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# Severe Fetal Manifestation of Hemifacial Microsomia

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**Summary.** Hemifacial microsomia is a heterogenous complex lesion including predominantly unilateral face and head malformations mainly in the region of the first and second branchial arch, vertebral anomalies and varying accompanying malformations. A severe manifestation of this condition is demonstrated in a fetus by means of 5 mm thick sections of the whole head. Abortion had been induced because extreme microcephaly simulated fetal anencephaly in prenatal ultrasound examination. Alpha-Fetoprotein values were normal.

**Key words:** Hemifacial Microsomia – Goldenhar syndrome – Fetopathology – Oculoauriculovertebral dysplasia.

## Introduction

Congenital unilateral face and head malformations, combined with different vertebral and sometimes internal anomalies, are frequently described heterogenous complexes which are not well understood. Goldenhar (1952) emphasized the close association of some cases of mandibulo-facial dysostosis (Franceschetti and Klein 1949) with vertebral abnormalities, epibulbar dermoids and preauricular appendices, in the syndrome 'oculoauriculovertebral dysplasia' (syn. Goldenhar syndrome). This and other designations, such as 'hemifacial microsomia' (Gorlin et al. 1963), 'first and second branchial arch syndrome' (Grabb 1965), 'intrauterine focal necrosis' (Poswillo 1973) or 'lateral facial dysplasia' (Ross, 1975) indicate attempts to characterize the malformation complex by the principle anomaly of morphogenesis or by the clinical features and to delineate it from coincidental combinations of anomalies (Günther 1948).

The present case of hemifacial microsomia was examined by morpho-histological and radiological methods.

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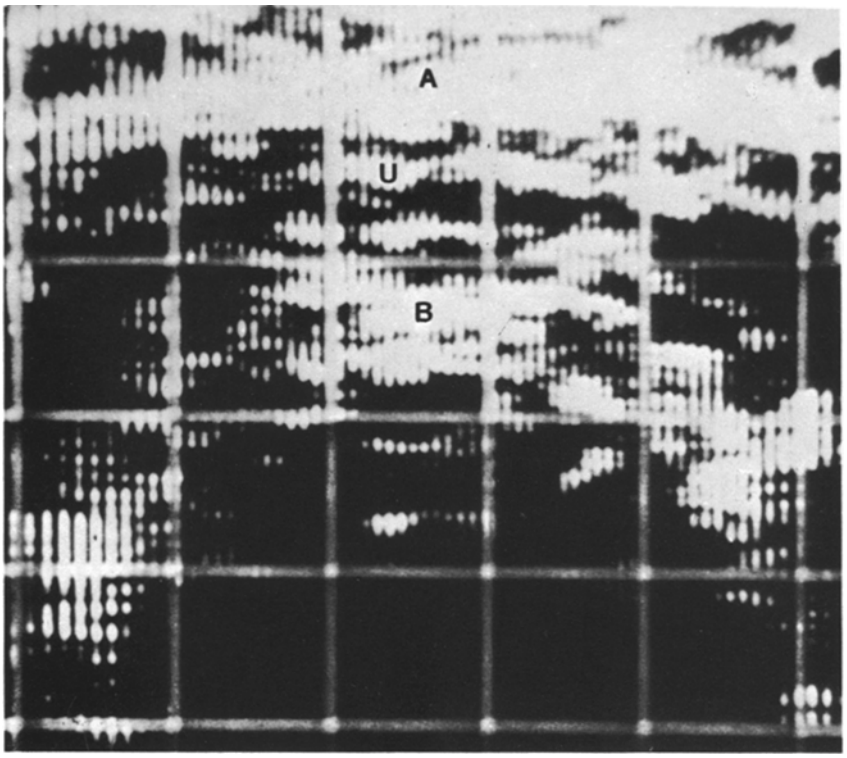


**Fig. 1.** Ultrasound real time display (Vidoson) showing fetal skull with open contour lines in suprapubic transverse body scan. *A*, abdominal wall; *U*, uterine wall; *B*, fetal skull base

