









Case Report

An Unusual Etiology of Proteinuria and Hematuria in a Case with IgA Vasculitis Nephropathy: Nutcracker Syndrome

IgA Vaskülitli nefriti Tanılı bir Olguda Proteinüri ve Hematürinin Farklı bir Nedeni: Nutcracker Sendromu

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ABSTRACT

IgA vasculitis is the most frequent type of vasculitis in children and progresses with the involvement of skin, gastrointestinal system, joints and glomerulonephritis. The most frequent findings of IgAV nephritis are microscopic hematuria and proteinuria ranging from trace amounts to nephrotic levels. The nutcracker syndrome (NCS) is a phenomenon that refers to compression of the left renal vein between the abdominal aorta and superior mesenteric artery. The presenting manifestations are hematuria, orthostatic proteinuria, abdominal pain or left flank pain. Herein we reported a case diagnosed with NCS with regard to persistent microscopic hematuria, intermittent macroscopic hematuria and a fluctuating proteinuria in non-nephrotic levels during the follow up of IgA vasculitis nephritis. A 4,5 year-old boy with rashes extending from the dorsal foot to the sacral regions, arthritis of the ankles and abdominal pain had been admitted to hospital and diagnosed with IgA vasculitis. The total urine analysis revealed +3 proteinuria, and +2 erythrocyte. Nephrotic range of proteinuria was detected in 24-hour urine analysis. The renal biopsy was in accordance with grade II IgA vasculitis nephritis according to the ISKDC classification. The patient was started on an ACE inhibitor and fish oil. In further follow-up, intermittent microscopic hematuria and non-nephrotic range of proteinuria reappeared. The amount of proteinuria was measured in the urine collected during the daytime and the nighttime urine and it was observed that the proteinuria was orthostatic. The patient was re-evaluated regarding etiologies for proteinuria and hematuria. Renal Doppler ultrasonography revealed that the angle between the abdominal aorta and SMA was 14 degrees. Abdominal computed tomography angiography demonstrated that the left renal vein was trapped between aorta and SMA, so the case was diagnosed with NCS. In conclusion, non-glomerular etiologies should be kept in mind in the differential diagnosis of patients with hematuria and/or proteinuria although they are being followed for glomerular pathologies.

Keywords: Proteinuria, hematuria, Nutcracker syndrome, IgA vasculitis nephritis

ÖZET

IgA vaskülit, çocuklarda en sık görülen vaskülit türüdür. Bu vaskülit, IgA nefropatisine benzer şekilde deri, gastrointestinal sistem, eklem ve glomerülonefrit tutulumu ile ilerler. IgAV nefritinin en sık bulgusu mikroskobik hematüridir. Bazı durumlarda eser miktardan nefrotik seviyelere kadar değişen proteinüri de izlenebilmektedir. Nutcracker sendromu, sol renal venin abdominal aorta ile superior mezenterik arter arasında sıkışması sonucu gelişen bir fenomendir. Başlıca bulguları; hematüri, ortostatik proteinüri, karın ağrısı veya sol yan ağrı

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sıdır. Burada IgA vaskülitisi nefriti tanısı ile takibi sırasında persistan mikroskobik hematüri, aralıklı makroskopik hematüri ve non-nefrotik proteinüri ile Nutcracker Sendromu tanısı konan bir olguyu sunduk. 4,5 yaşındaki erkek çocuk; ayak dorsalden sakral bölgeye uzanan döküntü, ayak bileklerinde ağrı ve karın ağrısı şikayetleri ile başvurdu. IgA vaskülitisi tanısıyla izleme alınan olgunun tam idrar analizinde +3 protein, +2 eritrosit saptandı. 24 saatlik idrar analizinde nefrotik düzeyde proteinüri (54mg/m²/saat) tespit edildi. Nefrotik düzeyde proteinüri gelişimi nedeni ile olguya böbrek biyopsisi yapıldı. Böbrek biyopsisi ISKDC sınıflamasına göre evre II IgA vaskülitisi nefriti ile uyumlu saptandı. Olguya ACE inhibitörü ve balık yağı tedavileri başlandı. İzlemlerde persistan mikroskopik hematüri, aralıklı tekrarlayan makroskopik hematüri ve non- nefrotik düzeyde proteinüri izlenen olgu, etyolojiye yönelik yeniden değerlendirildi. Gündüz saatlerinde toplanan idrardan ölçülen proteinüri miktarı 8,6 mg/m²/s, gece idrarından ölçülen proteinüri miktarı ise 2,6 mg/m²/saat olarak ölçülerek proteinürinin ortostatik nitelikte olduğu görüldü. Renal doppler ultrasonografide abdominal aorta ile SMA arasındaki açının 14 derece olduğu görüldü. Abdominal bilgisayarlı tomografi anjiyografisinde sol renal venin aort ile SMA arasında sıkıştığı görülünce olguya NCS tanısı konuldu. Sonuç olarak, hematüri ve/veya proteinürisi olan hastaların glomerüler patolojiler nedeniyle takip edilmelerine rağmen ayırıcı tanısında glomerüler dışı etiyolojiler akılda tutulmalıdır.

