

Why did this happen?

When children are conceived the parents' 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 in plants and animals and is not due to your lifestyle or anything you did to cause a change in the KIF11 gene.

In approximately 40% of families the sequence change in KIF11 occurs out of the blue (de novo). In approximately 60% of families, one parent may have the same genetic change as their child.

Can it happen again?

The possibility of having another child affected by a rare gene disorder depends on the genetic code of the parents. For KIF11 associated disorder where parents do not carry the same change (mutation) the chances of having another affected child would be considered very small. Empirically, this risk would be considered less than 1%. The reason why there is some residual risk of recurrence is due to a rare phenomenon called 'gonadal mosaicism'. This is when a parent carries a genetic change, but it is limited to a small cluster of egg or sperm cells. The genetic change would not, therefore, be detected on this parent's blood test. If the genetic analysis of the parents of a child with KIF11 associated disorder shows that one of them carries the same variant, the chance of it happening again is much higher (50%).

For specific advice about the chance of this happening again, it would be sensible to speak to a clinical geneticist or genetic counsellor.

Families say ...

"My son has learning difficulties and is visually impaired. We make sure he is seen by specialists and has specific input from education including support from a Visual Impairment Teacher. Not all children will need to do this but my son is learning Braille and how to use a cane to help increase his independence skills for the future."

Families say ...

"Our daughter is a very special young lady, the "glue" in our family - everyone who meets her adores her! She is boss of her big brothers despite her small size. We are fortunate that other than her small head, her petite stature (though she is expected to grow to normal height) and a possible genetic condition at the back of her eyes, her development is as expected for her age." 2½ years

Inform Network Support

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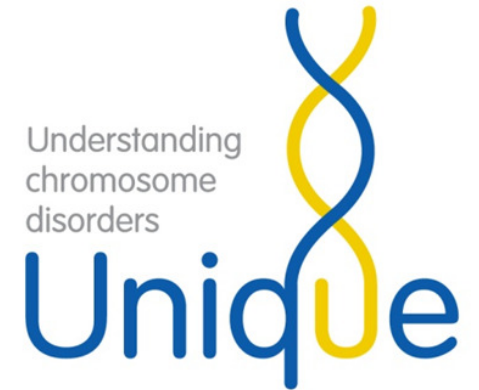


There is a Facebook group [www.facebook.com] called Microcephaly KIF11 Group

Unique lists external websites and webpages in order to be helpful to families looking for information and support. This does not imply that we endorse their content or have any responsibility for it.

This guide is not a substitute for personal medical advice. Families should consult a medically qualified clinician in all matters relating to genetic diagnosis, management and health. Information on genetic changes is a very fast-moving field and while the information in this guide is believed to be the best available at the time of publication, some facts may later change. Unique does its best to keep abreast of changing information and to review its published guides as needed. This guide was written by Dr Gabriela Jones, Speciality Trainee in Clinical Genetics, St George's University Hospital, London UK. 2015 Version 1 [PM] Copyright © Unique 2015

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KIF11 associated disorder (MCLMR)

rarechromo.org



What is KIF11 associated disorder?

KIF11 associated disorder is a recently defined condition that affects the brain, eyes and lymphatic system. The condition is also known as Microcephaly, Chorioretinopathy, Lymphoedema and Mental Retardation (MCLMR). A proportion of cases are caused by alterations in the KIF11 gene, although there are likely to be other as yet undiscovered genes. The condition occurs when one of a person's two copies of the KIF11 gene does not function normally. Genes are instructions which have important roles in our growth and development. They are made of DNA and are incorporated along with many other genes into organised structures called chromosomes. The KIF11 gene is located on chromosome 10 in band 10q23.3 at base pairs 94352824-94415151 [hg19 genome assembly]. The exact role of *KIF11* is still unknown, but it is likely to be important in the development of the brain, eyes and lymphatic system.

What causes the disorder?

KIF11 is a gene which is important for the development and maintenance of the brain, eyes, and lymphatic system. A disruption or the absence of this gene results in poor head growth (microcephaly), and abnormalities in the structure of the eyes (chorioretinopathy, myopia, hypermetropia, astigmatism, microphthalmia, retinal folds) and lymphatic system resulting in lymphoedema (fluid build up usually affecting the feet).

Most people with KIF11 associated disorder have:

- Small head size (microcephaly)
- Scars at the back of the eye (chorioretinopathy) or other eye changes
- Swelling of the legs (lymphoedema)
- Learning difficulties

Affected people will not necessarily have all of these features, but they have been found to be the most common. In addition, people who carry a change in the KIF11 gene with no clinical features of the condition have been reported.

Medical concerns

Chorioretinopathy and other eye changes

Approximately 80% of people with KIF11 associated disorder have eye changes consistent with the diagnosis. The most common feature is chorioretinopathy (scars of the back of the eye), however people may be short sighted (myopia) or long sighted (hypermetropia), or have astigmatism (a common condition that causes blurred vision). Small eyes (microphthalmia) and folds in the retina have also been described. Depending on the severity of the changes this may affect vision. Everyone with this condition needs to be assessed by an ophthalmologist.

Lymphoedema

Approximately 50% of babies with the condition are born with swelling of the feet due to fluid build up. This is often the presenting feature of the condition. The swelling typically improves with time, but if problematic a referral to a specialist clinic for further management with compression bandaging may be required. The swelling can sometimes reappear intermittently in adult life. Families have also noticed swelling of the hands and arms.

Seizures

A small proportion of people with the disorder may develop seizures.

Heart problems

Structural heart anomalies have been reported in several children although it is not yet clear whether this is a definite feature of the condition. Your child's doctor may request a heart scan (echocardiogram).

Hearing problems

Hearing loss has been reported in several children with the condition, but it is not yet clear whether this is a definite feature of the condition.

Can this be cured?

There is no cure as the effects of the genetic change took place during development in the womb. However, knowing the diagnosis means that appropriate monitoring and treatment can be put in place.



Development

■ Growth

Most babies are usually born at an average weight and length and continue to grow appropriately. A significant proportion of children have a small head at birth which remains below the expected size for age. This may be seen in up to 85% of children with the condition. However this feature can be very variable. A few babies and children have a head size at the lower end of the normal range, while in others it may be significantly reduced.

■ Physical development

Some children may have a delay in reaching their motor milestones compared with other children of the same age. However, the majority will be able to walk independently.

■ Learning

Some children may require support with their learning. A proportion may need to attend a special school where the right support can be given and non-academic and daily living skills focused on.

■ Behaviour

On the whole, children with KIF11 associated disorder do not have behavioural problems, however problems maintaining attention and with sleep have been reported in a few cases. Some families have also reported hyperactivity and behaviour problems.

■ Speech

Some children may have a delay in the development of their speech and may need the support of a speech and language therapist.

Management recommendations

Community paediatricians should oversee care so that development and behaviour can be monitored and the best help can be given early if required. A hearing test may be suggested if there are concerns. Children with lymphoedema may need to be referred to a specialist clinic for management (bandaging and compression garments) and monitoring. All children should be referred to an ophthalmologist for a detailed assessment. Regular eyesight checks may subsequently be recommended. Your child may have an echocardiogram and further follow up with a cardiologist if abnormalities are detected. Children with seizures should be assessed by a neurologist.