GATAD2B-associated neurodevelopmental disorder (GAND) GATAD2B syndro

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De novo pathogenic variants in the GATAD2B gene have been associated with a syndromic neurodevelopmental disorder (GAND) characterized by severe intellectual disability (ID), impaired speech, childhood hypotonia, and dysmorphic features. Since its first description in 2013, nine patients have been reported in case reports and a series of 50 patients was recently published, which is consistent with the relative frequency of GATAD2B pathogenic variants in public databases. We report the detailed phenotype of 19 patients from various ethnic backgrounds with confirmed pathogenic GATAD2B variants including intragenic deletions. All individuals presented developmental delay with a median age of 2.5 years for independent walking and of 3 years for first spoken words. GATAD2B variant carriers showed very little subsequent speech progress, two patients over 30 years of age remaining non-verbal. ID was mostly moderate to severe, with one profound and one mild case, which shows a wider spectrum of disease severity than previously reported. We confirm macrocephaly as a major feature in GAND (53%). Most common dysmorphic features included broad forehead, deeply set eyes, hypertelorism, wide nasal base, and pointed chin. Conversely, prenatal abnormalities, non-cerebral malformations, epilepsy, and autistic behavior were uncommon. Other features included feeding difficulties, behavioral abnormalities, and unspecific abnormalities on brain MRI. Improving our knowledge of the clinical phenotype is essential for correct interpretation of the molecular results and accurate patient management.