Leber's Hereditary Optic Neuropathy (LHON) – 2 Case reports

Anja Palmowski-Wolfe
University Hospital Basel, University Eye Hospital, Basel, Switzerland

Background on LHON, ORPHA 104: Rare: 1-9:100 000

First described by Theodor Leber 1871

Point mutation in mitochondrial genome -> maternal inheritance pattern
11778 (50-70%), 3460 (bad prognosis) 14484 (vision may improve more), > 45 mutations

complex I affected -> ↓ ATP synthesis, ↑ oxidative stress-> ↑ apoptosis
Affects retinal ganglion cells. Why?: Thin and unmyelinated intraocular nerve fibres have less mitochondria for high energy demand

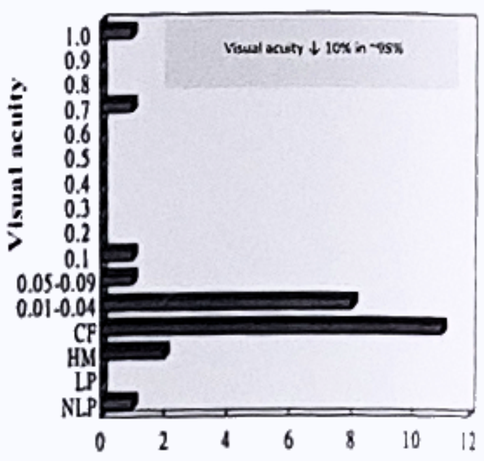
-> thin fibres affected first -> papillpomacular bundle [1]

Purpose:

To emphasize the importance of history-taking and of electrophysiology in the diagnosis of LHON based on 2 case reports.

LHON- Mitochondriopathy 11778

- negative family history ~57%
- 82% >
- Age of manifestation: 15-35 yrs(8-60)
- Bilateral start noticed:~55%
- If interval: ♦ 2 months, (up to 8 yrs)
- Rarely unilateral
- Vision loss occurs over ~4 months (0-24)
- Red-green affected
- Mostly not complete blindness
- Peripheral vision allows independent life [2,3]



Patient 1:

Presentation with loss of vision OS.
OD amblyopia post accident,
corneal scarring
Snellen acuity:
OD: 0,1
OS: 0,4 // pinhole= 0,63!

→ **? Corneal dystrophy**

2 days later
OS lubricated and refracted to 0.8

→ Dx: **posterior polymorphous corneal dystrophy** OD>OS

3 weeks later Snellen acuity:
OD: cc 0.1 (0.3)
OS: cc 0.1, central scotoma

→ cMRI (& Venographie): normal 2x!
Neurology
LP: opening pressure normal
barrier dysfunction (Albumin-ratio: 15.2)

Steroids
-> No improvement

6-7 cigaretts/day
1-2 beers

2 months after presentation:
blurred margin of optic disc!

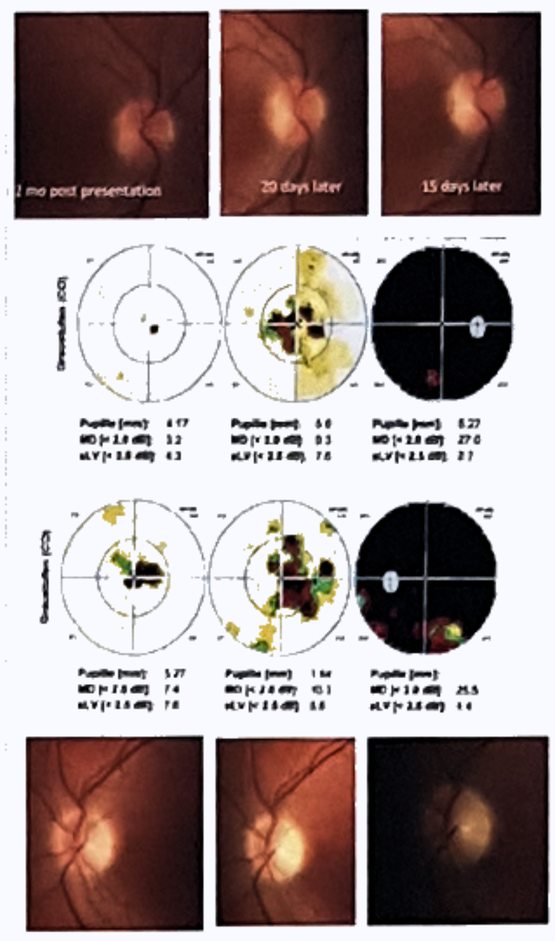
- DD:
- LHON
- (N)AION,
- PION
- paraneoplastic ON
- Tabac alcohol ON

