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Oto-Palato-Digital syndrome in four generations of a large family

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A new large family, affected by O-P-D syndrome is reported. Nine members in four consecutive generations have been studied.

Computerized tomography study of spine and skull showed abnormalities to be confined to mesodermal derivates, while nervous structures were normal.

Transmission pattern may be X-linked with intermediate expression in the female or autosomal dominant with sex limitation of expression.

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Oto-Palato-Digital syndrome was first recognized by Taybi in 1962. Since then other cases have been reported (Aase 1969, Gorlin & Poznanski 1973, Kozlowski et al. 1977, Jaeger & Refior 1969, Langer 1967, Singh et al. 1970) and it has been firmly established that this is a genetic condition although its mode of transmission is still uncertain (Dudding et al. 1967, Gall et al. 1972).

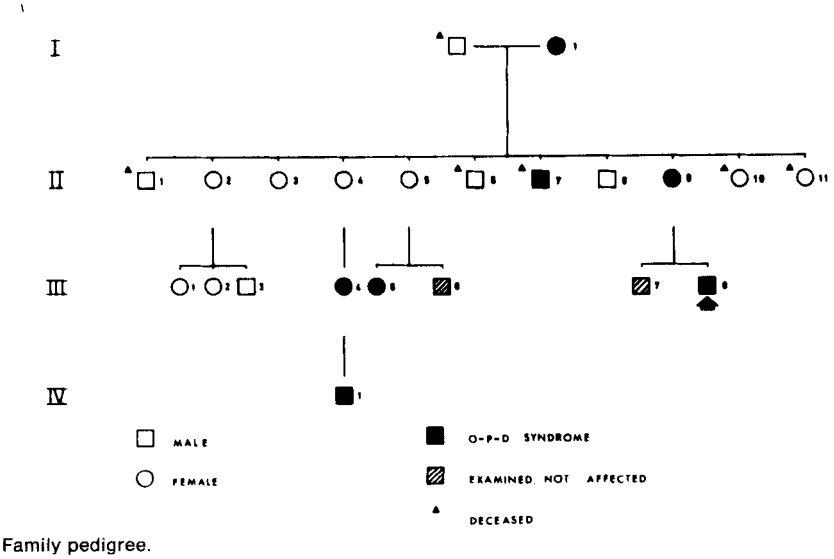


Fig. 1. Family pedigree.

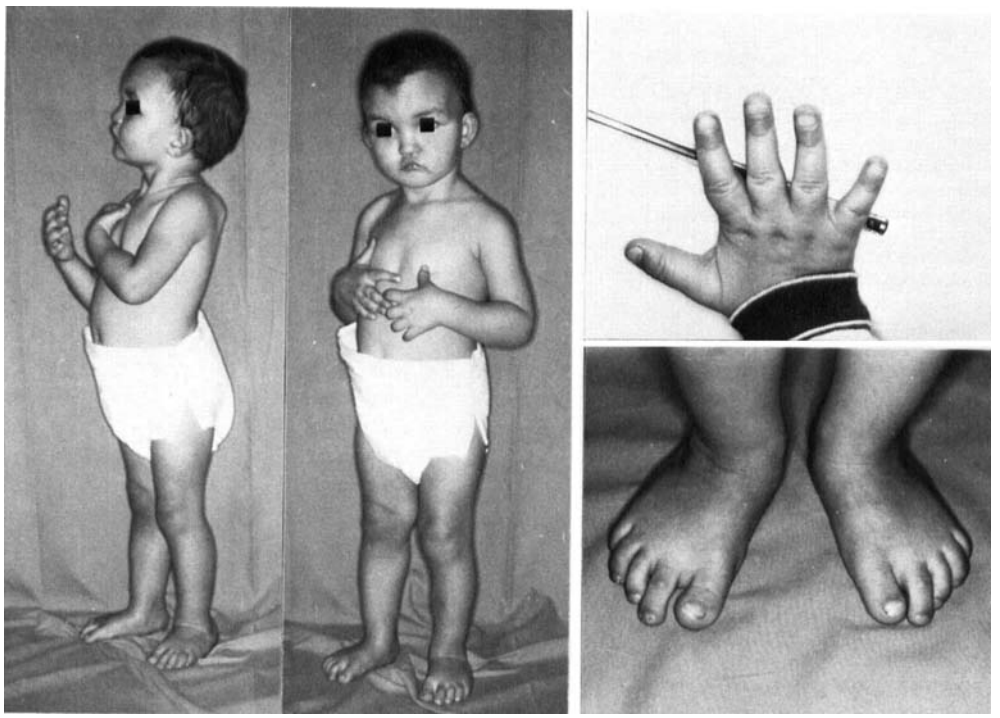


Fig. 2. Features of member IV1.

