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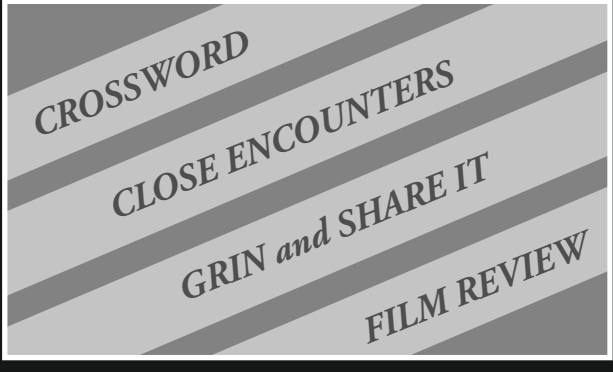

HIGHLIGHTS OF THIS ISSUE

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Wolters Kluwer Medknow

Siblings with Depressed Nasal Bridge due to Fetal Warfarin Syndrome

A 24-year-old mother who underwent a mitral valve replacement surgery for rheumatic heart disease, conceived and gave birth to two successive babies while she was on oral warfarin (5 mg/day). In both pregnancies, she remained unaware of having conceived till the end of the first trimester. The first issue was a girl born at 29 weeks gestation by cesarean section due to premature rupture of membranes. Her birth weight was 1370 g, and she was discharged at 34 post menstrual age. The second issue (born after 2 years) was a boy born at term by cesarean delivery and weighing 3050 g. Both babies had a depressed nasal bridge [Figure 1]. Other features of warfarin embryopathy (craniofacial deformities, microcephaly, optic atrophy, dorsal or ventral midline dysplasia, limb defects, digital hypoplasia, and skeletal stippling) were not found. Since other syndromes with depressed nasal bridge (Down syndrome, achondroplasia, cleidocranial dysostosis, congenital syphilis, Stickler and Williams syndrome) were excluded by the absence of associated anomalies, the final diagnosis was FetalWarfarin Syndrome (FWS).

Warfarin sodium inhibits the synthesis of Vitamin K-dependent clotting factors, and is therefore useful in patients at risk of developing thromboembolic events. Its low-molecular weight allows easy placental passage, manifesting as FWS (also known as de Sala Syndrome). *In utero*, warfarin blocks the recirculation of Vitamin K that may lead to hemorrhage within several organs. It also interferes with Vitamin K reductase activity, disrupting the synthesis of proteins such as osteocalcin and Gla matrix, which are essential for nasal bone and cartilage growth. Inhibition of arylsulfatase results in features mimicking chondrodysplasia punctata.[1] The classical clinical phenotype includes a variable combination of nasal hypoplasia, depressed nasal bridge, short limbs and digits, and stippled bone epiphysis.[1,2] There are reports of isolated neurological manifestations like hydrocephalus, or isolated cleft lip and palate. The incidence of FWS ranges from 0% to almost 30% of exposed pregnancies, with an average risk of 6%.

Children with FWS require multidisciplinary management according to the anomalies present. Women with prosthetic valves should be on lifelong anticoagulation, and warfarin is the preferred anticoagulant. Due to the high risk of FWS (15%–25% when dose >5 mg/day and 1.5%–2.5% when ≤5 mg/day), professional bodies have recommended the replacement of warfarin by heparin in the first trimester (between 6 and 12 weeks) during organogenesis.[1,2,3] However, since warfarin has a long half-life, substitution even at the 6th week may still be too late to prevent embryopathy. In addition, substitution may cause an increase in thromboembolic events in the mother, so a one-on-one discussion with the expecting couple needs to be undertaken explaining the maternal risks of switching vis-à-vis the fetal risks involved. Prenatal diagnosis of warfarin embryopathy is difficult, and even high detail ultrasonography may not detect the anomalies. Warfarin should be discontinued again after the 34–36th weeks of gestation.

Figure 1: Siblings with FWS: (a) first born preterm girl on 20th day of life; and (b) second born term boy on 1st day of life. FWS: Fetal warfarin syndrome

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understands that her name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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