Keywords: Proteinüri, hematüri, Nutcracker sendromu, IgA vaskülitisi nefriti

INTRODUCTION

IgA vasculitis (IgAV) is the most frequent type of vasculitis in children and is characterized by the storage of IgA1 dominant immune deposits usually found in capillaries, arterioles and venules. This vasculitis progresses with the involvement of skin, gastrointestinal system, joints and glomerulonephritis similar, with IgA nephropathy (1,2). The renal involvement is usually seen in more than one out of three patients (20-55%) and observed in 30-40% of patients 4-6 weeks after the beginning of IgAV (3). The most frequent finding of IgAV nephritis is microscopic hematuria. In some cases, there may be proteinuria ranging from trace amounts to nephrotic levels. Macroscopic hematuria is also present, among other symptoms. Despite the rarity of progression to chronic renal failure in some cases, renal involvement may be seen in late periods (4). It may be seen in 85% of the patients in the first four weeks, 91% of the patients in the first six weeks and in 97% of the patients in six months. Therefore, it is advised to follow cases with IgAV for at least six months for renal involvement (5).

The nutcracker syndrome (NCS) is a phenomenon that refers to compression of the left renal vein (LRV) between the abdominal aorta and the superior mesenteric artery (SMA). The presenting manifestations are hematuria (often microscopic), orthostatic proteinuria, abdominal pain or left flank pain, varicocele and gynecological symptoms, including dyspareunia and dysmenorrhea (6,7).

Herein we reported a case surprisingly diagnosed with NCS due to intermittent macroscopic hematuria, persistent microscopic hematuria and fluctuating orthostatic proteinuria during the follow up for IgAV nephritis.

Case Report

A 4,5-year-old boy with rashes extending from dorsal foot to the sacral regions, edema on feet, arthritis of the ankles, abdominal pain and bloody diarrhea had been admitted to another clinic and diagnosed with IgAV. He was referred to our clinic for further examination with the suspicion of renal involvement of IgAV.

On admission, his total body weight was 19 kg (50-75p), height was 112cm (50-75p), blood pressure was 90/54 mmHg (<95p/<95p). There were purpuric rashes on the lower extremities and gluteal regions and no other pathology was detected in physical examination.

The laboratory analyses were as follows: hemoglobin: 13g/dL, MCV: 87.9 fL, Platelet count: 450K/uL, APTT:18.5 s, PZ:11.3 s, INR:0.98. Erythrocyte sedimentation rate: 2mm/h, C-reactive protein: 0.1mg/L. Renal function tests and hepatic enzymes were in normal ranges. The total urine analysis revealed +3 proteinuria, +2 erythrocyte. Nephrotic range of proteinuria (54mg/m²/h) was detected in 24-hour urine analysis. Diffuse dysmorphic erythrocytes were detected in urine microscopy. The size, echogenicity and parenchymal thicknesses were normal for both right and left kidneys in abdominal ultrasonography. Renal biopsy revealed 75 glomeruli, some of which had minimal segmental mesangial cell proliferation. There was no sclerosis or hyalinization. Mesangial granular C3 (++) and IgA (++)/+++ deposits were detected in the immunofluorescence staining. The renal biopsy was in accordance with grade II IgAV nephritis according to the ISKDC classification. Angiotensin-converting enzyme inhibitor and fish oil were prescribed. During the one-year follow-up, microscopic hematuria was resumed although there was no macroscopic hematuria or proteinuria. The fish oil was stopped at the end of the first year. In further follow up when the patient was eight years old, inter-

ge of proteinuria reappeared. He had no complaints and there were not any pathological findings in physical examination. His body weight was 28 kg (50-75p and his height was 125 cm (25-50 p). The patient was re-evaluated regarding etiologies for proteinuria and persistent microscopic hematuria. The protein excretion measures were: 8.6 mg/m²/h for daytime and 2.6 mg/m²/h for nighttime compatible with orthostatic proteinuria. In urine examinations to differentiate glomerular and non-glomerular hematuria, diffuse isomorphic erythrocytes were detected. Renal Doppler ultrasonography revealed that the radius of proximal LRV between SMA and mesenteric region of aorta was 1.3 mm, the radius of the distal LRV between SMA and hilus was 7.2 mm with distal/proximal ratio above 4 and the angle between abdominal aorta and SMA was 14 degrees. The case was considered to be compatible with NCS. Abdominal computed tomography angiography was performed to confirm the diagnosis in this patient, who had a previous history of glomerular disease and presented with proteinuria. The angiography demonstrated that the LRV was trapped between aorta and SMA, so the case was diagnosed with NCS (Figures 1-2). The parents' of this patient consent was obtained for this study.



