Mandibular malformations: growth characteristics and management in hemifacial microsomia and Nager syndrome

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This review article describes normal and abnormal development of the mandible. The focus is on the characteristics of the mandible and its attached muscles in the various types of hemifacial microsomia and in Nager syndrome. Management protocols for these two types of malformations are presented in relation to development stages. □ *Classification; hemifacial microsomia; Nager syndrome; treatment*

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Etiologic factors

The mandible, the temporomandibular joint, and the outer and middle ear structures are derived from the first and second branchial arches. Disruption of cell migration and/or proliferation, such as could occur by a vascular insult, have been implicated as etiologic factors in hemifacial microsomia, which is the most frequently occurring congenital anomaly affecting these structures. The malformations seen in mandibulofacial dysostosis syndrome are thought to be due to disturbance of migration or differentiation of neural crest cells (1). This autosomal dominant disorder has recently been shown to be caused by mutations in gene *TCOFI* on chromosome 8 (2). It is possible that mutations in this gene also cause the malformations seen in other branchial arch syndromes. Animal models mimicking clinical findings in humans have been developed by various experimental methods (3–5).

Hemifacial microsomia

Hemifacial microsomia (HFM) is primarily a unilateral congenital birth defect with involvement of several skeletal, neuromuscular, and other soft tissue components of the first and second branchial arches. The term hemifacial microsomia covers a wide spectrum of craniofacial anomalies and may also include ocular, renal, spinal, and cardiac involvement. Dysmorphologists and others have created a variety of terms to describe the broad spectrum of phenotypes, but HFM remains the most widely used name. Other terms include oculoauriculovertebral (OAV) spectrum, craniofacial microsomia, otomandibular dysostosis, and lateral facial dysplasia (6–8). Oculoauriculovertebral dysplasia may be considered a separate category of HFM, also referred to as Goldenhar syndrome. The additional characteristics of this type are epibulbar dermoids and cervical spine abnormalities. There is a higher incidence of oronasal clefting in this type, and most likely there are specific etiologic factors causing this constellation of birth defects. HFM is the second most common congenital craniofacial anomaly after cleft lip and palate. The most frequently quoted incidence estimate is 1 in 5,600 live births (7, 9). There seems to be agreement that there is male predominance of 3:2 and a right-side predominance of 3:2 (10). For an extensive overview of the very heterogeneous phenotypes in this spectrum, the reader is referred to Cohen et al. (6) and to Peterson-Falzone (8). In the mildest form of HFM the only clinical manifestation may be ear tags with or without malformed ears. The most severe cases may present with malformed ear, temporal bone involvement including missing glenoid fossa, malformed or absent joint structures, and mandibular ramus including both coronoid and condylar processes.

Classification by phenotype

Tenconi & Hall (11) distinguished between the classic type, microphthalmic type, bilateral asymmetric type, complex with limb deformity type, frontonasal type, and Goldenhar type. The 'infant of diabetic mother' type has recently been added (12–14). Of the 67 subjects included in their study, Tenconi & Hall found that 14.9% had some type of cardiac malformation, 5.9% had renal system malformations, 17.6% had microcephaly, and 13.3% had developmental delay. They did not assess cervical spine abnormalities, but our findings at the Center for Craniofacial Anomalies and those of others (15–18) indicate that close to 50% have some type of cervical spine abnormality.

The OMENS classification attempts to include all of the most prominent features of HFM: O = orbit, M = mandible, E = ear, N = facial nerve, and S = skeletal. Each entity is graded from 1 to 3 according to severity. Others have suggested additions such as presence of non-craniofacial involvement that could be annotated by an asterisk (OMENS*) (19–21).

