DiGeorge Syndrome, Severe Combined Immunodeficiency and more

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The DiGeorge Syndrome results from microdeletion in a small segment of the chromosome 22. When inherited from parents, it follows autosomal dominant patterns. There are variable clinical features related to the DiGeorge Syndrome. The most common ones are congenital heart diseases, thymic hypoplasia, learning difficulties, characteristic facial appearance, hypocalcaemia, and psychotic disorders later in adolescence.

Definition

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
- 22q11.2 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 patterns from affected parents. The frequency of DiGeorge Syndrome is 1 in 4000 births.
22q11.2 deletion syndrome is inherited in an autosomal dominant pattern.

Signs and Symptoms of DiGeorge Syndrome

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

- **Congenital heart disease**, 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 cyanosis**
- Palatal defects, particularly cleft palate, and velopharyngeal incompetence
- **Affected individuals have characteristic facial features** like hypertelorism, tubular nose,

[Image: “Facial appearance of Patient VC901 with atypical 22q11.2 deletion. Note the broad square face, hypotelorism, narrow nasal base and broad nasal bridge, overhanging nasal tip, deviated nasal tip (state post cleft lip repair), short philtrum, narrow mouth, chin dimple and broad neck.” by BMC Med Genet. License: CC BY 2.0](#)

and hooded eyes (these 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**, 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
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
- Renal ultrasound

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
- **Early intervention and developmental evaluation is the key**
References


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