Genetic and Radiological Screening of First Degree Family Members of Patients with Familial Liver Adenomatosis

Published: 27-05-2008
Last updated: 07-05-2024

To determine if LA is a familial disease. To identify germline mutations in HNF-1 alpha, ß-catenin and CYP1B1 genes in LA patients. To screen first degree relatives of patients diagnosed with liver adenomatosis for the presence of liver adenomas and...

Ethical review	Approved WMO
Status	Pending
Health condition type	Hepatobiliary disorders congenital
Study type	Observational invasive

Summary

ID

NL-OMON31682

Source
ToetsingOnline

Brief title
Familial Liver Adenomatosis

Condition

- Hepatobiliary disorders congenital
- Hepatic and hepatobiliary disorders
- Hepatic and biliary neoplasms benign

Synonym
benign liver tumor, liveradenomatosis

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum

Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: adenomatosis, familial, gene mutation, liver

Outcome measures

Primary outcome

- Hepatic lesions on ultrasound and/or contrast-MRI in all patients

- Genetic abnormalities (CYP1B1, HNF-1 alpha, ß catenin) in LA index-patients

- Genetic abnormalities in first line relatives of LA patients diagnosed with

germline mutations.

- Genetic abnormalities in first line relatives diagnosed with adenomas on

imaging studies

Secondary outcome

-Hepatic fat content (MRS) and metabolic profile (blood analysis) in LA patients

-Hepatic fat content (MRS) and metabolic profile (blood analysis) in first

degree familymembers with germlinemutations and/or adenomas on imaging studies.

Study description

Background summary

Liver adenomatosis (LA) is a rare disease consisting of multiple adenomas in the liver. Originally, Flejou et al. defined LA as the presence of at least 10 adenomas in the absence of glycogen storage disease and androgen steroid use, and suggested a normal distribution between men and women. However, recent studies have shown that this number of adenomas is rather arbitrarily and not an evidence based parameter for LA diagnosis. Instead, more focus has come on the genetic abnormalities found in these patients. More specifically, germline mutations in hepatocyte nuclear factor 1 alpha(HNF-1alpha) and CYP1B1 are associated with familial liver adenomatosis whereas a mutation in the *-catenin gene is associated with simple liver adenomas. It has also been found that

liver adenomatosis is associated with the presence of steatosis.

Study objective

To determine if LA is a familial disease.
To identify germline mutations in HNF-1 alpha, ß-catenin and CYP1B1 genes in LA patients.
To screen first degree relatives of patients diagnosed with liver adenomatosis for the presence of liver adenomas and liver adenomatosis related germline mutations in HNF-1 alpha, ß-catenin and CYP1B1.
To investigate the association between LA and steatosis using MR-spectroscopy

Study design

Patients diagnosed with LA, and their first line relatives are asked to participate in our study. After obtaining informed consent, an ultrasound and an MRI are performed for the detection of adenomas and an MRS for steatosis detection. Blood samples are drawn for assessment of liver enzymes, hepatic synthesis function, hepatic tumor marker for hepatocellular carcinoma (alpha-foetoprotein) and determination of features of the metabolic syndrome associated with steatosis (Insulin resistance and lipid spectrum). Genetic analysis is performed on our 10 index patients (CYP-1B1, HNF-1 alpha, ß catenin); if germline mutations are present, their first line relatives will also be screened for these mutations. Furthermore, first line relatives diagnosed with adenomas on imaging studies will also undergo genetic analysis.

Study burden and risks

Study subjects will undergo a venous blood sample for gene, liver and metabolic abnormalities which poses no risk for the patient. An ultrasound, MRI and MRS will be performed for possible detection of adenomas and assessment of the steatosis degree. An MRI will be performed using an intravenous contrast agent (Primovist®). There is a very small risk of an allergic reaction after contrast administration. Other than that, these are all non-invasive radiological methods which are not associated with any substantial risk.
Possible detection of adenomas or a genetic defect in designated genes in the relatives of LA patients could pose a psychological burden. Presumed healthy subjects could be diagnosed with a possible liver disease, adenomas or possible other (unlikely) hepatic lesions, by the radiological examinations. This could eventually even lead to hospitalization and treatment of these lesions. The department of clinical genetics has a specialized clinical psychologist for this purpose.
On the other hand, the detection of the adenomas in an early phase could prevent possible malignant degeneration of the adenomas, or even life-threatening bleeding from the adenomas, by surgical or radiological intervention and close follow-up; a substantial benefit of this study. The

department of clinical genetics can offer specialised psychosocial assistance if healthy subjects are diagnosed with a disease.

Contacts

Public
Academisch Medisch Centrum

IWO-1-155 Meibergdreef 9
1105 AZ Amsterdam
NL
Scientific
Academisch Medisch Centrum

IWO-1-155 Meibergdreef 9
1105 AZ Amsterdam
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Patients diagnosed with liver adenomatosis by histology or imaging studies
2. First line family members of 1.
2. Minimal age 18 years old
3. Informed consent must be obtained

Exclusion criteria

1. Patients under 18 years of age
2. Patients who are pregnant
3. Patients who are claustrofobic (MRI)
4. Patients who have magnetic or radiofrequency sensitive implants (MRI)
5. Patients with extreme obesity (MRI+US)

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-02-2008
Enrollment:	40
Type:	Anticipated

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	NL20223.018.08