The SAT classification addresses only three main features: S = skeletal, A = auricle, and T = soft tissue (22). In this system there are five levels of skeletal deformity (S1

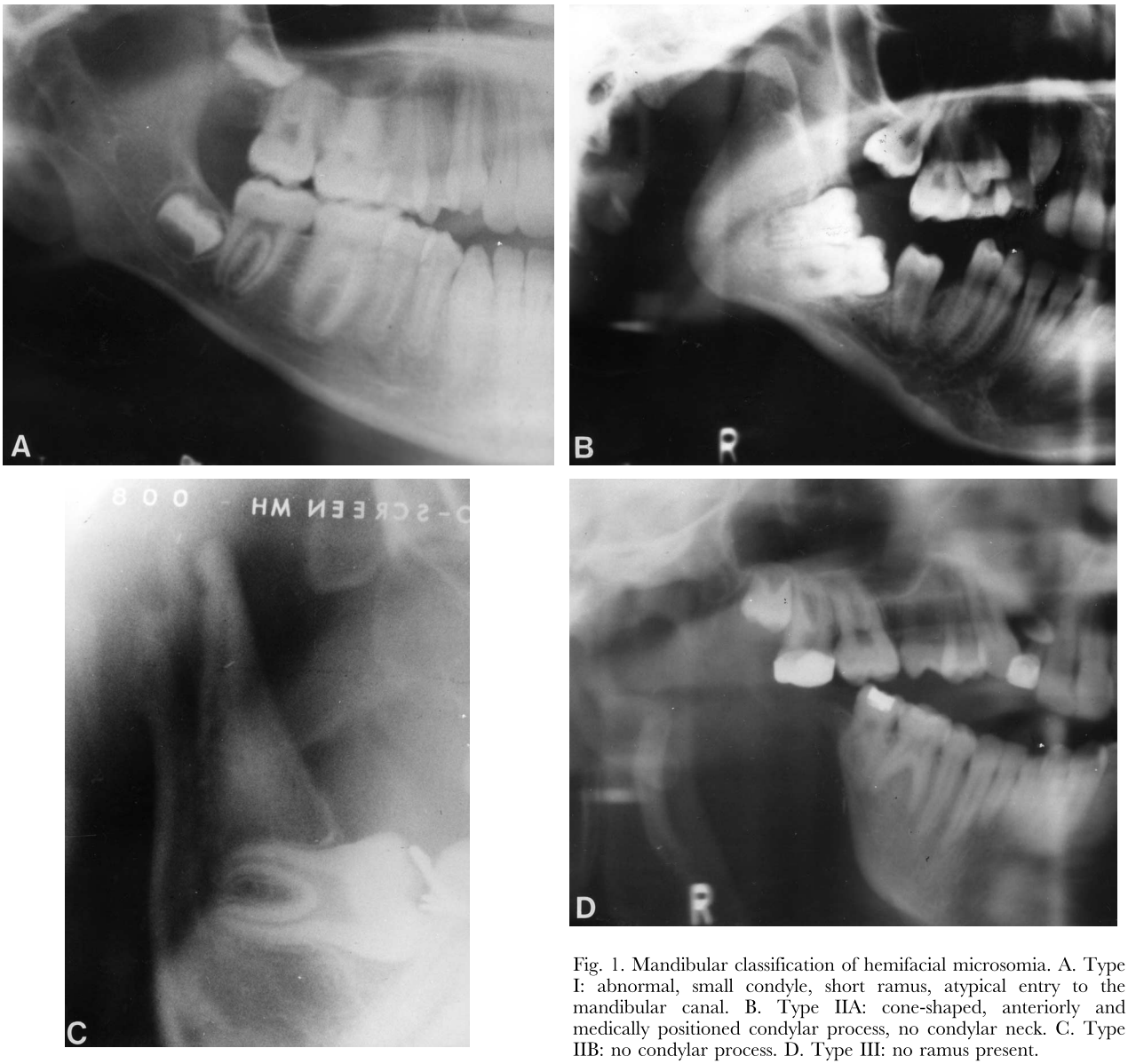

Fig. 1. Mandibular classification of hemifacial microsomia. A. Type I: abnormal, small condyle, short ramus, atypical entry to the mandibular canal. B. Type IIA: cone-shaped, anteriorly and medically positioned condylar process, no condylar neck. C. Type IIB: no condylar process. D. Type III: no ramus present.

through S5), four levels of auricular deformity (A0 through A3), and three levels of soft tissue deformity (T1 through T3). For example, they indicate that a person with minimal deformity might be classified as S1A0T1, while one with severe deformity would be S5A3T3. It does not appear that this system has clear advantages over the OMENS system, and it falls short of including all of the most essential elements involved (21).

