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CORRESPONDENCE

Amyotrophic Lateral Sclerosis due to *ALS2* Pathogenic Variant Masquerading as Cerebral Palsy

Vykuntaraju K. Gowda[1] · Sharath Babu[1] · Uddhava Kinhal[2] · Varunvenkat M. Srinivasan[3]

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To the Editor: Biallelic variants in *ALS2* gene [OMIM*606352] can cause a spectrum of phenotypes ranging from infantile ascending hereditary spastic paraplegia to primary lateral sclerosis and juvenile amyotrophic lateral sclerosis [1]. Here we report a child with *ALS2* variant masquerading as cerebral palsy (CP).

A three-year-old girl born to consanguineously married couple, delivered by cesarean section for fetal distress, cried immediately after birth, admitted at seventh day of life for encephalopathy, treated conservatively and discharged on day 10 of life. She presented to us at 2 y of age with not able to walk and progressive tightness of limbs predominantly in lower limbs, with delay in attaining milestones more so in motor domain. On examination, weight- 10.5 kg (-2 to -3 SD), head circumference- 48 cm (0 to -1 SD), marked spasticity in lower limb more than upper limb, with ankle clonus were noted. She was diagnosed as CP but MRI of the of brain was normal which further led to investigate other causes; with metabolic workup being normal, exome sequencing identified a known homozygous pathogenic nonsense variant c.4261C>T p.(Arg1421*) in exon 27 of *ALS2* gene, thus confirming the diagnosis of juvenile amyotrophic lateral sclerosis.

Cerebral palsy is usually a non-progressive disorder of neurodevelopment that predominately affects locomotion and posture [2]. As per a recent large cohort, the overall rate of birth asphyxia accounts to less than 10% as a cause of CP [3]. The yield of exome sequencing in identifying pathogenic variants is 53% among patients with CP born full term with normal neuroimaging [4]. The points which were red flags against CP in the current case were consanguinity, regression, and normal neuroimaging. Making the right diagnosis becomes essential, as CP would rarely recur, however, *ALS2* related disorder can recur. To conclude, genetic testing should be considered among children labeled as CP, even those with risk factors with normal MRI of the brain.

Declarations

Conflict of Interest None.

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✉ Vykuntaraju K. Gowda
drknvraju08@gmail.com

[1] Department of Pediatric Neurology, Indira Gandhi Institute of Child Health, Near NIMHANS, Bengaluru, Karnataka 560029, India

[2] Department of Pediatrics, Indira Gandhi Institute of Child Health, Bengaluru, Karnataka, India

[3] Department of Clinical Genetics, Indira Gandhi Institute of Child Health, Bengaluru, Karnataka, India

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