Journal of the Turkish Academy of Dermatology
eISSN 1307-394X

Case Report DOI: 10.6003/jtad.16104c6

A Young Adult Presenting with Nail-Patella and Nephrotic Syndrome: A Case Report

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Published:
J Turk Acad Dermatol 2016; **10 (4)**: 16104c6
This article is available from: http://www.jtad.org/2016/4/jtad16104c6.pdf
Keywords: Patellae, iliac horn, nephrotic syndrome

Abstract

Observation: The Nail-Patella syndrome is a rare autosomal dominant disorder that involves skeletal abnormalities, nail abnormalities and renal disease. Iliac horns are pathognomonic of the disease. Almost all of the patients have patellar aplasia or hypoplasia. It is usually diagnosed at early childhood. Herein we present a 20-year-old man who diagnosed Nail-Patella syndrome with nephrotic syndrome.

Introduction

The Nail-Patella syndrome (NPS) or hereditary osteo-onychodysplasia (HOOD) is a rare autosomal dominant disorder, with an incidence of 1 per 50,000 in the World [**1**]. NPS involves skeletal abnormalities, nail abnormalities and renal disease [**1, 2, 3, 4, 5, 6**]. We report a patient with NPS and nephrotic syndrome secondary to focal segmental glomerulosclerosis with nail abnormalities.

Case Report

A 20-year-old man presented with nephrotic syndrome was referred for nephrological assessment. On physical examination he was found to have short stature, blood pressure was 100/60 mmHg. There was bilateral pitting pedal edema. There was neither purpura nor rash and the thumbnail of the left hand was hypoplastic. The thumbnail of the left hand was hypoplastic. And triangular lunulae was seen on the second and third digit of the left hand (**Figure 1**). He had flexion contractures of both elbows. Patellae of both were asymmetric and dislocated (**Figure 2**). On pelvic roentgenogram the characteristic 'iliac horn' change of NPS was seen (**Figure 3**). Her family history was unremarkable.

Pertinent laboratory data included a BUN 25 mg/dl, serum creatinine 1.4 mg/dl, albumin 2.25 g/dl, LDL cholesterol 208 mg/dl. Urinalysis showed 4(+) proteinuria without any red or white blood cells. Twenty-four-hour urine collection revealed proteinuria of 8.5 g/24 h. Serum serologies including ANA, ANCA, complement levels, and hepatitis panel were all negative. Renal ultrasound showed a right kidney of 9.7 cm, left kidney size of 10 cm in length.

On light microscopy, renal biopsy representing both cortex and corticomedullary junction was

