Screening and diagnostic aspects of Endolymphatic sac tumor (ELSTs)

Marie Louise Mølgaard Binderup
Department of Cellular and Molecular Medicine, University of Copenhagen

In collaboration with

In Denmark:
Marie Louise Bisgaard, Steen Gimsing, Carsten Thomsen,
and the Danish vHL Coordination Group

International Collaborators:
Spain: Jose de Campos, Daniel Aguirre
London: Sally Watts
Singapore: Min-Han Tan
Japan: Hiroshi Kanno
India: Ashok Pillai

What are ELSTs?

- Benign, but locally aggressive tumors of the endolymphatic duct/sac in the inner ear

Normal function of the endolymphatic sac

The endolymph is essential to the function of the inner ear
Cells in the endolymphatic sac remove the endolymph from the inner ear and thereby maintain the fluid homeostasis and pressure of the inner ear

ELSTs and vHL

- ELSTs in up to 16% of vHL patients
- In vHL patients, ELSTs are bilateral in 11-30%
- Almost all (96%) of reported ELST patients had audiovestibular symptoms at diagnosis (sensorineural hearing loss (91%), tinnitus (64%), vertigo (52%))
- ELST of all sizes can lead to severe hearing loss
- Surgical treatment can preserve and in some cases improve hearing level and early excision is recommended

Outline of the talk

- What are endolymphatic sac tumors (ELSTs)?
- ELST diagnosis: imaging of the inner ear
- Challenges in ELST screening
- Our experience: international collaborative ELST study
- The use of audiometry in ELST screening
- ELST screening recommendations
Mechanisms of ELST-related hearing loss

- Sensorineural (Inner Ear Type) Hearing loss
  - About 50% Sudden hearing loss
  - About 50% Progressive hearing loss

ELST Size
- Small
  - Intralabyrinthine bleeding
  - Endolymphatic hydrops
- Large
  - Erosion of the labyrinth and surrounding bone
  - Invasion of neighboring structures

How is ELST diagnosed?
Traditionally based on symptoms and MRI of the inner ear

Large ELSTs are easiest to diagnose
- Hard to miss with imaging
- Unfortunately they have often already had catastrophic effects

The challenge is to diagnose the ELSTs at early stages to prevent development of permanent hearing loss

ELST diagnosis:
What does an ELST look like on an MRI of the inner ear?

MRI characteristics
- Larger ELSTs
  - Hard to miss! Location depends on progression
  - Non-enhanced T1: Heterogeneous signal intensity with areas of hyperintensity (cystic or necrotic areas and intratumoral hemorrhage)
  - Very large ELSTs: Flow voids (tumor vascularization)
- Small ELSTs
  - Mass centered in the retrolabyrinthine area
  - Isointense tumor (T1 and T2)
  - Homogeneous contrast enhancement

Image from: http://www.hkcr.org/
**ELST diagnosis: What does an ELST look like on an MRI of the inner ear?**

**MRI characteristics**

- Small ELSTs
  - Mass centered in the retrolabyrinthine area
  - Isointense tumor (T1 and T2)
  - Homogeneous contrast enhancement

**Imaging as screening tool**

- Thin slices (1 mm)

---

**Challenges in ELST diagnosis and screening**

**How do we make sure that ELSTs are detected at early stages?**

Prophylactic screening of all vHL patients regardless of whether or not they have symptoms of an ELST

**What is the best screening strategy for ELST in vHL patients?**

- MRI not accessible at regular intervals in all countries
- We propose audiometry as a first-line screening tool

---

**Our experience: An international collaborative study about ELST and hearing loss among vHL patients**

**Prospective cohort study**

**Objective:** How can audiometry be used in ELST screening among vHL patients?

1) Establish audiological characteristics among vHL patients with and without ELST
2) Investigate whether audiometric patterns correlate to ELST development

