



CASE REPORT

Oromandibular-limb hypogenesis syndromes: a case of aglossia with an intraoral band

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SUMMARY. Oromandibular and limb syndromes feature primarily in sporadic case reports because of their low incidence. They include Moebius syndrome, aglossia-adactylia syndrome, Hanhart syndrome, glossopalatine ankylosis syndrome, limb deficiency-splenogonadal fusion syndrome and Charlie M. syndrome. There is confusion in the classification of these patients because of the associated anomalies and the frequency of overlapping features.

This paper presents a patient with oromandibular malformations associated with major defects in the upper and lower limbs. Aglossia in the presence of an intraoral band is a peculiar association demanding classification.

This case confirms that aglossia – adactylia syndrome and the glossopalatine ankylosis syndrome are variants along a spectrum.

Congenital malformations involving the limbs and the tongue (Oromandibular-limb Hypogenesis Syndromes – OLHS) are extremely rare, with a few sporadic cases reported in the literature.¹

The aetiology of these dysplasias is not known. Some authors suggest the influence of intrauterine environmental factors such as amniotic bands² or vascular accidents,^{3,4} while others ascribe them to teratogenic drugs.⁵⁻⁷ The persistence of embryonic membrane has also been postulated^{8,9} as a genetic defect.¹⁰

Several syndromes are conventionally included under the umbrella of OLHS: Moebius syndrome, aglossia-adactylia syndrome (AA), Hanhart syndrome, glossopalatine ankylosis syndrome (GA), limb deficiency-splenogonadal fusion syndrome and Charlie M. syndrome.¹ Some patients are difficult to classify because their stigmata bridge two or more syndromes.^{1,7,11,12}

The limits between the GA and the AA Syndrome are particularly confusing, with the central difference represented by the presence of an intraoral band in GA,⁷ while AA features a more severe tongue deformity even to the extent of aglossia.^{6,13}

To contribute to the understanding of the aetiology and classification of these complex malformations we report a patient, who shows a peculiar combination of deformities: aglossia with an intraoral band from the floor of the mouth to the soft palate causing him to straddle the classifications of GA and AA.

Case report

During a Medical Mission in the rural Philippines a 9-year-old boy, only child of unrelated parents, presented with abnormalities of the face, oral cavity, and all four limbs. He had been born by a spontaneous vaginal delivery at term after an uneventful pregnancy. There were no reported

malformations in the family history. The lower third of the face showed a massive deficit in growth of both the hard and soft tissues. (Figs. 1 and 2) The mandible was extremely hypoplastic, retrusive and edentulous. The body of the mandible was virtually absent. The TM joint was abnormal and opening was restricted. The lower lip was tight and severely hypoplastic. The palate was high arched, there was no tongue visible in the oral cavity, and a band of fan-shaped fibromucous tissue connected the palate with the anterior floor of the mouth. (Fig. 3)

The right hand showed hypoplastic digits functional enough to attend to personal care. The left arm was generally hypoplastic but the forearm was more severely affected and showed also transverse arrest. (Fig. 4)

The right foot was missing the second toe. The left lower limb was absent below the upper third of the tibia. (Fig. 5). The patient was wearing a prosthesis fitted 5 years before, which was obviously too short, but provided him the means to walk.

He was affected by severe scoliosis, which is thought to be secondary to the leg length discrepancy.

The patient, of average mental capacity, attended a normal school and had intelligible speech, even in the presence of a major anatomical abnormality. Surprisingly good speech in a child with aglossia has been documented previously by Eskew.¹⁴

Discussion

The presence of an intraoral band is an uncommon entity,¹⁵ more frequently observed between the upper and lower gums (syngnathia)^{16,17} or between the margin of a palatal cleft and the tongue (glossopalatine ankylosis).¹ The adhesion of a hypoplastic tongue to the lower lip midline has been described in Hanhart syndrome.³ Few cases with AA and a fusion of the gums have been reported in the literature.^{18,19} Puroit et al²⁰ presented a case that shows some similarity with



Figure 1—A 9-year-old boy with severe hypoplasia of the lower third of the face: all tissues are involved.



Figure 2—Profile view of the patient.

the one reported here: but a difference seems to be in the more anterior place of insertion of the intraoral band that Puroit described, situated between the floor of the mouth and the hard palate.

Two theories have been proposed to explain the intraoral band as a remnant of embryological process.^{8,9} The first theory relates the intraoral band to the buccopharyngeal membrane formed by the stomodeum endoderm and the foregut ectoderm, that normally disappears at the end of the 4th week of intrauterine life. Chandra et al,^{8,21} reported on three subjects born without communication between oral cavity and pharynx, where this membrane presumably did not disappear. Hall⁶ proposed that in GA this membrane remains, while in AA it caused the damage earlier and then disappeared.

The second theory links the intraoral band with the subglosso-palatal membrane, normally present between the sixth and the eighth embryonic week, and disappearing when the tongue begins to drop. Nakajima et al,⁹ reported a patient presenting a thick fan-shaped membrane from the subglossal region to the soft palate holding the tongue in a backward position. Hydrocephalus, a patent ductus arteriosus and digital dysplasias were present. The illustration in their article shows that the jaw is normal. They related this band to a remnant of the subglosso-palatal membrane.

The band present in the mouth of our patient fits well with the subglossopalatal membrane theory with respect to shape and location.

