MANDIBULO-FACIAL DYSOSTOSIS*† A FAMILIAL STUDY

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MANDIBULO-FACIAL dysostosis is the name given by Franceschetti and Zwahlen (1944) and Franceschetti and Klein (1949) to a complex of symptoms which together comprise a congenital oro-facial syndrome (Wildervanck, 1960).

Franceschetti and Klein (1949) reviewed the literature and described the typical characteristics of the syndrome as follows:

- (1) Antimongoloid palpebral fissures with either a notch or coloboma of the outer third of the lower lid, and occasional absence or paucity of the lashes of the lower lid.
- (2) Hypoplasia of the facial bones, especially the malar bones and mandible.
- (3) Malformation of the external ear, and occasionally of the middle and inner ear, with low implantation of the auricle.
- (4) Macrostomia, high palate, mal-occlusion and abnormal position of the teeth.
- (5) A typical hair growth in the form of tongue-shaped processes of the hair-line extending towards the cheeks in the pre-auricular region.
- (6) Association at times with other anomalies, such as obliteration of the naso-frontal angle, pits or clefts between the mouth and ear, and skeletal deformities.

Since this description was published, some of these features have come to be regarded as being of lesser importance and some have been emphasized in the diagnosis. Thus Axelsson, Brolin, Engström, and Lidén (1963) named the following features as "obligatory":

- (1) Antimongoloid palpebral fissures.
- (2) Anomaly of the lower lid: coloboma of the outer third, or deficient lashes, or both.
- (3) Hypoplasia of the malar bones.
- (4) Hypoplasia of the mandible.

Present Investigation

The propositus (V, 9 in Fig. 1) was seen at a routine school medical examination. Although not severely affected, he showed all the "obligatory" features, and also had large prominent pinnae with low implantation of the auricles, irregular dentition, and mal-occlusion. X rays revealed absence of the zygomatic arch and hypoplasia of the malar bones and mandible. There was no hearing loss. Because of the known familial incidence of mandibulo-facial dysostosis, the family tree was traced. There is no evidence of consanguinity, although the family represents a typical non-migrant section of what has been, until comparatively recently, a small closed community.

The pedigree (Fig. 1, opposite) consists of five generations and eight sibships. In Generations II and III, except III(6), reliance had to be placed on photographs and family reports, as all except III(6) had died or left the district before the start of this investigation. In all, sixteen members of the family were examined and a further fifteen were assessed from photographs. One sibship (IV, 5-7, reported normal) has been excluded because of lack of data.

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FIG. 1.—Pedigree of mandibulo-facial dysostosis in five generations. For lack of evidence, sibship IV (5, 6, 7) has been excluded from the study.

Audiometric examination and x-ray examinations of the skull and facial bones were carried out on all those who were examined personally.

No history of stillbirth or abortion was obtained from any member of the family who was interviewed.

Results of Investigation

Seven members of the family as well as the proband were found to be affected, a brother and sister of the proband, his mother, and four maternal relatives.

II (2), great-grandfather of proband.—Photographs showed antimongoloid obliquity of the palpebral fissures; colobomata of both lower lids with absence of lashes; flattening of the naso-frontal angle; depression of the malar bones, but a long beard effectively hid the lower third of the face.

III (6), grandmother of proband.—Examination showed antimongoloid obliquity of the palpebral fissures with absence of lashes on the lower lids; deformity of the left external ear and low implantation of the auricles; a pre-auricular tongue of hair extending forward onto the cheeks.

X rays confirmed the clinical impression of hypoplasia of the malar bones and mandible, and the absence of the zygomatic arch. There was slightly defective hearing consistent with presbycusis.

III (7), great-uncle of proband (Fig. 2, overleaf).—Photographs showed antimongoloid obliquity of the palpebral fissures but they were not sufficiently clear to demonstrate the condition of the lower lids. There was a marked deformity of the left external ear and a history of deafness and mental retardation from infancy. The malar bones were hypoplastic, and the mandible, although partly obscured by a small beard, markedly hypoplastic. The beard in itself is probably significant as this photograph was dated 1925, a time when beards were extremely rare especially amongst young men.

