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CASE REPORT

Frontonasal Dysplasia in Yangon, Myanmar

Nang Kham Oo Leik[1*], Rhanye Mac Guad[2], Yuan Seng Wu[3], Shwe Yi Wai[4]

[1] Department of Reproductive Health, Faculty of Medicine and Health Science, Universiti Malaysia Sabah, Kota Kinabalu, Sabah, Malaysia
[2] Department of Biomedical Science and Therapeutics, Faculty of Medicine and Health Science, Universiti Malaysia Sabah, Kota Kinabalu, Sabah, Malaysia
[3] Department of Biochemistry, School of Medicine, Faculty of Medicine, Bioscience and Nursing, MAHSA University, Jenjarum, Selangor, Malaysia,
[4] Department of Surgery, North Okkalapa General and Teaching Hospital, Yangon, Myanmar

*Corresponding author's email: nangkhamooleik@ums.edu.my

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ABSTRACT

Frontonasal dysplasia (FND) is an uncommon congenital anomaly affecting the eyes, nose and forehead. In this case report, a baby of a 22-year-old mother was diagnosed with a midline facial cleft, bifid nose and hypertelorism during an ultrasound scan at 29th week of gestation. Besides a history of miscarriage on first pregnancy, no other abnormalities findings were found in laboratory or radiological examination of the newborn. Counselling about abnormality and psychological support were given by both obstetrician and neonatologist during the antenatal period. The patient delivered vaginally at 36th week with spontaneous labour and no complication was observed. Further interventions including corrective treatment have been planned as they often interfere with important functions such as breathing and feeding. Thus, the paediatric surgical team decided to do the operation when the baby reaches one year old as then tissues have been developed to 90% of their eventual form to give optimal treatment results. Further life expectancy depends on the severity of the malformation and whether or not surgical intervention can improve the associated health problems. This case report raises the importance of awareness on the nutritional value of pregnant mothers especially carotene and folic acid intake which may be associated with the organ maldevelopment. Overall, this report outlined the management of this rare condition experienced by the patient, particularly in a resource-limited setting like Yangon in Myanmar and also reviewed the literature about the presentation and classification of this condition.

INTRODUCTION

Frontonasal dysplasia (FND) is a very rare congenital anomaly affecting the eyes, nose and forehead[1]. Approximately 100 cases have been reported so far in the literature[1, 2]. This is an interesting case report as the average global prevalence rate is one in every 700 population, wherein in Myanmar one in every 800 to 1,000 babies every year according to the health report of Central Women's Hospital of Yangon in 2015[3]. The underlying causes of this condition are nutritional deficiency, including folic acid requirement[4]. Due to the facts that most of the affected individuals are often associated with the lack of health knowledge, unbooked pregnancies and poor quality of diet, including vitamin supplements during the antenatal period[5, 6]. This is an interesting clinical case in a resource-limited country like Myanmar to achieve optimal patient care and to avoid complications of FND if left untreated, such as feeding, speech and language delay or difficulties, dental and ear infections, hearing loss due to the risk of middle ear fluid formation as well as psychological problems in the affected individuals.

FND can have a variety of phenotypes[7]. However, the classical definition of FND is based on Sedano et al.[6] and Sedano and Gorlin[8]. The diagnostic criteria include at least two of the following features[8, 9], such as (1) anterior cranium bifidum occultum, (2) v-shaped or widow's peak of frontal hairline, (3) true ocular hypertelorism (IP distance >97th centile), (4) broadening of nasal root, (5) lack of nasal tip formation, (6) median facial cleft (nose and/or upper lip and palate) and (7) unilateral or bilateral clefting of the alae nasi. Besides, the severity of the malformations can determine the life expectancy of affected individuals. In some cases, both the front and back parts of the palate are open and have problems with breathing, feeding and speaking clearly in later life. They also might have hearing problems and ear infection.