Several hypotheses have been proposed on the aetiology of the OLHS. Genetic causes have been postulated²² but almost all the reported cases occurred sporadically. Recent advances have been made in the basic research on the molecular bases of embryonic development, leading to the identification of a group of genes, called homeobox genes, which play a role in

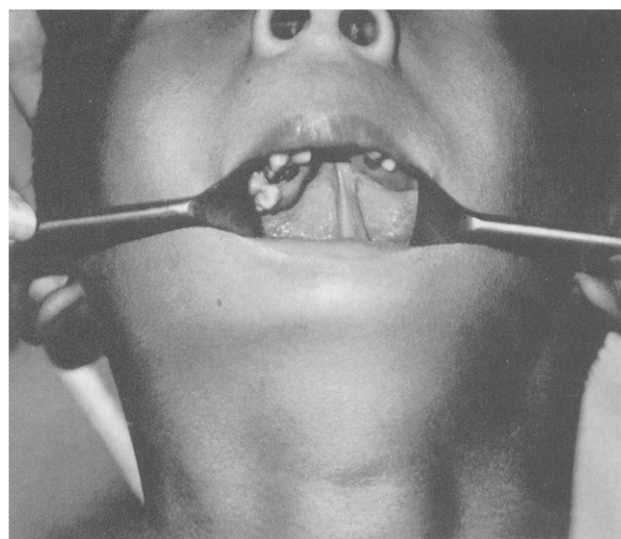


Figure 3—Close up view in maximal mouth opening, showing the presence of a fibrous band from the floor of the mouth to the palate.

craniofacial, limb and body axes development.^{23,24} In the mouse, transcripts of the *Msx2* gene, a homeobox gene, are localised in neural crest derived mesenchyme of the first to the fourth branchial arches, osteogenic tissue of the mandible and maxilla, developing teeth, apical ectodermal ridge and underlying mesenchyme of the limb bud.^{25,27} A report of a dominantly inherited mutation in *Msx2* akin to Boston-type craniosynostosis, in which some affected individuals also exhibit limb anomalies and cleft of the soft palate²⁸ might suggest an *Msx2* involvement in limb development.

Due to the lack of technology and manpower, the case reported here was not submitted to sophisticated analysis, to establish the presence of a mutation of the



Figure 4—The upper limbs of the patient showing a global hypoplasia on the left limb with a transverse arrest of the forearm, and hypoplasia of the digits on the right hand.



Figure 5—The lower limbs of the patient. The right foot is missing a toe, the left leg is absent below the knee joint.

human homeobox genes that might be suggested by the phenotype observed.

Uterine environmental factors have been blamed. Torpin² suggested that rupture of the amnion during

early pregnancy may produce membranous strands. These, if swallowed, could produce the intraoral adhesions. This seems a simplistic explanation of rather complex intraoral deformities.

Table Classification of syndromes of oromandibular and limb hypogenesis

<i>Hall (1971)</i>	<i>Chicarilli (1985)</i>
Type I: A. Hypoglossia B. Aglossia	Type I: <i>Micrognathia</i> (mandibular) Pierre Robin syndrome Hanhart syndrome
Type II: A. Hypoglossia – hypodactilia B. Hypoglossia – hypomelia (peromelia) C. Hypoglossia – hypodactylomelia	Type II: <i>Microglossia</i> Hypoglossia Hypoglossia – hypodactyly
Type III: A. Glossopalatine ankylosis B. With hypoglossia C. With hypoglossia – hypodactilia D. With hypoglossia – hypomelia E. With hypoglossia – hypodactylomelia	Type III: <i>Dysgnathia</i> (maxillo-mandibular) Glossopalatine ankylosis Glossopalatine ankylosis – hypodactyly
Type IV: A. Intraoral bands and fusion B. With hypoglossia C. With hypoglossia – hypodactilia D. With hypoglossia – hypomelia E. With hypoglossia – hypodactylomelia	Type IV: <i>Other</i> Moebius syndrome Charlie M syndrome (Amniotic band syndrome)
Type V: A. The Hanhart syndrome B. Charlie M. syndrome C. Pierre Robin syndrome D. Moebius syndrome E. Amniotic band syndrome	

David et al³ hypothesised that a vascular accident followed by tissue necrosis could play an important role in the pathogenesis. The case reported by Scott⁴ presenting oromandibular limb hypogenesis with organised thrombi in the fetal stem vessels on microscopic examination of the placenta seems to support this theory.

Firth et al,²⁷ after a survey of children exposed to chorionic villus sampling, reported that this procedure could play an aetiological role in producing isolated limb defects or a phenotypic overlap with oromandibular limb syndromes; suggesting but not confirming yet the traumatic factor theory.

Apart from this problem of aetiology, the literature contains ambiguity in classification of the different cases, presenting with a variable range of anomalies affecting the tongue, mandible, maxilla and limbs, included under the name of OLHS (Table). Hall in 1971⁶ recognised five main categories, with the only criteria necessary for inclusion is the occurrence of hypoglossia, with the exception of category Type V, which contains a miscellany of syndromes. Aglossia is classified under the I type and the presence of intraoral bands is in the IV type. Chicarilli in 1985¹⁰ proposed a new classification which took into consideration the embryologic origin and the clinical presentation. He recognised four major classes: type 1 showing micrognathia, type 2 based on microglossia as the primary disorder from subtle microglossia to total absence of the tongue, type 3 presenting with glossopalatine ankylosis, including all intraoral bands that span the intermaxillary space, type 4 including Moebius and Charlie M. syndrome.

The case we reported cannot be included in any of the cited classifications.

In conclusion we believe that this case, with the stigmata of either the glossopalatine ankylosis or the aglossia-adactylia syndrome, confirms the descriptions of a phenotypic overlap among the different OLHS syndromes,^{1,7,11} supporting the thesis of a common root with different expressions.

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