Introduction

Nail-patella syndrome is a hereditary osteoonychodysplasia (HOOD), also known as Fong disease, Osterreicher-Turner syndrome, and Turner-Kieser syndrome. It is a rare autosomal dominant disorder that has both ectodermal and endodermal origin [1]. It results from the mutation in gene LIM homeobox transcription factor 1 beta on long arm of chromosome 9q34. About 12.5% of cases has sporadic gene mutation without family history of NPS. The estimated incidence of the disease is about 1/50,000 live birth. [2, 3].

Following changes are frequently observed in the patient with NPS [4, 5]:

- **Nail changes** - The most common abnormality occurs in 98% of cases include: aplasia, hypoplastic or dystrophic nail, longitudinal or horizontal ridges resulting of nail splitting, pitting or triangular lunulae.

- **Skeletal changes** - Knee abnormalities occur in 74% of cases. Patella that may be aplastic or hypoplastic with instability, locking and clicking of the knee joints with prominent tibial tuberosity. Dysplasia of the elbow joints is also common with limited extension, pronation, and supination. Iliac horn is a bilateral conical projection at posterior-lateral of the central part of the iliac bone (pathognomonic sign). Rarely genu valgum/varum, pectus excavatum, talipes equinovarus, dysplasia of finger and toe, scoliosis, spina bifida, congenital hip dislocation, and arthrogryposes multiplex at birth.

- **Renal abnormalities** - Nephropathy occur in 40% of cases and manifests as proteinuria, microscopic hematuria, and hypertension. In 5-10% of cases, it may progress to nephrotic syndrome and progressive renal failure.

- **Other manifestations** - Lester’s sign (pigmentation of iris), glaucoma, gastrointestinal (constipation, irritable bowel

**CASE REPORT**

**NAIL-PATELLA SYNDROME WITH NEPHROTIC SYNDROME AND DEAFNESS: A CASE REPORT**

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**Abstract**

Nail patella syndrome (NPS) is a rare hereditary disorder, characterized by typical dermatological and musculoskeletal abnormalities. It is an autosomal dominant condition resulting from the mutation of LMX1b gene at chromosome 9q34. We herein report a case of NPS aged 18 years, having Nephrotic syndrome with atypical involvement of deafness. She had classical features of a syndrome like absent patella, deformed elbow, dysplastic nail of fingers and toes, and iliac horn.

**Keywords:** Nail patella syndrome, Gene LMX1B, Nephrotic syndrome, Deafness

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syndrome), attention deficit disorder, and depression.

Case Report

An 18 years old female came in a walk-in clinic with acute pharyngitis. We observed that she was physically and functionally impaired with deformed nail, elbow and knee joints, and deafness. She had no history of trauma or bony fracture, hematuria, body swelling, hypertension, and shortness of breath. She had a strong family history of congenital nail, elbow and knee deformities in three maternal cousins and two of them expired due to renal failure. Her mother, four maternal uncles, and aunts had congenital deafness without any physical anomalies.

On clinical examination she had normal vitals with blood pressure 110/72, her height was 131cm and SMR stage IV. She had poor oral hygiene with dental caries, high arched palate, dystrophic nail of all fingers and toes, clinodactyly of the little finger, swan neck deformities of other fingers (figure.1), and webbing of elbow joint with restricted extension (figure. 2). She also had pectus excavatum, scoliosis at lower lumbar region, bilateral absent kneecap with prominent sulcus of femoral condyles and tibial tuberosity, click observed on extension and flexion of knee joints, and bilateral Talipes equinovarus (Figure 3). Other systemic examinations were unremarkable.

The radiological evaluation shows bilateral posterior Iliac Horn (Figure 4), scoliotic deformity of the spine, hypoplasia of radial head leading to the subluxation of elbow joints (Figure 5), patellae are absent bilaterally (Figure 6), and Madelung deformity of the wrist. Other investigations reveal hypoalbuminemia (2.9g/dl), hypercholesterolemia (375mg/dl), significant proteinuria (spot urine Protein-to-creatinine ratio is 3 mg/mg, 24 hours urinary protein 2604 mg/dl). Urea, creatinine, renal ultrasound, and hematological parameters were within normal limits. Audiometry shows bilateral sensorineural hearing loss.

Figure 1. Dystrophic nails.

Figure 2. Hyperextension at PIP joints and flexion at DIP resulting “swan neck” appearance of fingers & webbing of elbow joint.
Figure 3. Bilateral absent kneecap with prominent sulcus of femoral condyles and tibial tuberosity on knee flexion, and talipes equinovarus.

Figure 4. X-ray of pelvis showing iliac horns.

Figure 5. X-ray of elbow showing a hypoplasia of radial head leading to subluxation of the elbow joint.

Figure 6. X-ray of pelvis showing absent patella.
Discussion

NPS is a clinical condition that involves predominantly nail, skeletal system and renal system. It results from a mutation at LMX1b gene, which is involved in the development of the skeleton, brain, formation of glomerular basement membrane in kidney and differentiation of anterior eye chamber, its mutation will lead to manifestations of the disease [6].

NPS can be diagnosed early in infancy with clinical manifestation likes dysmorphic nail, absent patella, elbow dysplasia, and confirmed by radiological evaluation [7]. If there has been a significant family history of NPS, it can be diagnosed prenatally at the time of anomaly scan by assessing the orientation of long bones and the limb movements in the foetus or by using chorionic villus sampling in 1st trimester [8]. Definitive diagnosis is by means of gene analysis which detects a mutation in LMX1b gene at chromosome 9q34.

About 10-40% of cases develop renal abnormalities which are more common in the female. It is a physiological defect characterized by progressive thickening and disorganization of glomerular basement membrane (GBM), defect in glomerular capillary permeability and podocyte function [5]. Age of presentation and severity of renal disease is extremely variable. The initial sign of renal involvement is asymptomatic proteinuria with or without haematuria. 5-10% of patients develop nephrotic syndrome. It may progress to end-stage renal disease if it remains undiagnosed for many years. It is a genetic disorder, so corticosteroid has no role in the management of disease and renal transplant is a corrective treatment option in ESRD[3,5]. We started ACE inhibitor therapy for persistent proteinuria with significant results.

In Bongers MHF et al study, 45% of NPS had a Sensorineural hearing loss that may be unilateral or bilateral but mean age of detection was 46.7 years (range 17.5–69.2 years), interpreted as mildly accentuated presbycusis [9]. In our index case, she was deaf since birth with family h/o deafness without NPS feature, and NPS without deafness that may give suspicion of two different types of diseases occur in two generations of index family and present in a single person or it may be a feature of NPS, needs further studies.

Conclusion

NPS is a rare autosomal dominant condition that involves predominantly nail, skeletal and renal system, with 50% risk of transmission in all generations. This is an atypical case of NPS associated with congenital deafness and nephrotic syndrome. Nephrotic syndrome is a co-morbid condition in NPS, which plays a key role in the progression of kidney damage to renal failure.

References