

THE OAV-SPECTRUM AND ASSOCIATED ANOMALIES IN 77 PATIENTS

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ABSTRACT

We have studied 77 patients belonging to the OAV-spectrum. These patients were grouped into four different categories according to their clinical signs: Goldenhar syndrome, oculoauriculovertebral dysplasia, typical hemifacial microsomia, and those only with pre-auricular tags, in order to compare the frequency of associated anomalies and recurrence rates. We have listed and compared our clinical findings with those found in the literature. There are few associated anomalies in the last group (pre-auricular tags) when compared with the other three groups, indicating that pre-auricular tags could represent a distinct anomaly.

INTRODUCTION

The term OAV (Oculoauriculovertebral) spectrum includes the classical Goldenhar syndrome (auricular anomalies, pre-auricular pits and/or tags, and epibulbar lipodermoid of the eye); the OAV-dysplasia (auricular anomalies, epibulbar dermoids, spinal anomalies); the facial microsomia (facial asymmetry often associated with auricular malformations and transverse clefts); and the pre-auricular ear tags (Goldenhar, 1952; Rollnick and Kaye, 1983; Gorlin *et al.*, 1990). However, there still exists controversy about the clustering of these different phenotypes under a unique eponym.

MATERIAL AND METHODS

We examined a sample of 82 patients belonging to the OAV-sequence spectrum. This sample included patients with Goldenhar syndrome (ear malformation, pre-auricular tag/pit, epibulbar dermoid, facial asymmetry), hemifacial microsomia (facial asymmetry, ear malformation), OAV-dysplasia (ear/eye anomalies, facial asymmetry, transverse cleft and spinal involvement); and patients with pre-auricular tags (without associated anomalies). Five patients presenting some of these signs, but diagnosed as having other syndromes were excluded from the sample. Each patient was ascribed to one category only. The categories were named as follows:

Goldenhar syndrome (GS): ear malformation, pre-auricular tag/pit, epibulbar dermoid;

Hemifacial microsomia (HFM): marked facial asymmetry (mandibular hypoplasia), ear malformation;

Oculoauriculovertebral dysplasia (OAV): spinal involvement associated with two or more of the following signs: eye anomaly other than epibulbar dermoid, ear anomalies, facial asymmetry, transverse cleft;

Pre-auricular tags (PT): pre-auricular tags without other features of the three conditions mentioned above.

All patients were examined personally at the Serviço de Genética Clínica do Hospital de Pesquisa e Reabilitação de Lesões Láblio-Palatais da Universidade de São Paulo, Bauru, SP, Brazil. Skull and spine roentgenograms, as well as orthopantomographies were performed when indicated.

The frequencies of associated minor/major anomalies were compared among patients from different categories, as well as with the frequencies found in the literature.

RESULTS

The total sample included 43 female and 34 male patients. Forty-seven patients had bilateral involvement, whereas 23 and 17 were affected unilaterally, respectively on the right and left sides. Fourteen patients were included in groups GS, 13 in group HFM, 46 in group OAV, and four in group PT.

Frequencies of associated anomalies found in this sample are shown in Table I. Type and frequency of eye and ear anomalies are shown in Tables II and III. The frequencies of associated anomalies were compared with the data of Cohen *et al.* (1989) (Table IV). The following isolated anomalies occurring in some patients were not included in the tables: scar in the auriculo-buccal line, bifurcation of the third metatarsal, recto-aginal fistula, anteriorisation of the anus, sacral dimple, and umbilical hernia in group GS; paresis of cranial nerves other than the 7th, buccal synechia, asymmetry of

upper limbs, renal agenesis, hemangioma, and alopecia areata in group HFM; skull, hemispheric and ventricular asymmetry, hydrocephalus, oro-nasal fistula, long philtrum, buccal tumor, reflux, clavicular asymmetry, asymmetry of sacral region, pulmonary stenosis, hemimelia, triphalangeal thumb, camptodactyly, precocious puberty together with fibrous dysplasia constituting the McCune-Albright syndrome, linear hypopigmentation, and ectodermal dysplasia in group OAV; postaxial polydactyly, and hip dislocation in group PT.

Table I - Associated anomalies in the different groups of patients belonging to the OAV-spectrum.

	GH	HFM	OAV	PT	Overall frequency (%)
Postnatal growth retardation	-	+	+	-	6.9
Mental retardation	-	-	+	-	5.2
Hypertonia	-	+	+	-	2.6
Convulsions	-	+	+	-	2.6
Frontal encephalocle	-	-	+	-	3.9
Macrocrania	+	+	-	-	2.6
Prominent forehead	-	+	+	-	5.2
Paresis of facial nerve	+	+	+	-	13.0
Facial asymmetry	+++	+++	+++	-	71.4
Eye anomalies	+++	++	+++	-	51.9
Ear anomalies	+++	+++	+++	+++	97.8
Large/high nasal root	+++	++	+	-	27.2
Nasal cleft	-	-	+	+	2.6
Macrostomia	++	++	++	-	44.2
Cleft lip/palate	++	+	+	++	32.5
Cleft palate	+	+	+	+	24.7
Cleft tongue	+	-	+	-	2.6
Short frenulum	+	-	+	-	3.9
Micro-retrognathism	+	+	+	-	20.8
Prognathism	-	-	+	-	2.6
Radiological anomalies	++	+	+	-	37.7
Thoracic asymmetry	-	+	+	-	2.6
Dextrocardia	+	-	+	-	2.6
Interventricular communication	-	-	+	-	2.6

Continued

Table I - Continued.

