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ORIGINAL ARTICLE

Left renal vein entrapment: a frequent feature in children with postural proteinuria

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Abstract In most Asian subjects with postural proteinuria, ultrasonic imaging and Doppler flow scanning disclose entrapment of the left renal vein in the fork between the aorta and the superior mesenteric artery. Little information is available on the possible occurrence of left venal rein entrapment in European subjects with postural proteinuria. Renal ultrasound with Doppler flow imaging was therefore performed on 24 Italian or Swiss patients with postural proteinuria (14 girls and ten boys, aged between 5.2 years and 16 years). Signs of aorto-mesenteric left renal vein entrapment were noted in 18 of the 24 subjects. In conclusion, aorto-mesenteric left renal vein entrapment is common also among European subjects with postural proteinuria.

Keywords Aorto-mesenteric left renal vein entrapment · Postural proteinuria · Proteinuria

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Introduction

Postural proteinuria is a common and benign condition characterized by increased protein excretion when individuals are in the upright position, but normal protein excretion when they are in the supine position [1, 2].

The etiology of postural proteinuria is poorly understood. In most Asian [3–6] subjects with postural proteinuria real-time ultrasonic imaging and Doppler flow scanning demonstrate entrapment of the left renal vein in the fork between the abdominal aorta and the proximal superior mesenteric artery, close to its origin (before the vein merges into the inferior vena cava). In addition, left renal vein entrapment has been demonstrated in three Turkish children [7, 8] and in a Swiss man [9]. It has been therefore suggested that partial obstruction of the flow in the left renal vein in the upright position alters glomerular microcirculation, leading to increased protein filtration [10].

The purpose of the our study was to investigate the frequency of aorto-mesenteric left renal vein entrapment, subsequently referred to as left renal vein nutcracker phenomenon [11], in a case series of Italian and Swiss children with postural proteinuria.

Patients and methods

Between 2001 and 2008, renal ultrasonic imaging and Doppler flow scanning were performed on a routine basis on 24 consecutive children and adolescents with postural proteinuria (14 girls and ten boys, aged from 5.2 years to 16 years, median 14 years). A complete physical examination of the patients failed to disclose pathological findings, and both systolic and diastolic blood pressure were <90th centile for gender, age, and height [12]. Furthermore, the urine sediment did not disclose hematuria (defined as more than five red blood cells per high power field) or cell casts, and circulating creatinine levels were normal. The diagnosis of postural proteinuria was based on the determination of the urinary total protein-to-creatinine ratio in two untimed urine samples collected in the morning immediately after the subjects had risen ("supine") and after they had been standing for at least 60 min ("standing"), respectively. The upper reference value for the urinary total protein-to-creatinine ratio is 30 mg/mmol.

The patients' body mass index was calculated as the body weight in kilograms divided by squared height in meters and subsequently plotted on the body mass index-for-age charts developed by the National Center for Health Statistics [13].

Renal ultrasonic imaging and Doppler flow scanning of the 24 patients were performed while they were in the supine position. The antero-posterior diameter and the peak flow velocity of the left renal vein were measured at the hilar and aorto-mesenteric portions to detect the possible occurrence of a compression in the fork between the abdominal aorta and the proximal superior mesenteric artery before the vein merges. The diagnosis of left renal vein nutcracker phenomenon was made when the antero-posterior diameter at the hilar portion divided by that at the aorto-mesenteric portion (= diameter ratio) or when the peak flow velocity at the aorto-mesenteric portion divided by that at the hilar portion (= flow velocity ratio) were >4.0 [5]. The cut-off values of 4.0 for both the diameter ratio and the flow velocity ratio represent the mean + 2 standard deviations (SD) obtained in healthy children and adolescents. The values are almost identical to the mean + 2 SD reported by Cho et al. [5].

The two-tailed Mann–Whitney–Wilcoxon test for two independent samples, the χ^2 test, and simple regressions with the Spearman rank correlation coefficient were used for analysis. The results are given either as median and interquartile range (which extends from the value at the 25th to that at the 75th centiles and includes half of the data points) or as relative frequency. Statistical significance was defined as a P value of <0.05.

Results

In the 24 patients the "standing" total protein-to-creatinine ratio was pathologically increased and ranged between 44 mg/mmol and 601 mg/mmol, median 91 mg/mmol. The "supine" urinary total protein-to-creatinine ratio was normal and ranged between 2.1 mg/mmol and 29 mg/mmol, median 15 mg/mmol. The age- and gender-specific body mass index varied between the 6th and the 54th centiles, median 19th centile.

