A Rare Presentation of FOXP1 Neurodevelopmental Disorder and Its Craniofacial Manifestations

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Introduction

Foxp1 is an important transcription factor involved in the development of many systems including the brain, heart, lung, esophagus, immune system, and spinal motor neurons.[1,2] Therefore, a single mutation can cause very detrimental consequences. Some of the clinical features of the Foxp1 deletion include prominent forehead, short nose with broad tip, down slanting palpebral fissures, ocular dysmorphic features, thick vermillion, high arched palate, macrocephaly, and malformed ears.[1,2,3,4] Physical features are not the only consequences of this deletion. Foxp1 deletions also result in global developmental delays, intellectual disabilities like autism, language and speech disorders, and other learning disorders.[3,4] Among all cases, several share similar deformities that prevent adequate feeding, speech, and development.[5,6] These physical malformations also translate into more infections of the skin and ear.[7] Many of these cases arise de novo without any inheritance pattern or background from parents or family. [8,9]

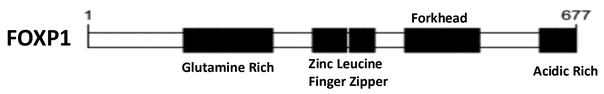

Figure 1. Foxp1 Chromosome
Elsevier. *FOXP1*. In: *ScienceDirect Topics in Neuroscience*. Published 2025. Accessed September 24, 2025. https://www.sciencedirect.com/topics/neuroscience/foxp1

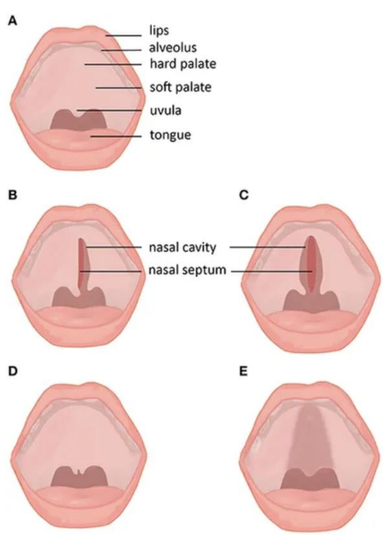

Figure 2. Subtypes and subclinical forms of cleft palate. (A) Normal lip and palate. **(B)** Unilateral cleft palate. **(C)** Bilateral cleft palate. **(D)** Cleft uvula. **(E)** Submucous cleft palate.
Bacon C, Rappold GA. The distinct and overlapping phenotypic spectra of FOXP1 and FOXP2 in cognitive disorders. Front Physiol. 2016;7:67. doi:10.3389/fphys.2016.00067

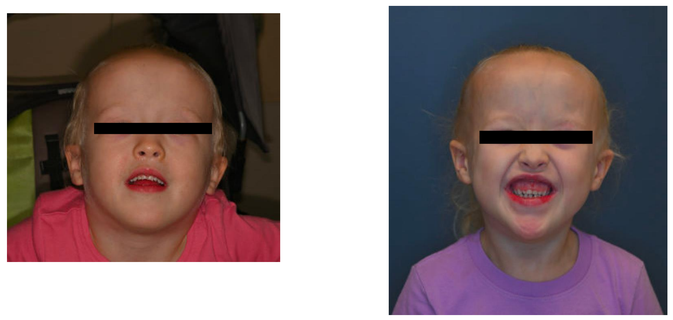

Figure 3. Craniofacial Features of Foxp1 in Patient.
11/2023 (left) and 12/2024 (right) showing patient with prominent forehead, wide nasal bridge with a broad tip, down slanting palpebral fissures, thick vermillion, and wide spacing between teeth consistent with Foxp1 Craniofacial features of Foxp1

Case Presentation

We present the case of a 5-year-old female (born 2019) with a de novo autosomal dominant **FOXP1 neurodevelopmental disorder (NDD)**, confirmed in the setting of unaffected parents. Her clinical course is notable for a constellation of congenital and developmental anomalies, including:

Craniofacial/ENT: central cleft palate with associated eustachian tube dysfunction, bilateral inferior turbinate hypertrophy, strabismus with right eye esotropia, frontal bossing, positional plagiocephaly, chronic mouth breathing, and speech delay.

Cardiac/Renal: atrial septal defect, heart murmur, and chronic kidney disease.

Neurologic/Developmental: global developmental delay and feeding difficulties.

This case highlights the **phenotypic variability** of FOXP1-related NDD, particularly the association of **cleft palate with other craniofacial anomalies** such as strabismus, esotropia, frontal bossing, and plagiocephaly. The breadth of multisystem involvement underscores the importance of **multidisciplinary care** across craniofacial, otolaryngologic, cardiac, and renal domains.

Acknowledgements

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Discussion

FOXP1-related neurodevelopmental disorder (NDD) is a rare condition characterized by intellectual disability, speech impairment, and multisystem congenital anomalies. Craniofacial findings such as prominent forehead, broad nasal tip, and high-arched palate have been reported. In our patient, the presence of a central cleft palate associated with eustachian tube dysfunction with the constellation of with strabismus, esotropia, frontal bossing, and plagiocephaly broadens the craniofacial phenotype associated with FOXP1.

This case further demonstrates the breadth of multisystem involvement, including cardiac (atrial septal defect, murmur), renal disease, ocular anomalies, and additional craniofacial dysmorphisms (inferior turbinate hypertrophy, chronic mouth breathing). These findings highlight the need for multidisciplinary management, with otolaryngology playing a central role in addressing airway, speech, hearing, and cleft-related concerns.

Only a limited number of FOXP1 cases with craniofacial anomalies have been described in the literature. Our report contributes to this growing body of evidence and strengthens the association between FOXP1 mutations and cleft-related pathology, underscoring the importance of genetic evaluation in children with syndromic cleft palate presentations.

Conclusion

This case expands the craniofacial phenotype of FOXP1-related NDD by demonstrating the occurrence of cleft palate associated with eustachian tube dysfunction in addition to several craniofacial findings in a patient with a confirmed de novo FOXP1 mutation. Recognition of these associations has direct implications for ENT specialists managing airway, feeding, and speech outcomes in affected children. Early genetic testing should be considered in syndromic cleft palate cases, as it can inform long-term multidisciplinary care and improve anticipatory guidance for families.

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