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DYSCHONDROSTEOSIS WITH TIBIA VARA —REPORT OF THREE CASES—

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Summary Three sporadic cases of dyschondrosteosis associated with marked tibia vara deformity are reported. The possibility of the associated appearance of these two anomalies has not been described to date, despite the fact that X-ray findings in the distal part of the radius in Madelung's deformity are very close to those in the proximal part of the tibia in tibia vara deformity, or Blount's disease, and the possibility that they might have the same etiological basis.

Dyschondrosteosis has been considered to be an autosomal dominant disease. Three sporadic cases reported here might be new mutants.

INTRODUCTION

Dyschondrosteosis is a heritable bone dysplasia characterized by moderate dwarfism, symmetrical shortening of the forearms in comparison with the upper arms, symmetrical shortening of the lower legs in comparison with the thighs (mesomelic micromelia) and fork-like deformity of the arms at the wrist regions known as Madelung's deformity. Since the first report by Leri and Weill in 1929, a number of cases of dyschondrosteosis have been reported in the French (Kaplan *et al.*, 1951; Berthaud and Auplat, 1954; Morel-Pescarolo, 1954; Maroteaux and Lamy, 1959; Sauvegrain and Nahum, 1963, and Fournier *et al.*, 1971), German (Brocher and Klein, 1962; Kirchmair, 1962, and Holenstein and Buchs, 1967) and Spanish (Gareiso *et al.*, 1937) literature. In 1965, Langer reported seven cases of this anomaly in English for the first time. Subsequently several cases were reported by different authors (Berdon *et al.*, 1965; Pinals and Heimann, 1965; Herdmann *et al.*, 1966; Henry and Thorburn, 1967; Felman and Kirkpatrick, 1969, 1970; Kozlowski and Zychowicz, 1971; Hoeffel *et al.*, 1972, and Carter and Currey, 1974).

This paper describes three sporadic cases of dyschondrosteosis associated with

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marked tibia vara deformity, *i.e.*, Blount's disease which appeared to be the first cases among Orientals.

CASE REPORTS

Case 1. Y. K., a 14-year-old male

He was born following a normal pregnancy and delivery and weighed 4,000 g at birth. His mother was 24 years old and his father, 27, when he was born. He had no siblings. The parents were normal and not consanguineous. There was no family history of malformation and/or short stature (Fig. 1a).

Since early childhood, abnormalities, such as short stature, fork-like deformity of the wrist, bowleg deformity and mental retardation were noted. He was studied by the authors on account of his short stature and bowleg deformity.

Physical examination. Physical examination revealed markedly short stature, *i.e.*, 135 cm (standard stature of a 14-year-old Japanese male is 160.5 cm), and shortening of the limbs especially of the forearms and lower legs. In each wrist region, the ulna protruded markedly to the dorso-distal direction and the radius curved toward the volar side at the distal end resulting in bilateral Madeling's deformity (Fig. 2). In

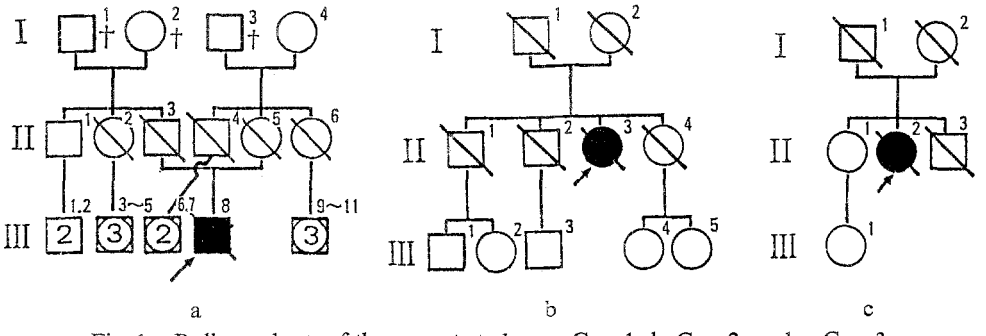

Fig. 1. Pedigree charts of the present study. a, Case 1; b, Case 2; and c, Case 3.

