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Nail-Patella Syndrome Diagnosed During Evaluation of Chronic Renal Failure
—Report of two Cases—

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慢性腎不全の経過観察中に発見されたnail-patella症候群の2症例

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nail-patella症候群は，外，中胚葉性の形成異常を特徴とする稀な遺伝性疾患である．欧米では数多くの報告をみるが，本邦でのそれは少なく我々の調べた限りでは13例の報告をみるに過ぎない．本症候群では爪，骨格系の異常が多く認められるが，最近では合併する腎障害について関心が持たれている．骨格系の異常等は進行性に乏しいため，変化が軽度の場合見過ごされることも多いと思われる．ところが腎障害は年齢を重ねるごとに進行性を呈し腎不全に到ることもあるため，患者の予後に与える影響は大きい．この腎障害の可能性を早期に察知し，適切な処置を施すには，特徴的なX線学的所見を呈する骨格異常から本症候群の正確な診断を下すことが重要と考えられる．我々は増子病院において進行性の腎不全の経過観察中に発見された2症例を経験したが，これらは典型的な骨格異常を呈していたにも拘らず，多くの医療施設で本症候群の診断には到っていなかった．

Summary

The nail-patella syndrome (NPS) is a rare hereditary condition which is characterized by anomalies of both mesodermal and ectodermal structures.

Dysplasia of the nails and bones can be most commonly demonstrated, in addition, recent literature has reported the renal manifestation with NPS as its part.

We wish to present two cases of NPS, of which anomalies of the nails and bones are representative, being noted during evaluation of progressive chronic renal failure in our Masuko Institute for Medical Research.

Introduction

The tetrad of NPS consists of dysplasia of the nails, aplasia or hypoplasia of the patellae, elbow

changes with increased carrying angle and limitation of motion, and iliac horns.

Among these manifestations, slight bony anomalies tend to be overlooked, from a radiologic standpoint, because of their trend of poor progression and causing only slight motor dysfunction[1)2)].

In contrast to them, renal manifestation being reported as a part of NPS in recent literature is progressive so that it will considerably affect the prognosis of patient with NPS[3)].

It might delay correct diagnosis of renal manifestation being caused by NPS to overlook radiologic findings of these skeletal changes owing to it.

We experienced two cases of NPS in which only renal manifestation had been evaluated minutely as benign nephrosclerosis, whereas typical radiologic findings of NPS had been overlooked for a few years.

Case Reports

Case 1.

A 47-year-old-female with end-stage of chronic renal failure (CRF) was admitted to our hospital with

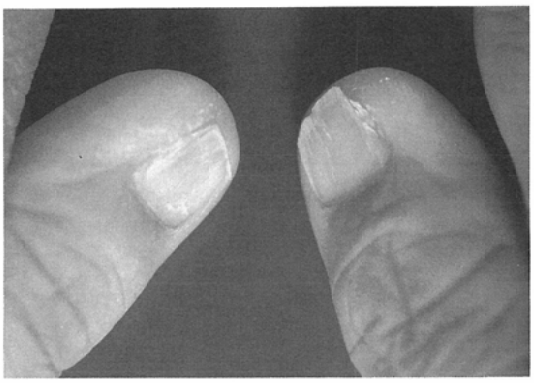

Fig. 1 Photograph of the bilateral thumbnails showing characteristic dysplasia of them.

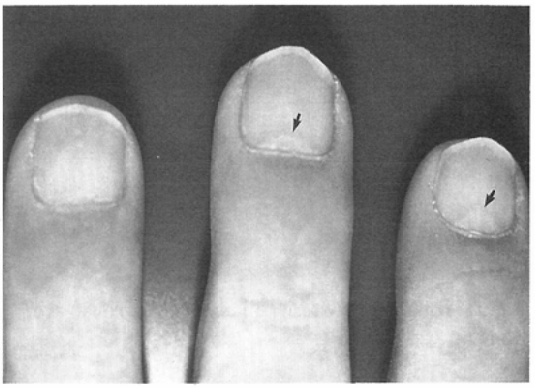

Fig. 2 Note triangular lunulae of the third and fourth fingernails (arrows) of right hand.

