Immunological (mis)communication in Langerhans Cell Histiocytosis

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Observational non invasive

Summary

ID

NL-OMON45196

Source
ToetsingOnline

Brief title
Immune-LCH-cell interactions

Condition

- Other condition
- Haematopoietic neoplasms (excl leukaemias and lymphomas)
- Epidermal and dermal conditions

Synonym
eosinophilic granuloma, histiocytosis X

Health condition

botaandoeningen

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: collectebusfondsen en particuliere stichtingen in en buiten Nederland

Intervention

Keyword: Immune cells, Langerhans Cell Histiocytosis, Pathogenesis, Somatic mutations

Outcome measures

Primary outcome

The primary outcome of our study is how certain genes, proteins (or

combinations thereof) expressed by LCH-cells or other leasional cells are

associated with LCH-free survival or with recurrence of LCH (LCH-reactivation).

Secondary outcome

Secondary study parameters are whether or not certain genes, proteins (or

combinations thereof) expressed by LCH-cells or other leasional cells are

associated with late effects such as neurological or hormonal dysfunction.

Study description

Background summary

Langerhans Cell Histiocytosis (LCH) affects both children and adults. The disease is characterized by the accumulation of aberrant histiocytes (LCH-cells) as well as inflammatory in one or more tissues or organs with bone and skin being the most affected sites. LCH can present in many different ways. Consequently, LCH can be misdiagnosed particularly in adults. The past five years, several somatic mutations associated with LCH, but also with many other types of cancer, have been identified. Based on these results., LCH is increasingly considered to be a neoplastic disorder of myeloid origin but with a clear immune component.
The impact of above mentioned mutations on the presentation, course and potential recurrence of LCH after treatment is unclear. In addition, the contribution of lymphocytes co-present in the inflamed LCH-affected tissues is

far from clear. There is a clear need from the field to identify (bio)markers at diagnosis which can adequatly predict progression of the disease or recurrence after treatment (LCH-reactivation). As the latter only occurs in a small proportion of patients, there is currently a significant number of patients who are subjected unnecessarily to prolonged therapy with steroids and/or chemotherapy.
As LCH is a rare disease, we can only collect reliable results from patient materials and clinical data through intensive collaboration. For this reason, we have set up multidisciplinaire research groups in 3 different Dutch centers (LUMC, AMC and EUR) wherein many different specialists who regularly treat LCH patients participate. We also collaborate with the Dutch Childhood Oncology Group (DCOG) which is participating in a large international study (LCH-IV) regarding long term outcome of various treatment protocols for children with LCH. Through these collaborations, we are able to enroll both new onset as well as former LCH patients, children and adults, in our study.

Study objective

The main objective of our study is to gain more insight into the molecular processes preceding the onset and course of LCH. Moreover, we try to understand the role of the immune system, if any, in the clearance of histiocytes which are typically present in LCH-affected tissues.

Study design

In our laboratory we study the gene and protein expression in leasional LCH-cells, immune cells, stromal cells as well as their presumed precursor cells which circulate in the blood or reside in the bone marrow. The DNA from these cells, as well as control genomic DNA extracted from a buccal swab, is tested for the presence of somatic mutations by standard PCR-based technology. Through these studies, we hope to understand how and where aberrant LCH cells arise, what their function is, how they are distributed throughout the body and why these genetic aberrant cells are usually not automatically eradicated by the immune system. To perform these studies, we make use of the remainder of freshly biopsied tissues which are collected for defining the diagnosis; alternatively, we use archived tissue blocks which are provided to us by our collaborators from the pathology department who are participating in our study group.

Study burden and risks

A significant proportion of LCH-affected patients concerns children and adolescents. It is therefore esstential to include especially patients below 18 years in our studies. For all patients enrolled, we aim to limit the burden and risks associated with the collection of biological materials from these patients as much as possible through combining the collection with routine

clinical procedures carried out during the work up or treatment of LCH. The sole exeption is the buccal swab. To avoid extra visits to our clinique, the collection of buccal swabs can be easily done at home at any given moment in time.

Contacts

Public
Leids Universitair Medisch Centrum

Albinusdreef 2
Leiden 2333ZA
NL
Scientific
Leids Universitair Medisch Centrum

Albinusdreef 2
Leiden 2333ZA
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Children (2-11 years)
Elderly (65 years and older)

Inclusion criteria

Patients with clinical features suspected of LCH (prospective study) or patients with clinically and histocology confirmed LCH with non active disease (retrospective study).

Exclusion criteria

Clinical features which do not lead to the (differential) diagnosis of LCH

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):	15-12-2010
Enrollment:	400
Type:	Actual

Ethics review

Approved WMO

Date:	03-12-2010
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	15-11-2011
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	18-11-2015
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	30-10-2017
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	31-01-2018
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

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	NL33428.058.10

Study results

Results posted: 16-11-2022

First publication
01-01-1900

URL result
Type
ext
Naam
pubmed.ncbi.nlm.nih.gov
URL