Volume : 4 | Issue : 9 | Sept 2015 • ISSN No 2277 - 8179

Research Paper

Nail Patella Syndrome: A Rare Cause of Nephrotic Syndrome

Medical Science

KEYWORDS : hereditary onycho-osteodystrophy, nail dysplasia, nephrotic syndrome, patellae dysplasia

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ABSTRACT

Nail-patella syndrome (NPS) is an autosomal dominant disorder reported in 1/50000 individuals, also known as hereditary onycho-osteodystrophy (HOOD). Diagnosis is usually based on clinical findings. We report a case of NPS which presented as nephrotic syndrome in a 3 year old male child. Physical examination revealed associated nail changes and bony deformities which were confirmed by the radiological evaluation.

Introduction:

Nail-patella syndrome (NPS), also known as Fong's Disease, Hereditary onycho-osteodysplasia (HOOD), Österreicher-Turner syndrome or Turner-Keiser syndrome, is a rare autosomal dominant hereditary disorder[1,2]. Its incidence is approximately 1 in 50,000. It is due to mutation of the LMX1B (LIM homeobox transcription factor 1-beta) gene located at the long arm of chromosome 9q34. LMX1B is required for dorso-ventral patterning of the limb, normal morphogenesis of the glomerular basement membrane (GBM) as well as anterior segment of the eye[3,4]. The phenotypic expression of the disease varies between individual due to variable penetrance, hence there is inter- and intrafamilial variability. Nail-patella syndrome is defined by three major features[5]: Nail anomalies- Changes in the nails represent the most constant clinical features of patients with NPS. Skeletal anomalies- the most frequent are: absent or hypoplastic patellae, iliac horns, dysplastic elbows. Other features- renal disease, glaucoma, depression, attention deficit disorder, lean habitus and difficulty to gain weight, gastrointestinal symptoms (constipation, irritable bowel syndrome). Renal disease found in approximately 40% of patients: proteinuria, microscopic hematuria, hypertension progression to renal failure has been reported in 3-15% of Nail-patella syndrome patients[6]. Diagnosis of NPS warrants further investigative work-up to assess the extent of the disease and possible dysfunction of the other organs. The management involves early identification of the systems involved and appropriate treatment.

Case History:

A 3 year old Indian male child with multiple congenital malformations was admitted in our pediatric department with complaints of generalized body swelling and reduced urine output for last 8 days. History of constipation and cool extremities since birth was also present. He was 5th child of a monogamous family of non-consanguineous marriage. Pregnancy and delivery was uneventful. There was history of similar malformation in two male siblings, who died in their neonatal period, nail changes and polydactyly in father and CTEV in paternal uncle.

Physical examination revealed pulse rate 94/min. RR 28/min. and BP 94/60mm of Hg. He had dysmorphic facial feature (high hair line, prominent nose and forehead, large ears, upward slant of eyes), winging of scapulae, club feet, facial puffiness and anasarca. Nails were absent in bilateral thumbs, dysplastic in index fingers and normal in rest fingers (fig-1). Hyperextension at PIP and flexion at DIP was present. Bilateral CTEV and dysplastic nails in 4th and 5th toe were present. On knee joint examination, there was complete bilateral absence of patellae.

Laboratory examination revealed hypercholesterolemia (419mg/dl), hypoproteinemia (4.28g/dl), hypoalbuminemia (0.86mg/dl), proteinuria (4+), hematuria (80 RBC/hpf), microcytic hypochromic anemia on peripheral blood film and leucocytosis (19100/µL). TSH, B.urea, S.creatinine and S.electrolyte were with in normal limits. Other routine laboratory tests were unremarkable. Ultrasound abdomen showed bilateral mild bright kidneys, hepatomegaly, b/l pleural effusion and moderate ascites. Radiographic examination showed absence of patella in b/l knee joints (fig.2) and overgrowth of scapular spines. X-ray pelvis was normal and didn't elicit iliac horn.

