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SCIENTIFIC LETTER

Recurrent Apnea in an Infant — Think Beyond the Usual

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To the Editor: A 2.5-mo-old girl, born of a nonconsanguineous marriage, term gestation, average weight with a ceft-lip anomaly, presented with recurrent apneic spells, occurring during both awake and sleep states. There was no association with feeding, choking, or seizure activity, and were aborted by tactile stimulation. On examination, she had microcephaly and generalized hypotonia. Her blood workup, electroytes, contrast esophagogram, and cardiac evaluation were normal. The magnetic resonance imaging (MRI) brain showed thickened, horizontally oriented and misaligned superior cerebellar peduncles with a deepened interpeduncular fossa and vermian hypoplasia, suggestive of the pathognomonic "molar tooth sign" of Joubert syndrome (JS). Respiratory stimulation by caffeine, continuous positive airway pressure (CPAP) and tactile stimulation during the episode was done. The apneas decreased from 2 to 3 episodes/d to once/wk and the child was discharged. Unfortunately, the child expired at age 7 mo. The mother's genetic analysis revealed 2 possibly pathogenic variations in Exon 15 of *RPGRIP1L* gene (MIM# 611560) and Exon 2 of *KIAA0586* gene (MIM# 616490) by next generation sequencing (NGS), which was further validated by Sanger sequencing. The father's genetic analysis revealed *KIAA0586* gene variant on targeted NGS. The pathogenic variant in the *KIAA0586* gene in mother was c.218-227delTGAATGGAAC: p.(Leu73Tyrfs*8) whereas the father had the c.3304-2A>G, a 3′ splice site pathogenic variant. The amniotic fluid analysis in the next pregnancy showed the presence of the former variation, but not the latter. The baby is now 2-y-old and healthy.

Joubert syndrome is an autosomal recessive brainstem maformation characterized by partial/complete absence of the cerebellar vermis. Fastigii nucleus ablation has shown not to alter eupnoeic breathing but markedly attenuate response to hypoxia and hypercapnea [1]. Fetal MRI from 20 to 22 wk of gestation has been earlier used as a method of antenatal diagnosis [2]. Thirty-seven genes have been listed as causative in the genetic testing registry. Multiple genes can simultaneously be tested by NGS [3, 4]. Most prevalent mutations in a European cohort was found in the genes: *C5orf42*, *TMEM67*, and *AHI1*, these 3 genes account for 30% of the identified mutations. *CEP90* gene accounted for upto 38% of variants in an Indian report [3]. The identification of the genetic defect in couples at risk allows for early prenatal genetic testing.

Compliance with Ethical Standards

Conflict of Interest None.

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