CHECKLIST: FABRY DISEASE?

FOCUS ON NEUROLOGY

COULD IT BE FABRY DISEASE? Focus on Neurology

Symptoms/Findings

- ☐ **TIA, stroke, muscle weakness**
- ☐ **Acroparaesthesia** → Burning pain in hands and feet
- ☐ **Small fibre neuropathy**
- ☐ **Pain crises**
- ☐ **Dyshidrosis** (hypohidrosis, rarely hyperhidrosis)
- ☐ **Temperature intolerance**
- ☐ **Gastrointestinal discomfort**
- ☐ Basilar ectasia/ ectatic vessels (vertebrobasilar)
- ☐ White matter lesions (WML)
- ☐ Reduced lacrimation and salivation
- ☐ Depression
- ☐ Fatigue

Diagnostics

- ☐ Doppler/duplex ultrasound, particularly of the basilar artery
- ☐ Cerebral MRI including MR angiography → WML, silent infarctions, spinal lesions, contrast medium enhancement
- ☐ Electroneurography
- ☐ "Bedside" thermal, vibration, and touch tests
- ☐ QST (small fibre neuropathy where diabetes, alcohol abuse, etc are excluded)
- ☐ Skin biopsy if necessary
- ☐ Assessment of pain/ quality of life using scales such as BPI, WHO-5, MDI-10, SF-36
- ☐ Questioning on sweating levels, temperature intolerance

Fabry disease possible →

Patient's Medical History

Any signs of kidney failure such as uraemia or hypocalcaemia?

Family Medical History

Any signs of kidney failure such as uraemia or hypocalcaemia in relatives?

Unexplained incidents of death in the family?

Fabry disease probable →

Fabry Diagnosis

Dry blood test determining:

- The genetic mutation
- The level of α-galactosidase A (α-Gal A) activity
- The biomarker lyso-Gb_3

and/or

Molecular genetic/ cytogenetic Fabry diagnosis from:

- EDTA blood test
- Serum
- Buccal swab

Engagement of an expert centre for conclusive diagnosis. In the event of confirmed Fabry disease diagnosis, further monitoring of progress and organ screening is recommended.

Note: this listing of symptoms/ findings and diagnostic tests may not be all-inclusive.

BPI, Brief Pain Inventory; EDTA, ethylenediaminetetraacetic acid; lyso-Gb_3, globotriaosylsphingosine; MDI-10, 10-item Major Depression Inventory; MR, magnetic resonance; MRI, magnetic resonance imaging; SF-36, Short-Form-36; QST, quantitative sensory testing; TIA, transient ischaemic attack; WHO-5, World Health Organization-5.

SIGNS AND SYMPTOMS OF FABRY DISEASE ACROSS ORGAN SYSTEMS

Kidneys

- **(Micro-) albuminuria**
- **Proteinuria (>300 mg/day)**
- **GFR decrease (GFR <60 mL/min/1.73 m²)**
- Oedemas in the hands and feet
  → Note relationship between leg oedema and protein excretion
- Parapelvic renal cysts
- Progressive renal failure
- Dialysis
- Rare: renal tubular acidosis and nephrogenic diabetes insipidus

Eyes

- **Cornea verticillata**
- **Fabry cataract**
- Corneal opacity
- Vascular anomalies of the conjunctiva
- Vascular tortuosity of the retina
- Optic neuropathy with visual field loss

Ears

- Hearing loss (often high frequencies)
- Tinnitus
- Dizziness

Heart

- **Cardiomyopathy/ left ventricular hypertrophy** (without/ mild hypertension)
- Myocardial infarction
- Congestive heart failure
- Intramyocardial fibrosis
- Cardiac arrhythmia
- Valvular disorder (mitral valve, aortic valve)
- Dyspnoea

Skin

- **Angiokeratomas**
- **Dyshidrosis**
- Telangiectasias

Quality of Life

- **Reduced physical capacity**
- Psychological problems
- Fatigue
- Pain

Differential Diagnosis

- Cryptogenic stroke
- Multiple sclerosis
- Dermatomyositis
- Ataxia, dysarthria
- Atherosclerosis
- Mitochondriopathy
- Vasculitis
- Neuropsychological disorders
- Ménière's disease
- Optic neuritis
- Osler's disease
- Cerebral vasculitis
- CADASIL syndrome
- Restless legs syndrome

CADASIL, cerebral autosomal dominant arteriopathy with subcortical infarcts and leucoencephalopathy; GFR, glomerular filtration rate.

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