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CASE REPORT: NEONATAL FATALITY ASSOCIATED WITH A PATHOGENIC INTERSTITIAL DELETION OF 9Q22.2-Q33.3

Neonatology

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ABSTRACT

Background: Interstitial deletions of the long arm of chromosome 9 (9q) are rare genomic events associated with a broad phenotypic spectrum. While distal deletions are often linked to Kleefstra syndrome, larger interstitial deletions involving the 9q22-q33 region present with significant multisystem involvement, including Gorlin-Goltz features and respiratory malformations. **Case Description:** We report a female neonate born at 35 weeks gestation presenting with multiple congenital anomalies, including cleft palate, retrognathia, low-set ears, and severe laryngomalacia requiring tracheostomy. 2D echocardiography revealed infiltrative cardiac disease. Whole Genome Sequencing (WGS) identified a large heterozygous pathogenic deletion of the 9q22.2 to 9q33.3 region, involving critical genes such as PTCH1, FOXE1, ROR2, and TGFBR1. Despite intensive neonatal care, the patient succumbed to respiratory complications three weeks post-discharge.**Conclusion:** This case highlights the critical nature of the 9q22.2-q33.3 region in neonatal development. The severity of the airway malformation and cardiac infiltration in this patient suggests that large deletions in this locus are associated with high neonatal mortality and require early, aggressive multi-disciplinary intervention.

KEYWORDS

INTRODUCTION

Chromosomal aberrations involving 9q22.2-9q33.3 are among the most clinically significant microdeletion syndromes, with an estimated incidence of approximately 1 in 4,000 live births when associated with epilepsy and cleft lip/palate phenotypes. Interstitial deletions in this region have been historically reported in both oncological contexts and congenital malformation syndromes [1,2,3]. While terminal deletions (9q34.3) are well-characterized as Kleefstra syndrome [4], interstitial deletions of the 9q22.2-q33.3 region present with higher phenotypic variability. This variability includes conotruncal cardiac defects, palatal abnormalities, hypocalcemia, and a spectrum of cognitive and psychiatric deficits [5]. This variant is recognized as pathogenic in the ClinVar database (Variant ID: 2671591).

We present a neonatal case that expands the known clinical manifestations of this deletion, specifically regarding severe airway and cardiac involvement.

Case Description

Clinical Presentation

A female neonate, the first child of a non-consanguineous healthy couple, was born at 35 weeks gestation via emergency cesarean section due to a non-reassuring non-stress test (NST). Birth weight was 2000 g (10th percentile) with Apgar scores of 8 and 9 at 1 and 5 minutes, respectively. There was no history of maternal viral exposure or teratogenic medication use.

The patient was initially admitted at the birth hospital for respiratory distress, requiring intubation and surfactant therapy. After three days of mechanical ventilation, she was transitioned to nasal oxygen. Enteral feeding was attempted via orogastric tube but was discontinued following the observation of dark green aspirates.

Evaluation at MAX Super Speciality Hospital

The infant was referred to our NICU in Mohali on March 15, 2025. Physical examination revealed:

- Craniofacial: Cleft palate, retrognathia, and low-set ears.
- Respiratory: Persistent distress and stridor; bedside laryngoscopy confirmed severe laryngomalacia with a malformed airway.
- Cardiovascular: 2D Echocardiography revealed infiltrative cardiac disease.
- Laboratory: Findings were consistent with late-onset neonatal sepsis, anemia, and hypocalcemia. Newborn screening (NBS) and metabolic profiles (GCS-TMS) were within normal limits.

Cytogenetics and Molecular Analysis

Whole Genome Sequencing (WGS) was performed at a mean depth of 80-100X using the GATK best practice framework on the DRAGEN BIO IT platform (v4.2.4). Analysis revealed a heterozygous pathogenic deletion of 9q22.2 to 9q33.3.

