severe compression of the LRV. Thus, he was diagnosed as having probable nutcracker syndrome resulting in severe hematuria. We also must emphasize the importance of early inclusion of nutcracker syndrome in the differential diagnosis of glomerulonephritis using the noninvasive procedure MRA. When a patient shows sudden onset of dark urine, MRA should be routinely carried out.[9]

Because the severe compression of the LRV between the aorta and the SMA causes left-sided renal bleeding, a proportion of patients with the syndrome have undergone surgical procedures[2–6] to decrease the pressure gradient between the LRV and the IVC. However, surgical treatment is substantially invasive and has not been established as the gold standard.[7] Moreover, the development of collateral veins from the LRV with time may resolve the pressure gradient between the major veins, although how long this takes is uncertain. Treatment of nutcracker syndrome remains controversial.[1–4,6]

Our patient was treated conservatively over a period of 6 years. Despite the substantial development of collaterals, which was confirmed by sequential MRA performed at the initial presentation and then again 4 years after the first MRA, his persistent, severe hematuria remained unchanged. Ultimately, the urine abnormalities completely subsided spontaneously over the 6 years after our first observation. Although the etiology of complete remission remains speculative, we think that his good physical development (i.e., approximately 10 cm taller than at the onset), which allows resolution of presumptive hemodynamic factors except for the development of collaterals, might be attributable. Based on his clinical course, we think that many pubertal patients with nutcracker syndrome can be treated conservatively for a relatively long time because spontaneous remission with time may be expected when the patient shows at least good physical development.

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