We report a new large family, in which the syndrome was followed in four consecutive generations.

Material and Methods

Nine members of the family were studied. Eight received a detailed physical examination and a radiologic bone survey. Computerized tomography of skull and spine was also performed in member III8.

Patient II7 was dead at the time of this study. The cause of death was reported to be respiratory failure secondary to a severe scoliosis, while the diagnosis of O-P-D syndrome was at that time missed. The patient's features were obtained from relatives' description, family portraits, and by the clinical and radiographic records of the hospital where the patient died.

Observations

Five males and four females were examined (Fig. 1). All females showed a variable expression of the disease both clinically and radiographically. Two of the five males were unaffected and three presented the complete phenotype of the syndrome.

Facial features of the proband and relatives were characteristic: they included overhanging brow, median frontal prominence, prominent occiput, prominent supraorbital ridges, broad depressed nasal bridge, anti-

Table 1

Clinical features of the affected males and females

	I1	II7	II9	III4	III5	III8	IV1
Short stature	−	−	−	−	−	−	−
Mental retardation	−	−	−	−	−	−	−
Deafness	−	−	−	−	−	−	−
Pectus excavatum	−	0	−	−	−	+/−	+/−
Scoliosis	−	+	−	−	−	−	−
Median frontal eminence	−	+	−	−	−	+	+
Overhanging bow	−	+	−	−	−	+	+
Prominent occiput	−	+	−	−	−	+	+
Prominent supraorbital ridges	−	+	−	−	−	+	+
Broad depressed nasal bridge	−	+	+	+	−	+	+
Antimongoloid slant	−	+	−	−	−	+	+
Laterally drooping upper lid	−	+	+	+	+	+	+
Hypertelorism	−	+	−	−	−	+	+
Flat mid face	+	+	+	+	+	+	+
Small jaw	+	+	+	+	+	+	+
Obtuse mandible angle	+	+	+	+	+	+	+
Cleft palate	−	0	−	−	−	−	−
High arched palate	+	0	+	+	+	+	+
Limited elbow extension-supination	−	0	−	−	−	−	−
Clinodactyly 2–3	−	0	−	−	−	+	+
Clinodactyly 5	−	0	−	−	−	+	+
Short 5th	−	0	−	−	−	+	+
Stub and spatulate thumb with short and large nail	+/−	+	+	−	−	+	+
Hip dislocation	−	−	−	−	−	−	−
Broad flat feet	−	0	−	−	−	−	−
Short great toe	+	0	+	+	−	+	+
Bulbous tip of great toe	−	0	+/−	−	−	+	+
Bulbous tip of other toes	−	0	+/−	−	−	+	+
Short and large nail of great toe	−	0	+/−	−	−	+	+
Short and large nail of other toes	−	0	+/−	−	−	+	+
Clinodactyly	−	0	−	−	−	+/−	+/−

+present; −absent; +/−questionable; 0 not investigated.

mongoloid slant of the eyes, a lateral drooping of the upper lid, hypertelorism, flat mid face, small jaw with an obtuse mandibular angle and high arched palate.

Hands and feet presented characteristic features: short and broad thumb and hallux, bulbous tip of the other fingers, clinodactyly. The nails of the affected fingers were flat, shorter and broader than normal (Fig. 2). These traits were fully evident and constant in the affected males, while in females they had a variable expression (Table 1).

The hand pattern profiles studied in six members of this family showed a considerable similarity with the mean pattern of O-P-D syndrome (Fig. 3), as well as among themselves (Poznanski et al. 1973).

The radiographic findings are summarized in Table 2. Member II7 showed a dorsal scoliosis of 130 degrees, which was responsible for the respiratory failure and the eventual death at the age of 34.

