Conotruncal Heart Malformations

**Alternative Names**
- CTHM
- Truncus Arteriosus Communis
- Conotruncal Anomaly Face Syndrome (CAFS)
- Double-Outlet Right Ventricle (DORV)

**WHO International Classification of Diseases**
Congenital malformations, deformations and chromosomal abnormalities

**OMIM Number**
217095

**Mode of Inheritance**
Autosomal recessive

**Gene Map Locus**
22q11.2, 2q21.1

**Description**
Conotruncal defects are defined as malformations of the outflow tract of the heart, presumably resulting from a disturbance of the outflow tract of the embryonic heart, or impaired development of the branchial arch and arteries, or both. This class of defects includes: truncus arteriosus, tetralogy of Fallot, interrupted aortic arch, double outlet right (or left) ventricle, and transposition of the arteries. Conotruncal defects of the heart are a frequent component of DiGeorge, velocardiofacial, or other syndromes caused by deletions of the human chromosome 22q11 region. In addition, some patients with isolated nonsyndromic conotruncal defects have been reported to have deletions of this region.

**Molecular Genetics**
Evidence shows that mutation in the CFC1 gene, located on chromosome 2q, plays a role in the etiology of double-outlet right ventricle. The CFC1 gene encodes a member of the epidermal growth factor (EGF)- Cripto, Frl-1, and Cryptic (CFC) family. EGF-CFC family member proteins share a variant EGF-like motif, a conserved cysteine-rich domain, and a C-terminal hydrophobic region. Members of this protein family play key roles in intercellular signaling pathways during vertebrate embryogenesis.

Mutations in the TBX1 gene, located on chromosome 22q, have been identified in heterozygous state in patients with phenotypes related to the 22q11.2 deletion syndrome, including conotruncal anomaly face syndrome. The TBX1 gene is a member of a phylogenetically conserved family of genes that share a common DNA-binding domain, the T-box. T-box genes encode transcription factors involved in the regulation of developmental processes.

**Epidemiology in the Arab World**

**Kuwait**
Abushaban et al. (2003) studied six cases of truncus arteriosus in four closely related families with a history of first-cousin marriages for generations. Analysis of karyotypes in these cases was normal. Family 1 has one affected male infant who was born in 1998. Family 2 has two affected children (one male and one female) who were born in 1989 and 1995, respectively. They have four other normal children. Family 3 has two affected children (one male and one female) who were born in 1981 and 1984, respectively. They have three other normal children. Family 4 has one affected male born in 1998 and another healthy child. All parents of all affected children are double cousins. The data in this study were suggestive for an autosomal-recessive inheritance, but multifactorial inheritance may also play a role.
Lebanon
Souki et al. (2003) reported a child with truncus arteriosus who developed bilateral proximal branch pulmonary stenosis, following total surgical repair of her condition with construction of the right ventricular outflow tract. The obstruction was relieved completely utilizing bilateral percutaneous stent implantation. Souki et al. (2003) indicated that their case was the first reported case of bilateral stent implantation to relieve branch pulmonary artery stenosis in Lebanon.

United Arab Emirates
Al Talabani et al. (1998) studied the pattern of major congenital malformations in 24,233 consecutive live and stillbirth at Corniche hospital, which is the only maternity hospital in Abu Dhabi, between January 1992 and January 1995. A total of 401 babies (16.6/1,000), including 289 Arabs, were seen with major malformation. Multifactorial disorders accounted for 26% of the cases. In their study, Al Talabani et al. (1998) observed one case of conotruncal heart malformations in a family from the United Arab Emirates. Recurrence was not reported in the family. Al Talabani et al. (1998) concluded that their study was very close to representing the true incidence of congenital abnormalities in the whole United Arab Emirates, as they investigated over 98% of deliveries in Abu Dhabi, the capital of United Arab Emirates.

References

Contributors
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