Case Report /Olgu Sunumu
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Jeune Syndrome with Proteinuria: A Case Report

Proteinüri ile İzlenen Bir Jeune Sendromu Olgusu

Nurcan Cengiz, Buket Kılıçaslan*, Tuba Canpolat, Şenay Demir***, Aytül Noyan**

Başkent Üniversitesi, Adana Uygulama ve Araştırma Merkezi, Pediatrik Nefroloji Bilimdalı, Adana, Türkiye

*Başkent Üniversitesi, Adana Uygulama ve Araştırma Merkezi, Çocuk Sağlığı ve Hastalıkları Anabilim Dalı, Adana, Türkiye

**Başkent Üniversitesi, Adana Uygulama ve Araştırma Merkezi, Patoloji Anabilim Dalı, Adana, Türkiye

***Başkent Üniversitesi, Adana Uygulama ve Araştırma Merkezi, Radyoloji Anabilim Dalı, Adana, Türkiye

Address for Correspondence/Yazışma Adresi: *Kılıçaslan MD, Başkent Üniversitesi, Adana Uygulama ve Araştırma Merkezi, Pediatrik Nefroloji Bilimdalı, Adana, Türkiye*
GSM.: +90 532 313 72 02
E-posta: drbuketk73@yahoo.com

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SUMMARY

Jeune syndrome, or asphyxiating thoracic dystrophy, is an autosomal recessive skeletal dysplasia with multiorgan involvement. Skeletal dysplasia is characterized by small, narrow thorax, short ribs, short squared iliac wings and short limbed dwarfism. Multiorgan involvement including renal, hepatic, pancreatic, and retinal complications may also occur. About 60% to 70% of children die from respiratory failure as infants or young children. Patients with Jeune syndrome who survive often develop problems with their kidneys, another serious feature of Jeune syndrome. We, herein, report a case of Jeune syndrome with proteinuria, due to its rarity. A 7-year-old girl presented to our hospital with poor growth for a year and urinary incontinence for 3 months with urgency and frequency. Skeletal survey showed findings consistent with Jeune syndrome. Laboratory examination demonstrated normal urinalysis and renal functions. Two years after her initial diagnosis with Jeune syndrome, the patient developed proteinuria. She was referred to pediatric nephrology department when proteinuria was noted. Because of persistent proteinuria, renal biopsy was performed. The histological diagnosis was consistent with chronic sclerosing glomerulonephritis. We wish to point out the progression of renal involvement of this uncommon syndrome over several years. The patients with Jeune syndrome should be followed closely for renal involvement and subsequently renal failure in corporation with pediatric nephrologists. (Journal of Current Pediatrics 2013; 11: 88-91)

Key words: Jeune syndrome, asphyxiating thoracic dystrophy, proteinuria, renal involvement

ÖZET

Jeune sendromu veya "asfiktik torasik distrofi", multiorgan tutulumu ile giden, otozomal resesif geçişli bir iskelet displazisidir. İskelet displazisi küçük, dar toraks, kısa kaburga, kısa kare iliak kanat ve kısa kollu cücelik ile karakterizedir. Multiorgan tutulumu ise böbrek, karaciğer, pankreas ve retina komplikasyonlarını içerebilir. Bebeklik ve çocukluk dönemlerinde %60-70'i solunum yetmezliği ile hayatını kaybetmektedir. Bu dönemde hayatta kalmayı başaran hastalar, Jeune sendromunun bir başka ciddi komplikasyonu olan böbrek tutulumu ile gelebilirler. Biz burada; seyrek görülmesi nedeniyle, proteinüri ile izlenen bir Jeune sendromu olgusu sunduk. Yedi yaşındaki kız hasta, hastaneye bir yıldır var olan büyüme geriliği ve üç aydır devam eden idrar kaçırma, idrara sıkışma ve sık idrar yapma şikâyetleri ile başvurdu. İskelet sistemi taraması Jeune sendromu ile uyumlu bulundu. Laboratuvar incelemesinde idrar analizi ve böbrek fonksiyon testleri normal sınırlarda idi. Başlangıçtaki Jeune sendromu tanısından 2 yıl sonra, hastada proteinüri gelişmesi üzerine pediatrik nefroloji bölümüne refere edildi. İzlemde, persistan proteinüri nedeniyle hastaya böbrek biopsisi yapıldı. Histolojik tanı, kronik sklerozan glomerulonefrit ile uyumlu bulundu. Biz bu olgu ile nadir görülen bu sendromdaki böbrek tutulumunun yıllar içerisindeki ilerlemesine işaret etmek istiyoruz. Jeune sendromu tanısı alan hastalar, böbrek tutulumu ve bunu izleyen böbrek yetmezliği açısından pediatrik nefrologlarla birlikte yakından izlenmelidir. (Güncel Pediatri 2013; 11: 88-91)

