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OCULO-AURICULO-VERTEBRAL DYSPLASIA (GOLDENHAR'S SYNDROME) CONCORDANT IN IDENTICAL TWINS

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SUMMARY

The first case of MZ twins concordant for oculo-auriculo-vertebral dysplasia is reported. In the light of the data from the literature concerning the etiology of the syndrome, this observation does not allow an absolute conclusion but points towards the possible existence of a genetic form of this syndrome.

Goldenhar (1952) recognized the combination of epibulbar dermoids or sometimes lipodermoids on the eyeglobe, with preauricular tags and fistulas, as a specific entity, and he supposed a relation with the mandibulo-facial dysostosis (syndrome of Franceschetti or Treacher-Collins syndrome).

Gorlin et al. (1963) and Gorlin and Pindborg (1964) analysed the described patients and gave an excellent review of the great variation in symptoms and associated malformations and underlined differences with the mandibulo-facial dysostosis. Because of the frequent deviations of the spinal column, he introduced the name " oculo-auriculo-vertebral dysplasia ", and indicated the relation with hemifacial microsomia.

Pashayan et al. (1970) described a patient with both the caracteristics of hemifacial microsomia and oculo-auriculo-vertebral dysplasia, and so confirmed Gorlin's thought that both syndromes are manifestations of the same dysmorfogenesis.

In the literature, there are but few indications for teratogenesis or heredity. As possible cause, Zarfl (1935) calls tubal gravidity, Jongbloet (1968) overripeness of the egg, and Hollwich and Verbeck (1969) a hormonal disturbance in the second month of pregnancy. Pashayan et al. (1970) mentioned consanguinity; occurrence in sibs was described by Saraux et al. (1963) and Krause (1970) and in successive generations by Summitt (1969). Six twin pairs have been described, all discordant for the syndrome.

Ours are the first concordant twins for oculo-auriculo-vertebral dysplasia and, also because of differences in clinical picture, form a new contribution to the knowledge of this syndrome.

Rec. 2. XII. 1971

Acta Genet. Med. Gemellol. (1972), 21: 116-124

CASE REPORT

In October 1965 female twins were born, both with multiple congenital malformations. The parents come from healthy families, have never been seriously ill, and denied consanguinity, radiation, and teratogenic contacts. At the birth of the twins the mother was 31 and the father 27 years of age. They had already a healthy son of 7 years and the mother never had a miscarriage. Between the birth of the son and of these twins they did not practise contraception because they very positively desired more children.

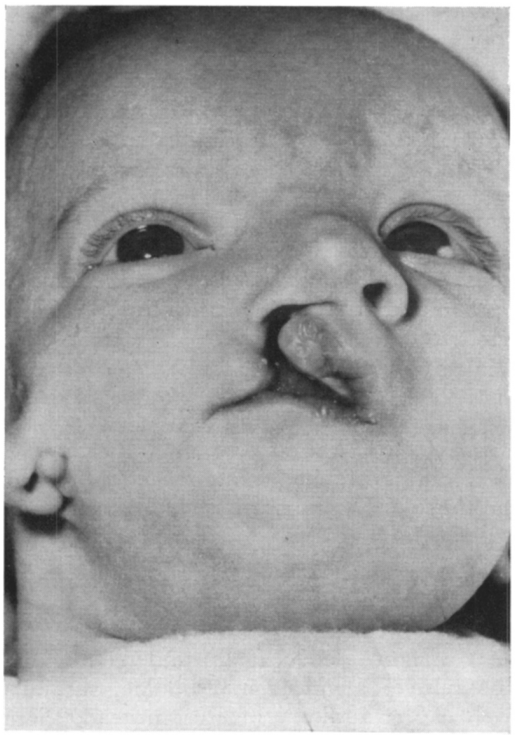
When the pregnancy came into the fourth month the boy got rubella and for precaution the mother was given a gamma-globulin-injection, though most probably she already had the disease in childhood. Because of hydramnion and oedema of hands and feet a saltfree diet was prescribed in the sixth month. In the thirty-third week of pregnancy the mother was admitted to a clinic because of a blood-stained vaginal discharge interpreted as caused by a placenta praevia lateralis. Two days later the twins were born spontaneously. No data are available on the composition of the placenta.

