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A NEW TYPE OF MAXILLOFACIAL DYSOSTOSIS, INHERITED AS AN X-LINKED OR AUTOSOMAL RECESSIVE TRAIT

by R.J.H. ENSINK¹, H.G. BRUNNER² and C.W.R.J. CREMERS¹

Summary: *A new type of maxillofacial dysostosis, inherited as an X-linked or autosomal recessive trait: Two brothers with congenital conductive hearing loss and phenotypic characteristics of maxillofacial dysostosis are described. In the oldest boy a malformed ossicular chain was present and the conductive hearing loss was improved by a malleo-vestibulo-plexy, with post-operative hearing gain of approximately 30 dB. Although superficially similar to Treacher Collins syndrome, the facial characteristics are more typical of maxillofacial than of mandibulofacial dysostosis. These cases most likely represent a new type of maxillofacial dysostosis inherited as an X-linked or autosomal recessive trait.*

Key-words: Maxillofacial dysostosis – Hearing loss – Mandibulofacial dysostosis – Autosomal recessive inheritance – X-linked inheritance.

Résumé: *Nouvelle forme syndromique de dysostose maxillo-faciale à transmission autosomique récessive ou liée au chromosome X: Deux frères présentant le phénotype d'une dysostose maxillo-faciale associé à une surdité conductive sont décrits. Chez le garçon aîné une malformation de la chaîne ossiculaire a été corrigée par une pexie malléo-vestibulaire, avec une amélioration de 30 db. Le dysmorphisme craniofacial ressemble plutôt à une dysostose maxillaire qu'à une dysostose mandibulo-faciale. Le tableau clinique présent chez deux frères est probablement le premier exemple d'une nouvelle forme de dysostose maxillo-faciale, à hérédité autosomique récessive ou liée au chromosome X.*

Mots-clés: Dysostose maxillo-faciale – Surdit  – Dysostose mandibulo-faciale – Transmission autosomique r cessive – H r dit  li e au chromosome X.

INTRODUCTION

Many distinct inherited syndromes have been described that originate from branchial arch defects (5). Midface hypoplasia, pre-auricular tags, fistulae, microtia, and cleft lip or cleft palate, are typical features of these branchiogenic syndromes.

The most common of these are mandibulofacial dysostosis or the Treacher Collins syndrome and the Goldenhar oculo-auriculo-vertebral syndrome.

A much rarer branchial arch syndrome was first described by Toriello and is cha-

racterized by intellectual dysfunction, microcephaly, short stature, protruding ears, midface hypoplasia, a high arched palate and an X-linked recessive pattern of inheritance (14).

We report two brothers who share several anomalies with the Toriello branchial arch syndrome. Maxillary hypoplasia was their most striking characteristic. However both had normal stature and intelligence.

The pattern of inheritance in this family with two boys is either X-linked or autosomal recessive. Other reports on maxillofacial dysostosis suggest autosomal dominant inheritance. The syndrome described here thus represents a new type of maxillofacial dysostosis of either

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X-linked or autosomal recessive inheritance.

CASE REPORTS

The index case, the first child of non-consanguineous parents, was born after an uneventful pregnancy with bilateral cleft lip and cleft palate. Bilateral preauricular fistulae were corrected surgically shortly after birth.

Hearing impairment was suspected at a young age; his language skills were poorly developed. Conductive hearing loss of 55 dB in both ears was confirmed audiometrically at four years of age. The external auditory canals were narrow. The boy also had small low set ears, a broad nasal bridge, malar and maxillary hypoplasia and hypoplastic zygomatic bones. A retrognathia is clearly present (Fig. 1). A diagnosis of the Treacher Collins syn-

drome was considered at that time. Mid-face hypoplasia was corrected the age of 15 years. On examination at the age of 18 years, he was 162 cm tall ($<P_3$) with a weight of 54 kg (P_{10}) and an occipital frontal circumference (OFC) of 54.2 cm (P_{25}). Inter canthal distance (ICD) was 34 mm (P_{75}); outer canthal distance (OCD) was 92 mm (P_{50-75}).