Ultrasonic imaging and Doppler flow scanning disclosed signs of aorto-mesenteric left renal vein entrapment in 18 of the 24 patients (75%). The diameter ratio and the flow velocity ratio were both >4.0 in 13 patients, the flow velocity ratio was >4.0 (but the diameter normal) in three, and the diameter ratio was >4.0 (but the flow velocity normal) in two patients. The diameter ratio and the velocity ratio were both normal, i.e. <4.0, in the remaining six patients. Children with and without evidence of left renal vein nutcracker phenomenon did not significantly differ with respect to female-to-male ratio, age, body mass index, blood pressure, plasma creatinine and standing or supine urinary protein excretion, as given in Table 1. In the 24 patients no significant correlation was noted between standing urinary protein excretion and either diameter ratio or flow velocity ratio.

Discussion

Aorto-mesenteric left renal vein entrapment, first reported more than 50 years ago, is a recognized cause of left renal

Table 1 Clinical and laboratory data of 24 children or adolescents affected by postural proteinuria with and without left renal vein nutcracker phenomenon. The results are given either as medians (with interquartile ranges between brackets) or as relative frequency

Parameter	Nutcracker phenomenon present	Nutcracker phenomenon absent
Number	18	6
Gender, girls:boys	10:8	4:2
Age, years	14 [13–15]	14 [12–15]
Body mass index, centile	22 [15–26]	16 [15–23]
Blood pressure		
Systolic, centile	40 [12–57]	45 [25–60]
Diastolic, centile	35 [11–50]	32 [20–55]
Plasma creatinine, μmol/l	65 [59–71]	61 [66–74]
Urinary total protein-to-creatinine ratio		
Supine, mg/mmol	14 [5.3–19]	15 [10–17]
Standing, mg/mmol	94 [74–145]	122 [75–152]

venous hypertension leading to the development of collateral veins with intrarenal and perirenal varicosities [10]. The main presenting features are recurrent gross hematuria, with or without left flank pain. Some patients present with left flank pain alone, and, in a few, varicocele is the only complaint [10].

More recently, left renal vein nutcracker phenomenon has been noted in more than 70% of approximately 100 Asian subjects with postural proteinuria [3–6]. The results of our study demonstrated that in rather slender Italian and Swiss subjects with postural proteinuria, real-time ultrasonic imaging and Doppler flow scanning disclosed signs of aorto-mesenteric left renal vein entrapment in three-quarters of them.

Retrograde phlebography with reno-caval pressure gradient measurement is the recognized gold standard for establishing the diagnosis of left renal vein nutcracker phenomenon [10]. Ultrasonic imaging and Doppler flow scanning, which have the advantage of being non-invasive and radiation free, are currently the single imaging technique for almost all patients with postural proteinuria [3–6]. The presently used ultrasonic imaging and Doppler evaluation techniques are not uniform and do not accurately quantify reno-caval pressure gradient but differentiate between critical and non-critical left renal vein nutcracker phenomenon. Sometimes, however, there is a considerable difference between estimates of left renal vein nutcracker by ultrasonic imaging or Doppler flow scanning and reno-caval pressure gradient [10].

The mechanisms underlying postural proteinuria are not well understood. In addition to left renal vein nutcracker phenomenon, the following mechanisms have been suggested: (a) since proteinuria increases with assumption of the upright posture in unaffected subjects, even though protein excretion remains within the normal range, postural proteinuria might sometimes represent an amplification of this response; (b) since renal biopsies show some minor glomerular lesions, including focal mesangial hypercellularity or basement membrane thickening in selected subjects with postural proteinuria, these minor alterations might require a superimposed hemodynamic abnormality to lead to postural proteinuria; (c) finally, postural proteinuria might be the consequence of an exaggerated release of angiotensin II and norepinephrine following the assumption of the upright position [1, 2]. In a Korean adolescent with left renal vein nutcracker phenomenon, postural proteinuria disappeared after the release of angiotensin II was blocked with a converting enzyme inhibitor [14–16]. This interesting observation indicates that sometimes at least two not mutually exclusive mechanisms underlie postural proteinuria.

In conclusion, left renal vein nutcracker phenomenon is frequent both in Asian and European subjects with postural proteinuria. We suggest that ultrasonic imaging and Doppler flow scanning might be useful in these subjects to evaluate whether left renal vein nutcracker phenomenon is implicated or not.

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