How common is RHOBTB2 syndrome?

RHOBTB2 syndrome is very rare. It was first described in 2018, and currently (2020) only about 13 children with a *RHOBTB2* gene variant have been reported in the medical literature. It is expected that more children and adults will be diagnosed with this condition over the next few years.

Why did this happen?

When children are conceived, the genetic material is copied in the egg and sperm that make a new 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 all children with RHOBTB2 syndrome known so far, the change in the *RHOBTB2* gene occurred out of the blue (*de novo*) and was not found in their parents.

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 *RHOBTB2* gene has been shown to be *de novo*, that means neither parent was found to carry it, the chance of having another child with RHOBTB2 syndrome is low (less than 1%). A clinical geneticist can give you specific advice for your family.

Can it be cured?

RHOBTB2 syndrome cannot be cured at the present time. However, knowing the diagnosis means that appropriate monitoring and treatment, e.g. for epilepsy, can be put in place.

Families say ...

“ She is an incredible, happy little girl and her laugh is truly infectious. She brings a smile to anyone who meets her and her big personality is really starting to shine through. She is finding her own way to communicate with us and she can make it very well known when she doesn't want to do her therapies! ” ~ *Age 2 years.*

“ As this syndrome is so rare, many of the professionals and aid services don't understand how it affects him. We would take away his suffering if we could, but would never want to change who he is. Hopefully this will help others to understand him so that they can meet him where he is and see the world from his unique perspective. ” ~ *Age 3 years.*

“ Since finding other families of children with the same condition, we are slowly starting to understand him, his condition and the varying presentation of RHOBTB2 children. Despite his complex medical and intellectual problems he continues to surprise and amaze us. He's a very affectionate, snuggly child, he's always 'busy' and like many of the other children usually has something in his mouth to chew. He's super motivated and determined, so we look forward to seeing what he's going to achieve next. ” ~ *Age 3 years.*

Inform Network Support

Rare Chromosome Disorder Support Group,
The Stables, Station Road West,
Oxted, Surrey. RH8 9EE. UK.
Tel +44(0)1883 723356
info@rarechromo.org
www.rarechromo.org

Websites, Facebook groups and other links:

https://www.facebook.com/groups/RHOBTB2/
https://www.kinderneurologie.eu/ziektebeelden/syndromen/RHOBTB2.php

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!

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Understanding Chromosome & Gene Disorders

RHOBTB2 syndrome

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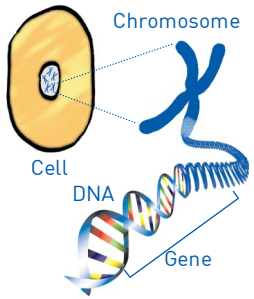
What is RHOBTB2 syndrome?

RHOBTB2 syndrome is a recently identified genetic condition. It is called a "developmental and epileptic encephalopathy" by medical professionals since it is associated with developmental delay/intellectual disability and epilepsy. Children with RHOBTB2 syndrome have seizures that can affect their developmental and cognitive function. Other features can include a small head circumference (known as microcephaly), growth delay, movement disorders, abnormalities in brain imaging, behavioural difficulties and additional medical concerns.

What causes RHOBTB2 syndrome?

RHOBTB2 syndrome is caused by specific changes (known as missense variants) to a gene called *RHOBTB2*. The *RHOBTB2* gene is located on the short 'p' arm of chromosome 8 in a region called 8p21.3. We have two copies of chromosome 8 in our cells, so two copies of the *RHOBTB2* gene.



Chromosome 8

RHOBTB2 syndrome occurs when only one copy of the gene is affected, this is known as autosomal dominant since the change occurred on an autosome (any of the chromosomes 1-22) and features are apparent when only one copy of the gene is altered (dominant).

The *RHOBTB2* gene is translated into the RHOBTB2 protein which is located in brain cells and has an important role in their functioning. The genetic changes that cause RHOBTB2 syndrome are located in a very specific and important region of the gene and disturb RHOBTB2 function in the brain. This results in the RHOBTB2 syndrome with epilepsy and intellectual disability.

RHOBTB2 syndrome features

Most people with RHOBTB2 syndrome have:

- developmental delay and intellectual disability
- epilepsy
- small head size (microcephaly)
- movement disorders
- brain abnormalities identified by MRI

Other possible features include:

- developmental regression (associated with seizures)
- hemiparesis (stroke-like symptoms associated with seizures)
- growth delay

Medical concerns

Epilepsy

So far, seizures have occurred in all children reported with RHOBTB2 syndrome. They commonly start within the first months of life. In the majority of children, seizures improve under antiepileptic treatment, but in some cases they can be difficult to control.

Brain abnormalities

MRI brain scans often reveal abnormal results. The changes seen are variable and include abnormalities of myelination (the sheath around brain cells) or the corpus callosum (the connection between the brains left and right hemispheres). Some children have experienced single or recurrent episodes of acute encephalopathy (damage to the brain) with long-lasting seizures, altered consciousness, swelling of the brain and subsequent loss of brain volume, fever and/or paresis (muscle weakness) of half of the body.

Movement disorders

Recurrent attacks of abnormal movements are common and include muscular spasms (dystonic), rapid, jerky, involuntary movements (choreatic) and impaired voluntary movements (dyskinetic).

Other neurological features

High muscle tone (hypertonia) and/or low muscle tone (hypotonia) is common.

Development

Physical development

Children with RHOBTB2 syndrome show significant delay in reaching motor milestones. Some children learn to walk later, 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. Most children need the support of special education and are not expected to be able to live independently as adults. Intellectual disability can be less severe in children with later onset of epilepsy. Some children have experienced regression (loss of acquired skills).

Speech and language

A few children acquire the ability to speak single words or two-word combinations. Most children, however, have a severe speech impairment 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 RHOBTB2 syndrome have behaviours such as autism or self-harm, some also grind their teeth.

Growth

Most babies are born with normal length, weight and head circumference. In the following months and years, head growth often slows down, resulting in a small head size (microcephaly). Some children also have a low body weight and short body length/height.

Management recommendations:

Children with RHOBTB2 syndrome should be under the care of a multidisciplinary team including paediatricians and neuropaediatricians and/or epilepsy specialists.