Nontuberculous mycobacterial cervicofacial lymphadenitis in children; diagnostic performance of the Capilia MAC antibody Elisa test and possible portals of entry

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This study intends to investigate the diagnostic potential of the Capilia mac antibody Elisa test in children with a clinical suspicion of NTM cervicofacial lymphadenitis.Moreover, this study aims at investigating whether NTM possibly access the...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Mycobacterial infectious disorders
Study type	Observational non invasive

Summary

ID

NL-OMON56039

Source
ToetsingOnline

Brief title
NTM cervicofacial lymphadenitis

Condition

- Mycobacterial infectious disorders

Synonym
Nontuberculous mycobacterial cervicofacial lymphadenitis/Atypical mycobacterial head and neck infcection of the lymph nodes

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Diagnosis, Lymphadenitis, Nontuberculous mycobaceria, Portal of entry

Outcome measures

Primary outcome

Sensitivity and specificity of the Capilia mac antibody Elisa test in patients

with a clinical suspicion for NTM cervicofacial lymphadenitis. A receiver

operating characteristic curve will be constructed and the overall accuracy

will be expressed by the area under the curve.

Secondary outcome

The assessment of microbial composition and identification of NTM in the oral

cavity, nose, oropharynx and excised lymph node material.

Study description

Background summary

NTM are acid fast bacteria that naturally occur in the environment. They are found in soil, water, food etc. They form a serious threat of generalized infections in immunocompromised people. Remarkably, NTM are also a common cause for (sub)chronic cervicofacial lymphadenitis in otherwise healthy children aged between 1-5 years. The reported incidence is 0,6-4,5 per 100.000 children below 4 years of age. Children with NTM cervicofacial lymphadenitis generally present without any symptoms of fever, malaise or fatigue. The clinical course of the disease is characteristic; at first, a painless mass presents with visible increase of vascularity. Then, the mass becomes fluctuant. After that, significant skin changes may cause a violaceous aspect of the lesion and the skin becomes *parchment-like*. In the last phase, the lesion breaks through the skin and fistualizes causing a draining wound. Ultrasonographically, all infected lymph nodes are hypoechoic, often with central necrosis, nodal matting

and adjacent soft tissue oedema. The submandibular lymph node is the most affected lymph node station.
Lindeboom et al. have shown, in a randomized controlled trial, that surgical excision is considered to be the most effective treatment compared to wait and see therapy and antibiotic therapy. Excision of the infected lymph nodes is considered to be the standard treatment for children with NTM cervicofacial lymphadenitis with a mean cure rate of 98%. Damage to the mandibular branch of the facial nerve and excessive scarring are possible complications of this treatment. The risk of facial paralysis depends on the proximity of the lesion to the facial nerve and the skills of the surgical team. Permanent facial nerve damage occurs in approximately 2% of the cases. Other treatment options are antibiotic therapy or wait and see therapy. However, these therapies have lower cure rates than surgical treatment.

Diagnosing NTM cervicofacial lymphadenitis is difficult. Definitive diagnosis requires a positive culture or polymerase chain reaction (PCR) result. However, these diagnostic procedures must be performed on infected lymph node material. The only way to obtain this material is by excision of the infected lymph nodes or by aspirating fine needle specimens. Both procedures are generally performed under general anesthesia in children. A non-invasive pre-operative diagnostic test is desired for NTM cervicofacial lymphadenitis to overcome this burden. The Capilia mac antibody Elisa* test is an in-vitro diagnostic test, which is developed to determine the levels of serum IgA to the glycopeptidolipid core of MAC
in serum samples.

It is still largely unknown in which way NTM enter the body. In the literature it is suggested that direct exposure to the mucosa during eruption be of importance, concluding that the oral cavity, nose and oropharynx might play a role as the portal of entry. There is no evidence of another possible portal of entry and no study has yet assessed the overall oral microbial composition (microbiome) in this group of patients. In this study, it is hypothesized that NTM could be found in the oral cavity, nose or oropharynx of patients with nontuberculous cervicofacial lymphadenitis. An aberrant microbiome could indicate an increased sensitivity to opportunistic infections.

Study objective

This study intends to investigate the diagnostic potential of the Capilia mac antibody Elisa test in children with a clinical suspicion of NTM cervicofacial lymphadenitis.
Moreover, this study aims at investigating whether NTM possibly access the body through the oral cavity, nose or oropharynx and if the patients carry an aberrant oral microbiome. Thus, the study will provide more insight regarding the pathophysiology of NTM cervicofacial lymphadenitis.

Study design

Prospective clinical observational study. Swabs of the tongue, tonsils, gingiva and nose are taken from patients with suspected NTM cervicofacial lymphadenitis. Moreover, 6mL blood samples are taken. All procedures are performed during surgery, which is the current best treatment for patients with a high clinical suspicion of NTM cervicofacial lymphadenitis. Real-time PCR and culture are performed on the material obtained by the swabs to confirm the possible presence of the NTM. To calculate diagnostic test accuracy values, the results of the Capilia mac antibody Elisa will be compared with the results of the reference standard being PCR and culture.

Study burden and risks

The additional risk of the study is small, as it is an observational study.

Due to the fact that NTM cervicofacial lymphadenitis only occurs in minors, it is not possible to carry out the study protocol with another patient population.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Children (2-11 years)
Babies and toddlers (28 days-23 months)

Inclusion criteria

Study group:

• Age between 0-15 years
• High clinical suspicion of NTM cervicofacial lymphadenitis, as defined by the following factors;
- Cervicofacial lymphadenopathy for a period longer than 3 weeks
- Typical clinical presentation as defined by Penn et al. (2011)
- Negative serologic tests for other kinds of (sub) chronical lymphadenopathy: Epstein-Barr virus, cytomegalovirus, Bartonella species, Adenovirus, and toxoplasmosis
- Ultrasonographically, hypoechoic lymph nodes, often with central necrosis, nodal matting and adjacent soft tissue oedema

Control group:
• Age between 0-15 years
• Indication for surgery under general anesthesia

Exclusion criteria

Study group:
- Known immunodeficiencies
- Usage of immunosuppressive drugs

Control group:
- Clinical suspicion of NTM cervicofacial lymphadenisis as defined above

Study design

Design

Study type: Observational non invasive

Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Basic science

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	23-10-2019
Enrollment:	96
Type:	Actual

Ethics review

Approved WMO Date:	13-06-2019
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	07-10-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	21-04-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	22-03-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	02-08-2023
Application type:	Amendment
Review commission:	MEC Academisch Medisch Centrum (Amsterdam)
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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	NL65321.018.18
Other	NL8371