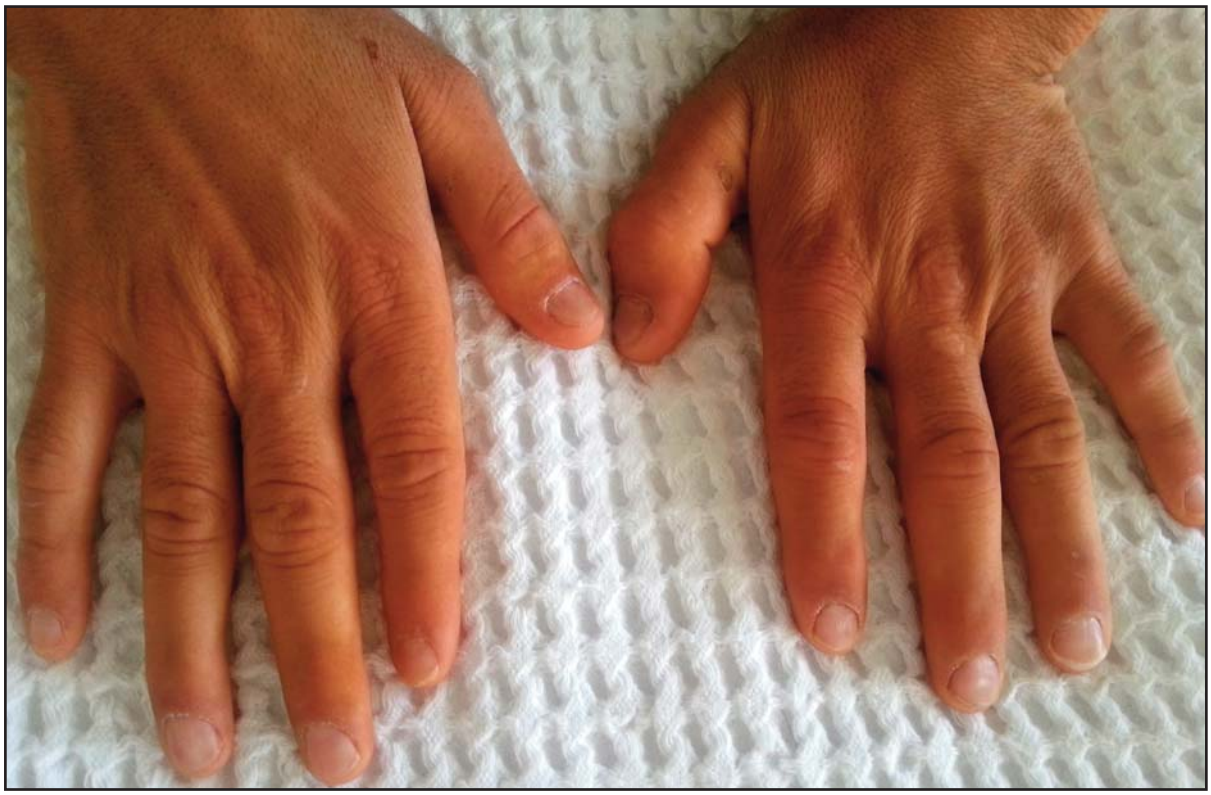

Figure 1. The thumbnail of the left hand was hypoplastic. And triangular lunulae was seen on the second and third digit of the left hand. All skin creases on the dorsal aspect of distal phalangeal joints was absent

consisted of about 41 glomeruli. Biopsy revealed total sclerosis in 5/41 (12%) of the glomeruli and focal and segmental sclerosis in 3/41 (%7) glomeruli. Some glomeruli enlarged and demonstrated mild focal mesangial hypercellularity. Immunofluorescence examination revealed depositions of C3 (2+) and IgM (1+/2+) in the mesangial areas, but no any depositions for IgG, IgA, C1q, fibrin, lambda and kappa light chains were seen.

Toluidine Blue stained semi-thin sections were consisted of 5 glomeruli. Uranyl acetate and phosphotungstic acid stained ultra-thin sections revealed cytoplasmic vacuolization in podocytes, effacements and fusions of foot processes of podocytes (**Figure 4**). There were no cross-banded (type III) collagen fibers or wide radiolucent enlargements in glomerular basement membranes (GBMs). These features in GBMs are characteristic ultrastructural findings for NPS. GBMs showed only focally mild thickening and thinning, and lamina densa was not clearly seen. In addition, there was no any electron dense deposit in glomeruli.

The pathological findings were compatible with focal segmental glomerulosclerosis. After renal biopsy was performed, the patient was treated with deflazacort (60 mg/day, p.o) and perindopril (10 mg/day) for 12 weeks, which resulted in partial response (serum creatinine 1.34 mg/dl, albumin 3.285 g/dl, proteinuria of 3.7 g/24 h). Partial remission was achieved by 12 weeks, we tapered deflazacort slowly over six months. The patient has been followed for 8 months and has had a stable renal function.

Discussion

Nail-patella syndrome is a rare autosomal-dominant pleiotropic genetic disorder and this genetic abnormality has been identified as a loss of function mutation in LMX1B (9q34) [**6**]. Almost all patients with NPS have nail and/or distal digital abnormalities. These abnormalities are typically bilateral. They include nail hypoplasia, nail dystrophic changes (discoloration, abnormal splitting, and triangular lunulae), distal digital changes (loss of the creases in the skin overlying the distal interphalangeal joint). Almost all patients have either patellar aplasia or hypoplasia, which may be irregularly shaped. Elbow abnormalities may include limited extension, limited pronation and these abnormalities may be asymmetrical. Iliac horns are bilateral symmetrical bone formations arising from the

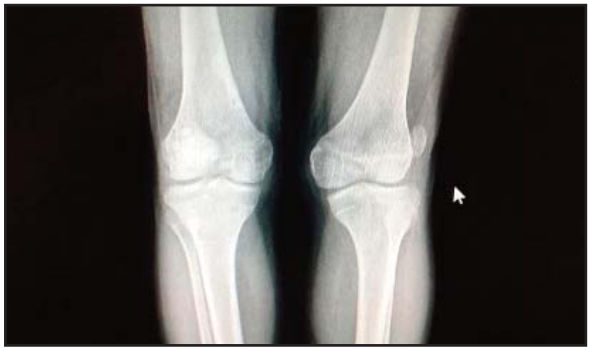

Figure 2. Right tripartite patella with lateral subluxation and left hypoplastic patella with lateral dislocation

