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References

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A case of suspected teratogenic holoprosencephaly

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SUMMARY A case of holoprosencephaly is reported in which the mother was prescribed high doses of oestroprogestins during the first 5 months of the pregnancy. Investigation of the family failed to reveal any sign of physical abnormality. A normal karyotype was detected in the proband. The authors suggest that this case may shed some light on the normal and abnormal way in which embryonic fields develop.

The action of teratogenic factors in the aetiology of holoprosencephaly has been studied experimentally using various animals (amphibia, birds, and mammals) and different agents (surgical removal of the prechordal mesoderm or its destruction by localised x irradiation, vitamin A excess, etc).1 2

The great majority of reports of this condition in man refer to cases with various chromosomal abnormalities,3–7 or Mendelian aetiology with autosomal dominant transmission in some families8–10 and autosomal recessive in others.1 11

Only a very few reported cases12 have well documented teratogenic mechanisms as causative factors. In the other cases Mendelian or chromosomal aetiology cannot be ruled out.

We report a case of alobar holoprosencephaly with a known exposure to a teratogenic agent.

Case report

The proband (fig 1) was a term newborn male (birth weight 3·5 kg, head circumference 40 cm) who died
The question of the teratogenicity in man of oestrogens and progestins, apart from the sexual differentiation of the fetus, is still controversial. In a large series of retrospective studies the use of oestrogen and progestogen during the early months of pregnancy has been found to be significantly associated with neural tube defect, VACTERL association, limb reduction defect, and congenital heart disease. Holoprosencephaly was reported by Batt et al but the patient also had trisomy D.

In the prospective survey of Hook et al in which 50 282 pregnancies were studied, a higher incidence of malformations was found after both early and late exposure to sex hormones in pregnancy. In contrast, a small number of prospective and retrospective studies have failed to confirm the teratogenicity of these drugs.

The embryotoxicity of oestrogens and progestins has been proved in mammals such as mice, rats, and mus rattus albinus. The most favoured interpretation of the facts is a teratogenic potential conditioned by genetic and other exogenous factors.

References

Tracheo-oesophageal anomalies in the Goldenhar anomalad

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SUMMARY A case of the Goldenhar anomalad is presented with a previously undescribed association with oesophageal atresia and tracheo-oesophageal fistula. This is the second instance of a tracheobronchial-oesophageal communication being found in association with the anomalad. Awareness of this combination may facilitate future diagnosis and treatment of the anomaly.

The Goldenhar anomalad is an association of facial and auricular anomalies resulting from errors in morphogenesis of the first and second branchial arches, accompanied sometimes by vertebral, ocular, and visceral malformations.1 We describe a case with previously undescribed anomalies including tracheo-oesophageal fistula, oesophageal atresia, and hypoplasia of the cerebellum.

Case report

A 2·025 kg female infant was delivered after 36 weeks of uneventful gestation to a 24 year old mother. The parents were unrelated Sephardic Jews and both they and their two children were normal and in good health. The Apgar scores were 6 and 9 at 1 and 5 minutes respectively. Increasing dysnoea and excessive salivation were soon noted and an attempt to pass an orogastric catheter was unsuccessful.

On examination the baby was noted to have an asymmetrical facies with maxillomandibular hypoplasia, bilateral preauricular skin tags, and microphthalmia with lipodermoids on both lower palpebrae (figure a). The cardiac impulse was felt over the right chest while breath sounds were heard over the left side only. The rest of the examination was considered normal. On chest x-ray a hyperinflated left lung with a complete rightward shift of the mediastinal structures and opacification of the right chest was seen. Extranumerary ribs and hemivertebrae of D1 to D4 were present. The visible tip of the orogastric catheter at D3 and the presence of gastric air suggested the presence of oesophageal atresia with a tracheo-oesophageal fistula. Bronchography showed a complete absence of the right bronchial tree (figure b). The baby died at 20 hours of age.

At necropsy the right lung and the right mainstem bronchus were absent. The left lung had three lobes. The upper portion of the oesophagus was separated from the lower half and ended blindly. The lower portion opened into the trachea. The cardiac chambers and valves were normal. The ductus arteriosus and the foramen ovale were patent. The pulmonary trunk divided into two branches, both supplying the

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14 Wilkins L. Masculinization of the female fetus due to the use of orally given progestins. JAMA 1960;172:1029–32.
16 Nora JJ, Nora AH. Preliminary evidence for a possible association between oral contraceptives and birth defects. Teratology 1973;7:24A.
23 Andrew FD, Christensen HD, Williams TL, Thompson MG, Wall ME. Comparative teratogenicity of contraceptive steroids in mice and rats. Teratology 1973;7:11–12A.

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