EUROPEAN STUDY OF THE CEREBELLAR MUTISM SYNDROME (CMS) IN CHILDREN WITH BRAIN TUMOURS OF THE POSTERIOR FOSSA

Published: 24-03-2023
Last updated: 30-01-2025

The purposes of this study are to uncover1. Which surgical methods are least likely to cause the CMS and if there is a difference in risk between primary surgery andreoperation2. Which patients may be genetically predisposed to developing the CMS 3...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Nervous system neoplasms malignant and unspecified NEC
Study type	Observational invasive

Summary

ID

NL-OMON53502

Source
ToetsingOnline

Brief title
European CMS Study

Condition

- Nervous system neoplasms malignant and unspecified NEC
- Nervous system, skull and spine therapeutic procedures

Synonym
Cerebellar Mutism Syndrome, unable to speak after brain surgery

Research involving
Human

Sponsors and support

Primary sponsor: University of Copenhagen - Rigshospitalet - Department of Clinical Medicine
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: cerebellum, mutism, neurosurgery, posterior fossa

Outcome measures

Primary outcome

To explore the relationship between different surgical methods for the removal

of posterior fossa tumours, and relate these to

the incidence and clinical course of the CMS (prospective observational study).

Hypothesis: Methods that spare the dentate nuclei and their efferents and focus

on minimally traumatic techniques lower the

risk of developing the CMS by 50%, and lessen its severity and duration by 40%

when compared to more invasive tumour

removal methods. The risk of getting the CMS is greater after reoperation(

s) when compared to primary surgery.

Secondary outcome

Genetics

To analyze the role of genomic variants on the development, severity and

recovery from the CMS by carrying out a broad genetic profiling of the study

participants (SNP analysis). Hypothesis: Genetic variants in inflammation,

vascularization, neuronal tissues, neurotransmitters, neurotransmitter

transporters, blood-brain-barrier tissues and/or lipoproteins explain at least

50% of the variation in incidence of CMS and explain at least 40% of the

variation in severity, duration and level of recovery from the CMS in those instances where tumour type, size, location and the surgical approach are similar.

Corticosteroids

To explore the effect that pre, intra and/or postoperative corticosteroids may have on the risk and severity of the CMS (prospective observational study). Hypothesis: Preoperative corticosteroids have a protective effect against the development of the CMS as they reduce vasogenic (tumour induced) cerebral oedema and thereby ICP. Intraoperative corticosteroids increase the risk of getting the CMS as the hyperglycaemia that they induce can cause acute neurological injury. Postoperative corticosteroids have a negative effect on the overall outcome of the CMS as earlier studies have shown a negative effect on the treatment of traumatic head injuries.

Other treatments

To investigate the effect of chemo and radiotherapy on recovery from CMS. Additionally information will be gathered on any medication specifically given to treat the symptoms of the CMS , with the aim of documenting what helps and does not help (prospective observational study). Hypothesis: Chemo and radiotherapy delay recovery from CMS.

Tumour type

To document the incidence of the CMS according to histological tumour type

(prospective observational study). Hypothesis: The risk of CMS depends on tumour type.

Handedness

To determine whether the risk of the CMS varies according to handedness (prospective observational study). Hypothesis: The risk of CMS is increased in lefthanded compared to righthanded and even more so in cases of medulloblastomas.

Comorbidities

To determine whether the presence of any comorbidities influences the risk of the CMS (prospective observational study). Hypothesis: The risk of CMS is increased in patients suffering from chronic comorbidities such as NF1, diabetes, heart diseases etc.

Language and speech

To analyze the speech and language deficits associated with CMS on shortas well as longterm basis, and to explore how preoperative language status affects the risk of developing CMS. Both have been done before, although in significantly smaller cohorts (prospective observational study). Hypothesis: Poor preoperative speech and language status increases the risk of postoperative speech and language deficits. The degree and type of impairment also depends on other patient and tumour variables.

Neuroradiology

To replicate and further extend the association between certain

neuroradiographic features and development of the CMS established by previous

studies (prospective observational study). Hypothesis: Different

neuroradiographic features carry different risks for the development and

progress of CMS.

Study description

Background summary

Central nervous system (CNS) tumours constitute 25% of all childhood cancers, and more than half of these are located in
the cerebellum. One of the most troublesome late effects after operation for such a tumour is the cerebellar mutism syndrome
(CMS) which is seen in up to 25% of children after surgery. It is characterized by mutism, hypotonia, ataxia and irritability, and
the exact causes have yet to be identified.
Although a cure may have been achieved with respect to their brain tumour, the CMS and its consequences can still
represent a lifelong challenge for these children. Since roughly half of all paediatric brain tumours reside in the posterior
fossa and require operative removal, the CMS constitutes both a common and severe problem in paediatric neurooncology.

Study objective

The purposes of this study are to uncover
1. Which surgical methods are least likely to cause the CMS and if there is a difference in risk between primary surgery and
reoperation
2. Which patients may be genetically predisposed to developing the CMS 3. The effect that corticosteroids may
have on the development and clinical course of the syndrome 4. Differences in incidence and clinical course of the CMS
according to tumour type, comorbidities, handedness, the effect of attempted symptomatic medication and chemoand
radiotherapy
We hope that the results will contribute to an overall reduction in incidence

and severity of the CMS as well as increasing understanding and awareness of the syndrome. Furthermore, this study can lead to harmonization of the treatment of these patients.

Study design

Multicenter prospective observational cohort study

Study burden and risks

Patients participating in the study will be treated according to the local standards. Additionally, we will take preand postoperative speech samples that take about 10 minutes each. We will also ask for one extra blood sample of 2 cc for genetic analysis, that can be taken at any time point during the study (for example, along with other routine blood samples). Participating in the study will not impact or interfere with the child*s treatment plan and the child will not be exposed to any additional risks or disadvantages by participating in this study except for the blood sample which carries minimal risks and discomfort.

CMS is almost exclusively seen in children. Very few cases of CMS in adults can be found in the literature, and thus it would not be possible to perform this study in an adult population.

Besides contributing to an increased understanding and awareness of the CMS this study has the direct prospect of reducing both the incidence and the severity of the syndrome, which would be a great advantage for other children with CMS.

Contacts

Public
University of Copenhagen - Rigshospitalet - Department of Clinical Medicine

Blegdamsvej 9
Copenhagen 2100
DK

Scientific
University of Copenhagen - Rigshospitalet - Department of Clinical Medicine

Blegdamsvej 9
Copenhagen 2100
DK

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Children (2-11 years)
Babies and toddlers (28 days-23 months)
Newborns

Inclusion criteria

- Age <18 years at the date of first imaging showing this tumour
- Tumour in the cerebellum/4th ventricle/brainstem with intention to treat with surgical resection or open biopsy. Second and further surgeries are also included.
- Signed Informed consent from custodial parent(s) and/or patient

Exclusion criteria

No informed consent

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	14-08-2023
Enrollment:	140
Type:	Actual

Medical products/devices used

Registration:	No

Ethics review

Approved WMO Date:	24-03-2023
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	07-03-2024
Application type:	Amendment
Review commission:	METC NedMec

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
ClinicalTrials.gov	NCT02300766
CCMO	NL81967.041.22