Introduction

DiGeorge Syndrome (DGS) is known as 22q11.2 deletion syndrome. It is a genetic disorder that is being recognized with increasing frequency with a documented incidence of approximately 1 in 4000 (Rimoin *et al.* 2007). It is the most common human deletion syndrome that typically presents early in life and is rarely considered in adult patients (Robin ,and Shprintzen 2005, Hiéronimus *et al.* 2006, Al-Jenaidi *et al.* 2007).

The syndrome was described in 1968 by the geneticist Angelo DiGeorge (DiGeorge 1968). It may be first spotted when an affected newborn has heart defects and hypocalcemia due to parathyroid hypoplasia and low levels of parathyroid hormone.

There are number of syndromes that were once thought to be separate entities and are now considered to be variant manifestations of a single disorder resulting from the 22q11.2 deletion. These include DiGeorge Syndrome, Velocardiofacial Syndrome (VCFS), Conotruncal Anomaly Face Syndrome (CAFS) and some cases of isolated conotruncal cardiac anomalies (Driscoll, Budarf ,and Emanuel 1992, Matsuoka *et al.* 1994). A collective acronym "CATCH22" has been used to include all the following slightly differing features: Cardiac Abnormality (especially Fallot's Tetralogy that caused by a combination of four heart defects affect the structure of the heart present at birth and this cause oxygen-poor blood to follow out of the heart and into the rest of the body. Children usually have bloe-tinged skin because their blood doesn’t carry enough oxygen), Abnormal Facies, Thymic Aplasia, Cleft Palate and Hypocalcemia.

Microdeletion of chromosome 22q11.2 is among the most clinically variable syndromes, with more than 180 features being associated with the deletion. The phenotype develops over time; therefore the clinical presentation may change (Robin ,and Shprintzen 2005). It has a variable

phenotypic expression, with no pathognomonic or obligatory clinical features, and requires a high level of awareness for its early diagnosis (Taylor *et al.* 2003, Hiéronimus *et al.* 2006).

The classical features are congenital heart disease particularly conotruncal malformations, dysmorphic facies, velopharyngeal insufficiency, immunodeficiency, learning disabilities and parathyroid dysfunction (Robin ,and Shprintzen 2005). Children with 22q11.2 deletion often have problems that involve many different bodily systems.

It is increasingly evident that a wide range of developmental communication disorders are present in patients with 22q11.2 microdeletion. Although some infants have acute medical problems such as cardiac, feeding or immunologic abnormalities, many patients with this syndrome have initially sought treatment for cleft-palate, speech disorders or feeding problems (Wang *et al.* 1998).

The syndrome is caused by genetic deletions (loss of a small part of the genetic material) found on one of the two 22nd chromosomes. Very rarely, patients with somewhat similar clinical features may have deletions on the chromosome 10 (Markert *et al.* 2007).

To understand how the chromosome 22q11.2 deletion occurs, it is essential to know the basic organization of human chromosomes. Chromosomes are thread-like structure located within the nucleus of every cell in our body. Each chromosome is made of protein and a linear deoxyribonucleic acid (DNA). Humans have a total of 46 chromosomes (23 pairs) comprising of 22 pairs of autosomes and one pair of sex chromosomes (Driscoll, Budarf ,and Emanuel 1992). The sex chromosomes determine the person's gender; presence of X and Y chromosome (XY) represent a male, while the presence of X chromosomes (XX) represent a female (Kok ,and Solman 1995). Each chromosome has a constriction point called cetromere, which divides the chromosome into two sections, or arms. The short arm of the chromosome is labelled the "p arm"

and the long arm is labeled the "q arm". The location of the centromere gives the chromosome its characteristic shape and can be used to help describe the location of specific genes.

People with 22q11.2 deletion have a very small piece of chromosome 22 missing, and q11.2 indicate that the missing piece is in a very specific gene region on the long arm of the chromosome (Solot *et al.* 2000). The mechanism that causes all associated features of the syndrome is unknown.

Most patients with DGS are identified to have deletion of about 3 million base pair (the building blocks of DNA) on one copy of chromosome 22 in each cell. This region contains about 45 genes, including the T-Box1 (TBX1) gene, but some of these genes have not been well characterized. Researchers believe that a loss of TBX1 gene, due to either a mutation in the gene or a deletion of part of chromosome 22, is responsible for many of the features of 22q11.2 deletion syndrome. Specifically, a loss of the TBX1 gene is associated with heart defect, an opening in the roof of the mouth (a cleft palate), distinctive facial features and low calcium levels, but does not appear to cause learning disabilities (Yagi *et al.* 2003).

DGS may pose difficulty in diagnosis because the disorder can cause a wide variety of signs and symptoms, the severity and combination being dependant on chromosome defect. One of the most telltale signs of DGS is its distinct facial features (hooded eyelids, bulbous nasal tip and malar flatness). Carelle – Calmels et al. 2009 (Carelle-Calmels *et al.* 2009), have identified some of the tests that will help in the diagnosis. They are:

(i) **Blood test:** Low levels of calcium (hypocalcaemia) and high levels of phosphorus in the blood (hyperphosphataemia), as well as low levels of T cells are associated with DGS.

(ii) **Chest X-ray:** Heart defects, if any may be identified and can be followed up with other tests for confirmation.

(iii) **Genetic studies:** the 22q11.2 deletion can be:

(a) **Cytogenetic analysis (karyotyping):** checking the microdeletion of chromosome 22 in each metaphase.

(b) **Molecular Cytogenetic Analysis:** Fluorescence in situ Hybridization (FISH) using DNA probes from the 22q11.2 chromosomal region (Carelle-Calmels *et al.* 2009).

(c) **Array- Comparative Genomic Hybridization (array-CGH):**

Less than 5% of individuals with clinical symptoms of the syndrome have normal routine cytogenetic studies and negative FISH testing. They may have variant deletions of DGS that may be detectable on a research basis only or with other more advanced clinical testing method such as array-CGH to detect any gain or loss in the whole genome (Restivo *et al*. 2006). In array-CGH two genomes, test (red) and reference (Feld *et al.*) are differentially labelled and competitively hybridized to specific microarray.

There is no genetic cure for 22q11.2 deletion syndrome but a certain individual features are treatable using standard treatments. Evaluations at regular intervals are recommended to monitor progress and assess changing needs. Typically, therapeutic needs are best met on an intensive and individual basis (Solot *et al.* 2000).