CHECKLIST: FABRY DISEASE?

FOCUS ON PAIN MEDICINE
**COULD IT BE FABRY DISEASE? Focus on Pain Medicine**

<table>
<thead>
<tr>
<th>Symptoms/Findings</th>
<th>Diagnostics</th>
<th>Patient's Medical History</th>
<th>Fabry Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acroparaesthesia</td>
<td>Medical history/physical examination</td>
<td>Any signs of kidney failure such as uraemia or hypocalcaemia?</td>
<td>Dry blood test determining:</td>
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<td></td>
<td>Assessment of pain/quality of life using scales such as the BPI, WHO-5, MDI-10, SF-36 health survey</td>
<td></td>
<td>• The genetic mutation</td>
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<td></td>
<td>Electroneurography</td>
<td></td>
<td>• The level of α-galactosidase A (α-Gal A) activity</td>
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<td></td>
<td>“Bedside” tests such as thermal, vibration, and touch tests; QST</td>
<td></td>
<td>• The biomarker lyso-Gb₃</td>
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<tr>
<td>Small fibre neuropathy</td>
<td>Skin biopsy if necessary</td>
<td></td>
<td>and/or</td>
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<tr>
<td>Pain crisis triggered by exercise, stress, temperature change/fever</td>
<td>Questioning on sweating levels, temperature intolerance</td>
<td>Any signs of kidney failure such as uraemia or hypocalcaemia in relatives?</td>
<td>Molecular genetic/cytogenetic Fabry diagnosis from:</td>
</tr>
<tr>
<td>Temperature intolerance</td>
<td>MRI</td>
<td>Unexplained incidents of death in the family?</td>
<td>• EDTA blood test</td>
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<tr>
<td>Dyshidrosis (hypohidrosis, rarely hyperhidrosis)</td>
<td></td>
<td></td>
<td>• Serum</td>
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<td>Gastrointestinal discomfort</td>
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<td>• Buccal swab</td>
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<td>Fibromyalgia</td>
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<td>Cluster headache/migraine</td>
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<tr>
<td>Joint pain</td>
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</tbody>
</table>

**Fabry disease possible**

**Fabry disease probable**

**Family Medical History**

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

Unexplained incidents of death in the family?

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.

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BPI, Brief Pain Inventory; EDTA, ethylenediaminetetraacetic acid; lyso-Gb₃, globotriaosylsphingosine; MDI-10, 10-item Major Depression Inventory; MRI, magnetic resonance imaging; SF-36, Short-Form-36; QST, quantitative sensory testing; WHO-5, World Health Organization-5.
## Signs and Symptoms of Fabry Disease Across Organ Systems

<table>
<thead>
<tr>
<th>Kidneys</th>
<th>Eyes</th>
<th>Heart</th>
<th>Skin</th>
<th>Nervous System</th>
<th>Differential Diagnosis</th>
</tr>
</thead>
</table>
| • (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 | • Cornea verticillata  
• Fabry cataract  
• Corneal opacity  
• Vascular anomalies of the conjunctiva  
• Vascular tortuosity of the retina  
• Optic neuropathy with visual field loss | • Cardiomyopathy/ left ventricular hypertrophy  
(without/mild hypertension)  
• Myocardial infarction  
• Congestive heart failure  
• Intramyocardial fibrosis  
• Cardiac arrhythmia  
• Valvular disorder (mitral valve, aortic valve)  
• Dyspnoea | • Angiokeratomas  
• Dyshidrosis  
• Telangiectasias | • TIA, stroke  
• Basilar ectasia/ ectatic vessels (vertebrobasilar)  
• White matter lesions  
• Depression/fatigue  
• Reduced lacrimation and salivation | • Inflammatory rheumatic diseases  
• Rheumatoid arthritis  
• "Growing pains"  
• Vasculitis  
• Recurrent fever syndromes  
• Porphyria  
• Peripheral, focal, or multifocal neuropathy  
• Peripheral, generalised neuropathy  
• Uraemic neuropathy  
• Central neuropathy  
• "Mixed pain" syndromes  
• Neuropathy due to diabetes mellitus or alcohol abuse  
• Psychogenic pain |

### Ears
- • Hearing loss (often high frequencies)  
- • Tinnitus  
- • Dizziness

### Quality of Life
- • Reduced physical capacity  
- • Psychological problems  
- • Fatigue  
- • Pain

GFR, glomerular filtration rate; TIA, transient ischaemic attack.
References

Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften e.V. Guidelines Catalog No. 030/134. Interdisziplinäre Leitlinie für die Diagnose und Therapie des Morbus Fabry.


Salviati A, Burlina AP, Borsini W. Nervous system and Fabry disease, from symptoms to diagnosis: damage evaluation and follow-up in adult patients, enzyme replacement, and support therapy. Neural Sci. 2010;31(2):299-306.