Common signs of branchial arch syndromes such as antimongoloid slanting colobomas and epibulbar dermoid of the eyes were absent. Visual acuity was normal. No cervical spine anomalies were present and there were no anomalies of the extremities. Cognitive development is normal. Exploratory tympanotomy revealed a monopodal stapes with no head and no incudial corpus. The malleus head and stapedial footplate were removed and the upper one third of the malleus handle was stripped away from the tympanic membrane. A 5 mm Teflon-Platinum piston

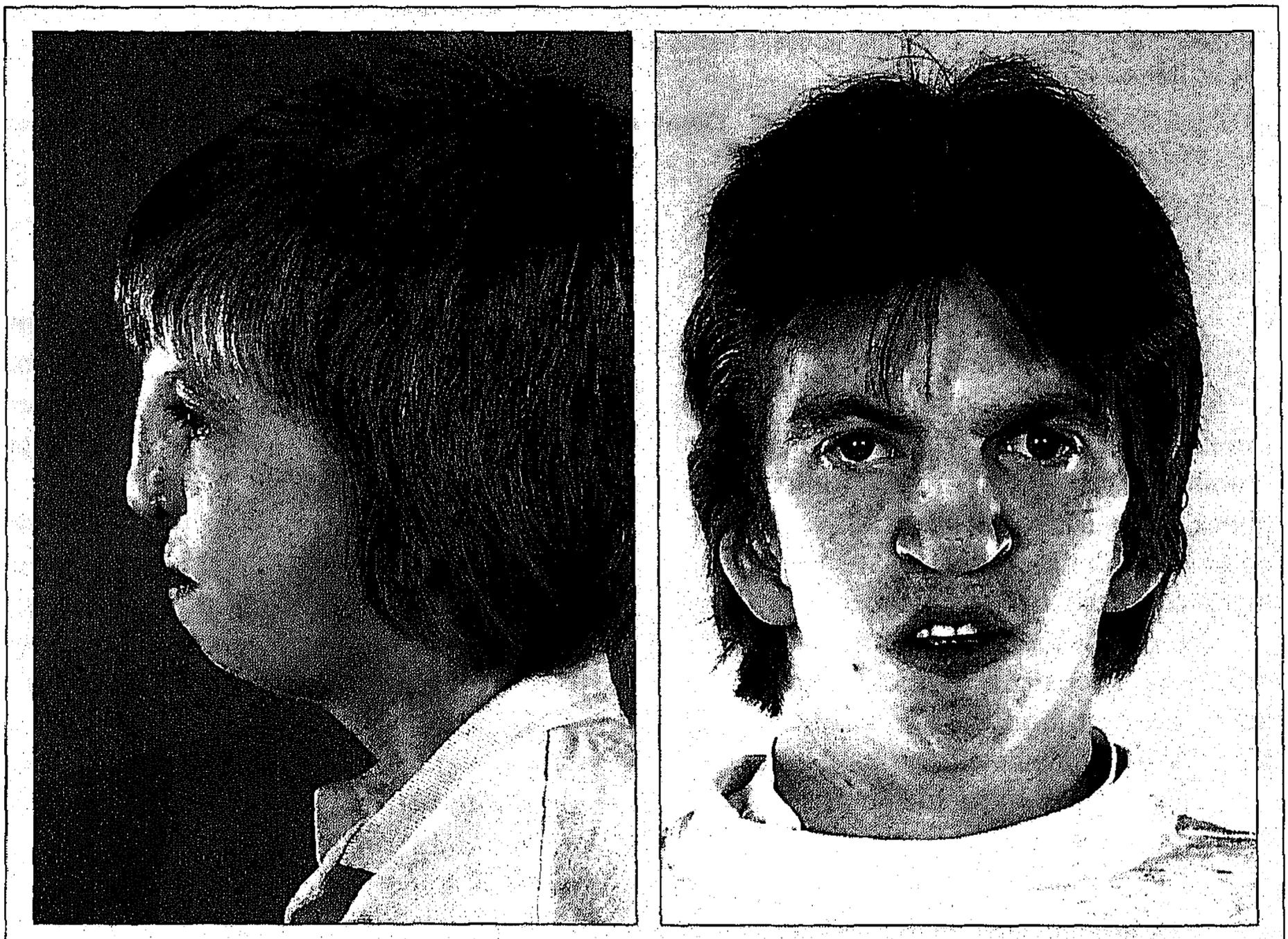


Figure 1: Facial appearance of the index case at the age of 11 years (left); note the maxillary hypoplasia and retrognathia; and facial appearance after zygoma osteotomy at the age of 18 yrs (right).

was fixed around the malleus handle and vestibulo-malleopexy was performed. Post-operative hearing improved to a conductive threshold of approximately 30 dB, which was maintained at a follow-up of 3 years.