Nancy

The first-born, with a length of 45 cm and a weight of 2950 g. She showed a clear underdevelopment of the right half of the face, a right-sided cleft lip and palate, and a deviation of the chin to the right because the ramus ascendens mandibulae was missing. The right external ear was missing, as well as the auditory meatus; instead, there was a rudimentary forming between the normal insertion of the ear and the corner of the mouth (Fig. 1). On the left eyeglobe an epibulbar dermoid was visible in the lower outer quadrant; and before the left ear, which was formed and put on normally, was a cutaneous tag. The cleft lip and palate were repaired by plastic surgery and in 1968 and 1970 a rib-transplant was placed on the underdeveloped right mandibula (Prof Huffstadt). Mentioning the psychomotor development, Nancy was able to sit when 7 and to stand when 10 months old, and walked within a year.

Examination at the age of 4.5 years. An asymmetrical face detrimental to the right, caused by hypoplasia of mandibula and maxilla. On the right side there is no external ear or external auditory meatus visible, but only the scar of the surgically removed rudimentary ear that was set on too low. There was no detectable fistula (Fig. 2). The nasofrontal angle is obliterated, due to a rather high nasal root. On the tip of the nose, on the right of the median, a fistula is visible. On the left side of the face an epibulbar dermoid (a relapse) is located in the lower outer quadrant of the eye, and before the left ear a supernumerary tag is seen without indications of fistula. The left ear and auditory meatus are normally shaped (Fig. 3). The remainder of the physical examination was normal, particularly the ophthalmoscopy e.c.g. and left-side audiogram. The girl is visiting nursery school and seems mentally normal.

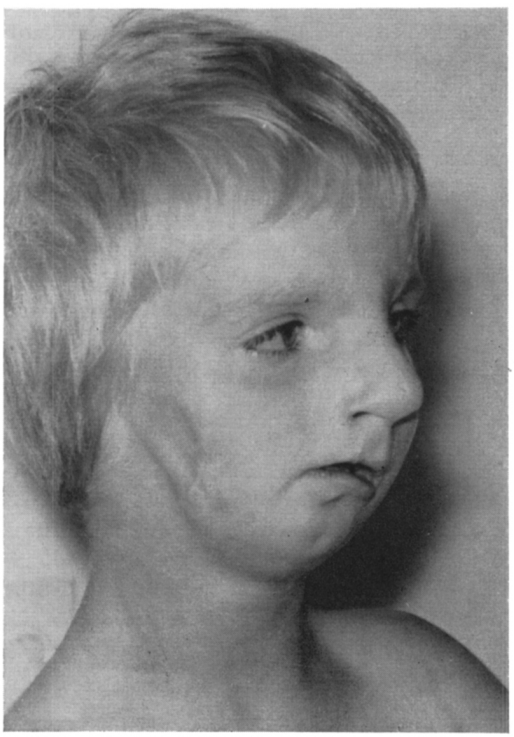
Röntgenological examination. The skull shows asymmetry of mandibula; maxilla, base of the skull, and ossa petrosa visible, detrimental to the right. On the Stenvers-Schülers-Chaussees there are no pecularities on the left, but on the right the external auditory meatus is lacking. On photographs of the spine no occipitalisation is visible but a synostosis of the vertebral bodies of C2 and C3 and the first and second ribs on the right side. Also, there are 13 ribs on the right side and 12 on the left.

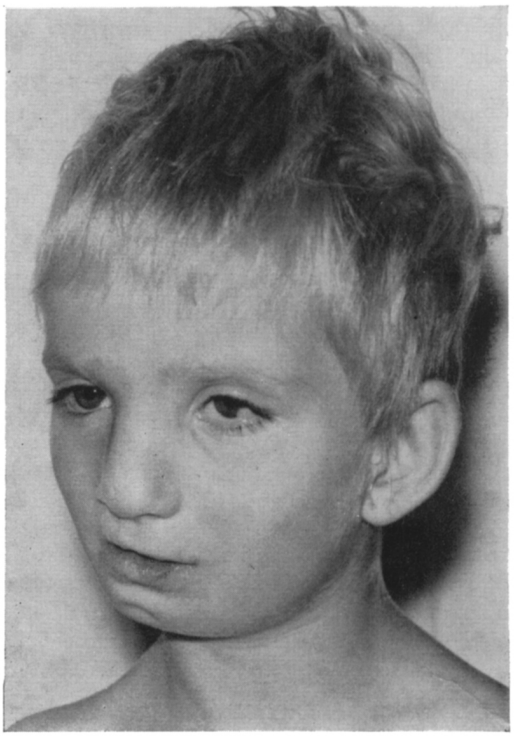


OCULO-AURICULO-VERTEBRAL DYSPLASIA

Nancy

Fig. 1: at birth





Figs. 2 and 3: at 4.5 years of age

https://doi.org/10.1017/S1120962300011173 Published online by Cambridge University Press