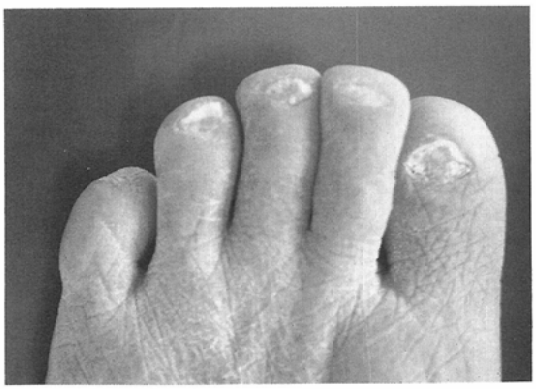

Fig. 3 Photograph shows dystrophy of the nails on left toes.

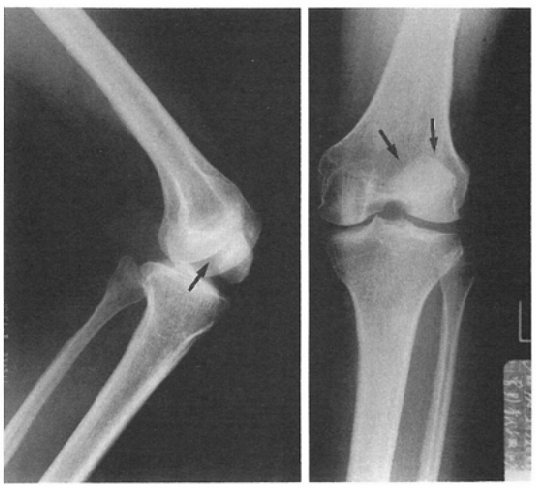

Fig. 4 Radiograph of the left knee joint in two views showing small patella (arrows) and hypoplastic lateral femoral condyle.

the view of the hemodialysis.

A history of instability on running from early childhood was noted. During the second pregnancy at 33 years of age, toxemia of pregnancy was pointed out. At 45 years of age, hypertension accompanied by qualitative proteinuria was indicated by a physician. During next 2 years, CRF became worse gradually so that hemodialysis was required.

On admission, physical examination revealed hypoplastic thumbnails (Fig. 1) and triangular lunulae of the third and fourth fingernails of either hand (Fig. 2). Further observation indicated dystrophy of the nails

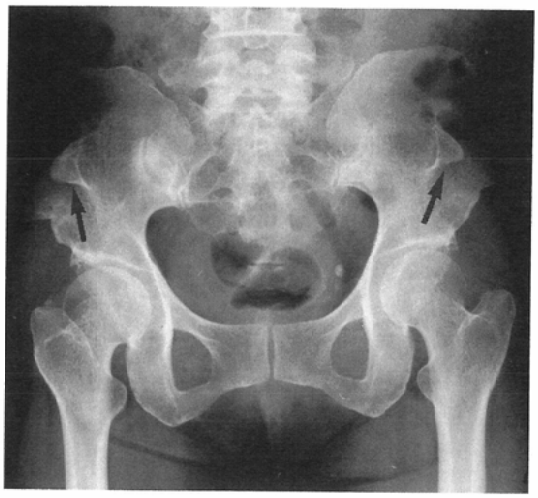

Fig. 5 Bilateral posterior iliac horns (arrows) are seen.

Fig. 6 Electron micrograph illustrating strands of collagen (arrows) in the glomerular basement membrane.

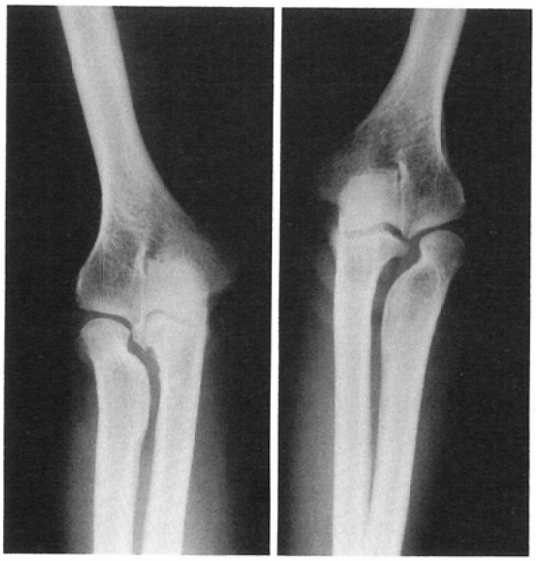

Fig. 7 Radiograph of the bilateral elbows showing hypoplastic radial heads with increase of carrying angle.