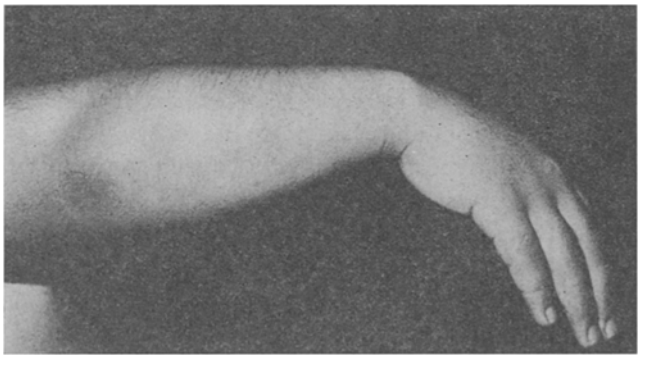

Fig. 2. External appearance of the right forearm showing Madelung's deformity in Case 1. See protruded end of the ulna toward the dorso-distal direction.

each knee region, marked tibia vara deformity was observed. The distance between the bilateral medial tibial condyles was 12 cm in the standing posture (Fig. 3). There was marked mental retardation showing a tendency to autism. Routine blood and urine examinations were normal. The Wassermann reaction was negative. Endocrinological examinations were also normal.

X-ray examination. Each radius showed marked shortening and bowing convex to the latero-volar direction. The shape of the distal radial epiphysis was triangular, the apex pointing to the ulnar margin. Premature fusion of the ulnar half of the epiphyseal line was observed. Each ulna was markedly protruded to the dorso-distal direction giving rise to the wedging of the carpal bones into the space between the distal end of the deformed radius and protruded ulna. Thus, the carpal bones formed a triangle configuration, the lunate being located at the apex of the triangle (Fig. 4). In the hands brachytelephalangy of each thumb and brachymesophalangy of each little finger were observed. There was marked deformity at the knee region. Due to severe ossification disturbance of the medial condyle, the articular surface showed oblique articulation resulting in tibia vara deformity, *i.e.*, Blount's disease (Fig. 5). In the feet, brachymetatarsy of each first metatarsus and brachybasophalangy of the left great toe were observed.

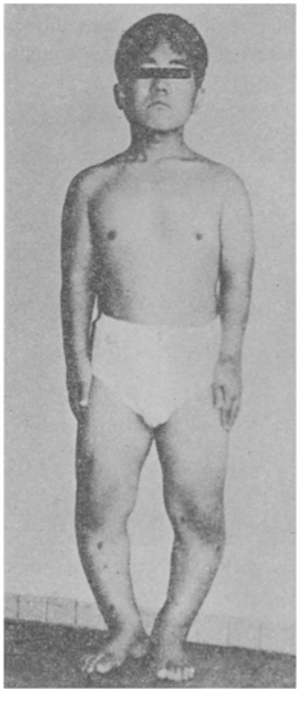

Fig. 3. External appearance of the whole body of Case 1 showing mesomelic dwarfism, Madelung's deformity and tibia vara deformity.

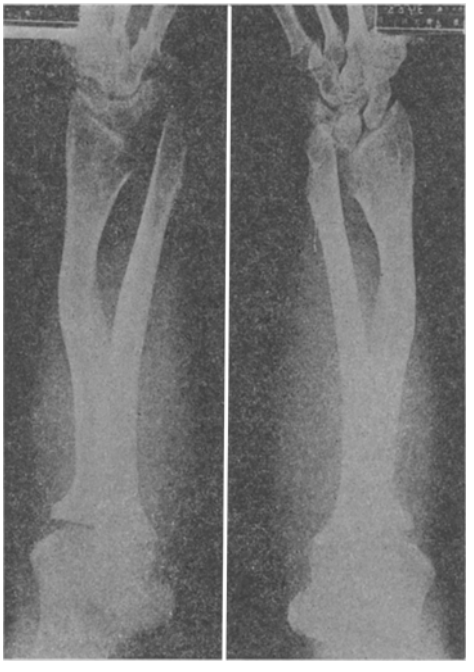

Fig. 4. Dorso-palmar X-ray picture of the forearms and wrists of Case 1 showing marked shortening of the forearms and typical Madelung's deformity at the wrist region.

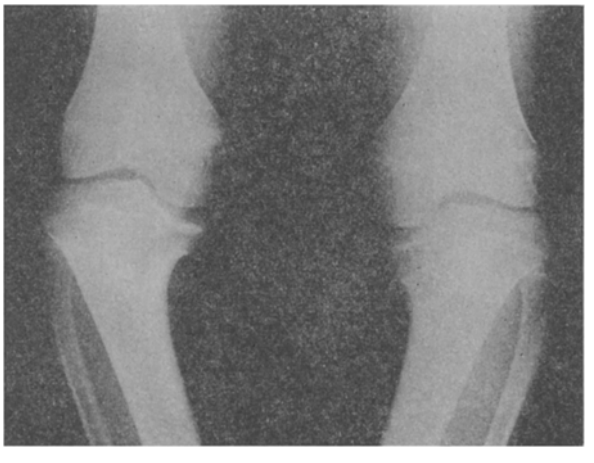

Fig. 5. Antero-posterior X-ray picture of both knee joints of Case 1 showing marked tibia vara deformity.