Classification by mandibular involvement

In this article the emphasis will be on the mandibular and temporomandibular bone and joint malformations and malfunctions. The classification system we use is an amalgamation of the classifications described by Pruzansky, Kaban et al., Harvold et al., and Vargervik & Kaban (23–26). Describing middle and lower face involvement, it is based on discrete findings of the presence or absence of critical elements of the mandible and temporomandibular joints and consists of Types I, IIA, IIB, and III (Fig. 1).

In Type I all parts of the affected side of the mandible and the attached muscles are present, but are hypoplastic to varying degrees. The glenoid fossa is usually missing, and translatory joint movement is minimal. Rotational movement of the condyle is usually not impaired, resulting in hinge movement on the affected side. During jaw opening, the mandible shifts to the affected side as translatory movement occurs on the contralateral side only. Quite frequently, the contralateral condyle moves excessively during maximum jaw opening.

Type IIA is characterized by a cone-shaped, anteriorly and medially displaced condyle, missing glenoid fossa, but presence of all masticatory muscles with variable degrees of hypoplasia. The jaws and face are usually very asymmetric. In Type IIB the condyle is missing along with the lateral pterygoid muscle. The coronoid process is usually small and the temporal muscle hypoplastic. Jaw and facial asymmetry are usually quite marked.

Type III represents congenital absence of the entire ramus of the mandible and most of the masticatory muscles. The mandible can be guided freely into various positions as the movements of the affected side are not limited by either joint structures or muscles and ligaments. All joint structures are missing, and frequently the temporal region is flat or even concave, resulting in a poor platform for the ear, which usually is affected and requires reconstruction.

Normal mandibular growth

In the embryo, mandibular bone formation starts in association with Meckel's cartilage and around the developing tooth buds. The osseous areas expand, coalesce, and become the body of the mandible. The neuromuscular and vascular networks are well established before bone formation starts and are presumably prerequisites for osteogenesis. During these early stages of development, the mandibular structures are carried forward by the growing Meckel's cartilage. The various muscle masses become attached to or included into the developing bone, probably by the same mechanisms that cause muscle reattachment (27). The posterior muscles extending into the temporal region provide the environment for development of the ramus with the condylar and coronoid processes. The condylar process and the developing temporomandibular joint structures, in association with the lateral pterygoid muscle, presumably take over the propulsive action, which up to that point had been provided by Meckel's cartilage. This new propulsive mechanism continues postnatally throughout the growth period and presumably functions by sensorimotor feedback, primarily from the joint structures (28). It appears that the periodic proliferation of condylar cartilage toward the glenoid fossa elicits activity in the lateral pterygoid muscle, which advances the condyle, thereby maintaining the optimal joint space. The various areas of the mandible remodel as the jaw is brought forward relative to its muscles and other structures. Bone apposition, which replaces cartilage in the interface between condylar cartilage and bone, appears to occur only when the cartilage is proliferating (29). The condylar cartilage is, therefore, a controlling factor during growth.

Growth in hemifacial microsomia

In patients with HFM, the very structures that are essential to mandibular growth are affected, and impairment of mandibular growth is therefore always present, varying in degree according to the primary tissue deficiencies. Characteristically, in most individuals with HFM, the affected side of the mandible and the associated muscles grow less than the contralateral side. However, it is interesting to note that even in Type III, where the entire ramus is missing, the length of the mandibular body increases as bone forms around each successively developing tooth bud. This side of the mandible is gradually brought forward to a small degree, presumably by the presence and function of the tongue and tissues in the floor of the mouth. Because the main propulsive factors in advancing the mandible (i.e. the condylar cartilage and lateral pterygoid muscle) are rudimentary or missing, it is understandable that jaw and facial asymmetry may increase, rather than improve, with growth.

