



Rhizomelic Chondrodysplasia Punctata, Type 2

Alternative Names

RCDP2
Dihydroxyacetonephosphate Acyltransferase
Deficiency
DHAPAT Deficiency
Glyceronephosphate O-Acyltransferase
Deficiency
GNPAT Deficiency
Peroxisomal Dihydroxyacetonephosphate
Acyltransferase Deficiency
Chondrodysplasia Punctata, Rhizomelic, due to
Dihydroxyacetonephosphate Acyltransferase
Deficiency

WHO International Classification of Diseases

Congenital malformations, deformations and
chromosomal abnormalities

OMIM Number

222765

Mode of Inheritance

Autosomal recessive

Gene Map Locus

1q42

Description

Rhizomelic chondrodysplasia punctata (RCDP) is a genetic peroxisomal disorder which is clinically characterized by rhizomelic shortening of the upper extremities, typical dysmorphic facial appearance, congenital contractures and severe growth and mental retardation. The peroxisomes in individuals with this disorder have four distinct abnormalities: deficient activity of three enzymes – acyl-CoA:dihydroxyacetonephosphate acyltransferase (DHAPAT), alkyl-dihydroxyacetonephosphate synthase (alkyl-DHAP synthase), and phytanoyl-CoA hydroxylase – and an abnormal form of another enzyme, peroxisomal 3-ketoacyl-CoA thiolase. However, a significant biochemical

heterogeneity within RCDP has been established recently. Individuals with all the clinical signs and symptoms of DHAPAT (RCDP type 2) have been identified. Clinical heterogeneity has also been observed, even among individuals with isolated DHAPAT deficiency: cases of a milder, variant form of chondrodysplasia punctata have been described in addition to those with the classic clinical manifestations.

Molecular Genetics

Patients with type 2 rhizomelic chondrodysplasia punctata (RCDP2) show deficiency of the enzyme acyl-CoA:dihydroxyacetonephosphate acyltransferase (DHAPAT). DHAPAT and alkyl-DHAP synthase are responsible for the first two steps of plasmalogen biosynthesis. As the etherphospholipid plasmalogens are major constituents of myelin phospholipids, defective development of myelin is expected in individuals with deficiencies of these enzymes.

Epidemiology in the Arab World

United Arab Emirates

Sztriha et al. (1997) described the cranial magnetic resonance imaging findings in three siblings with nonrhizomelic chondrodysplasia punctata due to isolated dihydroxyacetonephosphate acyltransferase (DHAPAT) deficiency. Areas of high signal intensity in a patchy distribution on the T2-weighted images were detected in the centrum semiovale in the eldest patient (a 6-year-old girl). The white matter of the second child (a 5-year-old boy) was spared, whereas the youngest sibling (a 2-year-old boy) manifested very severe white matter abnormalities. [See also: Yemen > Sztriha et al., 2000].



Yemen

Sztriha et al. (2000) reported a Yemeni girl with isolated peroxisomal acyl-CoA: dihydroxyacetonephosphate acyltransferase (DHAPAT) deficiency. She was born at term after an uneventful pregnancy, labor, and delivery to consanguineous parents. The girl had dysmorphic features, including upslanting palpebral fissures, depressed nasal bridge, long philtrum, thin upper lip, short neck, and disproportionately short proximal segments of the limbs (rhizomelia). The girl's chromosomal analysis was normal and a screen for TORCH (toxoplasmosis, other infections, rubella, cytomegalovirus infection, and herpes simplex) was negative. Bone X-ray confirmed rhizomelia and revealed punctuate calcification in the femoral and tibial epiphyses. The bone abnormalities were highly suggestive of a peroxisomal disorder. In addition, she had rhizomelic chondrodysplasia punctata, microcephaly, failure to thrive, delayed motor and mental development, and spastic quadriplegia. Magnetic resonance imaging showed abnormal white matter signal in the

centrum semiovale involving the arcuate fibers, while the corpus callosum was normal. Deficient de novo plasmalogen synthesis in her fibroblasts as a result of low DHAPAT activity was found, while her very-long-chain fatty acid profile, phytanic acid concentration, alkyl-dihydroxyacetonephosphate synthase (alkyl-DHAP synthase) activity, and peroxisomal 3-ketoacyl-CoA thiolase protein were normal.

References

- Sztriha L, Al-Gazali LI, Wanders RJ, Ofman R, Nork M, Lestringant GG. Abnormal myelin formation in rhizomelic chondrodysplasia punctata type 2 (DHAPAT-deficiency). *Dev Med Child Neurol.* 2000; 42(7):492-5.
- Sztriha LS, Nork MP, Abdulrazzaq YM, al-Gazali LI, Bakalinova DB. Abnormal myelination in peroxisomal isolated dihydroxyacetonephosphate acyltransferase deficiency. *Pediatr Neurol.* 1997; 16(3):232-6.

Contributors

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