Clinical research: PURA syndrome - refining the clinical phenotype

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Abstract:

PURA syndrome is a recently described disorder presenting with neonatal hypotonia, feeding difficulties, and frequent apnea and epilepsy. Affected individuals commonly have global developmental delay, intellectual disability, and severe language impairment. We describe 31 new individuals with *de novo* mutations in *PURA*. Epilepsy and congenital apnea were present in 48% of the subjects, however there was no concordance between these two findings. Autism and/or pervasive developmental disorder was identified in 3 subjects. However, we did not find additional *PURA* mutations in a cohort of 120 subjects with autism. Skeletal complications were also found in 48% of the subjects. We did not find significant strong clinical associations between *PURA* mutation type and/or location, however moderate associations were found between presence of a mutation within the PUR-II domain and infantile spasms (Pearson's correlation = 0.41, p = 0.02), nonframeshift mutations at any location and Lennox-Gastaut syndrome (Pearson's correlation = 0.52, p = 0.002), and any mutation within the PUR-III domain and Lennox-Gastaut syndrome (Pearson's correlation = 0.42, p = 0.02). Mutations in the PUR-I domain showed a modest negative correlation with increased clinical severity (Pearson's correlation = -0.39, p = 0.03). Although there was a trend in the direction of PUR-I domain mutations being less severe, PUR-II domain mutations somewhat more severe, and PUR-III most severe, these differences were not statistically significant. Further studies are indicated in larger cohorts of subjects with *PURA* syndrome clarify these genotype-phenotype associations.