Nail-patella syndrome: Clinical importance of diagnosis

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Sri Lanka Journal of Child Health, 2021: **50**(1): 170-172
DOI: http://dx.doi.org/10.4038/sljch.v50i1.9424
(Nail-patella syndrome, LMX1B gene, iliac horns, dysplastic nails)

Introduction

Nail-patella syndrome (NPS), an autosomal dominant genetic disorder, with a prevalence of 1 in 50,000, is associated with dysplastic or hypoplastic nails and patellae, elbow contractures, iliac horns in pelvic x-rays and risk of kidney disease[1-5]. We report an affected Sri Lankan family in whom accurate diagnosis was possible using the characteristic clinical and radiological features without resort to genetic testing. Establishing the diagnosis justifies follow-up to detect potential renal problems.

Case report

The male proband, aged 7.5 years, is the youngest of three siblings born to non-consanguineous parents. He was delivered at 38 weeks of gestation by elective caesarean section due to maternal preeclampsia. His birth weight was 1.9kg (< -3SD), occipito-frontal circumference 33cm (0 to -2SD) and length 49cm (-1SD). He required nasogastric feeding for a week but was breast fed subsequently. He had developmental delay (palmer grasp at 12 months, first spoken word at 20 months and independent walking at 23 months). He had normal vision and hearing. At presentation, his height was 121cm (-1SD) and head circumference was 49cm (-3SD). He had an average academic performance at his local school. On examination, he had hypoplastic and white fingernails, dysplastic thumb nails with a central, vertical ridge and hypoplastic, white toe nails (Figure 1).

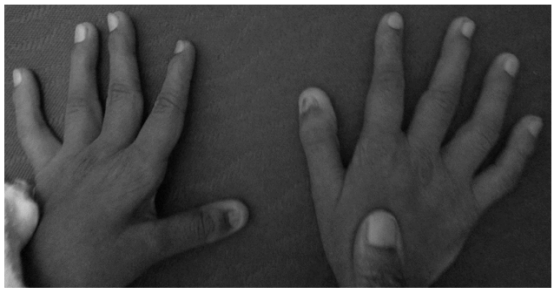

Figure 1: ***Hands showing hypoplastic thin whitish nails and dysplastic thumb nails with vertical, midline ridges***

He also had a flexion deformity of right elbow causing limitation of all elbow movements. Knee x-rays showed absent patellae (Figure 2) and x-ray pelvis showed the characteristic iliac horns (Figure 3). No dysmorphic features were noted. A clinico-radiological diagnosis of NPS was made.

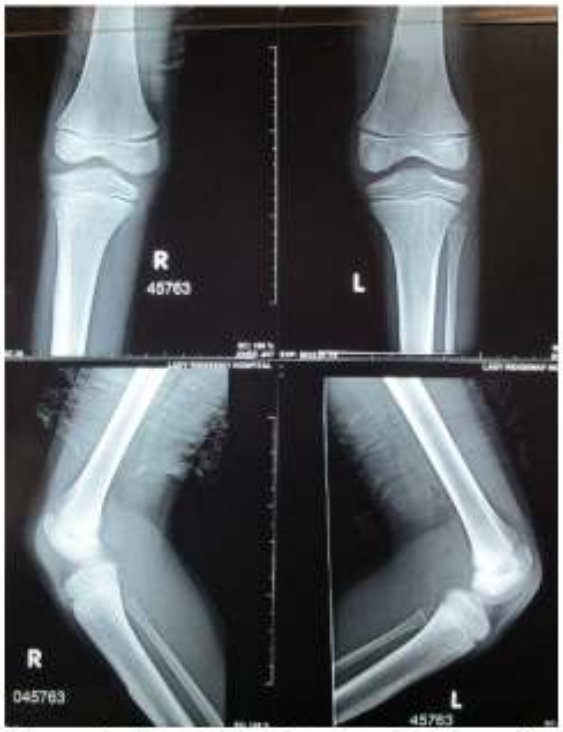

Figure 2: ***Knee x-rays showing absent patellae***

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(Received on 13 September 2019: Accepted after revision on 18 October 2019)
The authors declare that there are no conflicts of interest
Personal funding was used for the project.

