A Clinical, Molecular Genetic and Coagulation study in patients with Klippel-Trenaunay Syndrome and related entities

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Detection of mutations in AKT1 in patients with KTS

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Blood and lymphatic system disorders congenital
Study type	Observational non invasive

Summary

ID

NL-OMON35243

Source
ToetsingOnline

Brief title
Klipple-Trenaunay syndrome

Condition

- Blood and lymphatic system disorders congenital

Synonym
Klippel-Trenaunay 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: Etiology, Klippel-Trenaunay syndrome, Molecular analysis

Outcome measures

Primary outcome

Detection of AKT1 gene mutations

Secondary outcome

none

Study description

Background summary

Klippel-Trenaunay syndrome (KTS) is a congenital malformation syndrome characterised by combinations of vascular malformations (capillary, venous, lymphatic malformations), and localized disturbed growth of bone and soft tissues. Clinical presentation varies extensively. Occurrence is usually sporadic. The recognition of KTS is important because of its possible thrombotic complications. The pathogenesis of KTS is still unclear.
In an earlier part of the present study the clinical characteristics of 100 persons with KTS have been studied, radiological studies of blood vessels have been performed, and coagulation studies performed in a subset of patients. Molecular analysis was done in all patients and included a large set of genes involved in growth and blood vessel formation. No significant abnormality has been found.
Recently mutations have been found in AKT1 in patients with Proteus syndrome [Biesecker et al, N Engl J Med, in the press]. Proteus syndrome resembles KTS to a great extend both in tissues involved and distribution of manifestations; the difference is that Proteus syndrome patients are more severely affected. AKT1 is known to be involved in colon cancer and several other cancers in case of loss-of-function mutations. In Proteus syndrome gain-of-function mutations have been found. Importantly the mutations were not detectable in lymphocytes but only in other tissues.

Study objective

Detection of mutations in AKT1 in patients with KTS

Study design

The study will be performed in two steps:
- first, in 5 adult patients buccal swabs and skin biopsies will be studied for mutations. Patients are already participating in the earlier part of the study
- the second step depends on the results of the first step: if mutations will be detectable both in buccal tissue and fibroblasts, a series of 25 patients will be investigated using buccal swabs only. If mutations will be detectable only in fibroblasts, a series of 25 patients will be investigated using skin biopsies. Blood samples of all participating patients are already available and will be studied for mutations as well. All patients are already participating in the earlier part of the study.

Study burden and risks

buccal swabs: no risk
skin biopsy: very limited risk for infection and keloid formation. No pain if biopsy is performed under local anaesthesia. Only the formation of a scar of 3mm in diameter located at the inner part of the lower arm is a permanent sequella. As the benefit for the group of findings genes is considerable, and possibly even the patients themself may have benefit of the results of the biopsy if pharmacogenomics allows more directed thera[py, we consider it acceptable to perform a skin biopsy in a small series of patients.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Diagnosis Klippel-Trenaunay syndrome
Age >18yr

Exclusion criteria

Unreliable diagnosis
Age<18yr

Study design

Design

Study type: Observational non invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-09-2011
Enrollment:	30
Type:	Actual

Ethics review

Approved WMO
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	NL37695.018.11