Orofaciodigital syndrome type I associated with polycystic kidneys and agenesis of the corpus callosum

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SUMMARY We report a female case of orofaciodigital syndrome type I (OFD I) associated with polycystic kidneys and agenesis of the corpus callosum. She had chronic renal failure requiring maintenance dialysis and significant neurological deficits. Her mother had less severe OFD I associated with polycystic kidneys but her renal function was normal and there was no clinical or radiological evidence of a structural abnormality of the brain.

In 1954, Papillon-Léage and Psaume\(^1\) first described a syndrome of multiple congenital abnormalities which most characteristically affects the oral cavity, face, and digits. It has become known as the orofaciodigital syndrome type I (OFD I) and the inheritance appears to be X linked dominant with lethality in males. The majority of patients studied have had normal karyotypes.

Since 1964 several cases of OFD I have been reported in association with polycystic kidneys. The first two\(^2\) were females aged 38 and 72 years in whom the diagnosis was made at necropsy. Both patients had evidence of renal impairment before death. The third\(^3\) was the infant of an unaffected 13 year old mother. The infant died two hours after delivery due to extensive multiple congenital abnormalities and was reported as having orofaciodigital syndrome and polycystic kidneys. Then, from a series of 12 cases, polycystic anomalies of the kidney were described in five out of seven who had necropsies.\(^4\) Only two patients have been reported who have been treated with dialysis for renal failure. One, a female aged 48 years, required regular haemodialysis\(^5\) and the other, a female of 23 years, had regular peritoneal dialysis.\(^6\)

Mental retardation is frequently present in this syndrome and various structural abnormalities of the central nervous system are present in at least 13% of cases. Between 1955 and 1974 19 patients with central nervous system abnormalities were reported and five of these had agenesis of the corpus callosum.\(^7\) More recently, a case has been reported where computerised tomography showed agenesis of the corpus callosum.\(^8\)

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The female proband was born at term in October...
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1964 weighing 3230 g and was noted to have multiple congenital abnormalities. She was the only child of non-consanguineous parents. Her mother had had no spontaneous abortions. At the age of three years a diagnosis of OFD I was made. She had a cleft soft palate requiring plastic surgery and also a partial cleft of the hard palate. There was a hypertrophic irregular lingual frenum and thick fibrous bands between the buccal mucosa and alveolar ridges. The tongue was partially cleft into lobes and a typical nodule was present on the left margin (fig 1). There was clinodactyly affecting the fingers and toes and syndactyly of the fingers of both hands requiring surgical correction (fig 1). Patchy alopecia of the scalp and dry hair were also present and she had the typical facies with short upper lip and broad nasal root (fig 2). She grew along the 25th centile for height until she was 12 years of age but thereafter the height velocity diminished, possibly because of the development of renal failure, so that the final height of 151 cm was at the lower limit of normal, on the 3rd centile. Significant mental retardation was a major feature with an IQ of around 70 and she had marked dysarthria and a clumsy gait from early childhood.

By the age of 17 years she had established chronic renal failure and bilaterally palpable renal masses. Ultrasound and intravenous urography showed polycystic kidneys. There were no cysts seen in the liver or pancreas. Treatment was initially conservative, but after four months she required dialysis when the serum urea was 45 mmol/l, creatinine 1130 μmol/l, bicarbonate 9 mmol/l, and haemoglobin 6 g/dl. At this time she was established on continuous ambulatory peritoneal dialysis. She has since been transferred to maintenance haemodialysis and is awaiting renal transplantation.

At six years of age an electroencephalogram was performed and this showed non-specific diffuse abnormalities. At 20 years of age computerised tomography of the head showed cerebral and cerebellar atrophy and, in addition, serial tomograms showed total absence of the corpus callosum (fig 3).

Her mother also suffers from OFD I of lesser severity. She had had operative correction of oral malformations and of syndactyly affecting the fingers.
of her right hand. She has clinodactyly and tongue malformations similar to the daughter. Ultrasound examination again revealed polycystic kidneys. However, renal function is normal at 44 years of age with a serum creatinine of 88 μmol/L and urea of 5.8 mmol/L. She is of normal intelligence with no neurological dysfunction and computerised tomography of the head did not show any structural abnormality of the brain.

There is no known history of congenital malformation or of renal disease in the mother’s three brothers and three sisters, in the maternal grandmother, or in the maternal great grandmother.

Chromosomal studies of both the proband and her mother showed normal female 46,XX karyotypes on analysis of banding patterns after trypsin-Giemsa staining. Both had a large heterochromatic band on chromosome 1 visible on C banding; such a band is usually considered to be a normal population variant.

Discussion

These two patients add to the reported cases of OFD I associated with polycystic kidneys. The proband had end stage renal failure and is the third adult female with this combination requiring maintenance dialysis. Although a chance association with the relatively common adult type polycystic disease of the kidneys cannot be excluded, this report supports the evidence for polycystic renal changes being a distinct feature of the syndrome. Further information from the screening of patients of OFD I and, when possible, necropsies, will eventually reveal the true incidence of the renal abnormality.

As many as one-third of infants with OFD I die in their first year of life and it has been suggested that neuroradiological evaluation is a valuable guide to longevity and prognosis. Agenesis of the corpus callosum in combination with cerebral and cerebellar atrophy are the likely explanations for our patient’s mental retardation, communication difficulty, and clumsy gait. However, these clinical features are relatively mild and the severe structural abnormalities of the brain in her case have been compatible with a happy life in sheltered employment.

The inheritance of OFD I is usually considered to be by an X linked dominant gene with lethality in the hemizygous male. The inheritance in this family would be compatible with this interpretation.

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References


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An oculocerebral hypopigmentation syndrome: a case report with clinical, histochemical, and ultrastructural findings

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