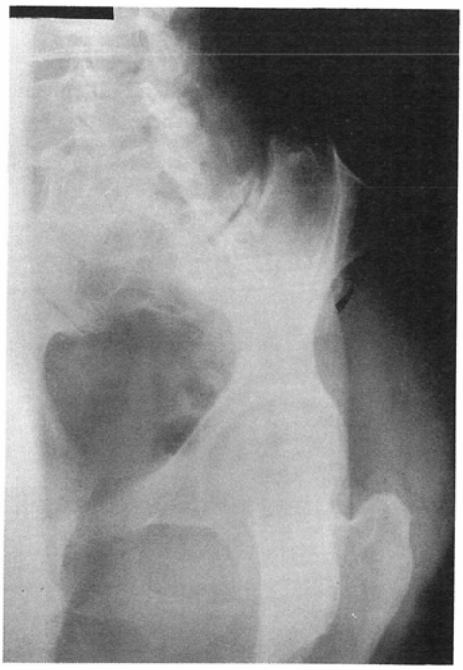

Fig. 8 Note left iliac horn (arrow) in left anterior oblique view.

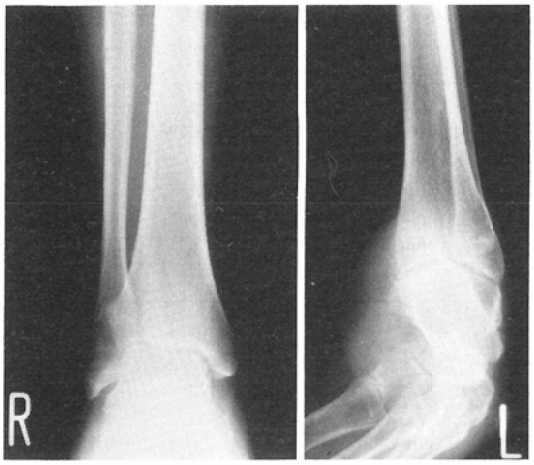

Fig. 9　Talipes equinovarus on left side is noted.

Table 1　Clinical findings in two cases

Findings	case 1	case 2
Hyponychia	(+)	(+)
Triangular lunulae	(+)	(+)
Iliac horn	(+)	(+)
Hypoplasia of capitulum and radial head	(+)	(+)
Hypoplasia of patella	(+)	(+)
Genu valgum	(+)	(+)
Scapular hypoplasia	(+)	(−)
Talipes equinovarus	(−)	(+)
Renal failure	(+)	(+)

on both toes (Fig. 3). Both elbows were held in slight flexion with limitted extension. She showed hypoplastic patellae and a genu valgum.

Radiologic examination of her knees showed hypoplastic patellae which were displaced leterally on extension, and a genu valgum with the hypoplastic lateral femoral condyles (Fig. 4). Bilateral posterior iliac horns were presented on the pelvic radiographic study (Fig. 5). Rentgenogram of the elbows showed hypoplastic radial heads with increase of carrying angle. Her relatives including father, the eldest brother, the eldest daughter and son showed similar physical changes attended by proteinuria. Those relatives as well as she had the group 0 blood.

On the basis of these features, she was diagnosed as NPS of hereditary nature and subsequent renal biopsy of her eldest daughter mentioned above was carried out. Electron microscopic examination of the renal biopsy specimen revealed deposition of collagen fibers in thickened glomerular basement membrane which were identical to those observed in NPS (Fig. 6).

Case 2.

A 56-year-old female was admitted for evaluation of CRF with hypertension.

At 44 years of age, hypertension with proteinuria was pointed out by a physician. During next 12 years, conservative therapy of CRF was practiced intermittently in several clinics. Because of the aggravation of it, she was awaiting hemodialysis at the time of her referral.

Physical examination on admission revealed the same findings as those of case 1 (Fig. 7) (Fig. 8), furthermore a talipes equinovarus on left side was noted (Fig. 9). These skeletal changes had been treated under diagnosis of polyomyelitis in those chinics.

Family history including the similar physical changes on her elder sister suggested hereditary disease in the same way as case 1.

Abnormal findings demonstrated in two cases are summarized in Table 1.

Discussion

We can find such many cases of NPS in Western countries, otherwise a small number of cases have been reported in Eastern countries. To the best of our knowledge, only 13 cases have been reported in Japan. Reports of NPS in Japan are shown in Table 2[4].

