British Journal of Oral Surgery (1981), **19**, 142-147 0007-117X/81/00230142$02.00

ORAL FACIAL DIGITAL SYNDROME—Case Report and Review of the Literature

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Summary. A patient is described with developmental deformities of the mouth, face and limbs. Patients with similar deformities have previously been described and referred to as the oral-facial-digital syndrome, Type I or Type II. This patient, however, had characteristics of both types in addition to malformation of the limbs and temporal lobe epilepsy features not previously described.

Introduction

In 1954 Papillon-Leage and Psaume described a new syndrome involving malformations of the face, oral cavity and digits. Subsequently, this syndrome became known as the oral-facial-digital syndrome (OFD I), and a number of cases have been reported (Gorlin & Psaume, 1962; Ruess *et al.*, 1962; Doege *et al.*, 1964; 1968; Dodge & Kernohan, 1967; Kernohan & Dodge, 1969; Solomon *et al.*, 1970; Wood *et al.*, 1975). The characteristic features are multiple hyperplastic lingual and labial frenula, lobate tongue, tooth anomalies (Lauterstein & Pruzansky, 1969) median clefts of the upper lip and palate, hypoplasia of the base of the skull and the facial bones (Aduss & Pruzansky, 1964; Schwartz & Fish, 1960), aplasia of the alar nasal cartilages and ocular hypertelorism.

There are variable digital malformations, syndactyly and brachydactyly being the most common. Mental retardation is seen in 30 to 50 per cent of cases (Gorlin & Psaume, 1962; Ruess *et al.*, 1962, 1965; Doege *et al.*, 1964, 1968; Solomon *et al.*, 1970; Wood *et al.*, 1975). Other features described are tremor (Gorlin *et al.*, 1961), cerebral anomalies (Wood *et al.*, 1975), polycystic disease of the kidneys and liver (Doege *et al.*, 1964; Tucker *et al.*, 1966), dry skin, milia and alopecia (Papillon-Leage & Psaume, 1954; Solomon *et al.*, 1970; Ruess *et al.*, 1965).

The incidence of OFD I is considered to be 15:1,000 persons with cleft lip and/or palate, or 0.0225:1,000 live births (Wahrman *et al.*, 1966). It occurs almost exclusively in females and is thought to be due to an X-linked or sex limited autosomal dominant trait with a lethal effect in males.

Several cases of OFD I have been reported in males (Kushnik *et al.*, 1963; Wahrman *et al.*, 1966; Mandell *et al.*, 1967; Theodoru, 1971; Chaurasia *et al.*, 1975), however, two of these had an XXY karyotype (Kushnik *et al.*, 1963; Wahrman *et al.*, 1966) and it is likely that others had the Mohr Syndrome (Mandell *et al.*, 1967; Chaurasia *et al.*, 1975).

In 1941 Mohr described a family, later restudied by Claussen (1946) in which four brothers and a male cousin had OFD malformations. This syndrome is inherited as an autosomal recessive trait. Parental consanguinity has been demonstrated (Claussen, 1946) and there have been several examples of the syndrome in siblings (Thurston, 1908; Mohr, 1941; Claussen, 1946; Rimoin & Edgerton, 1967; Gustavson *et al.*, 1971; Goldstein & Medina, 1974). The Mohr syndrome includes malformations found in

(*Received* 4 March 1980; *accepted* 2 July 1980)

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Table I

Oral and facial characteristics of OFD I, OFD II and case report patient (PM)

	OFD I	OFD II	Patient (PM)
Alveolar ridge	Thick bands cleave alveolar ridge	Normal or flaring	Normal
Nose	Alar cartilage hypoplasia Broad nasal root	Broad bifid tip Broad nasal root	Broad nasal root
Dentition	Mandibular incisors absent Duplication of canines Increased susceptibility to caries	Variable dental anomalies; often absent lower central incisors	Mandibular lateral incisors absent Caries + + + in adult life
Mandible	Hypoplasia of ramus	Hypoplasia of body	Normal
Palate and lip	Usually cleft in midline of upper lip Palate often cleft bilaterally	Midline cleft of upper lip Cleft palate in some cases	Broad phyltrum Multiple labial frenula
Tongue	Hamartomas Multiple frenula Bifid, trifid or quadrafid	Hamartomas Multiple frenula Cleft	Fatty Hamartomas Short frenulum

Table II

Clinical features found in patients with OFD I, OFD II and in case report (PM)