Overall management

The overall team management for a child with HFM involves attention to respiration, hearing, speech and language development, psychosocial issues, and management of associated problems such as cervical spine fusions, scoliosis, and epibulbar dermoids. Every child with HFM should have a renal sonogram, cardiac evaluation, spinal roentgenograms, computed tomography (CT) scans of ear structure, ophthalmology consultation, and management and intervention as needed.

Treatment of structural malformations

Phase I: early treatment intervention for jaw asymmetries. Our rationale for early treatment has been that some of the secondary unfavorable adaptations to the deficient growth of the mandible could be prevented and that, where condylar and coronoid structures exist (Types I and IIA), additional bone apposition could be achieved by providing a substitute for the normal advancing mechanisms (30–33). A functional appliance of the activator type, with or without a buccal shield, has therefore been used routinely in our HFM patients as an initial treatment phase. Generally, this treatment is started at the time of the eruption of the 6-year molars.

Phase II: mandibular surgery. The second treatment phase is surgical lengthening or reconstruction of the affected mandibular ramus. If done during the mixed dentition stage, it is often possible to avoid a surgical procedure on the maxilla by minimizing the secondary growth inhibition on the affected side (26, 31, 34). The exceptions are situations where the maxillary dental midline is severely deviated from the face midline and orthodontic correction of the dental midline discrepancy is impossible. It is generally not possible to correct a severely canted maxillary occlusal plane until an open bite has been created by surgical repositioning of the mandible. If maxillary surgery is anticipated, both jaw procedures can be postponed until most of the child's growth has been completed. The more general growth there is remaining in the child, the higher the probability that the asymmetry will redevelop owing to less growth on the reconstructed side than the contralateral

