The heart is always right

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Clinical case

- 76 years old woman without treatment
  - Past medical history: appendicectomy in 1958
  - In her family: mother and father died at 84 and 102 respectively. Her brother and sister are healthy.
  - Past professional activities: factory worker and cleaning
  - No addictions
  - Lives alone

- She comes to see the neurologist for a check-up, and her long, long story…
Clinical case:

- 1994: Hepatitis B vaccinations (3 doses)
  - Left eye pain: superficial punctuated keratitis
  - Repeated left superior member numbness, and elocution trouble
    - Clinical examinations shows: cerebellum syndrome mostly in left side and tetra pyramidal syndrome
  - CT scan: periventricular white substance hypodensity
  - Electroencephalogram, lumbar puncture are normal

- 1998: Brutal left hemiparesis and visual blur
  - Urgent brain MRI: symmetric periventricular leucopathy touching the thalamus
Brain MRI 1998

T2 FLAIR
Clinical case

- Neurologic symptoms:
  - Cerebellum syndrome
  - Pyramidal syndrome
  - Repeated brutal paresis
  - Visual blur

- CT scan and MRI: periventricular leucopahy increasing

- Echocardiography: hypertrophic cardiopathy caused by hypertension

- Clinical hypothesis?
  1. Strokes
  2. Multiple sclerosis
  3. CADASIL syndrome
  4. Other
Multiple sclerosis (MS)
- Treated with steroids and interferon B1

2002: Secondary progressive MS form
- Walks with a cane
- Cerebellum dysarthria, ataxia
- MRI: white substance symmetric anomaly, touching the external capsula

2006:
- Memory loss
- Left hemibody pain
- Balance issues
MRI 2003 (FLAIR)
MRI 2009

Many Microbleeds

External capsule affected
Clinical case

- 2010 – 2013:
  - Bilateral perception hypoacousia 45%
  - Cerebellum syndrome and cognitive troubles
  - Partial epileptic
  - Severe left ventricular hypertrophy (LVH)
    - Heart MRI: confirms LVH and inferior ischemic lesion

- To resume: neurologic and cardiac symptoms, perception hypoacousia starting at her 50’.

- Clinical hypothesis?
- One paraclinical exam to confirm the diagnostic.
- Ophthalmic examination: cornea verticillata
- Vascular leucodystrophy
- Myocardia biopsy: clarified myocytes, without fibrosis leading to a **Fabry’s disease**

- **Alpha galactosidase decreased**
  - Urinary globogluconosidase 3 increased
  - Heterozygote genetic mutation GLA gene
Take home message

- Patient’s global vision (neurologic, cardiac, ophthalmic and audition affected)
- Old diagnosis might be wrong (took 20 years to get it right)
- Stay alert in front of atypical diagnosis
- Heterozygotes genetic disorders can be revealed at adult age

Thank you for your attention!
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Fabry’s Disease
Review
- X-linked recessive transmission.
- Deficiency of alpha-galactosidase A
- Storage of neutral glycophosphingolipids (globotriaosylceramid et galgactosylceramid) in endothelium cells and other cell types.
- Causing kidney, heart, nervous system, skin alone or combination damage.
- Incidence estimated at 1/40 000 to 1/117 000 worldwide
Neuropathic pain, exercise intolerance, gastrointestinal symptoms, hypohidrosis, corneal changes, and angiokeratomas

Glycosphingolipid accumulation, hypoperfusion with inflammation fibrosis

Neuropathic pain, exercise intolerance, gastrointestinal symptoms, hypohidrosis, corneal changes, and angiokeratomas

Alpha-galactosidase A

Mild proteinuria, hyperfiltration, isosthenuria

Insuffisance rénale chronique

Insuffisance rénale chronique

Hypertrophic cardiomiopathy and LVH

Systolic and diastolic dysfunction Arrhythmias

MRI white grey matter and posterior circulation lesions

TIA and strokes
**Fabry disease**

- **Ophthalmologic affect:**
  - cornea verticillata (Early and almost pathognomonic sign)
  - One or more linear opacity irradiating from a point near the centre of the cornea
  - Do not interfere with visual acuity

- **Heart disease:**
  - Myocardial hypertrophy and diastolic dysfunction
  - Cryptogenic ventricular arrhythmias (short PR interval), bradycardia
  - Ischaemia (vasospastic or stenotic coronary artery disease)
Fabry disease

- Neurologic affect:
  - Neuropathic pain and acroparesthesia
    - Permanent or per crises
  - Small or median vessels occlusion.
  - Vascular dementia
  - Normal imaging in 25% of the homozygotes and 40% of the heterozygotes
    - Anomalies: strokes, intracerebral haemorrhages, ventricular dilatations, basilar arterial dilatation, specific T1 pulvinar hyposignal.

- Hearing loss: worse than in an aged-matched general population

- Gastrointestinal disturbance: nausea, vomiting, abdominal pain, diarrhoe (associated with meals)

- Angiokeratomas: characteristic reddish-purple skin lesions
- Renal failure and chronic renal disease:
  - Proteinuria, isosthenuria (inability to concentrate the urine)
- Decreased sweating (hypohidrosis)
  - Intolerance and decreased ability to exercise

Ranges of age at onset of different clinical manifestation in men with homozygotes Fabry’s disease
Diagnosis:

Men:
- $\alpha$-galactosidaseA activity in peripheral leucocytes or plasma if leucocyte analysis is unavailable
- $\alpha$-galactosidaseA gene sequencing and identification of disease-causing mutation or testing for all known familial mutations

Woman:
- $\alpha$-galactosidaseA gene sequencing and identification of disease-causing mutation or testing for all known familial mutations

Prenatal diagnosis:
- $\alpha$-galactosidaseA gene sequencing assessing for a known familial mutation

Treatment: $\alpha$-galactosidaseA enzyme replacement

- Serratrice C. Lipidose (II). Maladie de Fabry *EMC Neurologie* 200617-066-B-10

- Toyooka K. Fabry disease *Curr Opin Neurol* 24:463-468


- HAS Guide PNDS « Maladie de Fabry » Novembre 2010