Autosomal Recessive Spondylocostal Dysostosis, 1

**Alternative Names**
- SCDO1
- Vertebral Anomalies
- Jarcho-Levin Syndrome
- Spondylothoracic Dysplasia
- Costovertebral Dysplasia
- Spondylothoracic Dysostosis

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

**OMIM Number**
277300

**Mode of Inheritance**
Autosomal recessive

**Gene Map Locus**
19q13

**Description**
Autosomal recessive spondylocostal dysostosis type 1 is a member of the heterogeneous group of disorders termed the spondylocostal dysostoses that are characterized by multiple vertebral segmentation defects and rib anomalies. Radiologically, the disease is characterized by vertebral malformations including hemivertebra, block vertebra, fused vertebra and spina bifida and deformities of the ribs that include absent ribs and bifid or fused ribs, which give the typical “crab like”, or “fan like” appearance. In affected individuals, the entire vertebral column is malformed and is replaced by multiple hemivertebra giving rise to truncal shortening, abdominal protrusion and non-progressive spinal curvature. Associated malformations include those of the urogenital system, cardiovascular system, central nervous system and neural tube defects.

**Molecular Genetics**
Genetic studies have shown that autosomal recessive spondylocostal dysostosis type 1 is due to mutations in the somitogenesis gene, Delta-like 3 (DLL3). The DLL3 gene product is one of the ligands of the Notch signaling pathway, an evolutionarily conserved mechanism of interaction between cells involved in the boundary formation and somite segmentation in vertebrates. Delta-like 3 gene product is a membrane bound protein that is structured in different domains with different functions: a signal sequence at the 5-prime end of the protein; a Delta-Serrate-Lag2 domain, responsible for interaction with the Notch receptor; seven EGF domains; and a transmembrane domain, responsible for the membrane binding of the protein. To date, approximately 20 different DLL3 gene mutations have been reported.

**Epidemiology in the Arab World**

**Egypt**
Shehata et al. (2000) described a patient with spondylothoracic dysplasia (Jarcho-Levin syndrome) with diaphragmatic eventration. Shehata et al. (2000) pointed out that the subgroup of spondylothoracic dysplasia with diaphragmatic defect is a more severe subgroup of the syndrome rather than the other forms of this syndrome.

**Palestine**
Kimonis and Fathalla (1988) described a male infant born to first cousin parents with Jarcho Levin syndrome. On examination, he had a shortened neck and trunk and a deformed chest. X-rays showed multiple congenital deformities of the entire spine. At follow-up at 7 weeks the child was feeding well in spite of moderately severe tachypnea.

Turnpenny et al. (1991) examined seven members of a large inbred Arab kindred with autosomal recessive spondylocostal dysostosis. The subjects were three adults, one adolescent,
and three children under 3 years of age. One child was the offspring of a first cousin marriage which showed quasi-dominant inheritance. Six subjects had short stature owing to widespread vertebral dyssegmentation with variable reduction in rib number and rib fusion. One subject was of normal stature, had limited vertebral dyssegmentation, an extra rib, and no rib fusion. Five subjects showed the plagiocephaly-torticollis sequence. Four of the five male subjects had inguinal herniation on one or both sides. All subjects had normal renal ultrasonography. The youngest subject died of cardiopulmonary complications and is thought to represent one extreme in the expressivity of the gene.

Eliyahu et al. (1997) prospectively and repeatedly examined nine women from one Arab family with Jarcho-Levin syndrome by ultrasound examination of the fetus to evaluate the possibility of early diagnosis. Out of eight pregnancies, four fetuses were diagnosed as being affected by the disease as early as 12 gestational weeks. Three elected to terminate the pregnancy before viability and one was born at term. There were no misdiagnoses.

Turnpenny et al. (1999) performed genome wide scanning by homozygosity mapping in a large consanguineous Arab family in which there were 6 definite cases of autosomal recessive spondylocostal dysostosis. Significant linkage was found to 19q13, with a lod score of 6.9. This was confirmed in a second Pakistani family with 3 affected members, with a lod score of 2.4. The combined haplotype data identified a critical region between D19S570 and D19S908, an interval of 8.5 cM on 19q13.1-q13.3.

Tunisia
Marrakchi et al. (1996) reported six cases of Jarcho-Levin syndrome in Tunisia. No further details could be obtained.

United Arab Emirates

References


Contributors