Picture Story

A case of frontonasal dysplasia in a twin

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Sri Lanka Journal of Child Health, 2022; **51**(1): 157-159
DOI: http://dx.doi.org/10.4038/sljch.v51i1.10029
(Key words: Frontonasal dysplasia, Twin)

Introduction

Frontonasal dysplasia (FND), first described in 1967 by De Myer, is a rare congenital facial development disorder with about at least 100 cases reported in scientific literature up to date[1,2,3]. The condition is characterized by ocular hypertelorism, flat nasal bridge and a vertical groove in the mid face. There are 3 sub types namely FND -1, FND-2 and FND-3 which can be distinguished by genetics and clinical findings[2]. We report a neonate who was born with FND.

Case report

A baby girl was born as the second of a dichorionic diamniotic twin pregnancy at 33+6 weeks of gestation with a birth weight of 1.98 kg. This was the 7th pregnancy of non-consanguineous parents with 4 healthy living children. Mother was diagnosed with antiphospholipid syndrome in early pregnancy and was on enoxaparin and aspirin. Her pregnancy was also complicated with gestational diabetes mellitus, which was managed with insulin. Apart from the above medications, mother was not on any teratogenic drugs. The antenatal scans did not reveal any abnormalities. Babies were delivered via emergency caesarean section due to breech presentation and early labour. Both babies cried at birth. The second twin was found to have ocular hypertelorism, malformed nose with a vertical groove and a flat nasal bridge (Figure 1).

Figure 1: ***Baby with ocular hypertelorism, malformed nose with a Vertical groove and a flat nasal bridge***
**Permission given by parents to publish photograph*

Both nares were present and the tip of the nose was intact. There was no cleft lip or palate. Occipito-frontal circumference was 30 cm and the head was of normal shape. A grade 3 systolic murmur was audible over the left sternal edge. The spine, hips and limbs were normal on examination. There was no organomegaly.

Baby was admitted to the neonatal intensive care unit since she was dependent on nasal prong oxygen from birth and had poor feeding. She was treated for neonatal sepsis with intravenous (IV) antibiotics. Her C-reactive protein was 18.2 g/dL, chest x-ray had some inflammatory shadows over the right chest, and blood culture was negative. Baby was initially managed with IV fluids and later with gavage feeds and breast feeds. She was discharged on day 11 of life on full oral feeds.

Her ultrasound scans of the brain, abdomen and kidney were normal. 2D echocardiogram revealed a tiny restricted mid muscular ventriculo-septal defect and the electrocardiogram showed sinus rhythm. Skeletal survey was normal. Otolaryngology referral was done and choanal atresia was excluded. She was

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(Received on 11 July 2020: Accepted after revision on 21 August 2020)

The authors declare that there are no conflicts of interest
Personal funding was used for the project.

seen by the plastic surgical team and a review was planned at 3 months with a view to intervention. Genetic studies were not done due to scarcity of resources. The other twin did not have any facial dysmorphism.

Discussion

FND also known as median cleft face syndrome is a rare craniofacial development disorder with a sporadic occurrence with some familial cases. Though the aetiology is unknown, FND is thought to be due to deficient remodeling of nasal capsule which forms fronto-naso-ethmoidal complex prior to 28-mm crown-rump length stage in the embryo. Though the facial development is mainly affected, eyes, ears, brain and heart are also reported to be affected. The main features of FND are hypertelorism, broad nasal base, median facial cleft, underdeveloped or absent nasal tip, cleft lip & palate and widow's peak hairline[1,2,4]. The clinical findings may range from mild to severe defects such as notched broad nasal tip to completely divided nostrils, widow's peak hairline to cranium bifidum occultum and agenesis of corpus callosum, hypertelorism to laterally displaced eyes.

FND-1, FND-2 and FND-3 are caused by mutations in *ALX3*, *ALX4* and *ALX1* genes respectively, all of which are involved in nasal development[5,6]. FND-1 and 2 are autosomal recessive while FND-3 is autosomal dominant in inheritance[2,6]. Children with FND-1 have the main facial features of FND with some having associated cleft lip and/or palate, cranium bifidum occultum or brachycephaly. FND-2 is characterized by skull defects and coronal craniosynostosis. In some, there is partial or complete agenesis of the corpus callosum leading to varying degrees of intellectual impairment. It is also featured by broad variation in hair development and cryptorchidism in males. FND-3 is associated with more severe abnormalities such as anophthalmia. Some are reported to have congenital cyanotic heart lesions. Also a subtype of FND is described as acromelic frontonasal dysplasia which includes central nervous system and skeletal anomalies combined with craniofacial anomalies. Cranio-frontonasal syndrome is another syndrome associated with FND. The condition comprises of a number of severe craniofacial deformities inherited in an X-linked dominant fashion. These include bifid or underdeveloped nasal tip, severe hypertelorism, coronal craniosynostosis, longitudinally grooved or split nails, clavicle malformations and woolly hair. EFNB1 gene located on chromosome Xq13.1 (ephrin B1) mutation has been identified in affected cases[6].

Diagnosis of the condition is depended on thorough clinical evaluation. Genetic testing is still on research basis.

Since only a few cases of FND are reported, its management strategies are not well established and interventions are based on the severity of the physical deformities present. A series of surgical corrections including rhinoplasty might be needed depending on the deformities and cosmetic concerns. Multidisciplinary team approach is crucial. Genetic counselling of parents is important since the risk of recurrence in subsequent pregnancies is 25%[2,7].

Most children with FND have normal intelligence and a normal life span[1]. Babies with severe defects may have a shorter life span with interference of breathing and feeding. Repeated counselling involving parents and the child is warranted since FND affects self-image to a very distressing degree and may impact on self-esteem when the child grows.

Acknowledgement

We thank Dr. Romesh Gunasekera (Consultant Plastic, Reconstructive and Aesthetic Surgeon – Lady Ridgeway Hospital for Children) and his team for the collaborative management of the baby.

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