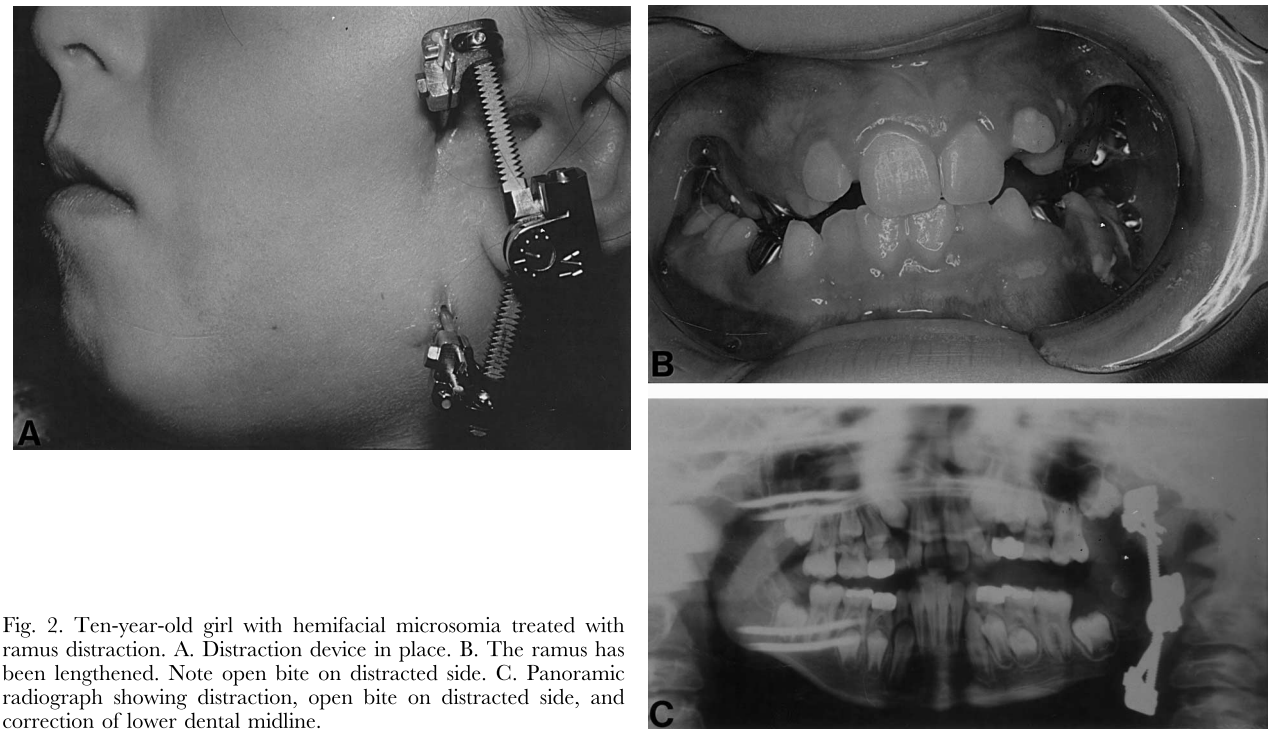

Fig. 2. Ten-year-old girl with hemifacial microsomia treated with ramus distraction. A. Distraction device in place. B. The ramus has been lengthened. Note open bite on distracted side. C. Panoramic radiograph showing distraction, open bite on distracted side, and correction of lower dental midline.

side of the mandible. A transplanted costochondral graft may also grow excessively, thereby creating an asymmetry to the opposite side.

Following the mandibular surgery, the position of the mandible relative to the maxilla is secured by a bite registration splint and interarch fixation wires. Depending on the type of mandibular surgical procedure, the length of the fixation may vary from 2 weeks, if rigid or semi-rigid fixation is achieved, to 6 weeks if the entire mandibular ramus has been reconstructed. Following removal of the interarch fixation wires, the splint is attached to the maxilla with elastics to allow removal for cleaning. Light guiding elastics are placed to the mandible to ensure precise and controlled mandibular movements into the splint (26, 31). This is a period for reattachment of muscles and ligaments, retraining of the neuromuscular system to a new position of the mandible, and new bone to form as the bone graft is gradually replaced and remodeled. This very important adjustment period should last several weeks. The progression of new bone formation and remodeling is monitored by panoramic radiographs. Continued growth of the reconstructed ramus/condyle unit is still unpredictable, and many factors play a role (35, 36).

Lengthening of the affected mandibular ramus by distraction has become popular lately (37–39) (Fig. 2). This technique has both advantages and disadvantages, and at this stage of technique development cases should be selected carefully. When distraction osteogenesis can be applied in such a way that significant muscle lengthening is achieved, this approach will have a major advantage over other lengthening procedures in selected cases.

Phase III: closure of open bite on the affected side. The postsurgical treatment phase blends into the next phase if it is expected that the unilateral maxillary underdevelopment can be corrected without a surgical procedure. The open bite created by lengthening of the affected mandibular ramus is protected by a maxillary bite plate. Auxiliary springs are placed on this plate for active extrusion of the maxillary teeth on the affected side.

Phase IV: orthodontic treatment. Full orthodontic treatment is started after eruption of the permanent teeth and after most of the jaw growth is completed. Standards for treatment outcome are the same for these patients as they would be for any other orthodontic patients. It is very important not to resort to interarch elastic mechanics that may contribute to redevelopment of the jaw asymmetry. It should be recognized that it may be very difficult, if not impossible, to completely correct unfavorable dentoalveolar adaptations. This is particularly challenging in the presence of an asymmetric palate and tongue.

