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SCIENTIFIC LETTER

# Childhood-Onset Neurodegeneration with Brain Atrophy in Association with c.628G>A in *UBTF* Gene

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*To the Editor:* A 10-y-old-boy, firstborn to non-consanguineous parents with a normal perinatal period, presented with developmental delay till three years of age, followed by neuroregression in motor, social, and cognitive domains since three years of age. He also had a history of myoclonic seizures and frequent falls while walking. There was no significant family history. On examination, he had microcephaly, spasticity, and brisk deep tendon reflexes (DTRs). He had a low intelligence quotient (IQ <70) suggestive of intellectual disability. Neuroimaging revealed significant cerebral, central cerebellar atrophy and diffuse white matter T2 hyperintensities. The differentials considered were neuronal ceroid lipofuscinoses, infantile neuroaxonal dystrophy, hypomyelinating leukodystrophy, and Lafora disease. Genetic testing revealed a pathogenic heterozygous missense variation c.628G>A(p.Glu210Lys) in exon 7 of *UBTF* gene (chr17:g.44212851C>T; Depth:169x) resulting in amino acid substitution of lysine for glutamic acid at codon 210, suggestive of Childhood-onset neurodegeneration with brain atrophy (CONDBA).

CONDBA (MIM#617672), a severe progressive neurodegenerative disorder, is due to heterozygous mutations in *UBTF* gene (MIM*600673) at chromosome 17q21.31 [1]. CONDBA is characterized by early onset loss of motor and cognitive skills at a median age of three (range 2-7) years [2]. To date, only 15 cases of c.628 G>A(p.Glu210Lys) variant-related CONDBA has been reported [2]. Over time, these patients develop frequent falls due to gait instability, seizures, ataxia, pyramidal signs including spasticity and hyperreflexia, extrapyramidal signs including rigidity, dystonia, chorea, and parkinsonism [2, 3]. The behavioral disorders reported are hyperactivity, impulsivity, and repetitive behaviors [4]. The common neuroimaging features include progressive supratentorial cerebral and cerebellar atrophy, symmetric and diffuse white matter T2 hyperintensities, thinning of corpus callosum, and bilateral thalamus involvement [2]. The index child has similar clinical progression and neuroimaging features as reported in the literature. Early recognition of this clinico-radiological phenotype may facilitate the diagnosis of CONBDA due to significant overlap with other neurodegenerative disorders.

## Declarations

**Conflict of Interest** None.

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