



Cardiofaciocutaneous (CFC) syndrome

What is Cardiofaciocutaneous (CFC) syndrome?

CFC syndrome is a rare genetic condition that typically affects the heart (cardio-), facial features (facio-) and skin (cutaneous). It is seen with equal frequency in males and females and across all ethnic groups. Children with CFC syndrome may have certain features that suggest the diagnosis, such as relatively large head size, down-slanting eyes, sparse eyebrows, curly hair, areas of thickened or scaly skin, and small stature. Most will also have a heart defect. While there is a wide spectrum of severity in CFC syndrome, most individuals will have some degree of learning difficulty and developmental delay. There are several characteristic facial features that are evident in CFC syndrome that may overlap with other conditions, particularly Noonan Syndrome (NS) and Costello Syndrome (CS). Therefore, accurate diagnosis is essential for proper medical management.

How common is CFC?

There are over 100 individuals reported in the literature. It is estimated that there are perhaps 200-300 individuals worldwide.

What are the features of the condition?

- **Facial features:** Large forehead, relative macrocephaly (large head), narrowing at the sides of the forehead, down-slanting eyes, ptosis (droopy eyelid), depressed nasal bridge, rotated ears.
- **Heart:** Pulmonic stenosis (narrowing of the artery going from the heart to the lungs), atrial septal defects (holes in the upper chambers of the heart), ventricular septal defects (holes in the lower chambers of the heart), hypertrophic cardiomyopathy (enlarged heart muscle)
- **Skin and hair:** Dry, thickened (hyperkeratotic), or scaly (ichthyotic), eczema (extreme dryness of skin and itchiness); sparse, curly, wooly or brittle hair; eyelashes and eyebrows may be absent or sparse.
- **Eye findings:** wide-spaced eyes (hypertelorism), strabismus (eyes turning in/out), nystagmus (jittery eyes), near-sightedness, small optic (eye) nerves. These may result in decreased vision and acuity.
- **Feeding/ Gastrointestinal (GI) problems:** Difficulty feeding, failure to thrive, reflux, vomiting, oral aversion; intestine malrotation, hernia, and constipation.
- **Growth:** May have normal birth weight and length, but they may drop to below the 5th percentile in infancy. Head remains on the growth curve (relative macrocephaly). Some may have growth hormone deficiency.
- **Neurologic findings:** Hypotonia (low muscle tone), seizures, abnormal EEG, hydrocephalus (fluid on the brain), other brain changes; cognitive impairment (ranging from mild to severe).

What causes CFC?

CFC syndrome is caused by a mutation (change) in one of our genes. Genes are the instructions which tell our body how to develop and function properly. If there is a change in one of our genes, it can affect how the gene is supposed to function and how the body develops. Recently, three different genes have been found to be associated with CFC syndrome (*BRAF*, *MEK1*, *MEK2*). Most individuals with CFC syndrome (87%) have a mutation in the *BRAF* gene and 13% have a mutation in *MEK1/2*. Molecular genetic (DNA) testing for mutations in all of these genes is clinically available.

How is it diagnosed?

In the past, the diagnosis of CFC was based on the clinical features, medical, and developmental history of the child. However with the recent discovery of genes that cause CFC, we are now able to offer genetic testing for any individual suspected of having the diagnosis. There are still some individuals with CFC syndrome who do not have a mutation in one of these genes, which suggests that there may be other genes associated with CFC syndrome that have not yet been identified.

What are the chances of having another child with CFC?

All cases of CFC syndrome have been sporadic, meaning that only one person in the family has CFC syndrome. As of yet, there have been no documented cases of CFC syndrome occurring in siblings or of a parent passing CFC on to a child. If neither parent has CFC syndrome nor a mutation in one of the genes, then the chance of having another child with CFC syndrome is very low (<1%). Prenatal diagnosis could be considered and offered to parents in subsequent pregnancies for reassurance. Individuals who have CFC syndrome, however, have a 50% chance of having a child with CFC syndrome. Currently, there is no way to predict the severity in offspring.

Is there a cure?

Currently, there is no cure to treat all of the symptoms of CFC syndrome. However, with proper management and early intervention, much can be done to improve the health of children with CFC syndrome. At present, treatment ultimately depends on the unique characteristics of each individual. These can include heart surgery to repair a structural defect, medications and lotions for the skin problems, or eye surgeries or corrective lenses to improve vision.

What other evaluations should my child have?

Management of the child with CFC syndrome should include the following evaluations:

- Neuropsychological assessment
- MRI of the brain to detect any structural changes of the brain
- Regular ophthalmology (eye) examinations
- Regular cardiac (heart) evaluations
- Electroencephalogram (EEG) if seizures are suspected
- Growth and psychomotor developmental monitoring
- Enrollment in early intervention therapies to promote growth, motor, and intellectual development – such as occupational therapy (OT), physical therapy (PT), or speech therapy.

Where can I get more information?

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