OCULO-AURICULO-VERTEBRAL DYSPLASIA

Jennifer

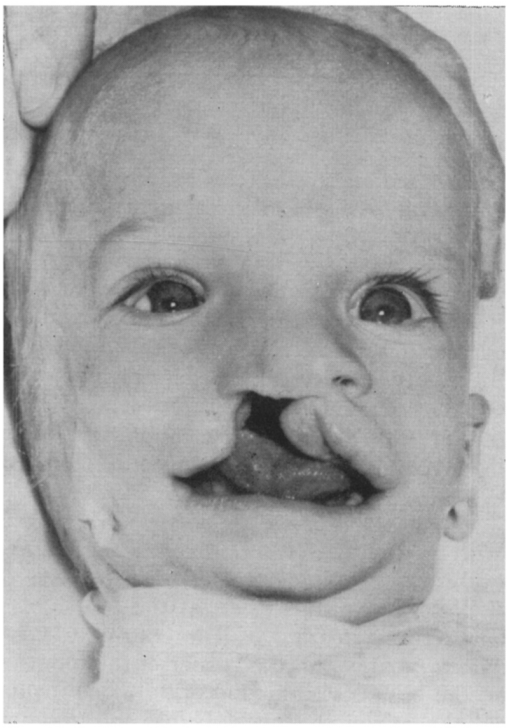
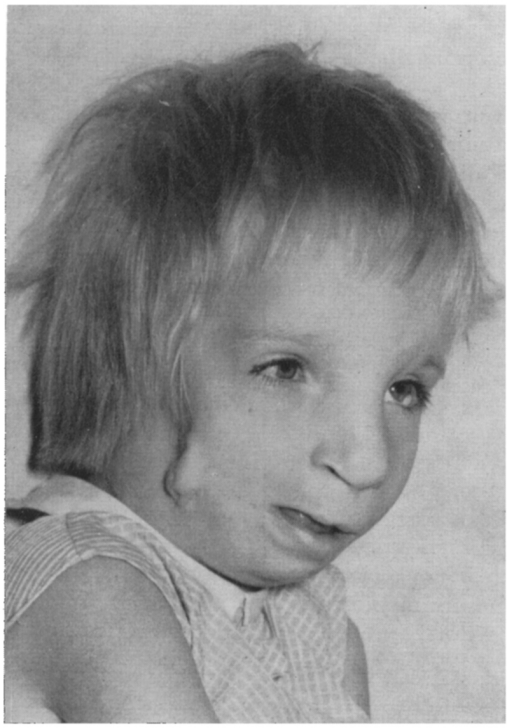
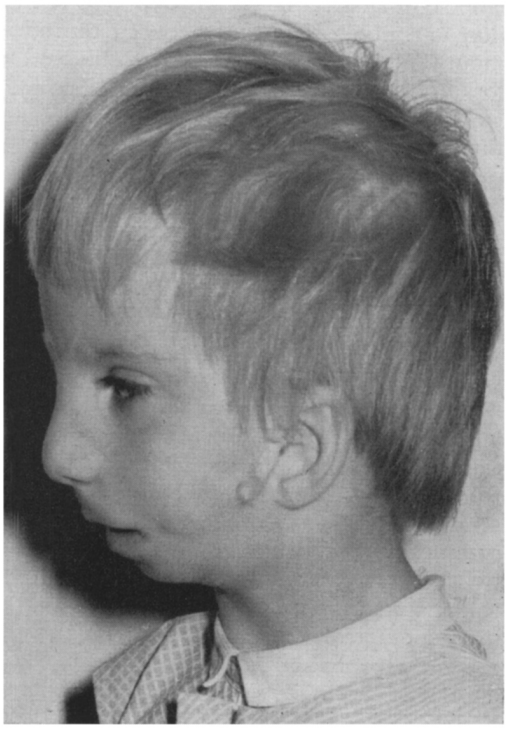


Fig. 4: at birth





Figs. 5 and 6: at 4.5 years of age

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JENNIFER

Immediately after the breech-delivery the conformity of the malformations was recognized: hypoplasia of the right half of the face, cleft lip and palate, deformed lowset ear, all on the right side, and epibulbar dermoids on both the eyeglobes and preauricular tags located in front of the left ear (Fig. 4). The chin was drawn back, due to hypoplasia of the mandibula, especially of its ramus ascendens on both sides (Prof. Boering). Remarkable was the bilateral macrostomia. The macrostomia, cleft lip and palate were corrected surgically, and because of the difficulties with swallowing, which made feeding by tube necessary during the first two years, a pharynx-correction according to Rosenthal was carried out (Prof. Huffstadt). The psychomotor development showed a clear retardation from the beginning: standing on 11 months, walking on 2.9 years. Speech has never developed and there is hardly any contact. At the age of 4.5 years she can only undress.

