HLA SUBTYPING IN ANTIBODY MEDIATED LIMBIC ENCEPHALITIS

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Autoimmune disorders
Study type	Observational invasive

Summary

ID

NL-OMON42370

Source
ToetsingOnline

Brief title
HLA in limbic encephalitis

Condition

- Autoimmune disorders
- Central nervous system infections and inflammations

Synonym
brain inflammation, Limbic encephalitis

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Nationaal Epilepsie Fonds

Intervention

Keyword: Autoimmune, HLA, LGI1, Limbic encephalitis

Outcome measures

Primary outcome

The frequency of HLA-A, B, C, DR and DQ alleles

Secondary outcome

If a specific HLA allele is detected in a subgroup of LGI1 patients, we will

analyze whether there are specific patient characteristics or disease

characteristics in this subgroup

Amendement: analyze the relevant LGI1 epitope (fragment of the protein to which

inflammatory cells bind)

Study description

Background summary

Limbic encephalitis is an autoimmune inflammation of the brain, causing subacute cognitive decline and seizures. Several antibodies causing this inflammation have been discovered in the last eight years, among which are anti-NMDA receptor antibodies (2007) are and anti-LGI1 antibodies (2010). Clinical syndrome depends on the antibody involved. Incidence is growing in all, probably due to better recognition of disease. Etiology of antibody production is unknown. A part of the patients have a tumor, autoimmune disease is suspected in the rest of the patients. The most important genetic marker for autoimmune disease is HLA genotype. Specific HLA subtype have been linked to several autoimmune diseases, but no studies analysed HLA genotype in antibody mediated limbic encephalitis. We have results of HLA subtyping in four patients with anti-LGI1 antibodies and found a common HLA-DR serotype in all.

Amendement: results of the first 11 LGI1 patients (plus 4 earlier patients) show a common HLA-DR allele. This strong association with a single HLA-molecule results in the question how this molecules binds the LGI1 protein. To address

this issue, we are planned to tap extra blood from the last five LGI1 inclusions to isolate inflammatory cells and analyze to which fragment of the LGI1 protein these cells bind. We hope to detect the relevant epitope.

Study objective

Our aims are to analyse whether there is a specific HLA allele or allelic combination associated with susceptibility to LGI1 encephalitis, and to perform a pilot study with HLA subtyping in patients with encephalitis due to antibodies to Caspr2, NMDAR, GABA-B and GAD65.

Amendement: the aim of extension of the study is to analyze which part of het LGI1 protein binds to the HLA-DR molecule, and how this binding occurs.

Study design

Case-control study

Study burden and risks

Blood sample will be taken once. Blood collection can be performed at a local laboratory of patients* choice. If possible, this will be combined with scheduled blood test. All patients are aware of the procedure since they have had venepuncture before. Puncture may cause moderate pain in patients. There is a risk for short-term feeling of light-headedness and a risk of hematoma.

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

- Limbic encephalitis due to antibodies to LGI1, Caspr2, NMDAR, GABA-B or GAD65, recently or in the past
- Current age > 18 years
- Caucasoid race

Exclusion criteria

- Not mentally competent to give informed consent
- Patient is withholding informed consent, or objects after initial consent

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	22-08-2015
Enrollment:	41
Type:	Actual

Ethics review

Approved WMO Date:	19-08-2015
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	03-02-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	NL53927.078.15