The main abnormalities of the spine were observed in the cervical and lumbar tract

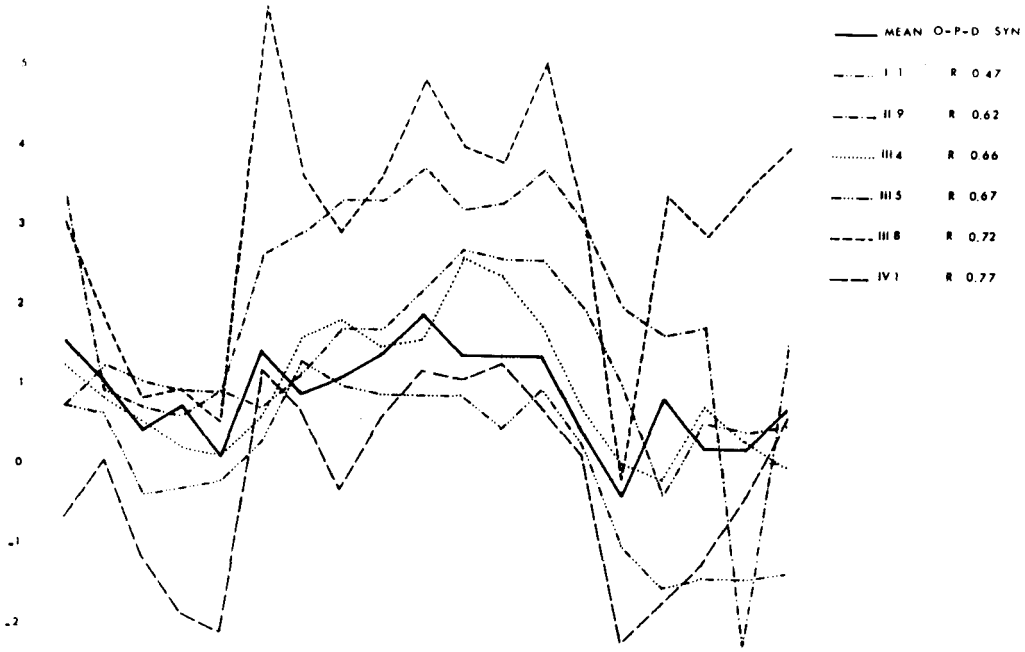


Fig. 3. Pattern profiles of the hands of six members of the family. R is the correlation coefficient of each of them to the O-P-D syndrome hand pattern profile.

and appeared exclusively in males. Vertebral bodies were larger than normal, with increased inter-peduncular distance and failure of fusion of the posterior arch. Vertebral bodies were shown to be enlarged by computerized tomography; otherwise they presented a normal appearance with a cortical wall of normal thickness and a regular trabecular pattern (Fig. 4). As a result of the vertebral body enlargement the interpeduncular distance was increased. There was a failure of fusion of the posterior arch on the median line, and the vertebral channel was consequently enlarged. In contrast, the transverse apophyses were of normal size.

Failure of fusion of the atlas anterior arch and a large foramen magnum were also present in the upper cervical spine. Medulla and spinal nerves were of normal size and morphology, contained in a very wide subarachnoid space. The vault profile of the skull presented irregular undulations which were more evident in correspondence with the frontal sinuses (Fig. 5). As a result of these irregularities the thickness of the skull vault was also very irregular. The brain was normal.

Karyograms of members II9 and III8 were, respectively, 46,XX and 46,XY (normal).

Discussion

In our family, as in the family reported by Gall et al. in 1972, no male-to-male trans-