Case 2. H. N., a 33-year-old female

She was born following a normal pregnancy and delivery and weighed 3,750 g at birth. Her mother was 26 years old and her father, 30, when she was born. There

were three normal siblings. The parents were also normal and not consanguineous. There was no family history of malformation and/or short stature (Fig. 1b). Since early childhood, abnormalities, such as short stature and, wrist and bowleg deformities, were noted. During two years period before her initial visit, skin pigmentation increased gradually. As shown subsequently, examinations disclosed endocrinological patterns indicating Addison's disease. Hydrocortisone, 20 mg daily, has been given for about a year. As the result, patient recovered endocrinologically and her skin pigmentation became less marked.

Physical examination. Physical examination revealed markedly short stature, *i.e.*, 140 cm (standard stature of the Japanese adult female is 155.0 cm), with marked bowleg deformity. The distance between the bilateral medial tibial condyles was 15 cm in the standing posture. In each wrist region, conspicuous Madelung's deformity was noted. Marked brownish skin pigmentation was also observed all over the body, especially on the knuckles, forearms and lower legs (Fig. 6). Pigmentation of the gingiva was also seen. Both pubic and axillary hair was conspicuously sparse.

Laboratory examinations. Chromosomal analysis was normal. The Wassermann reaction was negative. Routine blood and urine examinations were also normal. The daily amount of urinary 17-OHCS excretion was 5.2 mg and that of 17-KS excretion was 1.5 mg. Diurnal serum cortisol levels were low (undetectable at midnight,

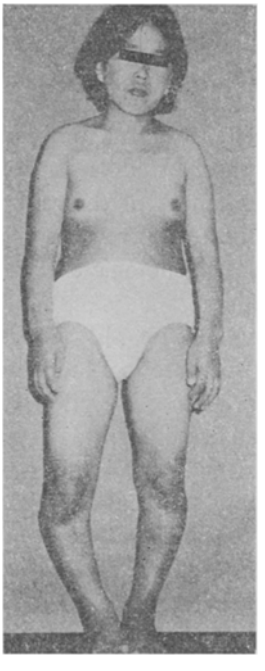

Fig. 6. External appearance of the whole body of Case 2 showing brownish pigmentation all over the body, mesomelic dwarfism, Madelung's deformity and tibia vara deformity.

3.2 μg/100 ml at 6 a.m., 4.6 μg/100 ml at noon and 3.9 μg/100 ml at 6 p.m.). Plasma ACTH levels were 1,600 pg/ml at 6 a.m. and 300 pg/ml at 6 p.m. The daily amount of urinary 17-OHCS excretion did not increase significantly by the intramuscular administration of ACTH or by the oral administration of SU-4885. T_3-RSU was 26.8%, and the serum thyroxine level was 12.4 μg/100 ml. The daily amount of urinary aldosterone excretion was 32.1 μg. Plasma renin activity was 515 ng/100 ml in the supine position. Fasting blood sugar was 62 mg/100 ml.

The findings are compatible with the patterns in Addison's disease.

X-ray examination. Exactly the same deformities of the wrists and knees as those seen in Case 1 were observed.

Case 3. K. S., a 25-year-old female

She was born after a normal pregnancy and delivery and weighed 3,600 g at birth. Her mother was 24 years old and her father, 28, when she was born. There were two normal siblings. The parents were also normal and not consanguineous. There was no family history of malformation and/or short stature (Fig. 1c).

Since early childhood, short stature and bowleg and wrist deformities were noted.

Physical examination revealed short stature, *i.e.*, 138 cm, with marked Madelung's deformity and tibia vara deformity, or Blount's disease. X-ray examination revealed exactly the same deformities of the wrists and knees as those seen in Case 1.

DISCUSSION

In 1878, Madelung described a painful abnormality of the wrist and forearm, which characteristically had its onset in adolescence without any history of previous injury or infection. The X-ray changes of the radius and ulna were described later by other researchers. Anton *et al.* (1938) reviewed the subject extensively. Dannenberg *et al.* (1939) introduced 12 roentgenologic criteria for the diagnosis of Madelung's deformity.