Table 1: Critical Genes Involved in the Deleted Region

Gene	Clinical Relevance	Associated Phenotype
PTCH1	9q22.32	Gorlin-Goltz Syndrome; skeletal anomalies
FOXE1	9q22.33	Cleft palate; Thyroid dysgenesis
ROR2	9q22.31	Skeletal and limb development
TGFBR1	9q22.33	Loeys-Dietz syndrome-like vascular features
FRRS1L	9q31.3	Early-onset encephalopathy/seizures
ZNF462	9q31.2	Ptosis, intellectual disability

Management and Outcome

Due to the complexity of the airway and the inability to maintain a patent airway without support, a tracheostomy was performed. The patient was eventually stabilized and discharged on home oxygen support via tracheostomy tube. Unfortunately, the infant was lost to follow-up and personal communication later confirmed she succumbed to acute-on-chronic respiratory failure three weeks after discharge.

DISCUSSION

The diversity of features in 9q deletions is largely attributed to the specific breakpoints and the resulting haploinsufficiency of genes within the deleted segment. As noted by Schinzel, while the severity of major malformations often correlates with the size of the deletion, the specific pattern of dysmorphism is less predictable [7].

The respiratory complications observed in our patient mirror the findings of Schimmenti et al. [8], whose subject presented with tracheomalacia and respiratory failure. Our patient's laryngomalacia and "malformed airway" led to an early tracheostomy, a requirement that appears to be a hallmark of the more severe interstitial 9q deletions. Furthermore, the presence of infiltrative cardiac disease in our case suggests that the 9q22.2-q33.3 region may contain genes critical for cardiac structural integrity that are not as frequently involved in smaller or more distal deletions.

The premature death of our patient, consistent with other reported cases of large interstitial deletions, underscores the poor prognosis when significant airway malformations are present.

CONCLUSION

The 9q22.2-q33.3 deletion syndrome represents a spectrum of severe developmental challenges. This case highlights that neonatal presentations can be particularly aggressive, involving life-threatening airway and cardiac anomalies. We suggest that chromosomal analysis and WGS be considered early in neonates presenting with cleft palate and severe laryngomalacia, as this microdeletion may occur more frequently than current literature suggests.

REFERENCES

1. Midro AT, Panasiuk B, Tumer Z, et al. Interstitial deletion 9q22.32-q33.2 associated with additional familial translocation t(9;17)(q34.11; p11.2) in a patient with Gorlin-Goltz syndrome and features of Nail-Patella syndrome. Am J Med Genet A. 2004;124A(2):179–191. doi:10.1002/ajmg.a.20400
2. Gamerdinger U, Eggermann T, Schubert R, Schwanitz G, Kreiss-Nachtsheim M. Rare interstitial deletion 9q31.2 to q33.1 de novo: longitudinal study in a patient over a period of more than 20 years. Am J Med Genet A. 2008;146A(9):1180–1184. doi:10.1002/ajmg.a.32266
3. Kulharya AS, Flannery DB, Norris K, et al. Fine mapping of breakpoints in two unrelated patients with rare overlapping interstitial deletions of 9q with mild dysmorphic features. Am J Med Genet A. 2008;146A(17):2234–2241. doi:10.1002/ajmg.a.32431
4. Kleefstra T, de Leeuw N. Kleefstra Syndrome. 2010 Oct 5 [updated 2023 Jan 26]. In: Adam MP, Mirzaa GM, Pagon RA, et al., eds. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993–2026.
5. Szalai R, Till A, Szabo A, et al. Overlapping interstitial deletions of the region 9q22.33 to 9q33.3 of three patients allow pinpointing candidate genes for epilepsy and cleft lip and palate. Mol Syndromol. 2023;14(2):109-122. doi:10.1159/000525976
6. Stalker HJ, Aymé S, Delneste D, et al. Duplication of 9q12-q33: a case report and implications for the dup(9q) syndrome. Am J Med Genet. 1993;45(4):456-459. doi:10.1002/ajmg.1320450412
7. Elliott AM, Chudley A. Ritscher-Schinzel Syndrome. 2020 Jan 23. In: Adam MP, Mirzaa GM, Pagon RA, et al., eds. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993–2026.
8. Schimmenti LA, Berry SA, Tuchman M, Hirsch B. Infant with multiple congenital anomalies and deletion (9)(q34.3). Am J Med Genet. 1994;51(2):140-142. doi:10.1002/ajmg.1320510212