	OFD I	OFD II	Patient (PM)
Inheritance	X-linked dominant	Autosomal recessive	Autosomal recessive or new mutation
Sex	Females only	Males and females	Female
Hair	Coarse and thin	Normal	Normal during youth – diffusely thin in past two years
Skin	Dry skin Milia	Normal	Normal until onset of rosacea four years ago
Digits	Clinodactyly Syndactyly Brachydactyly Polydactyly (less often)	Bilateral polydactyly of halluces Bimanual hexadactyly	Clinodactyly Syndactyly Brachydactyly Polydactyly
Skeleton	Increased cranial base angle Zygomatic hypoplasia Irregular reticular areas of short tubular bones	Zygomatic hypoplasia Metaphyseal irregularity and flaring	Bones of forearms bowed and shortened Elbow joints disrupted Gross deformity of tibia and fibulae necessitating below knee amputation
Hearing	Normal	Conductive hearing defect	Normal
C.N.S.	Mental redardation 30-50% of cases Tremor Hydrocephaly Porencephaly Hydrancephaly Partial agenesis of corpus callosum	Mental retardation Microcephaly Hydrocephaly Porencephaly Choroid coloboma Muscular hypotonia with poor co-ordination	Temporal lobe epilepsy

the OFD I snydrome, but there are distinct differences (Table I & II). The evidence accumulated from reported cases suggests that there are at least two distinct genetic entities associated with OFD malformations; the classical OFD syndrome or OFD I and the Mohr syndrome or OFD II (Rimoin & Edgerton, 1967).

This case report is of an adult female with a combination of malformations which are not entirely compatible with either OFD I or OFD II. She also exhibited two previously unreported features, severe malformations of the forearms and lower legs, and temporal lobe epilepsy.

Case report

PM was a 53-year-old caucasian female of normal intelligence. Her parents were unrelated. There was no family history of congenital anomalies.

At birth there were six toes on each foot and there were seven digits on one hand and six on the other. Some of the extra ulnar digits were removed at the age of one year. Bilateral below-knee amputations were performed at the age of 12 years because the lower legs remained disproportionately short with severe malformation of tibiae and fibulae. Similar abnormalities have been described by Büttner and Eysholdt (1950) and Wolf (1952). Temporal lobe epilepsy was first noted at the age of 40 years.

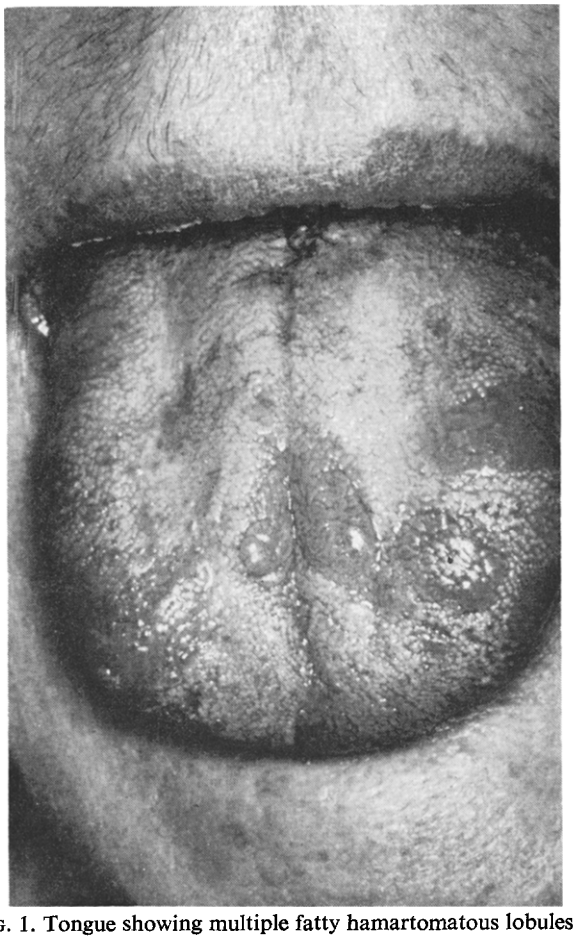

FIG. 1. Tongue showing multiple fatty hamartomatous lobules.

On examination the nasal root was broad and there was slight dystopia canthorum. She had ankyloglossia with a short lingual frenulum and there were hamartomatous lobules on the tongue (Fig. 1). Thick hyperplastic frenula extended across the labio-gingival sulcus (Fig. 2) and the phyltrum was broad. A prominent bony ridge extended along the midline of the hard palate. The mandibular lateral incisors were absent from birth, and she also had an extra tooth between the upper central incisors which was removed in childhood. The teeth have been extensively affected by caries, the lower central incisors having been removed for this reason.