In 1929, Leri and Weill reported a case of dwarfism showing roentgenologic changes of the forearm and wrist similar to those in Madelung's deformity, although no reference was made to Madelung's original description. They believed this case to be a previously undescribed generalized osseous dysplasia and designated it as "dyschondrostéose."

Regarding to the relationship between Madelung's deformity and dyschondrosteosis, Langer, in 1965, came to the following conclusion: "Madelung's deformity of the forearm is the most striking feature of dyschondrosteosis, and it is our feeling that all cases with this deformity, except when it is secondary to trauma or infection, should be included under the heading of dyschondrosteosis."

The three cases presented here showed typical characteristics of dyschondrosteosis and, as far as it is known, they are the first cases reported in Japan. Furthermore, tibia vara deformity, *i.e.*, Blount's disease, was presented in all cases. As to Made-

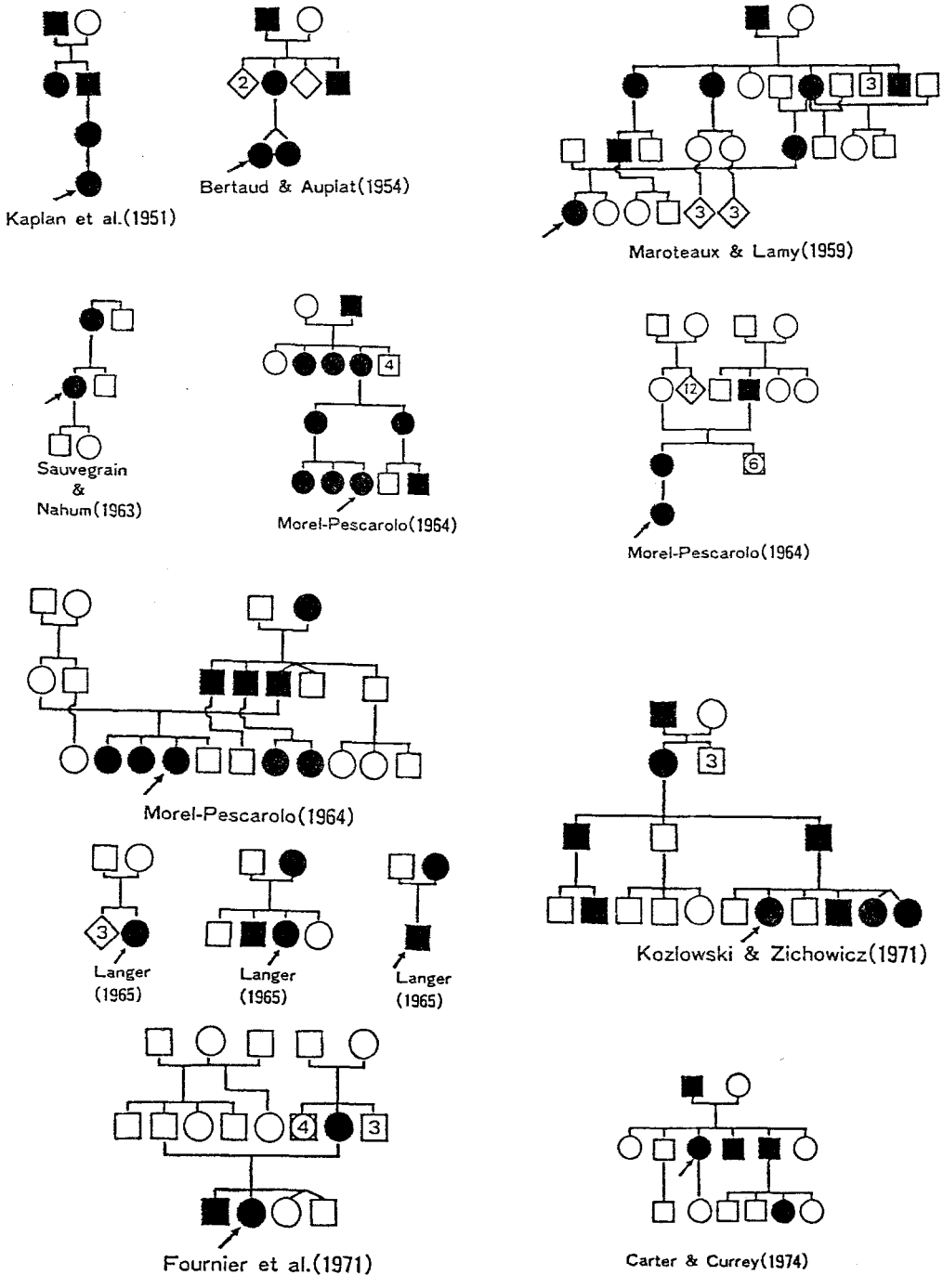

Fig. 7. Pedigree charts of dyschondrosteosis reported by different authors.