IV (1), maternal uncle of proband.—Examination showed antimongoloid obliquity of the palpebral fissures, absence of lashes of the lower lids, low implantation of the auricles, hypoplasia of the malar bones and mandible, and flattening of the naso-frontal angle. The absence of the

FIG. 2.—III (7), great-uncle of propositus, showing deformity of pinna and hypoplasia of mandible.

FIG. 3.—V (10), sister of propositus, showing antimongoloid palpebral fissures and absence of lashes on the lower eyelids.

zygomatic arch was confirmed by *x* ray. There was mal-occlusion of the teeth, and irregular dentition. A tongue of hair extended forward onto the cheek. There was no hearing defect.

IV (3), mother of propositus.—Examination showed antimongoloid obliquity of the palpebral fissures, paucity of lashes on the lower lid, and flattening of the naso-frontal angle. There was low implantation of the auricles and a tongue of hair extending forward in front of the ears and onto the cheek. *X* rays confirmed hypoplasia of the mandible and malar bones and absence of the zygomatic arch. There was abnormal dentition, and mal-occlusion of the teeth.

V (9), propositus.

V (10), sister of propositus (Fig. 3).—This was the most severely affected of those who were examined personally. The hypoplasia of the mandible and macrostomia gave the characteristic "bird-face" appearance referred to in some of the early descriptions of the syndrome. There was antimongoloid obliquity of the palpebral fissures, almost complete absence of the lashes of the lower lids, low implantation of the auricles which were large and prominent, and a tongue of hair extending forward from the ears and onto the cheeks. A high-arched palate, irregular dentition, and mal-occlusion were noted. *X* rays confirmed the hypoplasia of the malar bones, extreme hypoplasia of the mandible, and absence of the zygomatic arch. There was no significant hearing loss.

V (11), brother of propositus.—Examination showed antimongoloid obliquity of the palpebral fissures and paucity of lashes of the lower lids. *X* rays showed minimal hypoplasia of the malar bones and mandible and absence of the zygomatic arch. There was no hearing defect.

Discussion

Mandibulo-facial dysostosis is a familial congenital syndrome of malformations affecting the region derived from the first and second branchial arches, and the first branchial cleft and pouch (Waardenburg and Navis, 1949).

Few pedigrees described in the literature involve more than two generations, so that there is considerable diversity of opinion on the mode of inheritance and the role of exogenous factors.

It has been thought that the incidence increases in successive generations and that

the condition deteriorates until the mutation becomes a lethal gene (Debusmann, 1940).

For this reason, particular inquiry was made for abortion or stillbirth in this family, but there was no positive evidence of severely affected members who did not survive.

The present investigation does not therefore bear out the theory of deterioration; in fact, the most severely affected member was found in the third generation of the pedigree (III, 7).

In the family under consideration the gene responsible appears as a regular autosomal dominant showing complete penetrance; each affected individual had an affected parent, except II (2) of whose parents no description could be obtained. This is in accordance with the statistical results derived from the literature by Rovin, Dachi, Borenstein, and Cotter (1964).

Although the affected members of the family considered together show between them almost all the described features of mandibulo-facial dysostosis, there is comparatively little intra-sibship variation except in the degree of hypoplasia of the mandible.

Finally, there is insufficient evidence in this study either to confirm or to disprove the suggestion by Rovin and others (1964) that the children of affected females run an increased risk of inheriting the gene.

Summary

In a family affected by mandibulo-facial dysostosis, of 31 members traced, eight were found to be affected and are described.

The following conclusions are drawn from the data:

- (1) Mandibulo-facial dysostosis results from the transmission of a regular autosomal dominant gene with complete penetrance.
- (2) There is considerable variation between generations but little intra-sibship variation.
- (3) There is no increase in incidence or deterioration in successive generations in this study.

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