How common is TUBA1A - associated tubulinopathy ?

TUBA1A - associated tubulinopathy is very rare. Currently (2020) fewer than 200 children with a pathogenic *TUBA1A* gene variant have been reported in the medical literature. It is expected that more children will be diagnosed with this condition as awareness increases and genetic testing becomes more routine.

Why did this happen?

When a child is conceived, the genetic material is copied in the egg and sperm that makes that child. The biological copying method is not perfect, and occasionally random rare changes occur in the genetic code of children that are not seen in the DNA of their parents. This happens naturally and is not due to any lifestyle, dietary or environmental factors. No one is to blame when these changes occur, and nobody is at fault.

In nearly all children with *TUBA1A* - associated tubulinopathy diagnosed so far, the change in the *TUBA1A* gene occurred out of the blue (*de novo*) and was not found in their parents. A few parents have been found to carry the variant in a proportion of their cells (this is known as mosaicism) and have passed it on to their child (the parents have no or minimal symptoms).

Can it happen again?

The risk of having another child affected by a rare gene disorder depends on the genetic code of the parents. If the change in the *TUBA1A* gene has been shown to be *de novo*, that means neither parent was found to carry it, the chance of having another child with *TUBA1A* associated tubulinopathy is low (less than 1%). If a parent is found to be mosaic for the *TUBA1A* gene variant, this increases the chance of recurrence in a future pregnancy. A clinical geneticist can give you specific advice for your family.

Can it be cured?

TUBA1A associated tubulinopathy cannot be cured however, knowing the diagnosis means that appropriate monitoring and treatment can be put in place.

Families say ...

My son's needs are complex and he requires support with every aspect of life. Our starting point was being told he may never walk or talk but receiving such a rare diagnosis gave us the opportunity to believe anything was possible. After many hours of dedication, he can now walk and has speech and ways to communicate. We strive every day to help him reach his potential. His determination and wonderful personality push him forward.

Inform Network Support

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Websites and Facebook groups :

www.TubulinBiobank.org provides information and research project opportunities for families affected by different tubulinopathies

https://www.facebook.com/groups/1468134113494624/

Join *Unique* for family links, information and support

Unique is a charity without government funding, existing entirely on donations and grants. If you can, please make a donation via our website at www.rarechromo.org/donate Please help us to help you!

Version 1 (AP) 2020

Rare Chromosome Disorder Support Group Charity Number 1110661
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Understanding Chromosome & Gene Disorders

TUBA1A - associated tubulinopathy

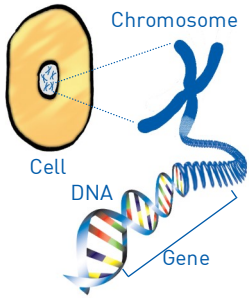
rarechromo.org

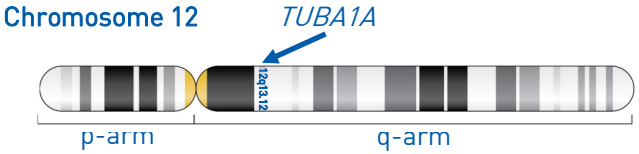
What is TUBA1A - associated tubulinopathy?

TUBA1A - associated tubulinopathy is a genetic condition caused by a change to a gene called *TUBA1A*. So far, most children with TUBA1A - associated tubulinopathy have been found to have developmental delay, altered brain formation and a small head. Epilepsy is also common. Many children have additional neurological symptoms that mainly affect muscle activity.

What causes TUBA1A - associated tubulinopathy?

TUBA1A - associated tubulinopathy is caused by specific changes (known as pathogenic variants) to a gene called *TUBA1A* (*TUBA1A* is an abbreviation of the gene's full name, tubulin alpha-1A, hence the name tubulinopathy). The *TUBA1A* gene is located on the long 'q' arm of chromosome 12 in a region called 12q13.12 (see below).





We have two copies of chromosome 12 in our cells, so we also have two copies of the *TUBA1A* gene.

TUBA1A - associated tubulinopathy occurs when only one copy of the *TUBA1A* gene is affected, this is known as autosomal dominant since the change occurred on an autosome (any of the chromosomes numbered 1-22) and features are apparent when only one copy of the gene is altered (this is known as dominant).

The *TUBA1A* gene sequence is used to make the TUBA1A protein. This protein can be found in most of our cells but is critical in the developing brain. The TUBA1A protein is used to form structures called microtubules that have many important roles, one of which is to ensure appropriate movement of nerve cells in the developing brain.

TUBA1A - associated tubulinopathy features

Most children with TUBA1A - associated tubulinopathy have:

- global developmental delay
- intellectual disability
- brain anomalies identified by MRI
- small head size (microcephaly)

Other possible features include:

- epilepsy
- tight muscles (spasticity)
- reduced muscle tone (hypotonia)
- eye problems

Medical concerns

Brain anomalies

MRI brain scans reveal a range of changes in the majority of children diagnosed with TUBA1A - associated tubulinopathy. The changes include underdeveloped or absent corpus callosum (the connection between the left and right hemispheres of the brain). Most children also have an abnormality of the ridges of the folding pattern on the surface of the brain (known as cortical malformation).

Epilepsy

Many children with TUBA1A - associated tubulinopathy reported in the medical literature are known to experience recurrent seizures. Types of seizures vary and include generalized tonic-clonic seizures, infantile spasms and focal seizures.

Other neurological features

Muscle tightness (spasticity) has been reported in a significant number of children with TUBA1A - associated tubulinopathy. A few children have also been found to have reduced muscle tone (hypotonia).

Eye problems

Some children are also diagnosed with eye problems, these include nystagmus (involuntary 'wobbly' eye movement), squint (when eyes do not properly align, also known as a strabismus) and underdevelopment of the optic nerve (optic nerve hypoplasia).

Development

Physical Development

Children with TUBA1A - associated tubulinopathy usually show significant delay in reaching motor milestones. Some children learn to walk later than expected, some can stand and walk with support and some do not learn to walk at all.

Intellectual Development and Learning

Children usually have severe learning difficulties or intellectual disability and may not be able to manage independently as adults. Many children need the support of a special education.

Speech and language

Difficulties in speech and language generally mirror intellectual disability. Most children have severe speech and language difficulties and do not use meaningful words, understanding is also usually limited.

Behaviour

Most children generally have a friendly and pleasant personality. A few children with TUBA1A - associated tubulinopathy also have neurobehavioural difficulties such as autism or autistic like features.

Feeding

Feeding can be problematic for children with TUBA1A - associated tubulinopathy. While some children manage to eat with the help of a parent or carer, others receive their nutrition (and medication) via a gastric PEG (percutaneous endoscopic gastrostomy) tube, which is when a tube is fitted directly into the stomach via the abdominal wall.

Management recommendations:

Children with TUBA1A - associated tubulinopathy should be under the care of a multidisciplinary team including paediatricians, neuropaediatricians and an epilepsy specialists if needed. Children should benefit from physio-, occupational, speech and language therapy as well as periodic evaluations by a developmental specialist. An ophthalmologic evaluation may be required.