FND is an autosomal recessive disorder[10]. In the majority of cases, it is caused by a gene mutation. Some common examples of gene mutation reported, including *ALX3* that causes FND type 1[11] and Homeobox Protein Aristaless-Like 4 (*ALX4*) gene can lead to FND type 2[12]. Additionally, a gene mutation on Homeobox Protein Aristaless-Like 1 (*ALX1*) causes FND type 3[11] has also been reported. Lastly, the mutation of both Eph-related receptor tyrosine kinases (*EFNB1*) and Zinc Finger SWIM-Type Containing 6 (*ZSWIM6*) genes can manifest to craniofrontonasal syndrome (CFNS) FND and acromelic frontonasal dysplasia (AFND), respectively. However, in some cases, such as oculo auriculo frontonasal syndrome (OAFNS) and AFND, the associated genes causing the syndromes remain unknown[10].

Each subtype of FND has its distinct phenotypic features (Table 1), and the phenotypes can generally be subdivided into six. CFNS phenotypes are more distinct in females, including severe hypertelorism, a bifid nasal tip, coronal craniosynostosis, malformations of the clavicle, longitudinally grooved nails and thick hair[10].

Table 1 Phenotypic classifications of the face in FND

Sedano-Jirásek classification	Characteristics	Causes of gene mutation
FND type 1	Hypertelorism, median nasal groove, and absent nasal tip	Homeobox Protein Aristaless-Like 3 (ALX3)
FND type 2	Hypertelorism, median groove or cleft face, with or without lip or palate cleft	Homeobox Protein Aristaless-Like 4 (ALX4)
FND type 3	Hypertelorism and notching of alae nasi	Homeobox Protein Aristaless-Like 1 (ALX1)
Acromelic frontonasal dysplasia (AFND)	Hypertelorism, median groove or cleft face, with or without lip or palate cleft and notching of alae nasi	Eph-related receptor tyrosine kinases (EFNB1) and Zinc Finger SWIM-Type Containing 6 (ZSWIM6)

For the FND1 phenotypes, it is characterised by short medial nasal region with a broad columella that attaches to the widely spaced nasal alae producing a distinctive concave shape to the nasal tip and a long philtrum with raised and fleshy lateral margins[10, 11] in addition to the CFNS prominent characteristics.

Besides, several characteristics attributed to frontorhiny type 2 (FND2) include hypertelorism, severely depressed nasal bridge, malar flattening, bifid nasal tip, cleft palate alae, craniosynostosis and hypoplastic clavaria, resulting in extensive brain abnormalities, including agenesis of the corpus callosum[11].

CASE PRESENTATION

The condition was noted on ultrasound scan showing a midline facial cleft, bifid nose and hypertelorism during a routine antenatal follow-up at 29th week of gestation (Figure 1). A history of miscarriage was reported in the mother's first pregnancy. The mother's fasting glucose level of 4.3 mmol/L and two hours postprandial of 6.2 mmol/L were within the normal range. Besides, other clinical and laboratory findings were not suspicious of any abnormalities. Genetic testing was not performed to confirm the karyotypes of the baby due to lack of facility in Yangon, Myanmar. As a standard guideline to prevent the complication of iron deficiency anaemia, ferrous fumarate tablets and Obimin AZ® were given orally to the mother. Moreover, extensive counselling, including psychological support, was given to the parents by both obstetrician and neonatologist throughout the antenatal period. Ultimately, the baby was delivered by spontaneous vaginal delivery at 36th week without any complications. The vital signs were stable and APGAR score was 5, 7 and 10 at 1, 5 and 10 minutes respectively. Ocular hypertelorism and a central cleft involving the nose, upper lip and palate were observed (Figure 2). The antenatal ultrasound diagnosis of midline facial cleft with hypertelorism, in this case, was confirmed following delivery of the baby. Moreover, cranial ultrasound and MRI also confirmed the defect and excluded other associated abnormalities.

