Rodriguez syndrome with an SF3B4 gene mutation: A case report

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Abstract

The case was a male neonate born by emergent cesarean section due to non-reassuring fetal status at 30 weeks of gestation. His manifestations were consistent with those of Rodriguez syndrome. Molecular analysis revealed an SF3B4 mutation.

Article type: Notes

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Keywords

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Key Clinical Message

When you see a neonate with upper limb phocomelia, lower limb anomalies, pulmonary hypoplasia, and central nervous system, cardiac, and urogenital anomalies, you should examine an SF3B4 mutation.

Acrofacial dysostosis encompasses a heterogeneous group of disorders characterized by craniofacial abnormalities resembling those observed in mandibulofacial dysostoses such as Treacher-Collins syndrome as well as additional limb and visceral anomalies. The well-known subtypes of acrofacial dysostosis include Miller syndrome (postaxial acrofacial dysostosis) and Nager syndrome (preaxial acrofacial dysostosis). The former is associated with postaxial limb deficiency (postaxial defects of all four limbs), whereas the latter is associated with preaxial limb deficiency (radial ray deficiency and only minor involvement of the great toes). Rodriguez syndrome is a lethal form of acrofacial dysostosis associated with upper limb phocomelia, lower limb anomalies, pulmonary hypoplasia, and central nervous system, cardiac, and urogenital anomalies.[1] However, it has been postulated that Nager and Rodriguez syndromes are allelic disorders caused by heterozygous mutations in the *SF3B4* gene mapped on 1q21.2.[2] Here, we report the case of a male neonate whose manifestations were consistent with those of Rodriguez syndrome. Molecular analysis revealed an *SF3B4* mutation.

The affected neonate was delivered by emergent cesarean section due to non-reassuring fetal status at 30 weeks and 3 days of gestation, immediately after emergent maternal transport, because of premature rupture of the membrane. Massive amniotic fluid leakage had occurred, suggesting polyhydramnios. The birth weight was 1160 g. The Apgar score was 5 at both 1 min and 5 min. At birth, the neonate was markedly hypotonic, with feeble respiration. He also showed Treacher-Collins syndrome-like facial features with severe micrognathia and phocomelia of the upper limbs and absent thumbs (Figure 1A-C). He did not respond well to resuscitation and passed away 1.5 hours after birth. Postmortem radiography showed hypoplasia of the scapular wings, severely hypoplastic, triangular-shaped humeri, elbow synostosis, radioulnar hypoplasia, and absence of the first digits. The axial skeleton and lower limbs were unremarkable. An autopsy performed after obtaining the parents' consent revealed severe post-ductal coarctation of the aorta and bicuspid aortic valves, intrapelvic right kidney, and absent lobulation of the left lung. The radial alveolar count was 3.0, suggesting mild hypoplasia of the lung. Molecular analysis, DNA extraction using PureLink® Genomic Kits, and Sanger sequencing of*SF3B4* revealed a heterozygous variant (c.1060dupC; p.Arg354Profs*132).

The variant was previously reported to be pathogenic for Nager syndrome.[3, 4] However, severe upper limb defects, association with multi-organ anomalies, and perinatal lethality in the present case warranted a diagnosis of Rodriquez syndrome rather than Nager syndrome. Our experience supports the notion that both types are phenotypic variations of the same disorder.

Ethics approval and consent to participate:

The study was conducted in accordance with the Declaration of Helsinki and national and institutional standards. The parents provided an informed written consent for the anonymous collection and use of the data for research purposes.

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Disclosure of interest: The authors have no potential conflicts of interest.

Author contribution: RN and RS carried out the literature search and drafted the first version of the manuscript. SH collected the sample and performed molecular analysis. MA and MY were responsible for designing. GN supervised the completion of this case report and substantively revised it. All authors read and approved the final manuscript.

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Figure 1: (A, B) Clinical photographs: note upper limb phocomelia with absent thumbs and facial abnormalities with micrognathia. **(C)** Postmortem radiographs: hypoplasia of the scapular wings, severely hypoplastic, triangular-shaped humeri, elbow synostosis, radioulnar hypoplasia, and absence of the first digits. The lower limbs are unremarkable.

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