Anahtar kelimeler: Jeune sendromu, asfiktik torasik distrofi, proteinüri, böbrek tutulumu

Introduction

Jeune syndrome or asphyxiating thoracic dystrophy is an autosomal recessive osteochondrodysplasia characterized by skeletal abnormalities including small, narrow thorax, short ribs, short squared iliac wings and short limbed dwarfism (1). Although most cases are ascertained by skeletal features, there is a wide spectrum of severity and occurrence of non-skeletal complications. Renal, hepatic, pancreatic, and retinal complications may also occur (2). While severely affected patients of this syndrome have poor prognosis, the mildly affected patients survived to teen ages, but they have varying degrees of renal involvements such as proteinuria and hypertension. Renal failure may also occur in the later period of this patient group. We would like to present the progress of the patient with Jeune syndrome and to discuss some insight into the progression and management of some types of renal involvement in patients with Jeune syndrome.

Case Report

A 7-year-old girl presented to our hospital with poor growth for a year and urinary incontinence for 3 months with urgency and frequency. She was the sixth child born to consanguineous (first cousins) parents, with a 30-year-old sister who had a narrow chest. There was a history of recurrent bronchitis and urinary tract infection in early infancy. The patient weighed 14 kg and was 108 cm tall. She was below the 3rd percentile for both weight and height for her age. Her vital signs were within normal li mits. She had short hands, short feet, and brachydactyly and pectus carinatum with significant narrowing of the chest (Figure 1). Her liver was 3 cm palpable below the costal margin and spleen was non-palpable on her abdominal examination. Laboratory examination demonstrated normal urinalysis, complete blood count, electrolytes, thyroid, liver enzymes and renal functions. Skeletal survey showed findings consistent with Jeune syndrome: narrow thoracic cage, short horizontal ribs with bulbous ends, handlebar clavicles (Figure 2), small pelvis with squared iliac bone, trident acetabular margin, sciatic notch spur (Figure 3) and metaphyseal abnormalities of the metacarpals (Figure 4). Vertebrae were normal. Echocardiogram revealed no abnormality. Pulmonary function testing showed decreased lung volumes consistent with restrictive lung disease. Abdominal ultrasonography (USG) revealed diffuse hepatomegaly with a normal hepatic structure, normal biliary tract, and normal portal flow pattern, and bilateral minimal pelvicaliectasis with normal echogenisity.

In the following two years, she was readmitted to the hospital several times because of respiratory and urinary tract infections. Two years after her initial diagnosis with Jeune syndrome, the patient developed proteinuria,

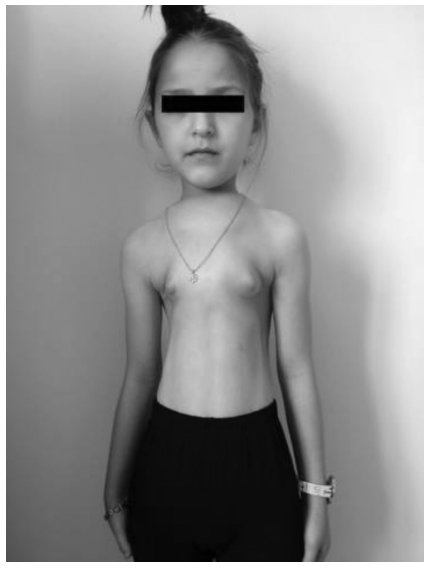

Figure 1. The patient has pectus carinatum with significant narrowing of the chest

