Autosomal Recessive Robinow Syndrome

**Alternative Names**
Costovertebral Segmentation Defect with Mesomelia
Covesdem Syndrome

**WHO International Classification of Diseases**
Diseases of the musculoskeletal system and connective tissue

**OMIM Number**
268310

**Mode of Inheritance**
Autosomal recessive

**Gene Map Locus**
9q22

**Description**
Robinow syndrome refers to a combination of short stature, mesomelic and acromelic brachymelia, thick abnormally modelled radius and ulna, characteristic face with hypertelorism, wide palperbral fissures, broad based nose and everted nares, large mouth, gum hypertrophy with irregular and crowded teeth, costovertebral anomalies, and micropenis in males. There is also endocrine dysfunction in autosomal recessive Robinow syndrome. Empty sella has been found in all children with the syndrome. There is also partial insensitivity of Leydig cells to HCG, low basal testosterone in prepubertal boys and a defective sex-steroid feedback mechanism. Phenotypic presentation is related to the inheritance pattern and patients with the recessive form have more severe dwarfism, more severe vertebral anomalies, more severe brachymelia, more digital defects, and the main discriminating feature is the occurrence of multiple rib and vertebral anomalies. Pulmonary or cardiac complications are common in affected individuals, and approximately 5-10% have a premature death in infancy and childhood. Intelligence is normal in most cases although some degree of mental retardation occurs in few (20%).

**Molecular Genetics**
Homozygous loss-of-function mutations in the gene encoding receptor orphan receptor tyrosine kinase 2 (ROR2), located on chromosome 9q22, are responsible for autosomal recessive Robinow syndrome. ROR2 contains nine exons and encodes a 4092 bp transcript. The protein product consists of 943 amino acids and is an orphan receptor tyrosine kinase that binds to an as yet unidentified ligand.

**Epidemiology in the Arab World**

**Egypt**
[See also: Oman > Soliman et al., 1998].

**Kuwait**
Teebi (1990) reported two brothers, born to first-cousin parents, with Robinow syndrome. Their paternal uncle also married a first cousin and had three similarly affected children (2 boys, 1 girl). The two affected brothers had short stature, mesomelic and acromelic brachymelia, characteristic face with hypertelorism, wide palperbral fissures, midface hypoplasia and large mouth, and hypogenitalism. Parental consanguinity and the presence of affected individuals in two sibships of common ancestry strongly suggested autosomal recessive inheritance. In 1991, Robinow also had reports of recessive cases from Kuwait (Source: OMIM).

Sabry et al. (1997) reported a child from a Kuwaiti consanguineous family with Robinow syndrome. The index case showed some unusual features including severe associated intrauterine growth retardation (IUGR), laxity of ligaments, hyperextensible joints, redundant skin folds, severe normocytic anemia, and
repeated infection associated with increased total T cells and an increased CD4:CD8 ratio.

Oman
Soliman et al. (1998) reported the characteristic features of 14 children with the recessive form of Robinow syndrome and the growth hormone (GH) response to provocation with clonidine and the serum insulin-like growth factor-I (IGF-I) concentration in 12 of these children. Children with Robinow syndrome, born at full-term, were short at birth (length, 41.4+/−2.1 cm) and had markedly slow growth velocity (GV) during the first year (13.1+/−2.1 cm/yr); consequently, they were significantly short at the end of the first year of life (length, 54.4+/−2.9 cm). This intrauterine and early extraterine growth delay reflected low growth potential. During childhood and early adolescence, boys with Robinow syndrome had low basal testosterone and a low testosterone response to HCG stimulation (3,000 IU/m2/d intramuscularly [IM] for 3 days). However, their basal and GnRH-stimulated FSH concentrations were normal. Two girls (Tanner II breast development) had a normal serum estradiol (E2) concentration but high LH and FSH responses to GnRH stimulation. This suggested either defective feedback of E2 on the hypothalamic-pituitary axis or hyporesponsiveness of the ovaries to gonadotropin. Four weeks of HCG therapy (2,500 IU/m2 IM twice weekly) in three boys with Robinow syndrome increased the penile length and testicular volume, denoting a significant Leydig cell response to prolonged HCG stimulation and the presence of functioning androgen receptors.

Saudi Arabia
Nazer et al. (1990) reported two children, born to first-cousin Saudi parents, with the ‘fetal face syndrome.’ Both of the children also had the Crigler-Najjar syndrome, as did two previously born sibs who did not have the fetal face syndrome. Both died at age 4 months. The parents lost two previous children at age 2 months with progressive jaundice but without fetal facial characteristics. Robinow (1991) also had reports of recessive cases from Saudi Arabia (Source: OMIM).

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. Single gene disorders accounted for 24% of the cases, 76% were due to autosomal recessive disorders. In their study, Al Talabani et al. (1998) observed one case of autosomal recessive Robinow syndrome born to a first cousin couple from the United Arab Emirates. Recurrence was also reported in the family. Al Talabani et al. (1998) concluded that their study is 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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