RHOBTB2 Syndrome

https://pubmed.ncbi.nlm.nih.gov/37982109/

Background:

Rho-related BTB domain-containing protein 2 (

RHOBTB2

) is a protein that interacts with cullin-3, a crucial E3 ubiquitin ligase for mitotic cell division.

RHOBTB2

has been linked to early infantile epileptic encephalopathy, autosomal dominant type 64

(OMIM618004), in 34 reported patients.

Methods:

We present a case series of seven patients with

RHOBTB2

-related disorders (

RHOBTB2

-RD), including a description of a novel heterozygous variant. We also reviewed previously published cases of
RHOBTB2
-RD.

Results:

The seven patients had ages ranging from 2 years and 8 months to 26 years, and all had experienced seizures before the age of one (onset, 4-12 months, median, 4 months), including various types of seizures. All patients in this cohort also had a movement disorder (onset, 0.3-14 years, median, 1.5 years). Six of seven had a baseline movement disorder, and one of seven only had paroxysmal dystonia. Stereotypies were noted in four of six, choreodystonia in three of six, and ataxia in one case with multiple movement phenotypes at baseline. Paroxysmal movement disorders were observed in six of seven patients for whom carbamazepine or oxcarbazepine treatment was effective in controlling acute or paroxysmal movement disorders. Four patients had acute encephalopathic episodes at ages 4 (one patient) and 6 (three patients), which improved following treatment with methylprednisolone. Magnetic resonance imaging scans revealed transient fluid-attenuated inversion recovery abnormalities during these episodes, as well as myelination delay, thin corpus callosum, and brain atrophy. One patient had a novel
RHOBTB2

variant (c.359G>A/p.Gly120Glu).

Conclusion:

RHOBTB2

-RD is characterized by developmental delay or intellectual disability, early-onset seizures, baseline movement disorders, acute or paroxysmal motor phenomena, acquired microcephaly, and episodes of acute encephalopathy. Early onsets of focal dystonia, acute encephalopathic episodes, episodes of tongue protrusion, or peripheral vasomotor disturbances are important diagnostic clues. Treatment with carbamazepine or oxcarbazepine was found to be effective in controlling acute or paroxysmal movement disorders. Our study highlights the clinical features and treatment response of

RHOBTB2

-RD.