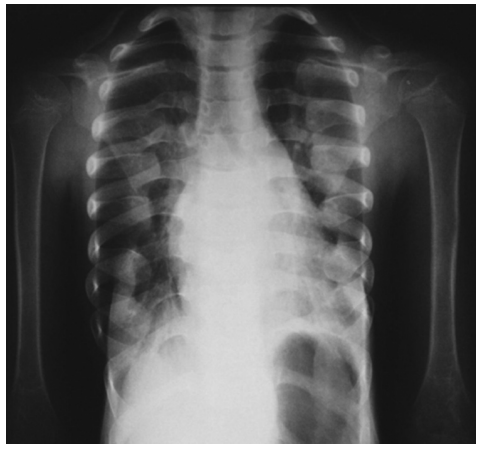

Figure 2. Anteroposterior (AP) plain film showing narrow thoracic cage, short horizontal ribs with bulbous ends

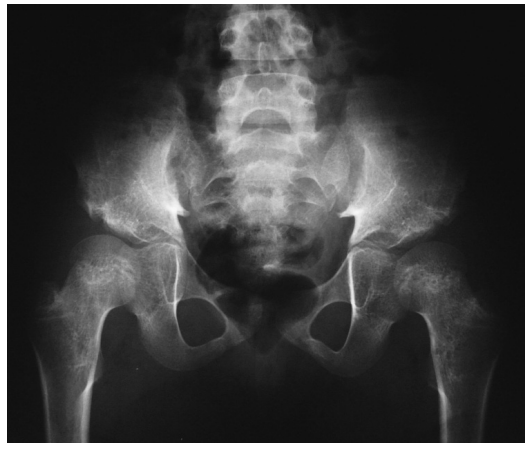

Figure 3. AP pelvis X-ray displaying small pelvis with squared iliac wings, trident acetabular margin, and sciatic notch spur

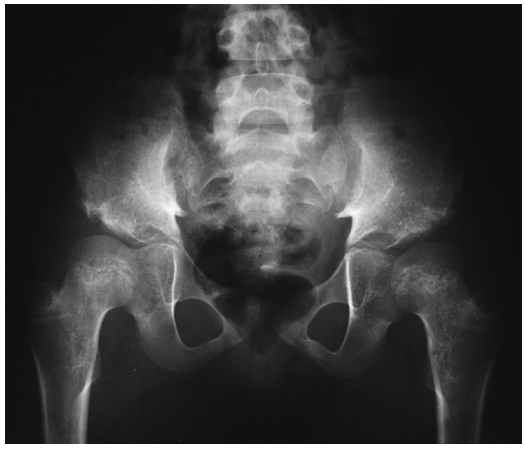

Figure 4. Apparent brachydactyly of especially distal phalanges and metaphyseal abnormalities of the metacarpals are seen at AP hand film

measured initially at 24 mg/m^2/hr. She was referred to pediatric nephrology department when proteinuria was noted. The levels of C3 and C4 complement components were normal. The tests including the antinuclear antibody and antiDNA were negative. Renal USG demonstrated bilateral grade-II parenchymal hyperechoic kidneys. Tc-99m dimercaptosuccinic acid (DMSA) scintigraphy and voiding cystourethrography (VCUG) were normal.

Because of persistent proteinuria, renal biopsy was performed. Percutaneous renal biopsy revealed diffuse interstitial fibrous changes, tubular atrophy, tubular hyaline casts, mononuclear inflammatory cell infiltration and glomerulosclerosis. Most of the glomeruli (8/11) were totally sclerosed. It was negative for amyloid reaction. Immunofluorescence microscopy showed negative staining for IgA, IgG, IgM, C19, and slightly positive for C3 in tubular epithelial cells. The histological diagnosis was consistent with chronic sclerosing glomerulonephritis.

Prednisolone (60 mg/m^2/daily), enalapril (0.3 mg/kg/daily) and omega-3-fatty acids were prescribed. Prednisolone was tapered within 2 months. In the one year follow-up, low dose prednisolone (10 mg/m^2/alternate daily) and enalapril was continued. Proteinuria decreased (7 mg/m^2/hr) after 6 months of therapy and her renal functions remained stable, and then prednisolone was discontinued. The patient developed hypertension and antihypertensive treatment was prescribed.

