



Autosomal Recessive Osteopetrosis

Alternative Names

OPTB1

Marble Bones, Autosomal Recessive

Albers-Schonberg Disease, Autosomal Recessive

Osteopetrosis, Malignant

WHO International Classification of Diseases

Congenital malformations, deformations and chromosomal abnormalities

OMIM Number

259700

Mode of Inheritance

Autosomal recessive

Gene Map Locus

16p13, 11q13.4-q13.5, 6q21

Description

Autosomal recessive osteopetrosis (OP) is a rare, lethal disorder in which osteoclasts are absent or nonfunctional, resulting in a bone marrow cavity insufficient to support hematopoiesis. It is one among disorders causing osteosclerosis of the trabecular bone and/or hyperostosis of the cortical bone. Four types of human osteopetrosis have been clearly defined, but patients with atypical symptoms are frequent, suggesting that there are additional forms. The most severe expression of this condition in its malignant form is inherited as an autosomal recessive disorder and it is usually fatal before school age. It presents with failure to thrive, severe hepatosplenomegaly, pancytopenia and nerve compression leading to blindness and deafness during infancy. Because osteoclasts are derived from hematopoietic precursors, allogeneic hematopoietic cell transplantation can cure the bony manifestations of the disorder.

Molecular Genetics

The TCIRG1 gene, encoding the alpha-3 subunit of the vacuolar proton pump, which mediates the acidification of the bone/osteoclast interface, is responsible for more than one-half of the osteopetrosis patients. Autosomal recessive infantile malignant osteopetrosis can also result from mutations in the CLCN7 gene. Mutation has also been detected in the human homolog of the mouse 'grey-lethal' gene (GL), also known as osteopetrosis-associated transmembrane protein-1 (OSTM1).

Epidemiology in the Arab World

Kuwait

Abdel-Al et al. (1994) diagnosed 19 Arab children (six boys and 13 girls) in ten sibships as having osteopetrosis over a 5-year period in various hospitals in Kuwait. Eighteen patients had an isolated autosomal recessive form. The mean age of diagnosis was 24 months. Parental consanguinity was high amongst them (68%). Anemia, hepatosplenomegaly, failure to thrive, recurrent infections and neurological manifestations were common. Associated congenital abnormalities were found in 26%. Deafness, hydrocephalus and dental caries were relatively less common. Abdel-Al et al. (1994) noted a high mortality rate (37%) owing to infection.

Palestine

In two Palestinian Muslim consanguineous families that lived in the same village, Dudin and Rambaud-Cousson (1993) found seven cases of lethal infantile osteopetrosis. In two of the seven persons, short-segment Hirschsprung disease (142623), a probably independent disorder, was also present. Both patients died early.

In a survey of 2000 different Palestinian Arab families Zlotogora (1997) diagnosed or strongly



suspected 601 individuals with autosomal recessive diseases. Among the common disorders, Zlotogora (1997) found a high prevalence of recessive osteopetrosis.

Subsequent to the chromosomal localization of the MOP gene in Arab-Bedouin families from the Negev region, Shalev et al. (2001) used linkage analysis for the prenatal diagnosis of osteopetrosis in Bedouin families at risk. Twelve cases were diagnosed, three fetuses were found to be affected, and one of the pregnancies was terminated. The other two pregnancies continued to term and the diagnosis of osteopetrosis was confirmed by X-ray immediately after birth.

Saudi Arabia

Al-Rasheed et al. (1998) observed, over a 10-year period, 28 Arab children with autosomal recessive osteopetrosis in two hospitals in Riyadh. Eighteen (64%) had osteopetrosis associated with metabolic acidosis probably due to a renal tubular defect; nine (32%) had a malignant infantile form of osteopetrosis and one had a mild form with delayed onset. Parental consanguinity was 56% and 40% among patients with and without acidosis respectively. Somatic and psychomotor retardation and recurrent bone fractures were common in both groups. Dental caries, cerebral calcification and optic atrophy were more frequent in patients with acidosis, while anemia, hepatosplenomegaly and deafness were more common in patients without acidosis.

United Arab Emirates

In a 5-year prospective study for newborns at Al Ain Medical District, Al-Gazali et al. (2003) defined the pattern and birth prevalence of the different types of osteochondrodysplasias in the United Arab Emirates. Among the 38,048 births during the study period, 36 (9.46/10,000

births) had some type of skeletal dysplasia of which one case, born to a consanguineous parents, had autosomal recessive osteopetrosis. Al-Gazali et al. (2003) calculated the birth rate of this type of osteochondrodysplasia in the United Arab Emirates to be 0.26/10,000 births.

References

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Contributors

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