Additional surgical procedures

Reconstruction of a malformed or missing ear usually requires three surgical procedures, which are generally started at about 6 years of age. Additional surgical procedures are often necessary to correct bony chin asymmetry, nasal septal deviation, and soft tissue deficiency. The asymmetric genioplasty and nasal septal reconstruction are done simultaneously. As the very last procedure, soft tissue augmentation may be indicated. If the soft tissue asymmetry is mild, the transferred tissue may be a double

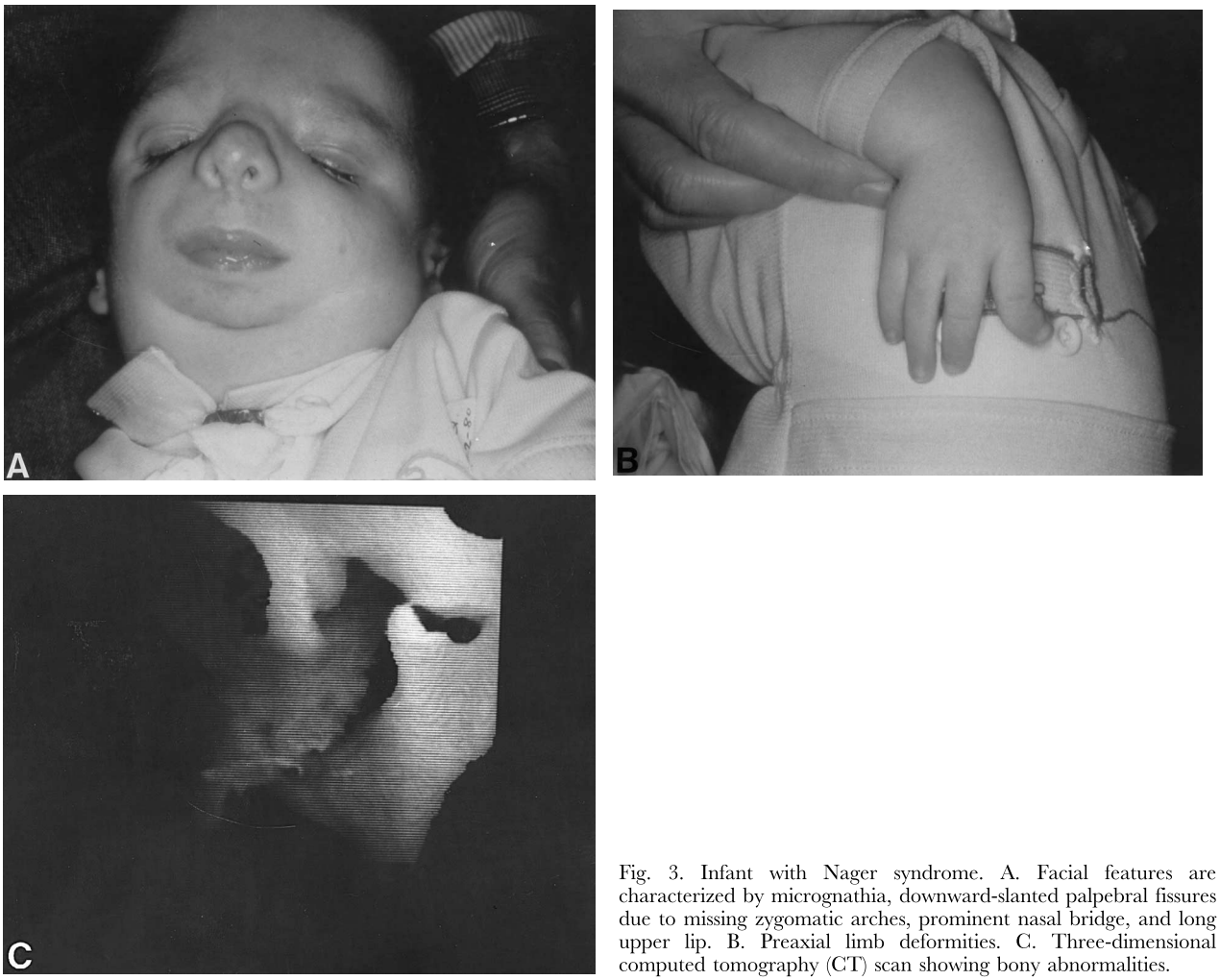

Fig. 3. Infant with Nager syndrome. A. Facial features are characterized by micrognathia, downward-slanted palpebral fissures due to missing zygomatic arches, prominent nasal bridge, and long upper lip. B. Preaxial limb deformities. C. Three-dimensional computed tomography (CT) scan showing bony abnormalities.

dermis graft obtained from the buttock (25). However, if more tissue bulk is needed, a muscle flap transfer by microvascular procedures may be the choice (40).

