The Journal of Laryngology and Otology
December 1992, Vol. **106**, pp. 1098–1099

Foetal Warfarin Syndrome—a complex airway problem Case report and review of the literature

J. D. T. MASON, F.R.C.S., A. JARDINE, F.F.A.R.C.S., K. P. GIBBIN, F.R.C.S. (Nottingham)

Abstract

Premature cartilaginous calcification and nasal hypoplasia following first trimester exposure to warfarin are known as the Foetal Warfarin Syndrome (FWS). There are over 40 cases reported in the literature, many of which describe breathing and feeding difficulties in the first few months of life. We report a case where a child had had difficulties breathing and feeding in the first months of life. These had been attributed to nasal hypoplasia. After proper ENT assessment the child benefitted from adenoidectomy.

ENT surgeons should be aware of the syndrome as more women of child bearing age are taking warfarin following cardiac surgery and treatment of thromboembolic disease. ENT surgeons may be asked to review these children who often present with airway and feeding problems which have been attributed to nasal hypoplasia.

Introduction

Warfarin is able to cross the placental barrier. Embryonic exposure during the first trimester is associated with premature cartilaginous calcification and nasal hypoplasia: the foetal warfarin syndrome (FWS). Warfarin taken during the second and third trimesters is associated with foetal haemorrhage and CNS abnormalities. Warfarin causes premature embryonic calcification by preventing the reduction of vitamin K and thus the gamma carboxygluttamation of osteocalcin. Osteocalcin is unable to bind calcium which is laid down in foetal cartilage (Hall *et al.*, 1980).

Di Saia (1966) first reported nasal hypoplasia in a baby associated with maternal ingestion of Warfarin during pregnancy. Hall *et al.* (1980) reviewed 418 cases of maternal warfarin ingestion and estimated that one sixth of pregnancies would result in live births with significant abnormalities, one half of these demonstrating the foetal warfarin syndrome.

We report a case of foetal warfarin syndrome who had specific upper airway problems which were attributed to nasal hypoplasia but the child benefitted markedly from adenoidectomy. There is clear evidence in other accounts of cases of FWS that these children benefit from a careful ENT assessment.

Case report

A 38-year-old woman had an unplanned pregnancy while taking warfarin following cardiac surgery for abberant electrical pathways. She had an elective Caesarian section at 37 weeks because of maternal cardiac problems. The child was a male weighing 2.82 kg. On examination he had mid-facial hypoplasia with a hypoplastic nose with small nares and small nasal passages. His head was large with an abnormally large occiput. He had short humeri, which were confirmed radiologically. Radiology demonstrated epiphyseal stippling of the sacrum, spine and talus. All features were consistent with the foetal warfarin syndrome.

At 12 months of age he was referred to the ENT department because of suspected poor hearing and sinus infection. Incidentally his mother also complained that he became particularly breathless when feeding unless his neck was extended and that he would not tolerate lying prone. The child was so dependent on lying supine that he had developed a flattened occiput. The flattened occiput was confirmed radiologically. There was otoscopic evidence of middle ear effusions. Radiological examination of the post nasal space suggested that it was completely obstructed by adenoidal tissue. The child was listed for adenoidectomy, sinus washouts and grommet insertion. In theatre, the child required a 4:0 rae endotracheal tube. Once intubated the child's oxygen saturation was difficult to maintain. Not until a sandbag was placed between the child's scapulae and the neck was extended further did the saturation return to normal. Large adenoids were removed and pus was found in the right maxillary sinus. Both sinuses were developed and patent. Grommets were inserted after fluid was aspirated from both middle ears. Six weeks following surgery the parents reported a marked improvement in the airway of the child. The child was able to feed easily and was able to lie prone.

Discussion

Over 40 cases of foetal warfarin syndrome have been reported in the literature. With the successful use of warfarin in female patients who have had cardiac surgery or suffered thromboembolic phenomena there will continue to be children with foetal warfarin syndrome, despite pregnancy being contraindicated in women taking anticoagulants.

These children may present to ENT surgeons with the following upper aerodigestive problems.