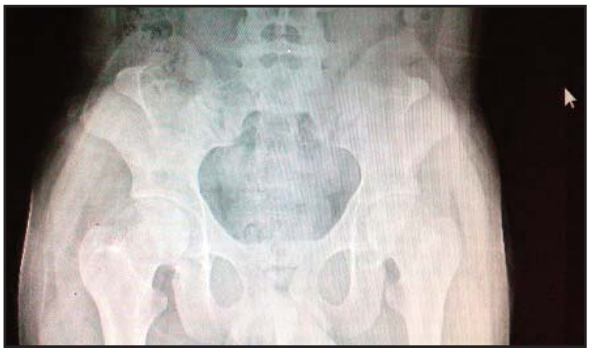

Figure 3. Bilateral posterior iliac horn

iliac crest, which are pathognomonic of NPS [**2, 3, 4, 5, 6**]. Patients with renal disease show proteinuria, microscopic haematuria. Proteinuria occurs in 30%-50% of affected patients, end-stage renal disease (ESRD) occurs in about 5% of affected patients [**7, 8**]. Nail-patella syndrome affect the nails. It most frequently involves the thumb. Other fingers may be involved too. In this syndrome the nails are absent or hypoplastic. The nail dystrophy is generally more visible on the ulnar side of the digit. A triangle-shaped lunula is usually seen. The toenails being only rarely affected. Nail changes include reduced size or absence, spoon-shape and fragility. Absent skin creases on the dorsal aspect of distal phalangeal joints represent another common finding of this syndrome. In our patient the thumbnail of the left hand was hypoplastic. And triangular lunulae was seen on the second and third digit of the left hand. All skin creases on the dorsal aspect of distal phalangeal joints was absent [**1, 2, 3, 4**].

Renal involvement in patients has been reported as ranging from 25 to 50% and manifests as proteinuria, microscopic hematuria, nephrotic syndrome and end-stage renal disease [**7**]. The severity of renal impairment varies significantly among patients.

NPS is distinguished from other diseases associated with proteinuria by the electron microscopic characteristic features of irregular and lucent rarefactions containing clusters of cross-banded collagen fibrils within the GBM. The clusters of fibrils are clearly demonstrated by staining with phosphotungstic acid [**8**]. Other types of glomerulopathy have also been reported in previous studies: membranous nephropathy, IgA nephropathy and crescentic glomerulopathy combined with NPS [**9, 10, 11**].

There is no specific therapy for the renal involvement in NPS. Management is directed towards identifying and treating complications. The use of RAAS blocking agents in various settings of proteinuria has been discussed and debated [**12**]. For patients with ESRD, successful renal transplantation has been reported [**13**].

We have herein described FSGS in a patient with NPS characteristic ultrastructural features of NPS were not found on electron microscopy. The combination has not previously been reported. Since corticosteroid responsiveness in NPS nephropathy is difficult to explain, it is possible that FSGS in the present patient with NPS was incidental. We suggest that renal histology should be examined in young subjects with NPS and nephrotic range proteinuria and nail examination should be done.

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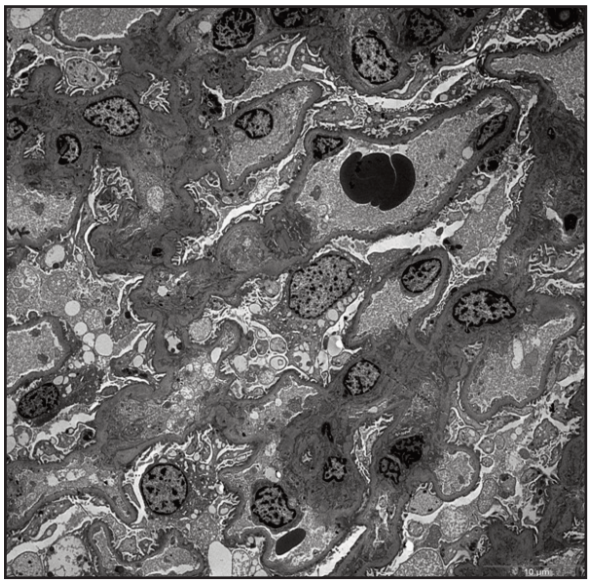

Figure 4. Cytoplasmic vacuolization in podocytes, effacements and fusions of foot processes of podocytes (EM)

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