



## Chondrodysplasia, Grebe Type

### Alternative Names

Achondrogenesis, Brazilian  
Grebe Chondrodysplasia  
Grebe Dysplasia  
Acromesomelic Dysplasia, Grebe Type  
AMDG  
Achondrogenesis, Type II, Formerly

### WHO International Classification of Diseases

Congenital malformations, deformations and chromosomal abnormalities

### OMIM Number

200700

### Mode of Inheritance

Autosomal recessive

### Gene Map Locus

20q11.2

### Description

Grebe type chondrodysplasia is a rare recessively inherited acromesomelic dysplasia, clinically characterized by dwarfism with severe marked micromelia with increasing severity in a proximo-distal gradient, and deformation of upper and lower limbs. Radiologically, it is characterized by short and deformed middle long bones, fusion of carpal bones and several metacarpal and metatarsal, and absence of proximal and middle phalanges. Other features include obesity and delayed mental development, but facial appearance and intelligence are normal with no vertebral abnormalities.

### Molecular Genetics

Grebe syndrome is caused by a missense mutation in the gene encoding cartilage-derived morphogenetic protein-1. The protein encoded by the CDMP1 gene is a member of the bone morphogenetic protein (BMP) family and the TGF-beta superfamily.

### Epidemiology in the Arab World

#### Jordan

Hattab et al. (1996) described a 9-year-old Arab boy presenting oral and dental abnormalities associated with a distinct variety of severe short-limb dwarfism. The affected boy had delayed development and eruption of teeth, severe oligodontia of permanent dentition, hypodontia, microdontia, supplemental incisor, enamel hypoplasia of primary teeth, doubled and abnormal frenal attachments, bifid uvula, hypoplastic maxilla, and malocclusion. Clinical and radiographic examinations revealed asymmetric dysplasia and anaplasia of long bones, craniofacial dysmorphism, prominent forehead, budlike fingers and bulbous toes, dysplastic nails, severe hearing loss, and reduced joint mobility.

#### Oman

In 2003, Al-Yahyaee et al. studied the clinical, radiographic, and genetic characteristics of an Omani family with four affected children. The affected individuals had normal axial skeletons, severely shortened, and deformed limbs with severity increasing in a proximo-distal gradient, and subluxated joints. The humeri and femora were hypoplastic with distal malformations. The radii/ulna were shortened and deformed whereas carpal bones were invariably rudimentary or absent. The tibia appeared rudimentary; fibula were absent in two children, and some tarsal and metatarsal bones were absent. The proximal and middle phalanges were absent while the distal phalanges were present. The father and mother had short first metacarpal and middle phalynx of the fifth finger and hallux valgus, respectively.

#### 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 Grebe type chondrodysplasia in a consanguineous family from the United Arab Emirates. Recurrence was also 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 studied over 98% of deliveries in Abu Dhabi, the capital of United Arab Emirates.

### **References**

- Al Talabani J, Shubbar AI, Mustafa KE. Major congenital malformations in United Arab Emirates (UAE): need for genetic counselling. *Ann Hum Genet.* 1998; 62 (Pt 5):411-8.
- Al-Yahyaee SA, Al-Kindi MN, Habbal O, Kumar DS. Clinical and molecular analysis of Grebe acromesomelic dysplasia in an Omani family. *Am J Med Genet A.* 2003; 121(1):9-14.
- Hattab FN, al-Khateeb T, Mansour M. Oral manifestations of severe short-limb dwarfism resembling Grebe chondrodysplasia: report of a case. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 1996; 81(5):550-5.

### **Contributors**

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