Nasal hypoplasia and choanal atresia. The airway difficulties that have been reported have been attributed to nasal hypoplasia and choanal stenosis (Hall *et al.*, 1980). In one third of the cases reviewed by Hall and colleagues an oral airway was used to overcome the problem of obligate nasal breathing in the presence of nasal hypoplasia and occasional choanal atresia. Stevenson *et al.* (1980) used a nasopharyngeal airway. Pauli *et al.* (1976) report the necessity of an oral airway to prevent the tongue falling back against the hard palate.

Robinson *et al.* (1978) and Richman and Lahman (1976) report the necessity of nasal prongs to dilate the nasal airway and highlight the value of regular nasal suction to keep the nasal airway patent. Whitfield (1980) describes ephedrine nasal drops as being beneficial.

Accepted for publication: 22 June 1992

Feeding. Feeding was difficult for the child in this report because of the difficulty of neck extension and feeding at the same time. Suckling is difficult for the neonate with FWS who has nasal obstruction (Whitfield, 1980; Lamontagne *et al.*, 1984; Zakzouk, 1986). Curtin and Mulhern (1980) and Harrod and Sherrod (1980) describe the necessity of nasogastric feeding in a neonate with FWS.

Laryngeal abnormalities. An abnormal larynx has been suspected but never confirmed in reports of the foetal warfarin syndrome.

Abbott *et al.* (1977) suspected laryngeal collapse prior to the death of a neonate with FWS but a post-mortem only revealed laryngeal calcification. Collins *et al.* (1977) performed a laryngoscopy and bronchoscopy on a neonate with FWS who was suffering apnoeic episodes; this revealed no abnormality.

Atlanto-axial subluxation. Atlanto-axial subluxation has been demonstrated in more than one case of the foetal warfarin syndrome with its associated risks on intubation (Kerber *et al.*, 1968; Whitfield, 1980).

Lesions of the central nervous system. CNS abnormalities and seizures are not part of the FWS but frequently occur in infants who have been exposed to second or third trimester warfarin in conjunction with FWS. It can be difficult on occasions to distinguish fits or hypoxia as causes for syncopal episodes (Collins *et al.*, 1977).

Protracted difficulties with the upper airway. Kerber *et al.* (1968) describe how a child required frequent nasopharyngeal suction but not until 11 weeks was a left choanal dilatation performed to give significant improvement to the airway. This child had seizures which could have been exacerbated by hypoxia. Shaul *et al.* (1975) describe a child who was slow to feed and gain weight and had several episodes of apnoea and bradycardia, but there is no mention as to whether there was a thorough assessment of this child's upper airway. Collins *et al.* (1977) report a child who had to be readmitted after initial discharge because of apnoeic episodes. The child required a McGovern nipple in the mouth to protect the airway for the first few months of life. The larynx was examined but no mention is made of the post nasal space. Raivio *et al.* (1976) report a child whose initial breathing difficulties subsided, but at three weeks returned with tachypnoea and died. A post-mortem revealed bronchopneumonia. No mention is made of a formal assessment of the upper airway apart from the nasal airways admitting thin catheters. Baillie *et al.* (1980) mention that a child with FWS had repeated dusky episodes until discharge, and had difficulty with feeding. No mention is made of an ENT assessment. Whitfield (1980) reported a case where feeding difficulties and respiratory distress lasted for eight months, the child requiring regular admissions. An ENT assessment is not mentioned. Lamontagne *et al.* (1984) relate a case of FWS where the baby was initially well once it was able to mouth breathe, but during the second month of life increasing episodes of apnoea occurred and the baby died aged two months. Again an ENT assessment is not mentioned apart from choanal stenosis being absent. Zakzouk (1986) reports a baby with FWS who had both feeding and breathing difficulties in the early weeks. Patent posterior nares were confirmed by passing catheters. Apart from this observation and noting a hypoplastic nose no other ENT examination was reported.

Difficulty maintaining oxygen saturation after endotracheal intubation. This is the only report where this is mentioned. The contributing factors were the midfacial hypoplasia, adenoidal hypertrophy and the relatively high position of the larynx found in all infants. These contributed to a small space and acute angle that the endotracheal tube had to turn through in order to get from mouth to larynx. Once the head was extended the mouth and the laryngeal inlet were more in line and the tube was less likely to get kinked or compressed.