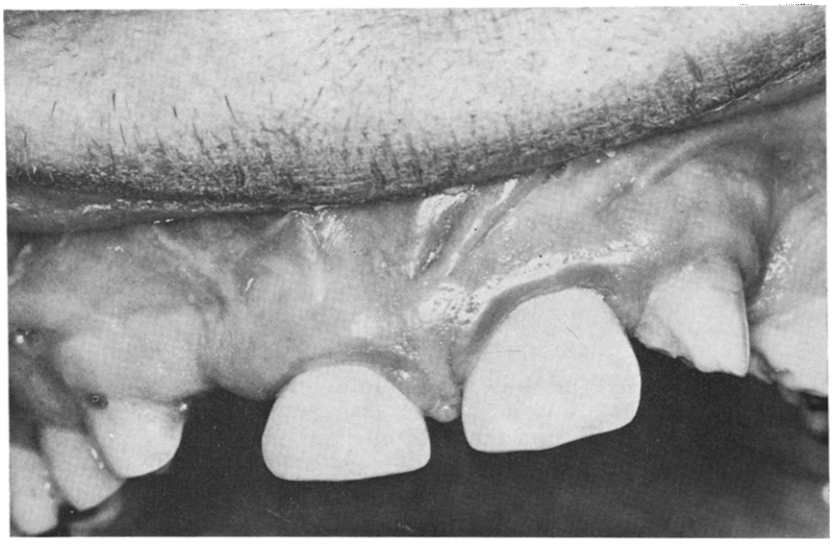

FIG. 2. Multiple hyperplastic frenula extending across the labio-gingival sulcus.

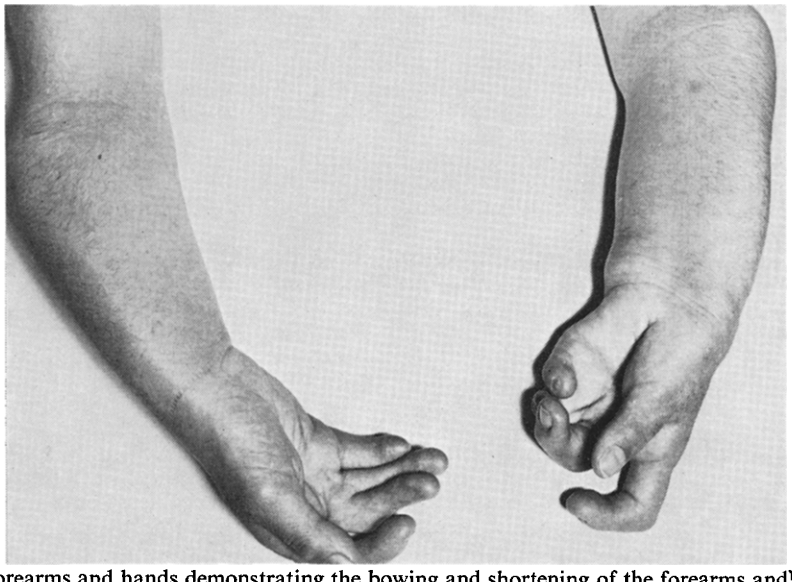

FIG. 3. Forearms and hands demonstrating the bowing and shortening of the forearms and brachydactyly, syndactyly and clinodactyly.

The forearms and hands were grossly deformed, the forearms being abnormally short and broad. She had six digits on the left hand and five digits on the right hand. These digits showed brachydactyly, syndactyly, and clinodactyly (Fig. 3). The radiological abnormalities were confined to the forearms and hands. There was bowing and shortening of the bones of the forearms associated with disruption of the elbow joints. The abnormalities of the digits as recorded above were demonstrated on radiographs.

Her hair had become diffusely thin during the two years before presentation but was previously normal. She developed rosacea four years before presentation. Chromosome studies showed that she had a normal female complement of 46 XX.

Discussion

It can be seen from Tables I and II that the case presented is typical of neither OFD I nor OFD II, although it is most compatible with OFD II. Studies of families with the OFD I syndrome have shown extreme variability in clinical manifestations. In some cases the syndrome can exist with minimal expression of the typical features and therefore it could appear to miss several generations before reappearing (Kernohan & Dodge, 1969). The multisystem involvement in the OFD syndromes suggests a chromosomal aberration involving more than one gene, but the evidence suggests that usually the amount of chromosome material involved is small (Dodge & Kernohan, 1969).

Inconsistent reports of a chromosomal abnormality have been published (Patan *et al.*, 1961; Gorlin & Psaume, 1962; Ruess *et al.*, 1962; Mandell *et al.*, 1967), however most patients have been found to have a normal chromosome pattern.

Since there is no family history, the OFD malformations in this case could have resulted from a spontaneous mutation, an autosomal recessive trait or an X-linked dominant trait with minimal expression in the preceding generations.

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