The younger brother of the proband was born with similar facial characteristics: low set dysplastic ears, bilateral preauricular fistulae, retrognathia and malar hypoplasia. Ptosis of the left upper eyelid was present (Fig. 2). Colobomas and epibulbar dermoid were not found. There was no facial clefting. Midface hypoplasia was corrected at the age of 15 years. Stature was within normal limits. No anomalies of the extremities were found. Intellectual development is normal. At the age of four years his receptive language skills were mildly delayed while his expressive language development was delayed by 1½ years. Non-progressive bilateral conductive hearing loss with a conductive thresh-

old of 40 dB was documented and has remained constant up to age 15 years. Exploratory tympanotomy has not been performed. Neither the boy's parents nor any other family member showed any of the above described anomalies.

DISCUSSION

The facial characteristics in these boys only vaguely resemble mandibulofacial dysostosis (Treacher-Collins syndrome) (5, 11). Facial characteristics of Treacher-Collins syndrome comprise mandibular hypoplasia, anti-mongoloid and downward slanting of palpebral fissures and coloboma of the lower eyelids with absence of medially localized cilia. A cleft lip-palate seen in our index case and ptosis of the upper eye lid which was present in the younger brother, are rare in this syndrome. Moreover, the Treacher-Collins

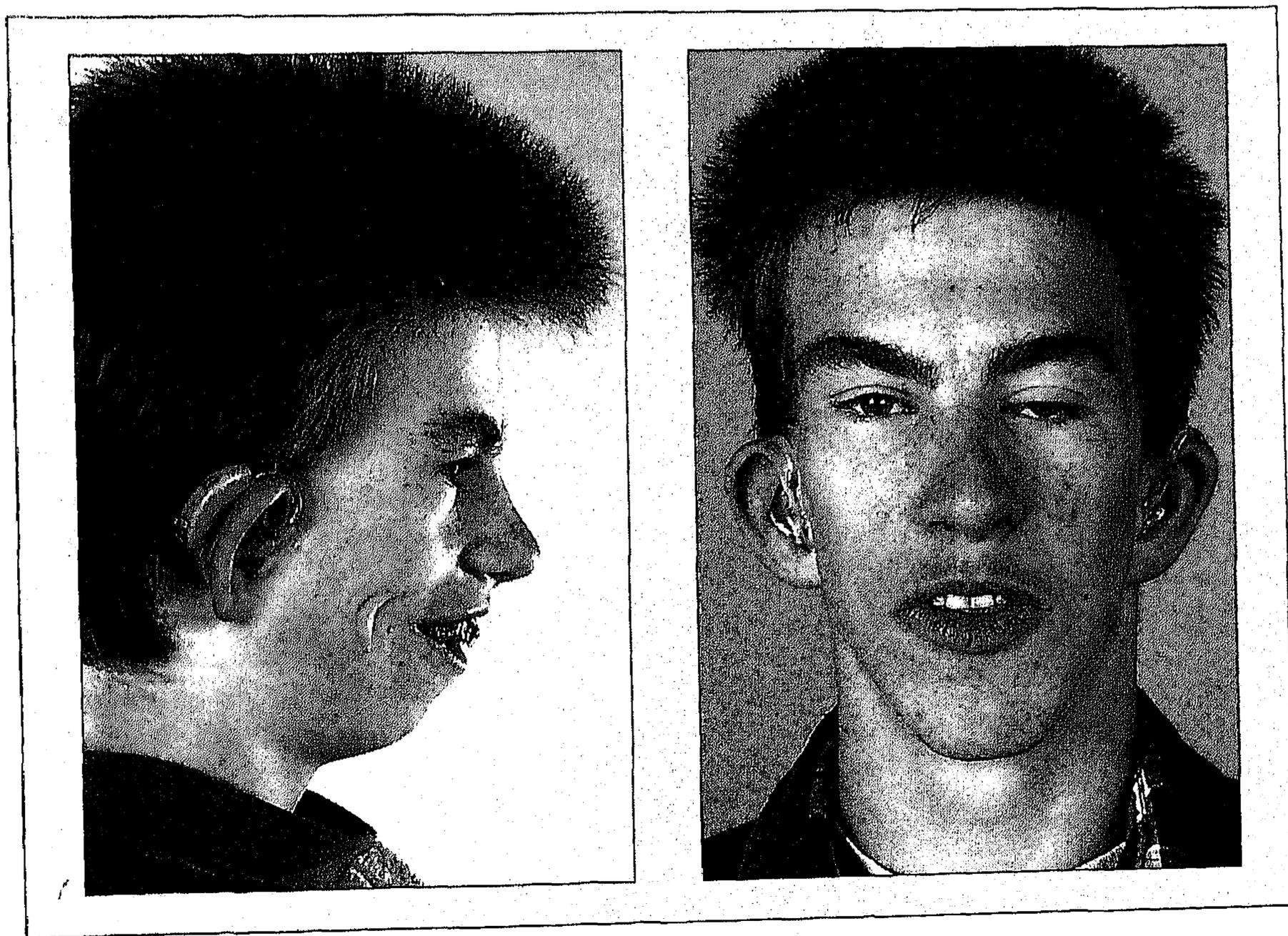


Figure 2: Facial appearance of the proband's younger brother at the age of 12 yrs (left); and after zygoma-osteotomy at the age of 17 years; note the ptosis of the left eye (right).