Nager syndrome (Nager acrofacial dysostosis)

The term acrofacial dysostosis relates to the extremities (acral). The preaxial limb abnormalities that characterize Nager syndrome are diagnostic and differentiate this syndrome from mandibulofacial dysostosis (Fig. 3). This is a very rare syndrome with only 35 cases published (41). Most cases are sporadic occurrences, but there is some evidence that an autosomal recessive inheritance pattern must be considered.

Structural characteristics

Nager individuals have extensive mandibular and temporomandibular involvement, often with extremely restricted jaw movement. In our center we have been caring for 15 children with Nager syndrome. In addition to the limb abnormalities, skeletal abnormalities including the spine, mandibular malformations including missing joint structures and severe restrictions in movement, zygomatic arch discontinuity, and ear abnormalities with bilateral hearing loss, there is also congenital absence of most of the soft palate (42).

Functional impairments

Respiration and feeding problems are primarily due to the retruded mandible and tongue and severely restricted jaw opening. The bilateral hearing loss varies according to the severity of the ear abnormalities. There may be speech problems due to the impaired hearing, but in the absence of a soft palate, velopharyngeal closure cannot be achieved, and the speech is therefore very hypernasal. In those individuals with very restricted jaw opening, chewing is not possible, and oral hygiene is a major problem for the same reasons. Severe dental decay without the option of

adequate treatment is very common. Owing to the hand and limb abnormalities, manipulating implements may be difficult, and self-care may not be possible.

Facial and jaw growth

Overall poor growth and short stature is expected in Nager syndrome. Owing to the missing temporomandibular joint structures, the ankylosis, and the overall mandibular, zygomatic, temporal bone, and masticatory muscle involvement, there is very little growth of the lower face. The nose and anterior portion of the maxilla appear prominent in relation to the deficient zygomatic areas and the extremely retruded mandible and chin. There is extreme crowding of teeth, and often particularly the posterior teeth will decay because of poor oral hygiene and poor access for treatment.

Overall management

Team care is essential for this complex entity. The immediate concerns are with breathing and feeding, which very often require placement of both a tracheostomy tube and a gastrostomy tube. Tube feeding may be necessary for a long time if jaw restrictions are severe. The following is a summary of our treatment protocol.

Treatment protocol for Nager syndrome patients

Immediate intervention. Tracheostomy and gastrostomy tubes should be placed to facilitate respiration and feeding.

Later, but as early as possible. Stimulation to oral feeding, placement of hearing aids, speech and language stimulation, and sign language should be instituted.