The airway and the feeding of the infant in this report was helped by adenoidectomy, but the referral to the ENT department was for the child's hearing problem. It had been assumed that the airway and feeding difficulties of the child were exclusively due to the hypoplastic nose and that nothing could be done for them. It is our opinion that ENT surgeons should be involved in the management of children with foetal warfarin syndrome and should be aware of the types of airway difficulty which they may encounter.

References

Abbott, A., Sibert, J. R., Weaver, J. B. (1977) Chondrodysplasia punctata and maternal warfarin treatment. *British Medical Journal*, **1:** 1639–1640.

Baillie, M., Allen, D. E., Elkington, A. R. (1980) The congenital warfarin syndrome. *British Journal of Ophthalmology*, **64:** 633–635.

Collins, P., Olufs, R., Karvitz, H., Babakitis, M. (1977) Relationship of maternal warfarin therapy in pregnancy to chondrodysplasia punctata: a report of a case. *American Journal of Obstetrics and Gynecology*, **127:** 444–446.

Curtin, T., Mulhern, B. (1980) Foetal warfarin syndrome. *Irish Medical Journal*, **73:** 393–394.

Di Saia, P. J. (1966) Pregnancy and delivery of a patient with a Starr Edwards mitral valve prosthesis. *Obstetrics and Gynecology*, **28:** 469.

Hall, J. G., Pauli, M. P., Wilson, K. M. (1980) Maternal and fetal sequalae of anticoagulation during pregnancy. *The American Journal of Medicine*, **68:** 123–140.

Harrod, M. J. E., Sherrod, P. S. (1980) Warfarin embryopathy in siblings. *Obstetrics and Gynecology*, **57:** 673–676.

Kerber, J., Warr, O. S. III, Richardson, C. (1968) Pregnancy in a patient with a prosthetic mitral valve prosthesis; associated with a fetal abnormality attributed to warfarin sodium. *Journal of American Medical Association*, **203:** 223.

Lamontagne, J. M., Leclerc, J. E., Carier, C., Bureau, M. (1984) Warfarin embryopathy, a care report. *Journal of Otolaryngology*, **18:** 127–129.

Pauli, R. M., Madden, J. D., Kranzler, K. J., Culpepper, W., Port, R. (1976) Warfarin therapy initiated during pregnancy and phenotypic chondrodysplasia punctata. *Journal of Pediatrics*, **88:** 506–508.

Raivio, K. O., Ikonen, E., Saarikoski, S. (1976) Fetal risks due to warfarin therapy during pregnancy. *Acta Paediatrica Scandinavia*, **66:** 735–739.

Richman, M. E., Lahman, J. E. (1976) Fetal anomalies associated with warfarin therapy initiated shortly prior to conception. *Journal of Pediatrics*, **88:** 509–510.

Robinson, M. J., Pash, J., Grimwade, J., Campbell, J. (1978) Fetal warfarin syndrome. *Medical Journal of Australia*, **1 (3):** 157.

Shaul, W. L., Emery, H., Hall, J. G. (1975) Chondrodysplasia punctata and maternal warfarin use during pregnancy. *American Journal of Diseases in Childhood*, **129:** 360–362.

Stevenson, R. E., Burton, O. M., Ferlauto, G. J., Taylor, H. A. (1980) Hazards of anticoagulants during pregnancy. *Journal of the American Medical Association*, **243:** 1549–1551.

Whitfield, M. F. (1980) Chondrodysplasia punctata after warfarin in early pregnancy. Case report and summary of literature. *Archives of Disease in Childhood*, **55:** 139–142.

Zakzouk, M. S. (1986) The congenital warfarin syndrome. *Journal of Laryngology and Otology*, **100:** 215–219.

Address for correspondence:
J. D. T. Mason, F.R.C.S.,
Department of ENT,
Queens Medical Centre,
Nottingham.

Key words: Foetal development; Foetal Warfarin Syndrome; Nasal obstruction