



Opitz Syndrome

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Introduction

Opitz syndrome is a genetic condition characterized by widely spaced eyes and, in males, hypospadias (an abnormal opening of the urethra on the underside of the penis).

Opitz is also known as oculo-genito-laryngeal syndrome and BBB/G compound syndrome.

About a quarter of all children with this syndrome have a cleft lip or palate. The syndrome can also include other facial abnormalities, such as a small jaw, ear abnormalities and a prominent forehead. Respiratory problems and congenital heart defects are also more common in children with Opitz syndrome.

The syndrome's impact on intelligence varies and depends on the severity of associated brain malformations.

Inheritance-

Opitz syndrome is caused by an inherited, genetic defect, demonstrated by heterogeneity. There are two forms of inheritance for Opitz syndrome. One is autosomal dominant, and other is X-linked form. This X-linked form of the syndrome primarily affects males. It is thought to affect between 1 in 50,000 and 1 in 100,000 males.

Genetics-

the X-linked form is caused by a mutation on the midline 1 (MID1) gene on the short (p) arm of the

X chromosome; the autosomal dominant form is due to a mutation on chromosome 22. Both forms of the disease result in physical deformities along the centreline of the body.

In X-linked type, the mutation in the MID1 gene leads to less functional midline-1 proteins. These proteins are responsible for binding to the cytoskeleton and assist the cell during cell division. It seems these issues with early cell division have a significant impact on the physical deformities that typically accompany the disease.

Autosomal dominant Type, endure a mutation on chromosome 22, most commonly at 22q11.2. Usually this form is classified as a part of a larger condition known as chromosome 22q11.2 deletion syndrome.

Medical Problems

A varieties of abnormalities can be seen in children with Opitz syndrome. However, it is unlikely that an individual child would have all of these abnormalities.

- Facial -prominent forehead, ocular hypertelorism, upward or downward slanting of palpebral fissure and epicanthal folds, broad flat nasal bridge, cleft lip with or without cleft palate, micrognathia, short

frenulum of tongue, thin upper lip, bifid uvula.

- Laryngo-Tracheo-oesophageal-laryngotracheal cleft, tracheoesophageal fistula, laryngeal malformation, high carina, hypoplastic epiglottis.
- Genitals— in males, hypospadias, cryptorchidism, bifid scrotum; in females, splayed labia majora.
- Musculoskeletal features- polydactyly of hands or feet, short, proximally placed thumb, other finger malformations, syndactyly of second and third toes
- Ocular – ptosis, strabismus.
- Respiratory features-recurrent pulmonary difficulty, recurrent aspiration, pulmonary hypoplasia etc.
- CNS -microcephaly, trigonocephaly, hypotonia, brain magnetic resonance imaging findings include agenesis or hypoplasia of corpus callosum, cortical atrophy, ventriculomegaly, pituitary macroadenoma, cranial osteoma.
- Performance-mild to moderate intellectual disability.
- Others-renal defect; cardiac defect, mostly conotruncal lesion; duodenal stricture; agenesis of gall bladder, hiatus hernia; imperforate anus; diastasis recti.

Diagnosis

There is Molecular genetic testing available to identify mutations leading to Opitz G/BBB Syndrome. X-linked type testing must be done on MID1 gene, since this is the only gene that is known to cause X-linked Opitz G/BBB Syndrome.

Two different tests can be performed: sequence analysis and deletion/duplication analysis.

In the sequence analysis a positive result would detect 15-50% of the DNA sequence mutated, while in deletion/duplication, positive result would find deletion or duplication of one or more exons of the entire MID1 gene.

Treatment

There is no specific treatment of Opitz syndrome but symptomatic treatment can relieve the conditions like-

- Speech and feeding therapy
- Tracheostomy or mandibular distraction to treat difficulty in breathing
- Regular heart monitoring if heart malformations are present
- Surgical correction of the following:
 - Laryngotracheoesophageal malformations
 - Cleft lip/palate
 - Heart defects
- Reflux medications to prevent risk of aspiration
- Educational support if intelligence is affected
- Neuropsychological support

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