Table 2

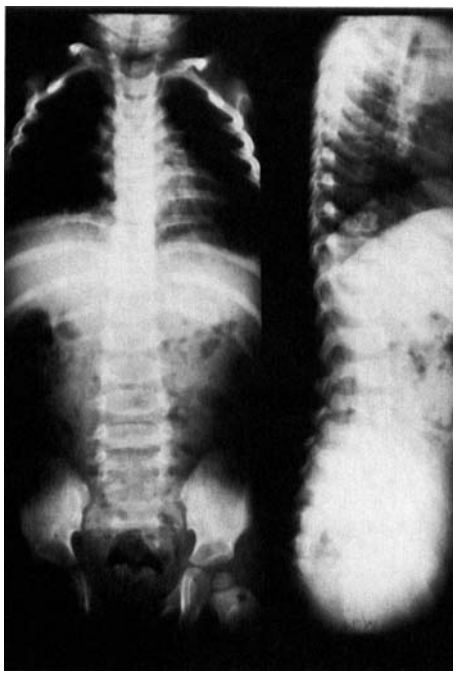
Radiographic findings of the affected males and females

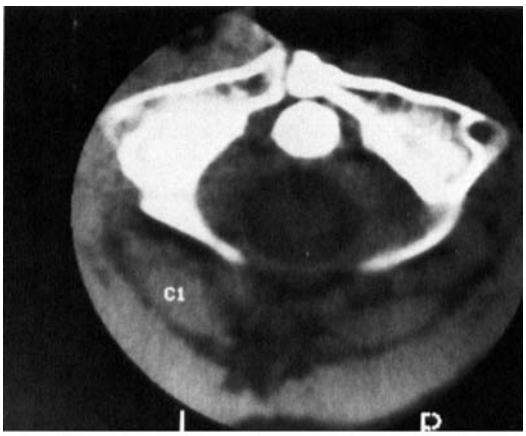
	II1	II7	II9	III4	III5	III8	IV1
Prominent frontal	0	0	−	0	0	−	−
Prominent occipital	0	0	−	0	0	−	−
Thick skull bones	0	0	+	0	0	+	−
Sinus hypoplasia	0	0	−	0	0	−	−
Poor mastoid pneumatization	0	0	+	0	0	+/−	+
Vertical clivus	0	0	+	0	0	+	+
Small mandible & obtuse mandible angle	0	0	+	0	0	+	+
Scoliosis	0	+	−	0	+	+	−
Abnormally large vertebral bodies	0	+	+	0	+	+	+
Widening of interpeduncolar distance	0	+	+/−	0	−	+	+
Failure of fusion of the post. arc	0	0	−	0	−	+	+
Absence of spinous apophyses	0	0	−	0	−	+	+
Posterior dislocation of the prox. radii	0	0	0	0	0	0	0
Clinodactyly or brachymesophalangia 5th	−	0	−	−	−	+	+
Broad 1st distal phalanx	−	0	+	−	−	+	+
Trapezium-scaphoid fusion	−L+R	0	+°	−	−	+L	0
Small carpals	−	0	+	+	−	+/−	0
Transverse capitate	−	0	−	−	−	+	0
Extra-carpal ossification	−	0	−	−	−	−	0
Capitate-hamate fusion	+L−R	0	+/−L	−	−	+	−
Trapezium-trapezoid fusion	−	0	+/−R	+L	−	−	0
Small iliac wings or flat angles	0	0	0	0	0	+	+
Dislocated hips	0	0	0	0	0	−	−
Coxa valga	0	0	0	0	0	−	+/−
Lateral bowing of femora	0	0	0	0	0	0	0
Lateral bowing of lower half of tibia	0	0	0	0	0	0	0
1st toe shorter than 2nd	+/−	0	+/−	+	−	+	0
Short 1st distal phalanx	+/−	0	+	+	+	+	0
Short 1st proximal phalanx	−	0	−	+	−	+	0
Prominent 5th MT base	+/−	0	−	+/−	+/−	−	0
Extra ossification center, base MT 5	−	0	−	−	−	−	0
MT 1 – medial cuneiform fusion	+°	0	+°	−	−	−	0
MT 2 – middle cuneiform fusion	+°	0	+°	−	+	+	0
MT 3 – lateral cuneiform fusion	+°	0	+°	+	+	+	0
MT – cuboid fusion	+°	0	+°	−	−	−	0
Involving cuneiform fusion or joint narrowing	+°	0	+°	+	+	+	0
Other tarsal fusion or joint narrowing	−	0	−	+	−	+	0

+ present; − absent; +/− questionable; 0 not investigated.
L = left; R = right; ° = bilateral.

mission of the trait has yet occurred. Therefore, both an X-linked transmission with intermediate expression in the female or an autosomal dominant with sex limitation of expression are possible. The full expression of the trait is evident only in males, where features of the face, hands and feet are easily recognizable.

