Familial Hemifacial Microsomia

KUTAY TAYSİ, M.D.
JEFFREY L. MARSH, M.D.
D. MILLER WISE, M.D.
St. Louis, Missouri 63178

Hemifacial microsomia, a relatively distinct clinical form in the Facio-Auriculo-Vertebral Spectrum is generally thought to be a sporadic event, although infrequent familial occurrences have been reported. In this communication, we describe a family with three males and two females in two successive generations affected with hemifacial microsomia. The pedigree is most compatible with autosomal dominant inheritance, although X-linked dominant or multifactorial inheritance cannot be excluded.

The anomalies found in Facio-Auriculo-Vertebral Spectrum primarily represent errors in morphogenesis of the first and second branchial arches which are sometimes associated with vertebral and/or ocular anomalies. The term Goldenhar syndrome has been used to describe the occurrence of epibulbar dermoids, with or without vertebral defects, in patients who have first and second branchial arch anomalies (Smith, 1982). Hemifacial microsomia (HFM), the term introduced by Gorlin (1963), refers to patients with predominantly unilateral anomalies including microtia, macrostomia, and failure of formation of mandibular ramus and condyle. However, the existence of transitional forms between Goldenhar syndrome and hemifacial microsomia (Pashayan, 1970), suggests that these two entities may represent the different expressions of a similar morphogenetic error. Furthermore, the great clinical variability in different affected individuals and the existence of sporadic as well as familial cases, possibly with different modes of inheritance, suggests heterogeneity in the etiology (Setzer et al., 1981).

Although the majority of patients with Facio-Auriculo-Vertebral Spectrum have been sporadic, infrequent familial occurrences were documented. We describe here another family with five individuals of both sexes, in two successive generations, affected with HFM.

Case Reports

Case 1. C.B.H. (III-2, Figure 1 and Figure 2), the proband, presented for emergency care with a mandibular fracture sustained in an altercation. On physical examination, several features of hemifacial microsomia were noted. The face was grossly asymmetric with receding mandible which deviated to the right. The occlusal plane was canted cephalad to the right and there was a right molar cross bite. The palate was high-arched with a hypoplastic right velum. There was no velopharyngeal incompetency. The temporalis and masseter on the right were hypoplastic and right mastoid prominence was small. Bilateral preauricular scars and chondrocutaneous remnants were noted. The positions of the right and left auricles were asymmetric. There were no ocular anomalies. Radiographs (Figure 3) demonstrated hypoplasia of the temporomandibular joint, mandibular condyle and ramus on the right. The maxilla and mandible showed deviation to the right and right sided hypoplasia.

Case 2. M.E.H. (III-3, Figure 1 and Figure 4), brother of the proband, had mild lower face hypoplasia, a right preauricular tag, and
occlusal cant cephalad to the left. No other facial anomalies were noted.

Case 3. S.J.M. (III-4, Figure 1 and Figure 5), sister of the proband, had a left preauricular tag. There were no other facial anomalies.

Case 4. B.H. (III-5, Figure 1 and Figure 6), brother of the proband, had right sided hemifacial microsomia. His past history included the removal of right sided preauricular skin tags in early childhood. He underwent alloplastic (silastic) augmentation of the right face to correct contour asymmetry in addition to the repair of right macrostomia at age 11. Physical examination during our evaluation revealed soft tissue deficiency and osseous hypoplasia of the right face, partially camouflaged by the alloplastic implant. There were well healed right preauricular and oral commissure incisions. Minimal microtia, hypoplastic tragus, and an epicanthic fold on the right were also noted. The right auricle was asymmetric in position compared to the left. Receding chin was deviated to the right. The occlusal plane was canted cephalad to the right. The palate was high arched with a hypoplastic velum. Velopharyngeal competency was normal. On the right, there was no masseter function and the temporalis function was diminished. Elevation of the upper lip

FIGURE 1. Family pedigree.