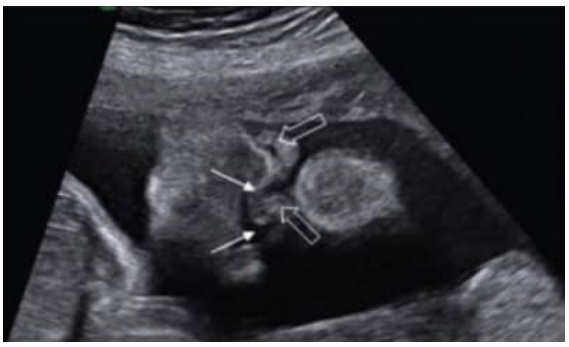

Figure 1 Ultrasound examination at 29th week of gestation showing a midline facial cleft, bifid nose and hypertelorism

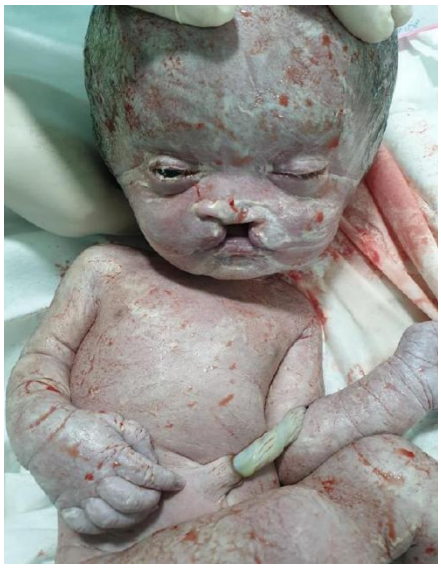

Figure 2 Frontal view showing ocular hypertelorism and a central cleft involving the nose, upper lip and palate.

DISCUSSION

According to Sedano's classification, this case is an example of type 3 FND[6]. The baby may require correction of hypertelorism in the future, whereby surgery is usually performed between 6 and 8 years of age because the cranial vault and the orbits are about 90% of their final size at that time. The paediatric surgical team has planned a primary surgery for the baby after the age of one year. The procedure is important because if the condition is left untreated, it could lead to many consequences, including speech delay. Furthermore, it helps to facilitate the child to adapt and integrate better in the family, society and school. Further correction surgery like rhinoplasty and cleft lip repair might also be needed. The baby is under currently under regular follow-up.

Frontorhiny type 3 (FND3) phenotypes are characterised by hypertelorism, a wide nasal base, isolated nasal alae, malformed orbits, microphthalmia, cleft primary and secondary palate as well as low-set and posteriorly rotated ears[10, 12]. While AFND phenotypes are characterised by hypertelorism, median cleft face, bifid nasal tips, widely spaced nasal alae, parietal defects and limb abnormalities (polydactyly, tibial hypoplasia and talipes equinovarus)[13, 14]. In some patients, it is manifested as marked mental retardation and brain malformations, including hydrocephalus, agenesis of the corpus callosum, interhemispheric lipoma and periventricular nodular heterotopia[15]. Lastly, OAFNS has several distinct phenotypic features, including microtia, preauricular tags, hemifacial microsomia and epibulbar dermoids[16].

Hypertelorism is the main and invariable component of FND. It is the main feature that differentiates FND from holoprosencephaly with median facial cleft[17]. FND can be an isolated feature or may be associated with other malformations, such as distal limb abnormalities including syndactyly, polydactyly, clinodactyly, tibial/fibular hypoplasia, acrocallosal syndrome or oral-facial-digital syndromes[9].

This case report is interesting as it happened in the economically deprived population in Yangon, Myanmar. Though, there is no obvious background condition that can lead to maldevelopment of the organs, the possibility of carotene and folic acid deficiency can be associated.

CONCLUSION

The described baby developed a congenital anomaly of FND type III. The baby is planned for correction of hypertelorism as well as a surgical intervention to avoid speech problems and psycho-social impact. This case report is important to emphasize the awareness of the nutritional value in pregnancy to the clinicians and population as a whole.

CONFLICT OF INTEREST

The authors declare that they have no competing interests in publishing this case.

CONSENTS

Written consent was obtained from the patient to publish the case with some related pictures. A copy of the written consent is available for review by the Chief Editor.

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