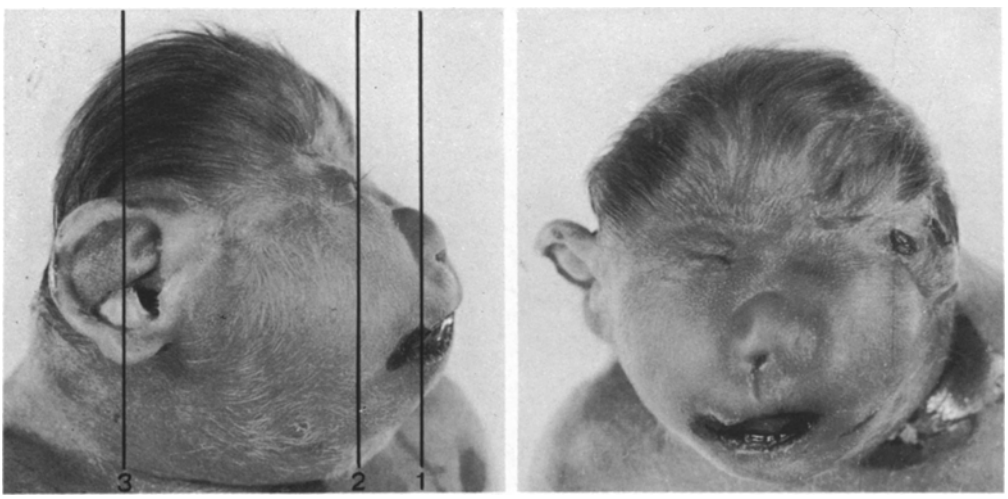


**Fig. 2.** Microcephalic fetal head with hemifacial microsomia. Longitudinal lines indicate levels of frontal sections

## Case Report

The female fetus was the third conceptus of a 35 year old woman and her 36 year old husband. She had previously given birth to two normal children. Pregnancy was uneventful until the 26th gestational week, when precocious onset of labour led to hospitalization. Ultrasonography displayed an anencephalic-like configuration of the fetal skull (Fig. 1). This was confirmed by X-ray examination. Although amniotic alpha-Fetoprotein (AFP) values were normal, abortion was induced in the 27th week of gestation.

The 32 cm female fetus displayed a closed, but extremely microcephalic malformation of the head. There was an asymmetry of the face with more distinct hypoplasia of the left side, frontal displacement of a rudimentary left pinna, defects of the left nostril and nasal cavity, and also of the left palpebral fissure (Fig. 2). The right side of the face showed milder anomalies including macrostomia with lateral facial cleft, macrotia and a very small palpebral fissure. Micro- and retrogenia, short neck with cutis laxa and bilateral clubfeet were present. On X-ray examination costal defects and multiple vertebral unomalies of the cervical spine were found, namely an occipitalisation of the atlas and vertebral block formation (Fig. 3).

