DiGeorge Syndrome (22q11.2 Deletion Syndrome) — Symptoms and Treatment

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DiGeorge Syndrome results from microdeletion in a small segment of chromosome 22. When inherited from parents, it follows an autosomal dominant pattern. There are variable clinical features related to DiGeorge Syndrome. Most common ones are congenital heart diseases, thymic hypoplasia, learning difficulties, characteristic facial appearance, hypocalcemia, and psychotic disorders later in adolescence. Microarray genetic testing is used to diagnose the syndrome. Early intervention and developmental evaluation is the key to treatment which includes multidisciplinary approach.

Overview and Definition of DiGeorge Syndrome

DiGeorge Syndrome is a result of a microdeletion in a segment of chromosome 22. Other names for this syndrome include:

- Velocardiofacial syndrome
- Shprintzen syndrome
- Conotruncal anomaly face syndrome
- 22 deletion syndrome

Deletion is heterozygous and involves the long arm, q, of chromosome 22 hence the name 22q11.2 deletion syndrome. Up to 50 genes may be affected as a result of such deletions. About 93 % of cases are de novo mutations during early fetal development.
while 7% are inherited in autosomal dominant pattern from affected parents. The frequency of DiGeorge Syndrome is 1 in 4000 births.
Autosomal dominant

Affected father

Unaffected mother

Affected son
Unaffected daughter
Unaffected son
Affected daughter

Unaffected

Affected
Signs and Symptoms of DiGeorge Syndrome

There are variable symptoms related to DiGeorge Syndrome and a marked variability in clinical expression among different individuals. **Commonly associated signs and symptoms include:**

**Congenital heart disease**

It is found in around 40% of the individuals. Common anomalies are:

- Interrupted aortic arch
- Patent truncus arteriosus
- Tetralogy of Fallot
- Ventricular septal defect

Poor circulation of oxygenated blood results in:

- Palatal defects, particularly cleft palate, and velopharyngeal incompetence.
- Affected individuals have characteristic facial features like Hypertelorism, Tubular nose, Hooded eyes

Features may be subtle.

Learning difficulties are found in 90% of the cases. Attention deficit disorders and cognitive deficits are common.

- Deficiency of growth hormone.

**Hypoparathyroidism**

It is found in around 50% of the cases. Hypoparathyroidism leads to hypocalcemia.

- Skeletal abnormalities
- Problems related to feeding
- Thymic aplasia due to failure to develop third and fourth pharyngeal pouches
Conductive and sensorineural hearing loss

- Seizures which may be due to hypocalcemia
- Anomalies of respiratory and digestive tracts (Laryngotracheoesophageal problems)
- Renal anomalies are found in up to 37% of the patients
- Autoimmune diseases such as Graves disease and rheumatoid arthritis
- Poor immunity due to reduced T cell
- Psychiatric disorders such as depression, bipolar disorder, attention deficit hyperactivity disorder (ADHD) and schizophrenia

Diagnosis of DiGeorge Syndrome

Variations in the phenotypes of DiGeorge syndrome make the diagnosis difficult. Patients who have one or more deletion signs are more likely to have 22q11.2 deletion syndrome.

Genetic testing is used for prenatal diagnosis using BACs-on-Beads or fluorescence in situ hybridization. Karyotyping may not detect microdeletions. Array-comparative genomic hybridization is used to detect deletions or duplications through screening the entire genome. Latest diagnostic methods include Quantitative Polymerase Chain Reaction and Multiplex Ligation-Dependent Probe Amplification Assay.

Other lab work and procedures include:

- ECG
- Cardiac echocardiography (ECHO)
- Serum calcium and phosphorus
- Thyroid profile test
- Chest x-rays to look for thymus
- Complete blood picture (CBC)
- Immunoglobulin levels
Treatment of DiGeorge Syndrome

There is no cure for the 22q11.2 deletion syndrome. Management is aimed at treating the associated features of the disease. Treatment revolves around a multidisciplinary approach with the aim to improve the function of affected organ systems.

Immune problems due to the absence of thymus are necessary to be identified in the early stages. Blood transfusions and live attenuated vaccines are used with precaution in the affected individuals. In rare cases, thymus transplantation is also possible.

Use of antibiotics for treating frequent bacterial infections. Lifelong calcium and vitamin D supplements are required to address hypocalcemia resulting from hypoparathyroidism. Treatment of structural abnormalities such as surgery for congenital heart abnormalities is recommended. Early intervention and developmental evaluation is the key.

References


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