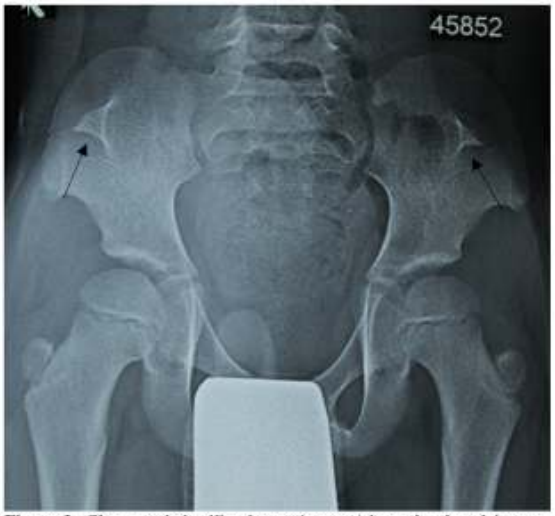

Figure 3: *Characteristics iliac horns (arrows) in patient's pelvic x-ray*

His mother and 18-year-old sister also had hypoplastic and dysplastic finger and toe nails. His sister had absent patellae and his mother had hypoplastic patellae. X-ray of his sister's pelvis also confirmed the presence of iliac horns. Blood pressure, abdominal ultrasound scans and renal function testing were normal in the proband, his mother and sister.

Discussion

The diagnosis of NPS is suspected in individuals with symmetrical nail changes, including absent, hypoplastic, pitted, discoloured or ridged (vertical or horizontal) nails with finger nails more affected than toenails. Thumbs are mainly affected with progressive lessening of severity from index to last finger and ulnar side more affected than radial[1,2]. These changes can be misinterpreted as fungal infections or injury. Iliac horns are identifiable in around 75% of affected cases[1]. The patellae may be small, irregularly shaped or absent and are prone to dislocation[1,2]. Elbow contractures are common and, as in this boy, can be asymmetric[1,2] and are due to dysplasia of radial head, hypoplasia of lateral epicondyle and prominent medial epicondyle[1,2,3]. The pathognomonic radiological feature of iliac horns, are present in about 70% of individuals with some being palpable[1,2,3]. These are usually asymptomatic requiring no medical intervention[1,2,3]. Approximately 30-50% of NPS cases develop proteinuria with end-stage renal failure in around 5% of cases[1,2,4]. Primary open angle glaucoma and raised intraocular pressure are also potential complications of NPS[1,2]. Associated medical problems include constipation, reduced peripheral sensation, vasomotor dysfunction and poor dentition[1,2].

Germline, mainly nonsense mutations in the *LMX1B* gene[1,5] cause NPS. The *LMX1* gene codes for a 402 amino acid protein with embryonic expression in the dorsal mesenchyme of the embryo (which gives rise to the limbs) and is involved in determining the dorsal-ventral axis of the developing limbs[1,5]. It also acts as a transcription regulator including regulation of expression of the α-3(IV) and α-4(IV) collagen normally expressed in the glomerular basement membrane[1,2]. Most cases have inherited the mutation from an affected parent but around 12% have a *de novo* mutation[1]. The children of an affected individual are at 50% risk of also inheriting the mutation[1].

The diagnosis can be established by identification of the clinical features affecting especially the nails and joints and this should trigger the search for the pathognomonic sign of iliac horns. Once the diagnosis is established in one individual in a family, parents and siblings have to be examined for diagnostic features of NPS. Affected individuals need to be screened for proteinuria, advised to avoid nephrotoxic drugs and need to have their blood pressure and renal function monitored. Ophthalmological evaluation and monitoring intraocular pressure would be advised. Genetic testing is needed in cases in whom the clinical features are atypical. There is a need to ensure that affected children continue to get monitoring in adolescence and adulthood as the complications associated with this condition may develop after childhood.

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