Perhaps the first documentation of NPS was by Chatelain in 1824, who described a family with anonychia of the thumbnails and aplasia of the patella. Then recognition is attributed to Little, who in 1897

Table 2 Reports of NPS in Japan

Reporters	No. of patients	Reference
Koizumi H. Nagao T. Yonemoto K.	2	Seikei Geka 18:133, 1967
Tsuchiya K. Kameshita K.	3	Yokohama Medical Bulletin 18:183, 1967
Takagi H. et al.	1	Jpn Med J 2647:30, 1975
Fukuzawa T. et al.	1	Jpn J Pediatr 82:469, 1978
Kuroda M. et al.	5	Jpn J Nephrol 20:909, 1978
Isoda K. et al.	1	Jpn J Nephrol 27:409, 1985
Total	13	

Table 3 Historical background of NPS

Reporters		Note
Chatelain	(1824)	A case with congenital anomaly of nail, elbow and knee.
Little	(1897)	42 cases including a family in whom 18 members over four generations.
Werde	(1909)	A cases involving cubital anomaly.
Firth	(1912)	Recognition of inheritance.
Trauner	(1925)	A family in whom 6 members including cubital change.
Turner	(1933)	Changes of nail, cubitus and knee were combined as triad.
Lester	(1936)	Lester iris meaning abnormal pigmentation of iris.
Kieser	(1939)	Report of iliac horn.
Fong	(1946)	Naming of iliac horn.
Mino	(1948)	Establishment of tetrad by additioning iliac horn.
Clarke	(1961)	Establishment of correlation with gene of ABO blood group.
Duncan	(1963)	252 cases.
Carbonara	(1964)	Investigation of incidence of renal manifestaion.
Simila	(1970)	Investigation of incidence of renal manifestaion.

described a series of patients with the nail and patellar dysplasias[5]. Table 3 summarizes historical background of NPS[6][7].

Typical clinical findings of NPS are those as follows:

i) dysplasia of the nail (anonychia, hyponychia, split nail, triangular lunulae) ii) aplasia or hypoplasia of the patella iii) subluxation of the cubital joint accompanied by hypoplasia of the capitulum and radial head iv) iliac horn v) ocular change (Lester iris, graucoma, microcornea) vi) renal manifestation (renal dysplasia, CRF, nephrotic syndrome) etc. Detalis and those incidence are shown in the Table 4[5].

Nephropathy is now a well established part of this syndrome. It has been considered to occur in up to 42% of cases with this condition[1][8]. Simila reported, 27% of patients with nepropathy in NPS had died of CRF[9].

In our case 1, the ultrastructural glomerular changes is identical to NPS, which is characterized by deposition of collagen fibers in a thickened glomerular basement membrane[10][11].

Correlation of NPS and gene of ABO blood group had been established by Clarke in 1961[12]. In our case 1, the blood group of the patient and her relatives are the same type, group 0 blood.

From the radiologic point of view, our two cases have typical bony changes designated above i), ii), iii), and iv) and they must have been demonstrated in previously performed radiographs, while they have been overlooked for a few years and only renal manifestation had been remarked as an independent symptom in certain clinics.

Clinical course of renal manifestation in NPS is resembling that of chronic glomerulonephritis so that typical radiologic findings of bony changes may be thought as a different problem from renal defect with

Table 4　Abnormal findings and their incidence of NPS

(Pechman, 1980)

1. cutaneous	95%	3. ocular	
anonychia		Lester iris	45%
hyponychia		glaucoma	
split nails		microcornea	
triangular lunulae		4. genitourinary	
2. orthopedic		renal dysplasia	40%
bilateral posterior iliac horns	30%	ureteral duplication	
hypoplasia of capitulum and radial head	90%	renal failure	25%
patellar aplasia	20%	nephrotic syndrome	
patellar hypoplasia or subluxation	70%	Goodpasture's syndrome	
scapular hypoplasia		chronic pyelonephritis	
scoliosis		5. others	
genu valgum		palmar-plantar hyperhidrosis	
talipes equihovarus		chronic neutropenia	
hypoplastic lateral humeral epicondyle		psychomotor retardation	
prominent medial humeral epicondyle			
hip flexion deformites			

NPS. Subsequently because of its poor trend of progression, it will not be brought up for discussion.

The evaluation of triangular lunulae has been settled as a clue in making diagnosis of NPS[13]. Besides it, radiologic findings are often the major criteria in establishing diagnosis of NPS[14].

Renal manifestation of NPS is progressive so that it will considerably affect the prognosis of patient with NPS, therefore it is of importance to make correct diagnosis of it by radiographs as early as possible. Close examiation of the kidney and urinary tact in the patient should be performed after correct diagnosis of NPS[6].

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