Figure 1. Left renal vein between aorta and SMA



Figure 2. Left renal venous congestion due to compression between aorta and SMA

DISCUSSION

Nutcracker syndrome is a rare anatomic condition secondary to entrapment of the LRV between the aorta and SMA. It usually presents with macroscopic or microscopic hematuria, orthostatic proteinuria, pelvic congestion, left varicocele, left flank pain, dysuria, dysmenorrhea, varicose vein formation at lower extremities and gluteal regions, and abdominal pain. The most frequent finding in NCS is hematuria, usually seen as microscopic and sometimes macroscopic attacks. The cause of hematuria seems to be the tearing of venular walls due to the increased pressure at the level of renal calyces (1,2,8). In the three-year follow up of our case diagnosed with IgAV nephritis, intermittent attacks of macroscopic hematuria, the persistence of microscopic hematuria and the presence of isomorphic erythrocytes necessitate searching for non-glomerular causes of hematuria. When vascular etiologies were evaluated, present hematuria and proteinuria were associated with NCS.

Orthostatic proteinuria is also observed in five to 10% of patients with NCS but the less frequent than hematuria (9). The etiology of the protein leakage from the calyceal system is increased pressure. Orthostatic proteinuria is the most frequent reason for persistent proteinuria among school children and adolescents (10). The presence of proteinuria in the non-nephrotic range at the upright position is called 'orthostatic proteinuria.' It may be related to the glomerular hemody-

dynamic changes and partial obstruction of the renal vein. The entrapment of LRV between the aorta and SMA was detected in 68% of the cases having orthostatic proteinuria (11). In our case, there was no protein excretion for the first year; however, he presented with intermittent proteinuria in non-nephrotic levels compatible with orthostatic proteinuria during the follow-up for IgAV nephritis.

Many patients with NCS tend to have a lower body mass index (12,13). It is believed that retroperitoneal fat widens the aortomesenteric angle and causes remission of symptoms (14-17). However, body mass index of our case was in normal percentiles.

In conclusion, to our knowledge, this is the first case with NCS is accompanied by IgAV nephritis reported in the literature. The non-glomerular etiologies should be kept in mind in the differential diagnosis in patients with hematuria and/or proteinuria, although they are being followed with known glomerular pathologies.

Conflict of Interest / Çıkar Çatışması

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REFERENCES

- Batu ED, Özen S. Pediatric vasculitis. *Curr Rheum Rep* 2012; 14: 121-9.
- Jennette JC, Falk RJ, Bacon PA, Basu N, Cid MC, Ferrario F, et al. 2012 revised International Chapel Hill Consensus Conference Nomenclature of Vasculitides. *Arthritis Rheum* 2013; 65: 1-11.
- Kiryuk K, Moldoveanu Z, Sanders JT, Eison TM, Suzuki H, Julian BA, et al. Aberrant glycosylation of IgA1 is inherited in both pediatric IGA nephropathy and Henoch-Schonlein purpura nephritis. *Kidney Int* 2011; 80: 79-87.
- Chen JY, Mao JH. Henoch-Schönlein purpura nephritis in children: incidence, pathogenesis and management. *World J Pediatr* 2015; 11: 29-34.
- Pohl M. Henoch- Schönlein Purpura nephritis. *Pediatr Nephrol* 2015; 30: 245-52.
- Gulleroglu K, Gulleroglu B, Baskin E. Nutcracker syndrome. *World J Nephrol* 2014; 3: 277-81.
- Berthelot JM, Douane F, Maugars Y, Frampas E. Nutcracker syndrome: A rare cause of left flank pain that can also manifest as unexplained pelvic pain. *Joint Bone Spine*. 2017; 84: 557-62.
- Lopatkin NA, Morozov AV, Lopatkina LN. Essential renal haemorrhages. *Eur Urol* 1978; 4: 115-9.
- Ekim M, Ozçakar ZB, Fitoz S, Soygür T, Yüksel S, Acar B, et al. The "nutcracker phenomenon" with orthostatic proteinuria: case report. *Chin Nephrol* 2006; 65: 280-3.
- De Schepper A. "Nutcracker" phenomenon of the renal vein and venous pathology of the left kidney. *J Belge Radiol* 1972; 55: 507-11.
- Mazzoni MB, Kottanatu L, Simonetti GD, Ragazzi M, Bianchetti MG, Fossali EF, et al. Renal vein obstruction and orthostatic proteinuria: a review. *Nephrol Dial Transplant* 2011: 1786-807.
- He Y, Wu Z, Chen S, Tian L, Li D, Li M, et al. Nutcracker Syndrome- how well do we know it? *Urology* 2014; 83: 12-7.
- Kurlisky AK, Rooke TW. Nutcracker phenomenon and nutcracker syndrome. *Mayo Clin Proc* 2010; 5: 552-9.
- Shin JI, Park JM, Lee JS, Kim MJ. Doppler ultrasonographic indices in diagnosing nutcracker syndrome in children. *Pediatr Nephrol* 2007; 22: 409-13.
- Shaper KR, Jackson JE, Williams G. The nutcracker syndrome: an uncommon cause of haematuria. *Br J Urol* 1994; 74: 144-66.
- Alaygut D, Bayram M, Soylu A, Cakmakci H, Türkmen M, Kavukcu S. Clinical course of children with nutcracker syndrome. *Urology*. 2013; 82: 686-90.
- Kavukcu S, Kasap B, Göktay Y, Seçil M. Doppler sonographic indices in diagnosing the nutcracker phenomenon in a hematuric adolescent. *J Clin Ultrasound* 2004; 32: 37-41.