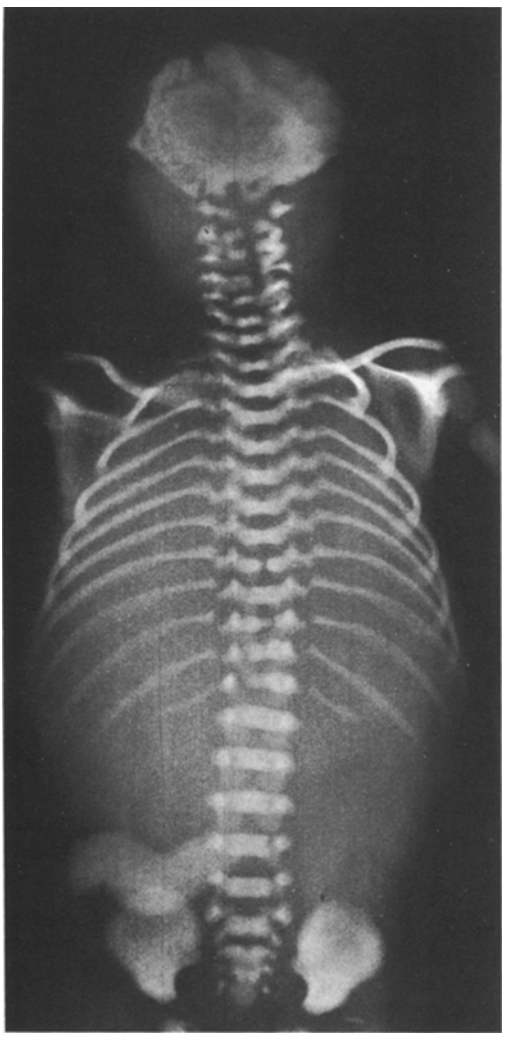

**Fig. 3.** X-ray picture of fetal skull and spine

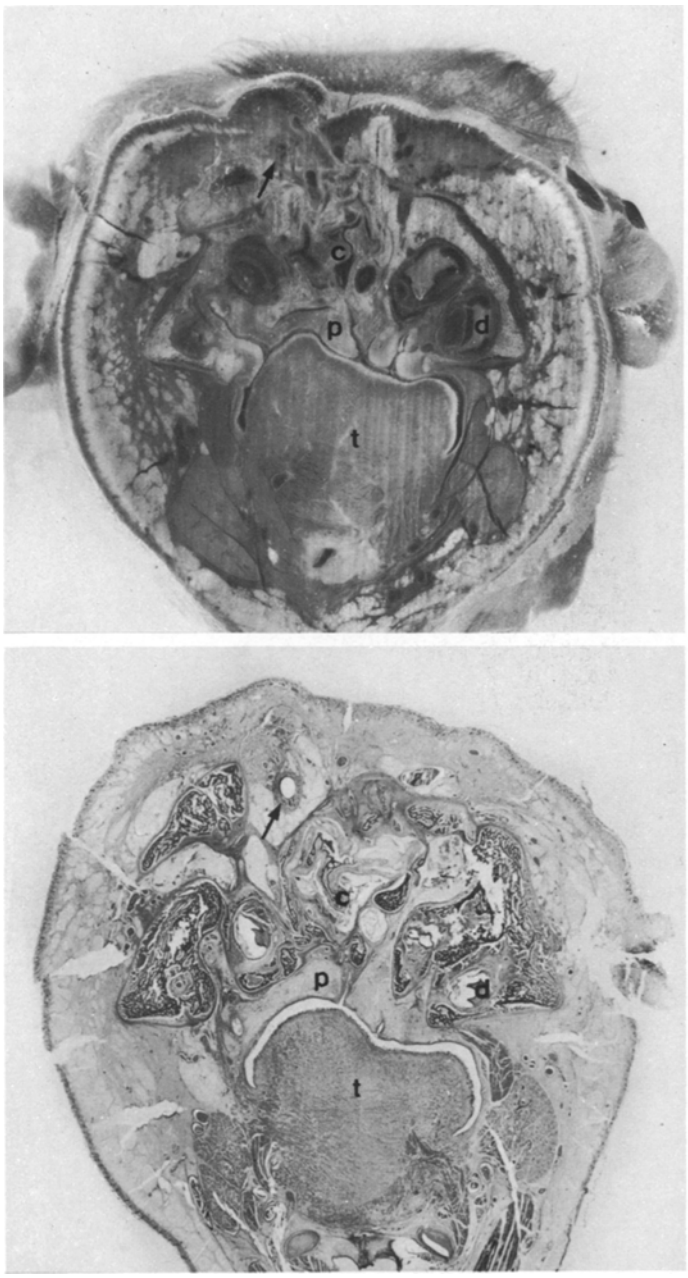


**Fig. 4.** Frontal section of the fetal head at level 2 (s. Fig. 2) displaying cryptophthalmic eye (↗) (s. Fig. 5), left sided defect of nasal cavity and conchae (*c*), dental anlagen (*d*), cleft palate (*p*) and hypoplasia of the left tongue (*t*). (×2,1)