syndrome has autosomal dominant inheritance. However, rare recessive forms of mandibulofacial dysostosis have been reported so far with a predominance in males. (1, 7, 10, 16) Also non-penetrance of Treacher-Collins syndrome has been reported (17).

Clinically a syndrome with dysostosis of the maxilla as most prominent feature is considered more likely. In many ways these boys also resemble the description by Lowry *et al.* (7) although the phenotypical characteristics are more severe in this family.

The earliest description of inherited maxillary hypoplasia originates from 1932 and concerns an affected grandfather, father and son. This autosomal dominant pattern of inheritance of maxillofacial dysostosis was confirmed and the phenotype was delineated as a distinct syndrome (15). As minimal diagnostic criteria for maxillofacial dysostosis the presence of anterior-posterior shortening of the maxilla anti-mongoloid slanting of the palpebral fissures and often nonfluent and inarticulate speech with normal intelli-

gence and hearing was proposed. Another possibly mild example of AD maxillofacial dysostosis was described by Kavshima and Tsuji (4).

Since both parents are clinically normal and the lack of other apparently affected family members, an autosomal recessive pattern or X-linked pattern inheritance is considered more likely. The delayed speech development in the youngest was probably the result of hearing impairment.

X-linked inheritance would be consistent with the Toriello variant of maxillofacial dysostosis (2, 14, 18). However, normal intelligence in these boys is not accordance with Toriello syndrome. Cryptorchidism and sub-valvular pulmonic stenosis both of which have been described in Toriello syndrome were not seen in our cases. The low set protruding ears and mild short stature, only present in the index case, as well as maxillary hypoplasia have been described in this syndrome. The anti-mongoloid slanting of the palpebral fissures were also present in our cases. In the Gdenhar syndrome epibulbar dermoid, cervical spine anomalies and facial

Table I: Characteristic findings in brancial arch syndromes.

Case 1	Case 2	Treacher Collins	Toriello syndrome	BOR syndrome	Maxillofacial dysostosis
Pre-auric. fistules	Pre-auric. fistules	Malformed pinna	Microcephaly	Branchial clefts; fistules; cysts	Anterior-posterior shortening n
Small low set ears	Small low set ears	Supra-orbital rim hypoplasia	Low set ears	Pre-auricular pits	Minor malformations auricles
Cleft lip-palate	Ptosis left eye	Narrow face	Webbed neck	Renal anomalies	Non-fluent inarticulate speech
Max. hypoplasia	Max. hypoplasia	Hearing loss	Hearing loss	Hearing loss	No hearing loss
Hearing loss	Hearing loss	Normal IQ	Mental retardation	Normal IQ	Normal IQ
Normal IQ	Normal IQ	Eye lid colobomata	Short stature		
		Deficiency cilia	Cryptorchidism		
		Receding chin	Sub-valv pulm sten.		
Normal parents	Normal parents	Aut. dominant (variable expressivity)	X-linked	Aut. dominant (variable expressivity)	Aut. dominant

ymmetry are frequently present but these were absent in the cases reported here (12). The combination of especially preauricular pits and abnormal pinnae might suggest a diagnosis of branchio-otorenal syndrome but cervical fistulae were absent. Moreover, maxillary hypoplasia is not a feature of the BOR syndrome (3). Differential diagnostic considerations are summarized in table I.

The Treacher-Collins syndrome is the brachial arch syndrome in which middle ear anomalies are best documented (8). Approximately 50% of patients have conductive hearing loss. Middle ear anomalies are mostly complex and are rarely amendable to reconstructive surgery. The presence of a malleus handle in the oldest index case made it possible to perform a malleo-vestibulopexy as this middle ear surgery procedure has good post-operative results in the majority of cases (13).

In summary we present a new form of maxillofacial dysostosis in which autosomal dominant inheritance is unlikely. Recognition of this clinical pattern of anomalies has important implications for patient counselling. Further reports are needed to clarify whether this form of maxillofacial dysostosis is inherited as an autosomal or X-linked recessive trait.

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