

ALX4-related frontonasal dysplasia sequence presenting with alopecia in a 12 year old girl

K L P D Seneviwickrama¹, S K P Lekamge², H M P Gunathilake²

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Abstract

Children with alopecia are frequently encountered in paediatric dermatological practice. Common causes include alopecia areata, and telogen effluvium. Herein we report a case of alopecia in a 12 year old girl as a part of ALX4-related frontonasal dysplasia (FND) sequence for its rarity.

Introduction

FND is a rare genetic disorder characterized by abnormal development of the head and face during embryonic development. Major physical characteristics include ocular hypertelorism, a flat broad nose, and a vertical groove involving the middle of the face. In some, the tip of the nose may separate vertically into two parts. In addition, anterior cranium occultum may present. There are three main types of FND that can be distinguished by clinical features and genetic testing.

Case report

A 12 year old girl was referred for the evaluation of hair loss since early childhood. She was the youngest child born to non-consanguineous parents following an uneventful ante-natal period. She was born by an elective caesarean section indicated by the past section. Her birth weight was normal. On routine neonatal examination, it was found to have scanty scalp hair and a wide anterior fontanelle. The rest of the examination was normal. She was evaluated and found to have an absence corpus callosum. During the development, her motor skills were delayed. Her mother noticed that the child was losing scalp hair periodically so she require haircuts very infrequently. After sometimes she gains regrowth of hair. She is attending a special school where she can do simple tasks equal to 7 year old child. Her family history was unremarkable.

Examination revealed a child with an average body built. She has hypertelorism with a broad nasal root and, a large skull defect in the middle of the forehead with pigmentation of skin over the defect (Figure 1).



Figure 1.

She has sparse short scalp hair (Figure 2). The hair-pulling test was negative. Hair microscopy was normal. Her eyebrows and eyelashes were normal. Her nail and teeth were normal. Her pubertal assessment was in tanner stage 1. Both cardiovascular and respiratory systems were normal. Neurological examination revealed clumsiness in movements.

Her ophthalmological examination, Echo cardiogram and hearing were normal. Considering her cranio-facial abnormalities possibility of FND was raised. In the absence of corpus callosum and scalp alopecia, ALX4-related frontonasal dysplasia sequence was

¹Consultant Dermatologist, ²Medical Officer in Dermatology, Sirimavo Bandaranaike Specialized Children's Hospital, Peradeniya, Sri Lanka.

diagnosed clinically. Due to financial constraints, genetic conformation wasn't carried out. She was referred to a paediatric endocrinologist for the follow-up of pubertal development.



Figure 2.

Discussion

FND also known as median cleft face syndrome was first described in 1967 by Sedano and Gorlin¹. It is characterized by midline defects involving the face, head and central nervous system. The FND is believed to be a result of abnormal development of the frontonasal prominence in craniofacial embryogenesis². In the embryonic development of the face, the persistent of the frontonasal process in its position prevents the orbits from reaching their normal position giving rise to hypertelorism and other mid-facial defects. It is very rare and approximately 100 cases have been reported in the scientific literature³.

Clinical features in FND are extremely varied and can present in any combination or severity. FND is clinically diagnosed based on at least two features including a median cleft in the skull (cranium bifidum occulta), broad nasal bridge, ocular hypertelorism, widened philtrum, median cleft upper lip and pallet, widow's peak in the frontal hair line, missing or

underdeveloped nasal tip. Other reported features include intellectual impairment, hearing defect, ocular changes, and agenesis of the corpus callosum, tetralogy of Fallots, alopecia. Inheritance is autosomal recessive or dominant. It may be associated with other severe abnormalities (syndromic) or has been reported independently. (Nonsyndromic).

Three main types of FND are caused by mutation in ALX genes. Type 1 is caused by a genetic mutation in ALX 3 gene. Type 2 and 3 are caused by changes in ALX 4 and ALX 1 respectively. Three main types of FND can be distinguished by clinical features and genetic testing. In addition to the common features in type 1 long philtrum, ptosis and nasal abnormalities are seen. Type 2 may present with alopecia, enlarged parietal foramina, male genetic abnormalities may present as cryptorchidism and agenesis of corpus callosum⁴. Type 3 is the most severe form where the patient gets anophthalmia or microphthalmia, low set ears.

The life expectancy of affected individuals depends on the severity of the malformations. No specific treatment is available⁵. Surgical intervention may be needed in cases with breathing and feeding problems as well as to improve the appearance. Multistage craniofacial surgery is needed to improve the patient's physical appearance⁶.

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