	GH	HFM	OAV	PT	Overall frequency (%)
CHD inespecific	-	-	+	+	2.6
Radial/ulnar hypoplasia	+	-	+	-	2.6
Clinodactyly	+	-	+	-	6.5
Brachydactyly	+	-	+	-	2.6
Simian creases	-	-	+	-	2.6
Hypospadias	+	-	+	-	3.9
Cryptorchidism	+	-	+	-	3.9
Phimosis	-	-	+	-	2.6
Rokitansky sequence	-	+	+	-	2.6
Inguinal hernia	-	-	+	+	2.6
Abnormal hair implantation	+	-	+	-	3.9
Synophrys	+	+	+	-	11.7

+ = < 40%; ++ = 40%-70%; +++ = > 70%; - = none found.

GH - Goldenhar syndrome; HFM - hemifacial microsomia; OAV - oculoauriculovertebral dysplasia; PT - preauricular tags.

Table II - Types and frequencies of eye anomalies.

	GH	HFM	OAV	PT	%
Epibulbar tumor	+++				18.2
Anophthalmia			+		5.2
Microphthalmia		+		+	7.8
Palpebral coloboma	+		+		5.2
Iris coloboma	+		+		3.9
Convergent strabism	+		+		5.2
Heterochromia	+				1.3
Ptosis			+		1.3
Epicanthal folds	+	+	+		11.7
Dacryostenosis			+		5.2
Asymmetric eye fissures	+	+	+		11.7
Absence of eyelashes	+				1.3

Table III - Types and frequencies of ear anomalies

	GH	HFM	OAV	PT	%
Anotia		+	+		3.9
External ear malformation	++	++	++		48.1
Pre-auricular tags	++	+	+++	+++	64.9
Deafness	+	+	+		22.1
Abnormal ear implantation	+		+		2.6
Prominent ears			+		2.6

Table IV - Frequencies in percent of associated anomalies compared with the data of Cohen *et al.* (1989).

	Present study	Cohen <i>et al.</i> (1989)
Facial asymmetry	71	65
Macrostomia	44	35
Cleft lip and/or palate	57	7-15
Epibulbar tumor	18	35
Palpebral coloboma	5	20
Eye motility disorder	5	25
Ptosis, an(micr)ophthalmia,	14	10
Hearing deficit	22	50
Cervical fusion	21	20-35
Facial nerve paresis	12	10
Cardiac involvement	7	5-58
Mental retardation	5	5-15

DISCUSSION

There is still controversy about the clinical spectra of GS, HFM and OAV, which could be variants of the same dysmorphogenetic process (Rollnick and Kaye, 1983). It has been suggested that ear tags might be a microform of the OAV-spectrum (Gorlin *et al.*, 1990); however, 1% of all newborns present ear tags, and 60% of them have no other associated anomalies (Rollnick and Kaye, 1983). Furthermore, there are many other syndromes in which skintag is part of the clinical spectrum. In our sample only four of 77 patients presented this anomaly.

Isolated associated anomalies were found in 86% of the patients. In the whole sample, vertebral and/or rib anomalies, eye involvement, and ear anomalies were present in 46%, 51.9% and in 98.7%, respectively, of the patients. Vertebral anomalies were found in 50% of the patients in group GS, in 58.3% in group HFM and in 44.4% in group OAV. In group GS there was of course by definition involvement of the eye in 100%; in group HFM this occurred in 46.2% and in group OAV in 44.4% of patients.

Comparing the present data with those reported by Cohen *et al.* (1989) (Table IV), the high prevalence of cleft lip and/or palate in our sample reflects the obvious bias of a sample collected in a Craniofacial Center attending mainly clefting patients.

A 3:2 (male:female) sex-ratio has been reported in most papers (Wilson, 1983; Rollnick *et al.*, 1987; Gorlin *et al.*, 1990), however we found a 3:4 ratio. Among our patients 61% presented bilateral facial involvement, which is discordant with the frequency of 10 to 33% reported in the literature (Grabb, 1965; Rollnick *et al.*, 1987). Among the patients with unilateral facial involvement, there was a 3:2 right side/left side ratio, in fair agreement with the published data (Cohen, 1971; Rollnick *et al.*, 1987; Gorlin *et al.*, 1990). Considering facial asymmetry, spinal anomalies, pre-auricular tags and other ear malformations as mild expression of the OAV-spectrum, a recurrence rate of 13% was found in our patients (21.4% in group GS; 7.7% in group HFM; 13% in group OAV; 0% in group PT). This rate is higher than the recurrence risk of 2-3% normally calculated on the basis of a multifactorial model (Grabb, 1965; Rollnick *et al.*, 1987). We did not find significant differences in frequencies of associated anomalies for the GS syndrome, HFM and OAV-dysplasia. This suggests that they are variants of the same condition, namely - the OAV-spectrum. Pre-auricular tags could represent a minor expression of this condition.

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RESUMO

Nós estudamos uma amostra de 77 pacientes pertencentes ao espectro OAV. Estes pacientes foram agrupados em quatro categorias diferentes de acordo com os sinais clínicos que apresentavam: Síndrome de Goldenhar, displasia oculo-auriculo-vertebral, microssomia hemifacial e aqueles que tinham apenas apêndices pré-auricular, no sentido de verificar se existia alguma diferença detectável relacionada às anomalias associadas ou às taxas de recorrência dentro destes grupos. No último grupo, quando comparado com os demais, observamos que existem poucas anomalias associadas indicando que apêndices pré-auriculares podem representar uma anomalia distinta.

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