Normal: OCT u OCT angiogram
Fluorecein & ICG angiogram

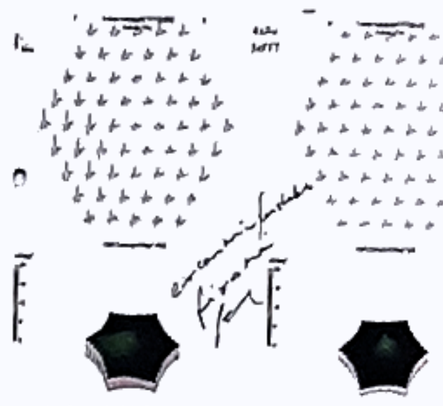
Light reaction direct & indirect, no RAPD

1 son, healthy
Parents: healthy, 1x glasses
Grandparents had been healthy
No siblings

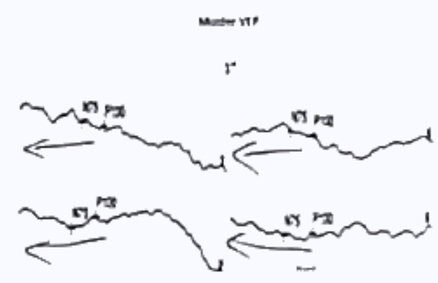
1. Genetic ? LHON
2. Low Vision
3. Psychosomatik



Optic nerve head and corresponding fields over time

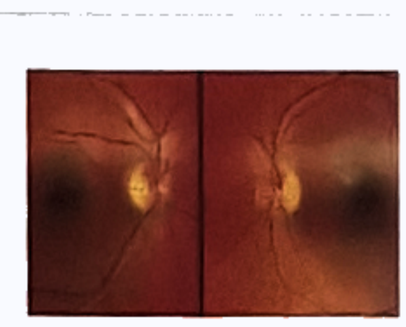


Multifocal ERG:
careful: nice waveforms, also in center.
Central «dip» caused by unstable fixation
-> does not confirm retinal disease!

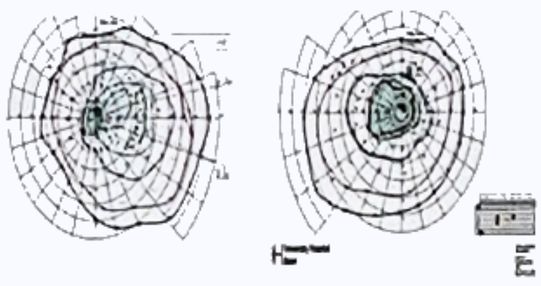


Pattern VEP:
No (reproducible) responses
-> Optic nerve pathology

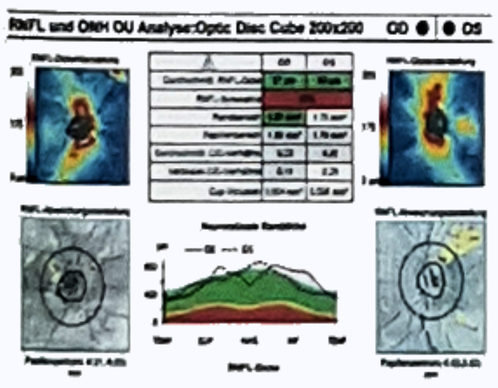
→ **5 months post presentation:** genetic confirmation of MT-ND4 m.11778G>A p.(Arg340His) homoplasmic (100%)

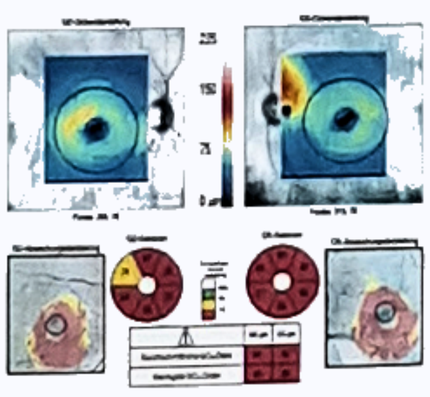


Bilateral temporal palor of the optic disc



Central visual field loss.





Thinning of the RNFL and GCL on OCT

Patient 2:

A 48 year old male with a known history of sleep apnoea initially presented elsewhere with reduced VA OU. ? PION

On presentation at our hospital 10 months later:
Snellen acuity OU: 0.5

Family history positive for LHON !!

Genetic testing confirmed LHON 11778

Conclusions:

Electrophysiology is helpful especially in patients with other underlying pathology (amblyopia, corneal dystrophy, pt 1)
History-taking can facilitate diagnosis-> so do not forget (pt 2)
Both are essential to diagnose LHON early and to initiate genetic confirmation.

This is becoming more important in view of treatment options such as N06BX13 Idebenon but also gene therapy which is becoming available for these mutations[4].

Literature

1.Sadun et al. 2013. doi.org/10.1111/j.1755-3768.2013.2664.x

2.Newman, *Arch Neurol.* doi:10.1001/archneur.1993.00540050082021

3.Hung et al. Chang Gung Med J 2003 http://cgmj.cgu.edu.tw/2601/260106.pdf

4.Yu-Wai-Man .JAMA Ophthalmol. doi: 10.1001/jamaophthalmol.2024.5375

www.LHONsociety.org

www.lhon.org