Examination at the age of 4.5 years. Clearly asymmetrical face, detrimental to the right, with an obliterated naso-frontal angle and a rather high nasal root. Very striking are the epibulbar dermoids located in the lower outer quadrants of both eyes. An indication of a slight epicanthus exists at the left side. The left ear is normally configurated but a bit low-set and in front of it an extra ear tag is found. On the line between the external auditory meatus and the corner of the mouth a knob-formed appendix with three little fistulae at the base is visible (Fig. 5). A pedunculated skin-process with a central opening is found on the left of the neck, before m. sternocleidomastoideus. Scars of the repaired cleft lip and palate and macrostomia are hardly visible. The chin is slightly deviated to the right. The right side of the face is hypoplastic as a result of the underdeveloped mandibula, maxilla, and nose. Halfway between the normal place for the auricle and the corner of the mouth, a primitive structure is to be seen, representing the lacking ear, without indications for an external auditory meatus (Fig. 6).

Further physical and neurological examinations offered no peculiarities, and the ophthalmoscopy, I.V.P., ECG, and EEG were considered as normal. A hearing test on this mentally retarded child indicated a certain ability to hear.

Röntgenological examination. Asymmetry of the skull detrimental to the right with hypoplasia of the ramus ascendens of the mandibula on both sides. There was no occipitalisation but there was a synostosis of the vertebrae C2 and C3 and also of the right-sided first and second ribs; in addition there were 13 ribs on the right side and 12 on the left.

Summarising, with the presence of epibulbar dermoids, auricular appendixes, and the bony anomalies of the spinal column in both children, the cardinal symptoms of oculo-auriculo-vertebral dysplasia are given. The macrostomia (Jennifer), the hypoplasia of the ramus ascendens, and the cleft lip and palate, are frequently described in this syndrome. The fistula on Jennifer's neck and on Nancy's nose (on the same place where Christiaens et al., 1966, described a tag in a patient with this syndrome) belong doubtless to the same complex of malformations. The most important symptoms and differences found in the twins are summarized in Table I. Because of their concordance, not only in hair and eye-colour and the 13 ribs on the right side, but mainly in blood groups and serology, where the genotypical differences between the parents are permitting sufficient variability, they are most probably MZ twins (Table II).

TABLE I
COMPARISON OF CONCORDANT AND DISCORDANT SYMPTOMS

Symptom	Nancy	Jennifer
Epibulbar dermoid	+	+
Dysplasia right ear	+	+
Cervical synostosis C2-3	+	+
Clift lip and palate	+	+
Auricular appendixes	+	+
Absence ext. auditory meatus	+	+
Unilateral facial hypoplasia	+	+
Aplasia mandibular ramus, right side	+	+
left side	—	+
Macrostomia	—	+
Preauricular fistulas	—	+
Nasal fistula	+	—
Cervical fistula	—	+
Psychomotor retardation	—	+

TABLE II
BLOOD-GROUP AND SEROLOGICAL CARACTERISTICS OF PARENTS AND TWINS

Father	Mother	Nancy/Jennifer
A	O	A
NNS+	MNS—	MNS—
P_1+	P_1+	P_1+
Lu(a—)	Lu(a—)	Lu(a—)
CcDee	ccDEE	CcDEe
K—	K—	K—
Fy(a+b—)	Fy(a+b+)	Fy(a+b—)
Jk(a+)	Jk(a—)	Jk(a+)
Gc 1-1	Gc 2-1	Gc 2-1
Hp 2-2	Hp 2-2	Hp 2-2
Gm(a—x—g—f+b+)	Gm(a—x—g—f+b+)	Gm(a—x—g—f+b+)
Inv(1—)	Inv(1—)	Inv(1—)

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DISCUSSION

Narog (1925) describes a three-days-old baby with an epibulbar dermoid in both eyes without further mentioning particularities. It would have been one of a pair of twins, but more information about conformities or even sex is lacking.

