Nutcracker Syndrome Mimicking Familial Mediterranean Fever

Ailesel Akdeniz Ateşini Taklit Eden Nutcracker Sendromu

Özet
Nutcracker sendromu sol renal venin abdominal aorta ve superior mezenterik artery arası sıkışması sonucu oluşan nadir görülen bir sendromdur. Burada 18 yaşında Ailesel akdeniz ateşi tanılı Nutcracker sendromu vakası sunulmaktadır.

Anahtar Kelimeler
Amiloidoz; Tuzak; Nutcracker Sendromu

Abstract
The Nutcracker syndrome (NCS) is a rare entrapment syndrome caused by compression of the left renal vein (LRV) between the abdominal aorta and the superior mesenteric artery. We present a case of Nutcracker syndrome in an 18-year-old patient with Familial Mediterranean fever.

Keywords
Amyloidosis; Entrapment; Nutcracker Syndrome

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Corresponding Author: Atalay Dogru, İç Hastağıklar Anabilim Dalı, Romatoloji Bilim Dalı, Süleyman Demirel Üniversitesi Tıp Fakültesi, İsparta, Türkiye.
GSM: +905063698747 F: +90 2462112830 E-Mail: atalay_dogru@hotmail.com
Introduction

Familial Mediterranean fever (FMF) is an autosomal recessive disease that is characterized by episodes of fever and serositis. Amyloidosis is one of the most important complications of the disease and proteinuria is the first symptom of amyloidosis [1]. The Nutcracker syndrome (NCS) is a rare entrapment syndrome caused by compression of the left renal vein (LRV) between the abdominal aorta and the superior mesenteric artery [2]. The symptoms vary from asymptomatic hematuria to severe congestion. The most common symptom is hematuria and/or proteinuria due to elevated LRV pressure. Symptoms are exacerbated by physical activity. Most symptomatic patients are in the second and third decades of life. Nutcracker syndrome can be confused with other causes of proteinuria [3]. Here we present a case of Nutcracker syndrome in an 18 year-old-patient with FMF.

Case Report

An 18-year-old male patient with FMF, who was diagnosed with episodic fever, abdominal pain, and M694V heterozygote mutation seven years earlier, was admitted to our clinic for sustained mild proteinuria. Colchicine treatment had been initiated seven years earlier and complete response was observed. He had suffered left flank pain exacerbated by physical activity 1-2 times per week for 6 months. Colchicine dosage was increased from 1.5 gr/day to 2 gr/day. 1+ proteinuria by dipstick test in the daytime urine and 350 mg/day of proteinuria were detected by 24-hour urine specimen. Physical examination was unremarkable. Laboratory investigations showed: sedimentation rate 12 mm/ h, CRP 3 mg / L (N: 0-5), serum amyloid A 5.6 mg/L (N:0-6.4), creatinine 0.8 mg / dL, total protein 7.1 g / dL, albumin 4.5 g / dL, and LDL 189. There were no clinical or laboratory findings suggestive of amyloidosis. Renal ultrasonography (USG) was performed to elucidate the other causes of proteinuria. In USG, the left renal vein was compressed and the left renal vein flow was reduced. Computed Tomography angiography was performed to show vascular structure. LRV was compressed between the aorta and the superior mesenteric artery (Figure 1-2). The distance was measured as 3.8 mm and the angle was 18 degree between the aorta and the superior mesenteric artery (Figure 3). The patient was diagnosed with Nutcracker syndrome. Interventional procedures were not applied because of mild symptoms. There were not severe symptoms such as severe unrelenting pain, severe hematuria, or renal insufficiency. Conservative treatment was recommended. There was no significant increase in proteinuria found at his 6 months follow-up.

Discussion

Nutcracker syndrome, which describes compression of the left renal vein between the aorta and the superior mesenteric artery, is characterized by intermittent hematuria with or without left flank pain. Clinical manifestations vary from asymptomatic hematuria to severe congestion. Hematuria is the most common symptom due to increased LRV pressure, leading to the development of collateral veins. Rupture of the thin-walled septum between the collateral veins and the collecting system causes hematuria [2]. Flank pain and abdominal pain are common symptoms that are exacerbated by physical activity and...
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exercise and radiates to the thigh or gluteus region. Pain is induced by inflammatory cascade triggered by venous congestion. Varicocele, seen in 5.5%-9.5% of men, usually occurs on the left side due to high LRV pressure and collateral circulation. NCS also causes mild to moderate proteinuria. The degree of proteinuria is variable and orthostatic proteinuria is common [4].

Entrapment of the left renal vein is one of the most common causes of orthostatic proteinuria. The pathophysiology of proteinuria is not fully understood. In a case with orthostatic proteinuria, the left kidney was found to be the source of proteinuria with bilateral ureteral catheterization [5]. In another case with Nutcracker syndrome, treatment of angiotensin-converting enzyme (ACE) inhibition was found to improve the proteinuria level. In this case, a left kidney biopsy was performed, but there were no significant abnormalities. The increase in the level of angiotensin 2 with compression of the renal vein is thought to cause proteinuria [6].

The normal angle between the SMA and the abdominal aorta is almost 51 ± 25º and the distance is 16 ± 6 mm in normal adults. Doppler ultrasonography, computed tomography angiography (CTA), magnetic resonance angiography (MRA), and retrograde venography are required to diagnose NCS. Doppler ultrasonography is the initial imaging method for the diagnosis of NCS because it is inexpensive, easy to apply, and non invasive. Doppler ultrasonography has a sensitivity of 78% and a specificity of 100% [4]. CTA and MRA provide detailed renal vein and SMA anatomy. Retrograde venograph is the gold standard imaging method. It is not usually performed because it is an invasive test [7].

The treatment of NCS should be based on the severity of symptoms, the patient's age, and the stage of the syndrome. Treatment options range from observation to nephrectomy. Conservative treatment is recommended for mild symptoms. Especially in patients younger than 18 years, seventy-five percent of patients with hematuria recover without medication. ACE inhibitors may be used to improve the proteinuria level. Surgical interventions, such as nephropexy, intravascular stent implantation, transposition of the LRV or SMA, gonadocaval bypass, renal autotransplantation, and nephrectomy, are used for severe symptoms [8].

In conclusion, NCS should be considered when proteinuria develops with or without hematuria in FMF patients. Especially in patients with normal acute phase reactants, flank pain, and unfavorable response to colchicine, proteinuria may be the manifestation of NCS. NCS should be considered in the differential diagnosis of amyloidosis.

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Conflict of Interests
The authors declare that there are no conflicts of interest.

References

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