Deafness, mental retardation, short stature and cleft palate observed in earlier reports (Dudding et al. 1967, Kozlowski et al. 1977, Jaeger & Refior 1969, Langer 1967, Nager & Char 1971, Spranger et al. 1974, Taybi 1962) were lacking in this family and they are probably not constant features of the syndrome.





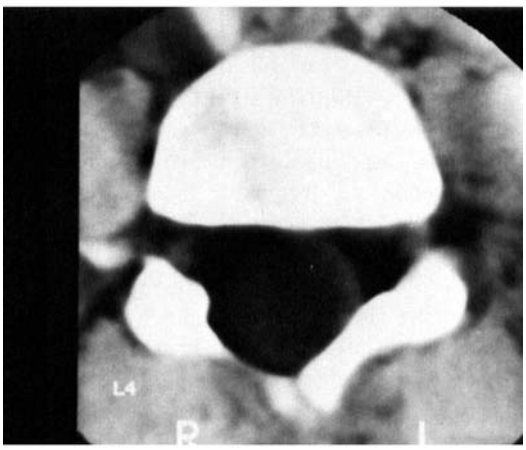


Fig. 4. Spine roentgenograms show large vertebral bodies and increased interpeduncular distance in both cervical and lumbar tract.
Computerized tomography: failure of fusion of the atlas anterior arch and a large vertebral channel of the cervical tract are observed. Lumbar vertebral bodies are enlarged, but medulla is of normal size.

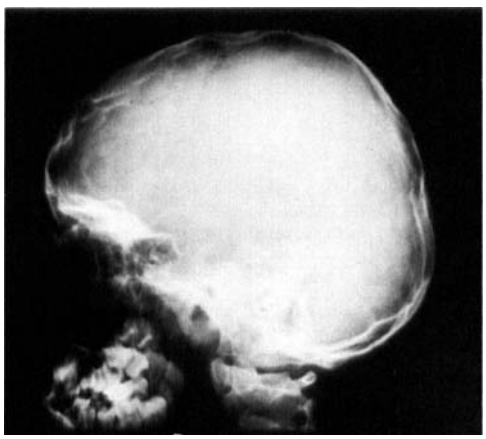


Fig. 5. Irregular undulations of the skull vault.

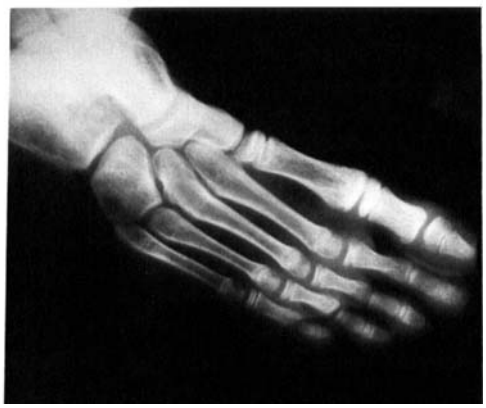


Fig. 6. Tarsal bone fusions are characteristic of the syndrome: scaphoid – 1st cuneiform; 2nd cuneiform – 2nd metatarsal; 3rd cuneiform – 3rd metatarsal. A broad distal phalanx of the first and second toes is also evident.

Scoliosis is found for the first time to be associated with O-P-D syndrome. The absence of scoliosis in the other male members of this family and in all the reported cases of this disease probably indicates that the two conditions have been fortuitously associated in this patient; nevertheless, the feature deserves to be investigated in further cases.

Computerized tomography has been carried out for the first time in O-P-D syndrome. It shows abnormal development to be confined to mesodermal derivates (vertebrae and skull), while nervous system structures are unaffected.

The expression of the O-P-D syndrome gene in females is variable; in three members of this family (II9, III4, III5) the traits were easily detectable clinically, while in the fourth (II), age and osteoarthritic changes of the hands and feet made them difficult to recognize. In this case the more reliable criteria were carpal and tarsal fusions (Fig. 6).

Members II4 and II5, females, were not available for the study, but they are obligate carriers of the gene.

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