A three-years-old boy was described by Bock (1951), having a bilateral epibulbar dermoid, hypoplasia of the right facial skull and a deformed low-set ear on the right. The twin brother was fully normal. Because of conformity in appearance, hair and iris colour, position of the teeth, and dermatoglyphics, Bock thinks them to be MZ twins.

The first patient described by Goldenhar (1952) was one of male twins. The brother was not affected and details about the nature of the twinship are lacking.

Berthelon and Cremer (1968) mention a boy with lipodermoids on both eyes and auricular appendixes on both sides. The left mandibula clearly shows on the röntgenphotographs a hypoplasia which was already suspected because of the underdevelopment of the left half of the face. Additionally, there existed a congenital atresia ani, hypoplasia of the right kidney, an arteria lusoria, an asymmetrical spinal column, and presumably a congenital heart malformation. The twin brother was fully normal, and the existence of monochorial, monoamniotic placenta is mentioned.

A pair of DZ twins with discordance for the oculo-auriculo-vertebral dysplasia was described by Heimann (1968).

Cordier et al. (1970) described MZ female twins of which only one shows the oculo-auriculo-vertebral dysplasia: bilateral epibulbar dermoids, auricular appendixes and underdervelopment of the left facial skull. The twins were proved to be MZ by blood-group and serological investigation, by anthropometric analysis, and with the help of skin transplantation.

In conclusion, the six pairs of twins up to now reported in the literature were all discordant for this syndrome.

It is perhaps remarkable that, while in the literature up to now about 80 patients have been described with oculo-auriculo-vertebral dysplasia, this is already found in 7 twin pairs. Although it is of course preferred to publish twins (though this counts more for concordant than for discordant pairs), this would mean that there must be about 300 patients with this syndrome, unless an etiological connection exists between the syndrome and twin pregnancy. This thought was born while reading the publication of Grabb (1965) where, among 101 unselected patients with the first and second branchial-arch syndrome, 5 pairs of twins are mentioned (4 nonidentical and 1 probably identical) which is remarkably high.

Reviewing the complete literature there are but few sound data to conclude for an exogenous or endogenous origin of oculo-auriculo-vertebral dysplasia. The absence of frequent consanguinity of the parents, the few familial accumulations (the great

majority of cases being indicated as sporadic), and also the absence of clear disturbances of pregnancy — all this does not give much information about the etiology.

The first concordant twin pair has here been reported, against 6 discordant ones reported in the literature. The concordance, however, is so striking that it seems possible to assume a genetic form of the syndrome. It may be only a genetic predisposition which is realised under unfavourable circumstances. The most extensive form of the syndrome we found in the girl, who seems to be delayed in growth, compared to her twin sister, and later appeared to be retarded, which perhaps can be imputed to worse intrauterine conditions. Both the forced sterility during years and the low implantation of the placenta, resulting in a placenta praevia lateralis, could be explained as a subnormal surrounding for the children. But if exogenous factors play a part in the etiology of this syndrome, this should be very early in the pregnancy, or even before in the sense of a gametopathy.

To the author, a genetical predisposition which can be luxated by exogenous influences seems to be the most attractive explanation.

ACKNOWLEDGEMENT. The author is greatly indebted to Prof. D. Boering, Prof. A.J.C. Huffstadt, Dr. L.E. Nijenhuis, and Dr. P.H. Jongbloet for their comments, and to the Departments of Medical Illustration of the Universities of Groningen and Nijmegen for their photographs.

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RIASSUNTO

Viene riportato il primo caso di gemelli MZ concordanti per la displasia oculo-auricolo-vertebrale. Alla luce dei dati eziologici ricavati dalla bibliografia, questa osservazione non consente conclusioni assolute, ma indica comunque la possibilità di una forma genetica di tale sindrome.

RÉSUMÉ

La première observation de jumeaux MZ concordants pour la dysplasie oculo-auriculo-vertébrale est rapportée. A la lumière des données étiologiques de la littérature, cette observation ne permet aucune conclusion absolue, mais indique toutefois la possibilité d'une forme génétique de ce syndrome.

ZUSAMMENFASSUNG

Das ist der erste in der Literatur beschriebene Fall von konkordanten EZ mit Augen-Ohren-Wirbeldysplasie. Die ätiologischen Angaben des Schrifttums gestatten es nicht, aus dieser Beobachtung absolute Schlüsse zu ziehen, doch zeigt diese, dass eine erbbedingte Form des Syndroms irgendwie möglich ist.

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