Based on above clinical and family history, physical examination (typical nail changes, absence of bilateral patella, bilateral CTEV and typical facial features), laboratory and radiological findings, the diagnosis of Nail Patella Syndrome (NPS) with renal involvement in form of nephrotic syndrome was made. This subject has classic feature of NPS involving musculoskeletal system, skin and kidney. Patient relatives refused for undergone renal biopsy. Ophthalmological examination showed no significant abnormality. He was managed according to protocol.

Figure-1, Absent nails in bilateral thumbs, dysplastic in index fingers and normal in rest fingers
Figure-2, X-ray lateral view of knee joint showing absent patella

Discussion:

The first description of NPS has been credited to Chatelaine in 1820, when he initially described a triad of patella, nail and elbow involvement[7], with Turner later describing the pathognomonic iliac horns in 1933[8]. Nail- Patella syndrome is usually characterized by nail dysplasia, patellar apoplasia/hypoplasia, iliac horns, elbow dysplasia, and progressive nephropathy. Other less common features include scapula hypoplasia, scoliosis, genu valgum, club feet, heterochromia and glaucoma.

Most of patients with Nail Patella Syndrome have affected fingernails, which may be partly or completely missing (80-100% of cases)[9]. Thumbs are affected severely as compared to other fingers, and the severity decreases toward the little finger. When toenails are affected, little toenails are most commonly involved[10]. The nail dysplasia may produce a triangular lunula, especially of the index and/or middle fingers. Other modifications of the nails may include narrowness, smallness, spooning, rarely thickening, a median groove or cleft, roughness, cracking, splitting, and/or brownish discoloration with distal fraying. The distal most joint which is actually closer to the nail may not have creases over it. Sometimes, fingers might seem to be double-jointed. Some of these patients with Nail Patella Syndrome are unable to fully straighten their joint.

Volume : 4 | Issue : 9 | Sept 2015 • ISSN No 2277 - 8179

One of the characteristic manifestations of nail patella syndrome is patellae dysplasia range from complete agenesis to moderate hypoplasia. If patella is present, it will be hypoplastic, and it may be located more distally than usual leading to recurrent dislocation. Abnormal projections of bone from the superior (upper) portion of both sides of the hip bone (bilateral iliac horns) are reported. These "horns" are very specific to this disease that are said to be pathognomic but reported to be present in 30–70% of patients and occasionally detected on clinical examination. Other bony manifestations described are hypoplasia of the scapulae, talipes (club foot) or "twisted feet", hypoplasia of the first ribs, dislocation of the head of the radius, prominent outer clavicle, malformed sternum (Pectus Excavatum), scoliosis, and lordosis[9].

Our patient had typical nail changes (absent in thumbs, dysplastic in index fingers and 4th and 5th toe) and skeletal system (bilateral absence of patella and club feet) involvement but did not have typical iliac horn.

The incidence of renal impairment in NPS is approximately 40%[11]. This is one of the most serious manifestations of NPS. Though it is common in adults, it has been described to occur in children also. The clinical manifestations include protienuria with or without hematuria, and hypertension. Nephrotic syndrome and progressive renal failure can occur. The course is rather benign with renal failure a late feature. Annual urine screening is recommended. Kidney biopsy is rarely required to diagnose the disease. Nephrotic syndrome due to NPS nephropathy is resistant to therapy with corticosteroids[12]. However, it has been reported that antiproteinuric treatment with combination of angiotensin converting enzyme inhibitor and angiotensin receptor blocker can provide complete remission in infantile nephrotic syndrome secondary to NPS[13]. On the other hand, nephrotic syndrome diagnosed as an incidental comorbidity in the setting of NPS without NPS nephropathy may respond to steroid treatment similar to the general population[12].

Conclusion

Our case serves as a platform to understand and diagnose patients with presentation of abnormal nails and skeletal development. The multi system involvement of NPS warrants further investigative work-up to assess the extent of the disease and early detection of other system involvement to prevent the associated complications and need for the physicians of different specialties.

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