IQSEC2-related Disorder

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IQSEC2 mutations are associated with IQSEC2-related intellectual disability (ID). Phenotypic spectrum has been better defined in the last few years by the increasing number of reported cases although the genotype-phenotype relationship for IQSEC2 remains overall complex. As for IQSEC2-related ID a wide phenotypic diversity has been described in Rett syndrome (RTT). Several patients harboring IQSEC2 mutations present with clinical symptoms similar to RTT and some cases meet most of the criteria for classic RTT. With the aim of establishing a genotype-phenotype correlation, we collected data of 16 patients harboring IQSEC2 point mutations (15 of them previously unreported) and of five novel patients carrying CNVs encompassing IQSEC2. Most of our patients surprisingly shared a moderate-to-mild phenotype. The similarities in the clinical course between our mild cases and patients with milder forms of atypical RTT reinforce the hypothesis that also IQSEC2 mutated patients may lay under the wide clinical spectrum of RTT and thus IQSEC2 should be considered in the differential diagnosis. Our data confirm that position, type of variant and gender are crucial for IQSEC2-associated phenotype delineation.