A case of TUBGCP2-associated tubulinopathy with a novel missense variant

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INTRODUCTION

Tubulinopathies are rare neurodevelopmental disorders associated with a wide range of malformations of cortical development.

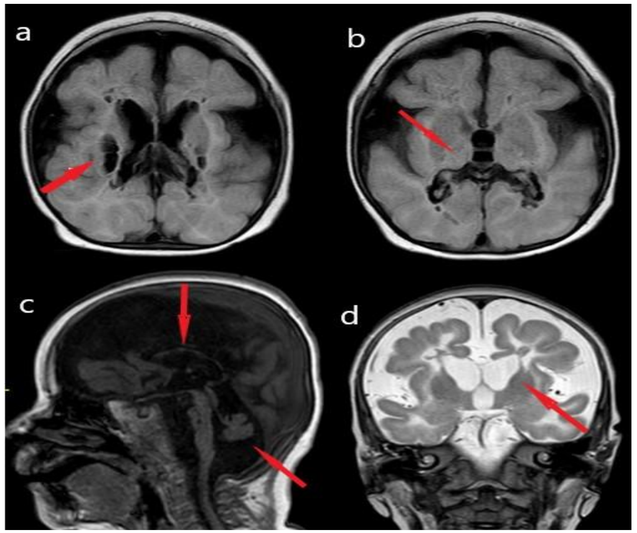
They caused by the abnormal function of microtubules. Some tubulin genes such as TUBA1A, TUBB2B, TUBB, TUBB3, and TUBG1 are highly expressed in the brain and have varying degrees of expression in all other tissues. Autosomal recessive variants in TUBGCP2, which encodes the G-tubulin complex 2 (GCP2) protein, have been reported to be associated with developmental delay, hypotonia, dysmorphic features, seizures, microcephaly, and malformations of cerebral cortical development, including pachygyria, agyria, and subcortical band heterotopia. We aimed to report a case of TUBGCP2-associated tubulinopathy with a novel homozygous missense variant.

CASE REPORT

A boy aged seven years and six months presented with global developmental delay, feeding difficulty, seizures, and microcephaly. He was born after uneventful pregnancy and delivery, with first degree cousin consanguineous marriage. His developmental milestones were reported as normal up to the age of five months. He developed seizures at this age and gradulally had deterioration in developmental milestones. On neurological examination, he had microcephaly (-5.3 SDS), truncal hypotonia, limb spasticity, hyperreflexia, bilateral Babinski's sign and clonus. Laboratory and metabolic tests revealed unremarkable. Electroencephalography showed slow background activity and a high incidence of generalized and focal spike-polyspike wave activity. Cranial MRI demonstrated dysgria, cystic encephalomalacia, periventricular band heterotopia, thin corpus callosum, atrophy of caudat nucleus and thalamus, atrophy of brainstem and cerebellum. Despite receiving appropriate doses of antiseizure medications including adrenocorticotropic hormone, phenobarbital, carbamazepine and levetiracetam, the seizures persisted. The next-generation sequencing identified a homozygous missense variant of c.815A>G (p.Asp272Gly) in the TUBGCP2 gene, and the variant was confirmed by Sanger sequencing.

CONCLUSIONS

This case expands the genotype-phenotype spectrum of TUBGCP2-related tubulinopathy. This variant in *TUBGCP2* may cause an autosomal recessive neurodevelopmental trait consisting of a neuronal migration disorder such as agyria, cystic encephalomalacia, and subcortical band heterotopia.



***Cranial MRI findings of the patient

a. Cystic encephalomalacia
b. Atrophy of thalamus
c. Thin corpus callosum, , atrophy of brainstem and cerebellum
d. Atrophy of caudat nucleus, dysgria

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