CHECKLIST: FABRY DISEASE?

FOCUS ON PAEDIATRICS

COULD IT BE FABRY DISEASE? Focus on Paediatrics

Symptoms/Findings

- ☐ **Acroparaesthesia** → Burning pain in hands and feet
- ☐ **Gastrointestinal discomfort**
- ☐ **Small fibre neuropathy**
- ☐ **Pain crisis** triggered by exercise, stress, temperature change/ fever
- ☐ **Heat intolerance**
- ☐ **Dyshidrosis** (hypohidrosis, rarely hyperhidrosis)
- ☐ **Cornea verticillata**
- ☐ Chronic pain in the extremities
- ☐ Tortuous vessels along the rim of the eye
- ☐ Angiokeratomas
- ☐ Proteinuria (>300 mg/day)
- ☐ Renal cysts
- ☐ Elevated cystatin C levels
- ☐ Tinnitus/hearing loss
- ☐ Lethargy/tiredness

Diagnostics

- ☐ Medical history/family tree/clinical examination
- ☐ Paediatric questionnaire on pain and quality of life
- ☐ Questioning on sweating levels, temperature intolerance
- ☐ ECG/24-hour ECG
- ☐ Renal function test: albuminuria/creatinine/ creatinine clearance/ GFR/protein → Serum analysis/ spontaneous urine/ 24-hour urine
- ☐ Slit lamp examination/ retroillumination/ retinal examination and photography
- ☐ Audiogram
- ☐ Cerebral MRI

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.

ECG, electrocardiogram; EDTA, ethylenediaminetetraacetic acid; GFR, glomerular filtration rate; lyso-Gb_3, globotriaosylsphingosine; MRI, magnetic resonance imaging.

SIGNS AND SYMPTOMS OF FABRY DISEASE ACROSS ORGAN SYSTEMS

Kidneys

- **(Micro-) albuminuria**
- **Proteinuria (>300 mg/day)**
- **GFR decrease**
- Rare: renal tubular acidosis and nephrogenic diabetes insipidus

Heart

- Impaired heart rate variability
- Arrhythmias
- ECG abnormalities (shortened PR interval)
- Mild valvular insufficiency

Eyes

- **Cornea verticillata**
- **Fabry cataract**
- Vascular anomalies of the conjunctiva
- Vascular tortuosity of the retina

Ears

- Tinnitis
- Hearing loss

Gastrointestinal

- **Abdominal pain, often after eating**
- **Diarrhoea**
- **Nausea**
- **Vomiting**
- **Bloating, early satiety**
- **Failure to gain weight**

Quality of Life

- **Poor physical, school, and social performance**
- Psychological problems
- Fatigue
- Pain

Nervous System

- **TIA, stroke**
- **Acroparaesthesia**
- **Small fibre neuropathy**
- **Pain crises**
- **Dyshidrosis**
- **Temperature intolerance**
- Depression/fatigue
- Reduced lacrimation and salivation

Differential Diagnosis

- Juvenile idiopathic or rheumatoid arthritis
- Rheumatic fever
- “Growing pains”
- Multiple sclerosis
- Irritable bowel syndrome

TIA, transient ischaemic attack.

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