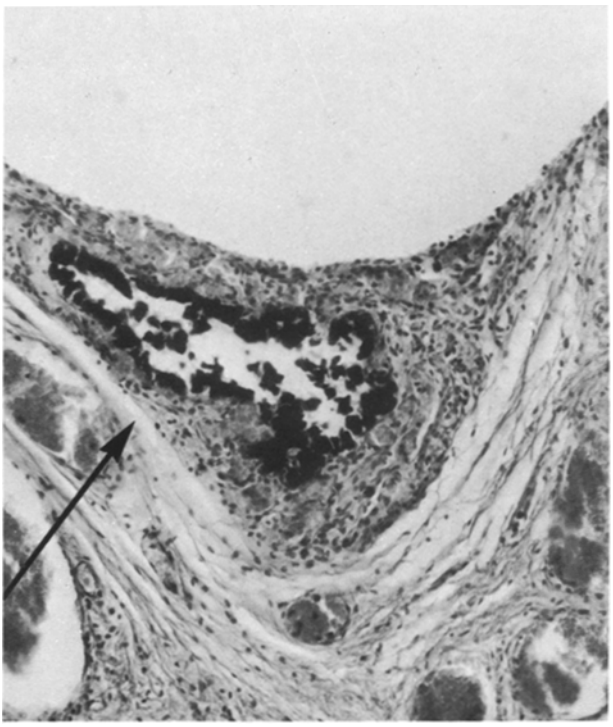

**Fig. 5.** Caudal pole of ophthalmic cyst with inclusion of pigmented epithelium, under higher magnification (s. Fig. 4) (×61)

Autopsy revealed additional internal anomalies such as bicuspid aortic and pulmonic valves, defect of the left umbilical artery, a bilobed right lung, malrotation of the intestine, and hypoplasia of the adrenals and thyroid glands.

For a more precise evaluation of the skull deformities 5 mm frontal sections of the head were photographed, X-rayed and paraffin embedded. Histological sections of the whole head were studied after hematoxylin-eosin and Goldener staining. They were compared to those of a normal control fetus of the same age.

Examination at the level of the nose (Fig. 2) showed the orbital region not to be included because of protrusion of the mouth region. Absence of the left nostril and nasal cavity were noted, but the dental anlagen were well developed and symmetrical development of the frontal mandibular was seen.

At the level of the right palpebral fissure (Figs. 2, 4) a bilateral defect of the orbital bones was found. There was complete left sided anophthalmia, while on the right a medially displaced small cystic structure was identified as an eye by the presence of a pigmented lining layer (Fig. 5), although lens, anterior chamber, and cornea were missing. This cryptophthalmic eye was surrounded by solid lipoid tissue. Left sided defects of the conchae and of medial parts of the maxilla causing cleft palate and radiologically verified aplasia of the left mandibular condyle and hypoplasia of the left tongue, were collectively responsible for unilateral microstomia. On the right side, hypoplasia of the mandibular condyle was combined with unilateral macrostomia. The parotid glands were symmetrical, though medially displaced, while other salivary glands seemed irregularly distributed on both sides. The left ear was included in this section because of frontal displacement. It showed a dysplastic pinna and the absence of a normal external auditory meatus. In contrast to control sections cerebral tissue was not recognized at this level.