lung's deformity, the X-ray findings of the patients were quite compatible with all the criteria mentioned by Dannenberg *et al.* The X-ray findings of the radius in Madelung's deformity are similar to those found in the proximal part of the tibia in tibia vara deformity reported by Blount (1937), Golding (1963) and Langenskiöld and Riska (1964). In Madelung's deformity, the distal growth plate of the radius, which is the primary site of the occurrence of abnormality, shows premature fusion of the antero-medial quadrant. As growth proceeds, the characteristic deformity begins to take place and advances. In tibia vara deformity, the postero-medial quadrant of the proximal tibial epiphysis is mainly affected so that the deformity becomes more marked as the unaffected part continues to grow.

Thus the association of tibia vara deformity with dyschondrosteosis would be logical, presumably on the same etiological bases of these conditions. In fact, associated tibia vara deformity was observable by the authors in the cases presented by Brocher and Klein, Holenstein and Buchs, and Kozlowski and Zychowicz. These researchers, however, did not make any comment of the cause of the combined appearance of these deformities.

It still remains unknown, however, whether marked mental retardation showing a tendency toward autism in Case 1 and Addison's disease in Case 2 are associated findings with dyschondrosteosis or mere coincidental findings.

Genetics. Familial occurrence of dyschondrosteosis was noted by Kaplan *et al.* (1951). Bertaud and Auplat (1954), Morel-Pescarolo (1954), Maroteaux and Lamy (1959), Langer (1965), Fournier *et al.* (1971), Kozlowski and Zychowicz (1971) and Carter and Currey (1974). The pedigree charts in these families shown in Fig. 7 indicate that the abnormalities were transmitted as an autosomal dominant character. Prior to the report by Kaplan *et al.*, it was stated that such abnormalities occurred predominantly in females. In reality, however, symptomes of this anomaly in males were incomplete in most cases. As was mentioned by Maroteaux and Lamy, and

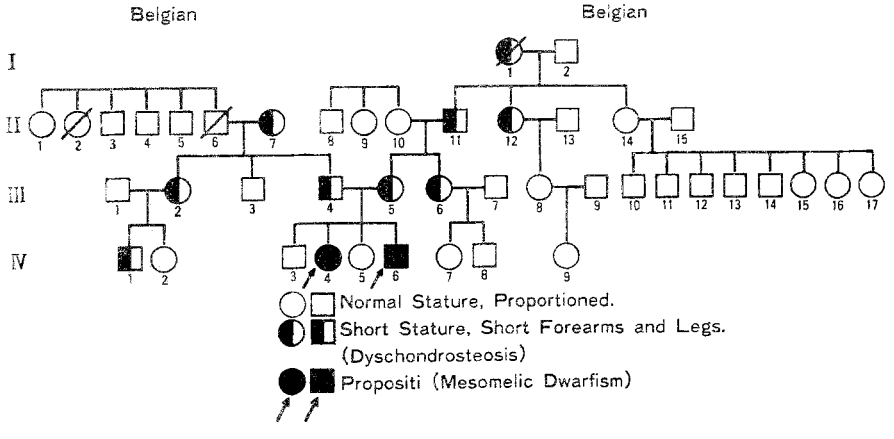

Fig. 8. Pedigree chart of mesomelic dysplasia reported by Espiritu *et al.*

Fournier *et al.*, more cases of subclinical, but definite, male patients would be detected if close X-ray examinations were performed on all members of related families. In the English literature, many reported cases of dyschondrosteosis are sporadic. The present three cases were also sporadic. Thus, there seems to be many sporadic cases of this anomaly. Most of them may be new mutants.

Espiritu *et al.* (1975) reported one family in which the parents and three other members showed clinical and roentgenologic features of dyschondrosteosis. The two propositi, a boy and a girl, had mesomelic dwarfism and hypoplasia of the mandibles, ulnae and fibulae (Fig. 8). It is their interpretation that mesomelic dysplasia (Langer type) is the clinical manifestation of the homozygous state for the dyschondrosteosis gene.

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