**Methods:**

- vHL patients over the age of 15 years
- Blinded assessment of audiometry
  (Ear-nose-throat specialist Steen Gimsing)
- Blinded assessment of MRI of the inner ear
  (within 12 months of audiometry - Professor of neuroradiology Carsten Thomsen)

---

**Collaborators**

- So far 80 vHL patients have been included in the study

---

**London**
Department of Clinical Genetics
Guy’s Hospital
Local project manager: Sally Watts

**Copenhagen**
Department of Cellular and Molecular Medicine
University of Copenhagen
Local project managers: Marie Luise Bisgaard and Marie Louise Mølgaard Binderup

**Madrid**
Neurosurgery Department, Fundación Jiménez Díaz
Universidad Autónoma de Madrid
Local Project Managers: Jose M de Campos and Daniel Mollehuanca Aguirre

**Kochi, Kerala**
Amrita Institute of Medical Science & Research Centre (AIMS)
Local project manager: Ashok Pillai

**Singapore**
National Cancer Center Singapore
Local project manager: Min-Han Tan

**Yokosuka**
Department of Neurosurgery
Yokosuka City Hospital
Local project manager: Hiroshi Kanno
Audiometry = Measurement of hearing

Normal hearing development with age
Average hearing in otologically normal males (selected age groups)

Audiogram assessment:
1) Compare with age-related expectations
2) Compare the two sides
3) Shape of the audiogram

Derived from: ISO 1999 (Database A).

Do audiometric patterns correlate to ELST development?

Hypothesis: Early-stage ELSTs may be associated with low-frequency hearing loss

- Almost half of ears with reported early-stage ELSTs have low-frequency hearing-loss. (Review of the literature of ELSTs with reported audiogram and tumor size (N= 18 ears with small ELSTs))

- Low-frequency hearing loss is known to be related to Meniere’s disease, caused by endolymphatic hydrops

References:
3. Lonser et al.: Tumors of the endolymphatic sac in von Hippel-Lindau disease. 2004
30-year old man, no subjective symptoms
4 mm right-sided ELST
Normal hearing level

26-year old man reported tinnitus 15 years later: 4 mm right-sided ELST
Low-frequency hearing loss

41-year old man, total deafness, tinnitus
3 x 4 mm right-sided ELST

48-year old woman
Subjective hearing loss
13 mm right-sided ELST
Low-frequency hearing loss

Marie Louise Mølgaard Binderup – mlmb@sund.ku.dk
What is the best screening strategy for ELST in vHL patients?

Screening recommendations:
First-line screening: Audiometry

- Annual hearing examination with
  - Pure tone audiometry (air- and bone conduction)
  - Tympanometry and Stapedial Reflexes

Important to remember:
- We are looking for very small hearing losses!
- Precise measurements by professionals
- Include low frequencies
- Serial audiometries: verify findings and detect progression

When should an ELST be suspected based on audiometry? (preliminary conclusion)

- Low frequency hearing loss (sensorineural) from 250 Hz extending to 1 or 2 kHz (two grades) in one or both ears and/or:
  - A sensorineural asymmetry of at least 15 dB at two neighboring frequencies (anywhere in the frequency range)

ELST suspicion based on audiometry

Diagnostic MRI of the inner ear

Screening recommendations: MRI of the inner ear

- High-resolution MRI with
  - T1- and T2-weighted images
  - Thin slices (1 mm) through the inner ear and 8th cranial nerve
  - T1 without and with i.v. contrast

- ELST screening included in annual surveillance MRIs of the CNS to spare patients an extra surveillance examination
  - Evaluated by trained professionals
International collaborative study

• New collaborators can still join!

Longitudinal prospective study, 10 years follow-up

Requirements for collaborators
All vHL patients can be included, regardless of whether or not they have an ELST
1) Audiological examination AND
2) MRI of the inner ear
No more than 12 month apart

More information: www.kortlink.dk/efxv
E-mail: mlmb@sund.ku.dk

QUESTIONS?