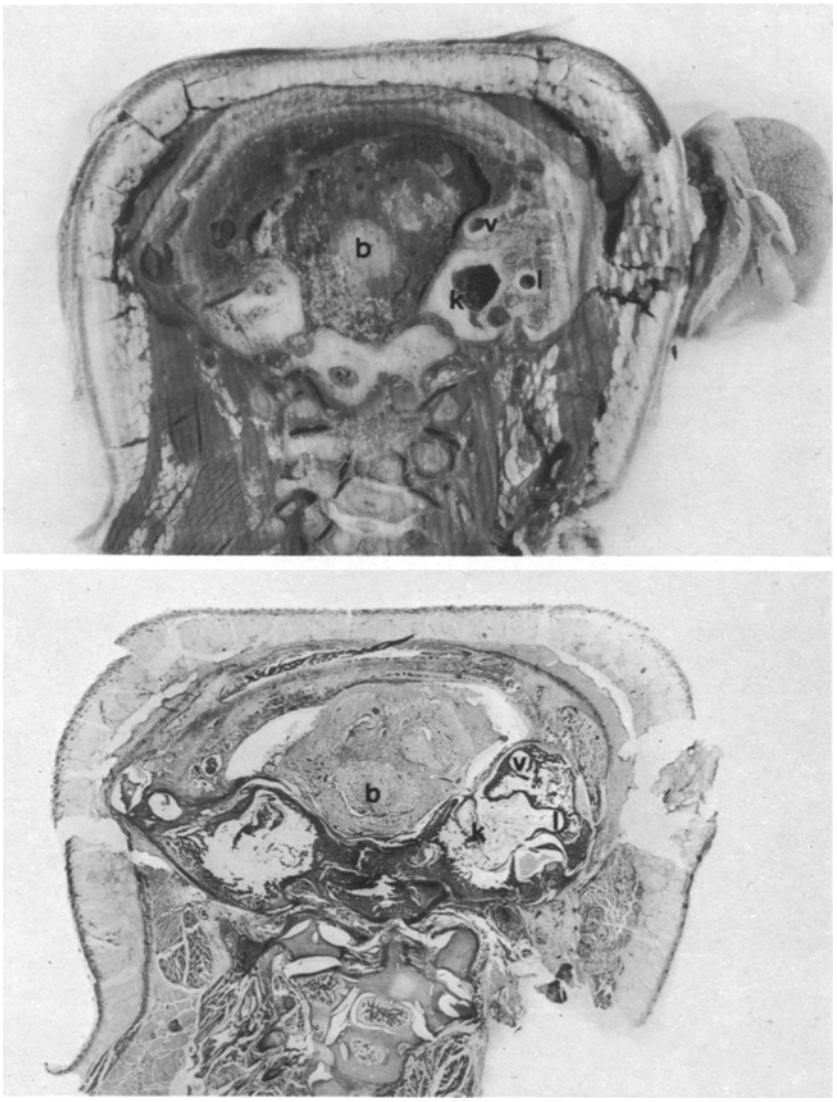


**Fig. 6.** Dorsal section of the fetal head at level 3 (s. Fig. 2) showing microencephaly with disorganized cerebral and mesenchymal tissue (*b*) as also ventral (*v*) and lateral (*l*) semicircular canals and cochlea (*k*) of the right inner ear. (×1,7)

At the level of the right ear (Figs. 2,6) semicircular canals and middle ear anlage could be identified macroscopically at the right side, whereas on the left there was a defect of the middle ear and a frontal displacement of the inner ear. This was verified by X-ray examination. The extremely small cranial cavity did not contain cerebral hemispheres nor cerebellum, but a highly vascularized mesenchyme surrounded a small area of disorganized cerebral tissue with glial cells and few clusters of neuroblasts. The cranial base was shortened and displayed a more distinct left sided hypoplasia. Radiological examination of this slide confirmed occipitalization of the atlas.

## Discussion

The nature of the cranial malformation of the aborted 32 cm female fetus explains the discrepancy between normal amniotic AFP-values and apparently anencephalic configuration of the fetal skull in ultrasonography. Extreme microcephaly had produced a misleading intrauterine diagnosis. The microcephalic malformation was associated with distinct facial asymmetry and defects of the cervical spine.

The coexistence of unilaterally accentuated facial anomalies and vertebral malformations was first described by Arlt (1892) and has often been studied in attemps to carve distinct clinical entities from this complex group. The variability of morphological expression, the fact that many transitional forms exist and that different modes of inheritance have been described, indicates a possible multifactorial aetiology in man (Gorlin et al. 1976).

An animal model in the mouse provided evidence that early unilateral facial haematomas in the region of first and second branchial arch may cause oculoauriculovertebral dysplasia by inducing focal tissue necrosis (Poswillo 1973). This demonstrates a possible pathogenetic pathway, but does not reveal aetiological principles.

With regard to our case, the unilaterally accentuated facial anomalies may well be due to focal damage of the first and second branchial arch area, but may also result from early disturbances of neural crest cell migration, since the cranial mesenchyme derives from this cellular system (Poswillo 1974). Moreover, the occurrence of extreme microcephaly suggests additional damage of either the neural plate or more likely of the early brain anlage.

According to earlier descriptions, all the present malformations, including the internal anomalies, have been associated with cases of oculoauriculovertebral dysplasia (Goldenhar 1951; Baum und Feingold 1973), hemifacial microsomia (Gorlin et al. 1976) or unilateral facial dysplasia (Ross 1975). However, they usually occurred in a less severe manifestation and with different combinations of the symptoms. Our case may be interpreted as an extreme and lethal manifestation of these variable conditions, detected in an earlier developmental stage. Since congenital diseases come to the observation of the paediatrician and geneticist only when less affected children survive, fetopathological studies may help to evaluate the earlier staged and the more severely affected cases of these diseases.

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