Discussion

Jeune syndrome also known as asphyxiating thoracic dystrophy, is a rare autosomal recessive skeletal dysplasia with an estimated incidence of 1 in 100 000 to 130 000 live births (3,4). It was first described in 1955 by Jeune et al. (2) Diagnosis is based on clinical and radiographic findings. The clinical presentation and severity of disease in children with Jeune syndrome varies greatly. Our case carries characteristic skeletal findings of Jeune syndrome including the narrow chest, brachydactyly, short stature and limb. She is also based on characteristic radiographic findings of a narrow thoracic cage, short horizontal ribs with bulbous ends, handlebar clavicles, small pelvis with squared iliac bone, trident acetabular margin, sciatic notch spur and metaphyseal abnormalities of the metacarpals and normal vertebrae (5,6).

The diseases that should be evaluated in the differential diagnosis of Jeune syndrome include short rib-polydactyl (SRP) syndrome (types 1-4) and Elis-van-Creveld (EvC) syndrome (7,8). Jeune syndrome differs from EvC syndrome with the absence of ectodermal dysplasia, and cardiac and dental defects, and from SRP syndrome with milder clinical and radiological manifestations. Facial abnormalities, ambiguous genitalia and cloacal abnormalities observed in SRP syndrome are also important in making the differential diagnosis. Jeune syndrome and SRP syndrome (type 3) have been suggested to be the allelic variants of the same disorder (9). Clinical variability of Jeune syndrome described in the literature may be due to genetic heterogeneity, as well as to clinical overlap with other similar syndromes (10,11).

Jeune Syndrome might occur within the same family as reported in the literature (2,12-14). In our case, there was a family history such as a sister who had a narrow chest. Besides skeletal dysplasia, multi-organ involvement may also occur in Jeune syndrome (9). Although hepatosplenomegaly was detected in all cases of Vries et al., in our case, we detect hepatomegaly without splenomegaly. Serum examination including liver function tests revealed no abnormalities which is similar as previous case reports except only one case (14).

Prognosis of Jeune syndrome is associated with pulmonary and renal involvement (15). The narrow thorax often results in respiratory distress and recurrent respiratory infections (14). There are several reports of mildly affected patients as presented by Keppler-Noureuil et al. primarily with narrow thorax and rib shortening with survival to teens; although most patients are severely affected and die in the perinatal or infancy period due to respiratory insufficiency (2,15). Our case had a history of recurrent bronchitis and she was complicated with restrictive lung disease. Vries et al. tested spirometry in 10 patients and no restrictive lung disease was reported (14).

Two different patterns of renal involvement have been identified within Jeune Syndrome. Severely affected patients who have renal involvement during neonatal and infancy period, exhibit various types of renal dysplasia with cortical or diffuse cystic changes, end-stage renal disease develops early, and they have poor prognosis. The mildly affected patients survive this period, but

should be followed for probable renal problems such as proteinuria and a urine concentrating defect including a defect in the phosphate and urate resorbtion that they may develop late progressive renal disease. In our case, proteinuria was typical for renal involvement. In the literature, atrophic and cystic dilatation of the tubules, diffuse interstitial fibrosis, tubular atrophy, periglomerular fibrosis and glomerular sclerosis are described as predominant histological findings (12,14,15). In our case, most of the histological abnormalities described above by percutaneous renal biopsy were consistent with the literature. Renal involvement is a well-known feature of Jeune syndrome, but most patients in the literature were diagnosed when renal failure developed (12). As similar with the literature, we diagnosed Jeune syndrome while we were investigating growth retardation but before renal failure. Whereas Özçay et al. diagnosed their case after he went into renal failure who was admitted with growth retardation (12). In the literature, Keppler-Noreuil et al. did not detect renal involvement in none of their 8 cases; although, Vries et al. detected renal involvement in 2 cases of 13 patients who were not in childhood age (2,14). Tüysüz et al. reported renal involvement in only one of 11 patients who died at 13 years old due to renal failure (13). Our case is still alive and detected renal involvement before renal failure. It was our chance to recognize Jeune syndrome with glomerulosclerosis before renal failure.

In conclusion, renal involvement in Jeune syndrome is significant. Renal failure occurred in 38% of those with kidney involvement (13,14). The predominant cause of death for patients aged 3-10 years is renal in origin (2). Because renal complications tend to develop insidiously, the patients with Jeune syndrome should be followed closely for renal involvement and subsequently renal failure in corporation with pediatric nephrologists.

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