Familial Marfan-like syndrome

Published: 25-06-2018
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Finding the cause of the phenotype that resembles Marfan syndrome in a single family.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Connective tissue disorders (excl congenital)
Study type	Observational non invasive

Summary

ID

NL-OMON45866

Source
ToetsingOnline

Brief title
Marfan-like

Condition

- Connective tissue disorders (excl congenital)

Synonym
Marfan-like syndrome; syndrome resembling Marfan syndrome

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: exome sequencing, functional studies, Marfan syndrome

Outcome measures

Primary outcome

Pathogenic variant in a gene that explains the phenotype in the family

Secondary outcome

Understanding the pathogenesis of the connective tissue disorder in the family

Study description

Background summary

Marfan syndrome is a well-known disorder characterized by widely spread signs and symptoms, of which the most important ones are dislocation of the lens, skeletal deformities including pectus carinatum formation, scoliosis and arachnodactyly, and decreased elasticity and firmness of the aorta and other large blood vessels which may lead to dissection. A multi-fold of additional signs and symptoms occurs, such as dural ectasias and striae. Marfan syndrome is caused by variants in the gene Fibrillin type I.
For years a family is known in the AMC with a connective tissue disorder that resembles Marfan syndrome to a very great extent. The affected family members fulfil the clinical criteria for the diagnosis Marfan syndrome. However, no variant could be found in Fibrillin type I or in one of the other genes of which it is known that variants may cause a phenotype resembling Marfan syndrome.

Study objective

Finding the cause of the phenotype that resembles Marfan syndrome in a single family.

Study design

Exome sequencing in 3 affected family members and 1 unaffected family member, checking for variants in genes present in affected members and not in the unaffected member. If the numberof candidate genes remain too high exome sequencing will be performed in two additional unaffected family members. We expect to find a small number of candidate genes,. Due to the extensive knowledge of proteins involved in establishing a normally functioning connective tissue we expect to be able to indicat which candidate gene is most likelt the cause in this family. Subsequently, further functional studies will

be performed.

Study burden and risks

Of all affected and non-affected family members DNA is stored at the time they have been investigated because of the familial connective tissue disorder. Therefore no further sampling is needed and the burden of the study is nil. If functional studies will be needed these will likely be performed in an animal model. However, if case these will be needed in one of the affected family members it will be performed in the affected adult male.

Contacts

Public
Academisch Medisch Centrum

Meibergdreef 9
Amsterdam 1105AZ
NL
Scientific
Academisch Medisch Centrum

Meibergdreef 9
Amsterdam 1105AZ
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Children (2-11 years)
Elderly (65 years and older)

Inclusion criteria

Patients:
Marfan-like syndrome
willing to participate
Control
Not affected by Marfan-like syndrome as it runs in the family
willing to participate

Exclusion criteria

none

Study design

Design

Study type: Observational non invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	12-02-2019
Enrollment:	4
Type:	Actual

Ethics review

Approved WMO

Date:	25-06-2018
Application type:	First submission
Review commission:	METC Amsterdam UMC

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL65695.018.18