Search for a **rare disease**

Very long chain acyl-CoA dehydrogenase deficiency

Disease definition

Very long-chain acyl-CoA dehydrogenase (VLCAD) deficiency (VLCADD) is an inherited disorder of mitochondrial long-chain fatty acid oxidation with a variable presentation including: cardiomyopathy, hypoketotic hypoglycemia, liver disease, exercise intolerance and rhabdomyolysis.

ORPHA:26793

Synonym(s):

VLCAD deficiency

VLCADD

Prevalence: **1-9 / 100 000**

Inheritance: **Autosomal recessive**

Age of onset: **Infancy**, **Neonatal**

ICD-10: **E71.3**

OMIM: **201475**

UMLS: **C3887523**

MeSH: -

GARD: **5508**

MedDRA: -

Summary

Epidemiology

Over 400 cases have been reported worldwide. Prevalence in Germany is of 1/50, 000.

Clinical description

VLCADD is a clinically heterogeneous disease, with 3 major phenotypes. Severe infantile VLCADD has an early onset, usually within the first 3-12 months of life and as early as the neonatal period, with high mortality and a high incidence of hypoketotic hypoglycaemia, liver disease, cardiac arrhythmias and cardiomyopathy. Pericardial effusion is also reported. Moderately severe infantile/childhood VLCADD has a later onset (early neonatal period to early childhood) and usually presents with hypoketotic hypoglycemia, lower mortality and rarely cardiomyopathy. Late-onset myopathic VLCADD presents in older children and young adults (usually >10 years of age) with isolated skeletal muscle involvement, exercise intolerance, myalgia, rhabdomyolysis and myoglobinuria usually triggered by exercise, fasting, cold/heat and/or stress but viral infection can also precipitate/exacerbate this presentation. In rare cases it can lead to renal failure and can be fatal. Some patients presenting with myopathic disease may have a previous history of hypoglycemia in infancy/childhood.

Etiology

VLCADD is caused by mutations in the *ACADVL* gene (17p13.1). Mutations of this gene lead to dysfunction of mitochondrial beta-oxidation of long-chain fatty acids.

Diagnostic methods

Abnormal plasma or blood acylcarnitine profile identifies virtually all patients with the severe/moderately severe phenotypes by demonstrating increased C14:1 and C14:1/C12:1 ratios together with elevations of C12, C16, C16:1, C18 and C18:1 species. Occasionally patients with mainly myopathic disease can give an essentially normal profile when metabolically stable. Crisis urine organic acid analysis generally shows a non-specific abnormal pattern of C6-C14 dicarboxylic and hydroxydicarboxylic acids. Newborn screening is available in Austria, Czech Republic, Denmark, Germany, Hungary, Iceland,

Netherlands, Portugal and Spain (milder "late-onset" patients may not be detected). VLCADD is confirmed by showing two pathogenic mutations in the *ACADVL* gene. Fatty acid oxidation flux assays in cultured fibroblasts or direct measurement of VLCAD activity in lymphocytes or fibroblasts can also clarify difficult diagnoses.

Differential diagnosis

Differential diagnosis includes other long chain fat oxidation defects. Myopathic carnitine palmitoyl transferase II deficiency (see this term) has a presentation identical to the myopathic presentation of VLCADD.

Antenatal diagnosis

Antenatal diagnosis is possible when mutation(s) have been identified within the family.

Genetic counseling

VLCADD is inherited autosomal recessively and genetic counseling is available.

Management and treatment

Dietary treatment along with strict avoidance of fasting is essential in infants/children and involves a low long-chain fat diet in combination with medium chain triglycerides. An emergency regimen should be available for each patient to use when they cannot tolerate their prescribed diet. Medical treatment should be sought immediately if there is evidence of decompensation. Those with a milder phenotype should limit exercise and cold/heat exposure and avoid fasting. Treatment with bezafibrate offers potential benefit in myopathic patients with residual enzyme activity, although this awaits full clinical evaluation.

Prognosis

VLCADD can be fatal but thanks to newborn screening programs, the outcome is improving for all phenotypes. Prognosis is much better for milder phenotypes provided that there is adherence to treatment protocols.

Expert reviewer(s): ***Dr Simon OLPIN*** *- Last update:* ***February 2014***

Detailed information

Professionals

› Summary information

Polski (2014, pdf)
Russian (2014, pdf)

› Emergency guidelines

English (2012, pdf)

› Clinical genetics review

English (2014)

Additional information

Further information on this disease

› Classification(s) (4)

› Gene(s) (1)

› Publications in PubMed

› Other website(s) (9)

Health care resources for this disease

› Expert centres (398)

› Diagnostic tests (107)

› Patient organisations (62)

› Orphan drug(s) (1)

Research activities on this disease

› Research projects (35)

› Clinical trials (6)

› Registries/biobanks (34)

› Networks (28)

Specialised Social Services

› Eurordis directory

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