FIGURE 2. Proband (III-2) with right sided hemifacial microsomia. Note hypoplastic facies on the right (a), and bilateral residual preauricular scars and tags (b,c).
FIGURE 3. Anteroposterior cephalometric radiograph of the proband (III-2). Note hypoplastic right maxilla and mandible with cant of occlusal plane. Mandibular midline is shifted to the right.

was weak. Radiographs (Figure 7) showed bilateral mandibular hypoplasia, more pronounced on the right. The temporomandibular joints were normal in configuration. However, the right condyle had retrusive seating while the left was slightly protrusive.

Case 5. N. H. (II-2, Figure 1 and Figure 8), mother of the proband, had right facial nerve, ramus mandibularis palsy, in addition to asymmetric masticatory muscles and a mild nasal deformity. Radiographs revealed hypoplasia of the right mandibular condyle with narrowing of the joint space (Figure 9).

Family history revealed no other similarly affected individuals. There was no consanguinity between the parents of the proband (Figure 1).

Discussion
The patients presented here have markedly variable expression of hemifacial microsomia, ranging from preauricular tags in two cases to a full blown syndrome in another. The proband (III-2) was moderately affected, while one of his brothers (III-5) had more overt features of HFM. Two other siblings (III-3 and III-4) had only preauricular tags and the mother (II-2) had unilateral mandibular condyle hypoplasia. Apparently the last three individuals had minimal expression of HFM.

In the majority of cases, HFM is sporadic in occurrence (Smith, 1982; Gorlin, 1976). However, infrequent families have been reported with multiple affected individuals in
FIGURE 4. M.E.H. (III-3). Note lower face hypoplasia (a), and preauricular tag on the right (b).

FIGURE 5. S.J.M. (III-4). Note the preauricular tag on the left.

both sexes, spanning successive generations with male to male transmission, all suggesting an autosomal dominant mode of inheritance (Grabb 1965; Herrmann and Opitz, 1969; Summitt, 1969; Setzer et al., 1981). Affected sibs with normal parents (Grabb, 1965; Kirke, 1970; Krause, 1970), and consanguinity (Pashayan et al, 1970) suggesting autosomal recessive inheritance, have also been reported. Kaye et al. (1979) considered multifactorial inheritance as the most likely genetic mechanism in the etiology of familial cases. Non-genetic environmental factors were also considered in the etiology when Poswillo (1973) induced hemifacial microsomia phenotype in primate embryos that were exposed to Triazine. The existence of mainly sporadic and infrequently familial occurrence, discordance in monozygotic twins (Setzer, 1981), and the possibility of non-genetic causation in some patients, support the etiologic heterogeneity in hemifacial microsomia.

The pedigree reported here with multiple affected individuals of both sexes in two successive generations, is most compatible with autosomal dominant inheritance with variable expressivity in different affected family members. However, X-linked dominant or multifactorial inheritance cannot be excluded. In the light of the extreme clinical variability of this disorder, one may even speculate that all published pedigrees can be explained by reduced penetrance of an autosomal dominant gene.

Since the clinical features in familial and sporadic cases are not different, recurrence risk counseling will depend on the segregation
FIGURE 6. B.H. (III-5). Note status post repair right macrostomia, silastic augmentation of hypoplastic right face, lower position of the right ear compared to the left (a) and deformed right tragus (b).

FIGURE 7. Anteroposterior cephalometric radiograph of B.H. (III-5). Note asymmetric deviations of the maxillary and mandibular midlines to the right.
pattern of the mutant gene in a given family where there are multiple affected individuals. However, counseling in families with sporadic occurrence remains difficult. Although the recurrence risk was thought to be about 2% in families (Grabb, 1965; Grabb and Smith, 1979), detection of the minor clinical or radiologic findings of the disorder in other family members will be valuable in clarifying the pattern of inheritance (Converse et al., 1973). In such families the recurrence risk would be as high as 50%.

References