Management of jaws and dentition. Fluoride treatment and

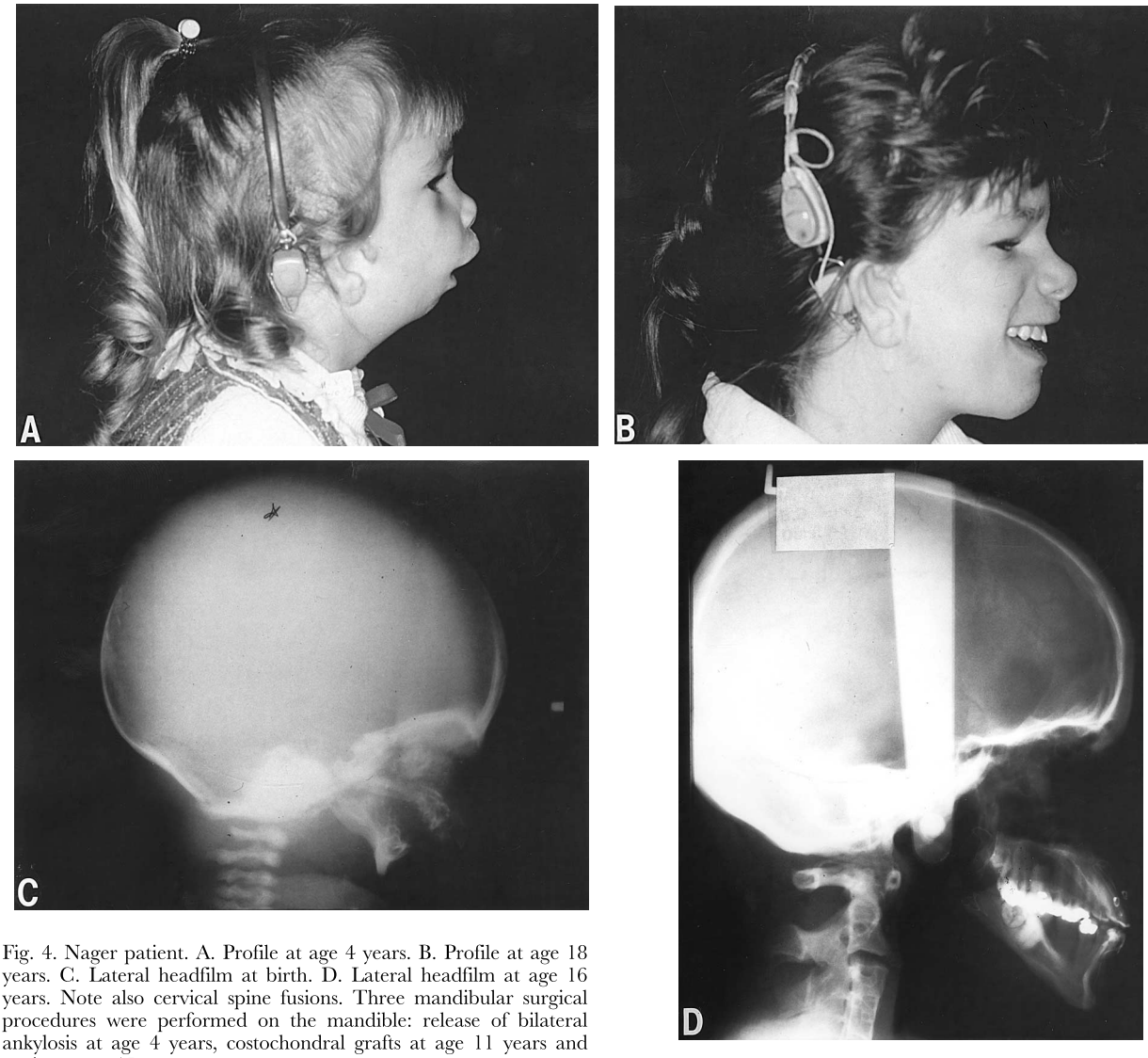

Fig. 4. Nager patient. A. Profile at age 4 years. B. Profile at age 18 years. C. Lateral headfilm at birth. D. Lateral headfilm at age 16 years. Note also cervical spine fusions. Three mandibular surgical procedures were performed on the mandible: release of bilateral ankylosis at age 4 years, costochondral grafts at age 11 years and again at age 15 years.

low sugar intake should be initiated to minimize tooth decay. At 3–4 years of age release of mandibular ankylosis should be undertaken, followed by splint or functional appliance therapy. A spring-loaded stretching device may be used as well. At age 6 or 7 years or later, depending on several factors, lengthening of the mandibular rami should be started. Depending on the characteristics of the case, this can be done by using bone grafts or distraction techniques. This treatment should be followed by splint and functional appliance therapy until orthodontic appliances can be placed after eruptions of permanent teeth. Additional surgical procedures may be indicated for the mandible (Fig. 4). The maxilla and zygomatic arches may need reconstruction as well. Severe scoliosis is a frequent finding, and physical and occupational therapy are usually indicated. The hypernasal speech remains a problem, as little can be done surgically because of the absence of a soft palate, and obturation is usually not possible owing to the poor condition of the dentition.

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