



CHECKLIST: FABRY DISEASE?

**FOCUS ON
RHEUMATOLOGY**

COULD IT BE FABRY DISEASE? Focus on Rheumatology

Symptoms/Findings	Diagnostics		Patient's Medical History		Fabry Diagnosis	
<ul style="list-style-type: none"> <input type="checkbox"/> Acroparaesthesia → Burning pain in hands and feet <input type="checkbox"/> Small fibre neuropathy <input type="checkbox"/> Pain crisis triggered by exercise, stress, temperature change/fever <input type="checkbox"/> Joint pain <input type="checkbox"/> Elevated erythrocyte sedimentation rate 	<ul style="list-style-type: none"> <input type="checkbox"/> Medical history/physical examination <input type="checkbox"/> Assessment of pain/quality of life using scales such as BPI, WHO-5, MDI-10, SF-36 health survey <input type="checkbox"/> Electroneurography <input type="checkbox"/> “Bedside” tests such as thermal, vibration, and touch tests; QST <input type="checkbox"/> Skin biopsy if necessary <input type="checkbox"/> Questioning on sweating levels, temperature intolerance <input type="checkbox"/> Rheumatological laboratory diagnostics <input type="checkbox"/> Lack of response to therapy for rheumatic diseases 	<p>Fabry disease possible</p> <p>→</p>	<p>Any signs of kidney failure such as uraemia or hypocalcaemia?</p>	<p>Fabry disease probable</p> <p>→</p>	<p>Dry blood test determining:</p> <ul style="list-style-type: none"> • The genetic mutation • The level of α-galactosidase A (α-Gal A) activity • The biomarker lyso-Gb₃ <p>and/or</p> <p>Molecular genetic/cytogenetic Fabry diagnosis from:</p> <ul style="list-style-type: none"> • EDTA blood test • Serum • Buccal swab 	<p>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.</p> <p>Note: this listing of symptoms/findings and diagnostic tests may not be all-inclusive.</p>
			<p>Family Medical History</p> <p>Any signs of kidney failure such as uraemia or hypocalcaemia in relatives?</p> <p>Unexplained incidents of death in the family?</p>			



BPI, Brief Pain Inventory; EDTA, ethylenediaminetetraacetic acid; lyso-Gb₃, globotriaosylsphingosine; MDI-10, 10-item Major Depression Inventory; QST, quantitative sensory testing; SF-36, Short-Form-36; WHO-5, World Health Organization-5.

SIGNS AND SYMPTOMS OF FABRY DISEASE ACROSS ORGAN SYSTEMS

Kidneys	Eyes	Heart	Skin	Nervous System	Differential Diagnosis
<ul style="list-style-type: none"> • (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 	<ul style="list-style-type: none"> • Cornea verticillata • Fabry cataract • Corneal opacity • Vascular anomalies of the conjunctiva • Vascular tortuosity of the retina • Optic neuropathy with visual field loss 	<ul style="list-style-type: none"> • Cardiomyopathy/left ventricular hypertrophy (without/mild hypertension) • Myocardial infarction • Congestive heart failure • Intramyocardial fibrosis • Cardiac arrhythmia • Valvular disorder (mitral valve, aortic valve) • Dyspnoea 	<ul style="list-style-type: none"> • Angiokeratomas • Dyshidrosis • Telangiectasias 	<ul style="list-style-type: none"> • TIA, stroke • Acroparaesthesia → Burning pain in hands and feet • Small fibre neuropathy • Pain crises • Dyshidrosis • Temperature intolerance • Gastrointestinal discomfort • Basilar ectasia/ectatic vessels (vertebrobasilar) • White matter lesions • Depression/fatigue • Headaches • Reduced lacrimation and salivation 	<ul style="list-style-type: none"> • Inflammatory rheumatic diseases • Rheumatoid arthritis • Rheumatic fever • Amyloidosis • Vasculitis • Raynaud's syndrome • Sjögren's syndrome • Multiple sclerosis
	<p>Ears</p> <ul style="list-style-type: none"> • Hearing loss (often high frequencies) • Tinnitus • Dizziness 		<p>Quality of Life</p> <ul style="list-style-type: none"> • 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.
- Burlina AP, Sims KB, Politei JM, et al. Early diagnosis of peripheral nervous system involvement in Fabry disease and treatment of neuropathic pain: the report of an expert panel. *BMC Neurol.* 2011;11:61.
- Eng CM, Germain DP, Banikazemi M, et al. Fabry disease: guidelines for the evaluation and management of multi-organ system involvement. *Genet Med.* 2006;8(9):539-548.
- Gal A, Hughes DA, Winchester B. Toward a consensus in the laboratory diagnostics of Fabry disease – recommendations of a European expert group. *J Inherit Metab Dis.* 2011;34(2):509-514.
- Germain DP. Fabry disease. *Orphanet J Rare Dis.* 2010;5:30.
- Haas S, Lampl C. Morbus Fabry – Neurologische Klinik und Möglichkeiten der Therapie. *J Neurol Neurochir Psychiatr.* 2004;5(1):40-43.
- Hajas A, Grubits J, Varga Z. Neurophysiologic examinations in patients with Fabry-Anderson disease. *Clin Ther.* 2012;14(4 suppl):e19-e20.
- Hoffmann B, Mayatepek E. Fabry disease – often seen, seldom diagnosed. *Dtsch Arztebl Int.* 2009;106(26):440-447.
- James RA, Singh-Grewal D, Lee S-J, McGill J, Adib N. Lysosomal storage disorders: a review of the musculoskeletal features. *J Paed Child Health.* 2016;52(3):262-271.
- Parchoux B, Guibaud P, Maire I, et al. Fabry's disease. Initial nephrogenic diabetes insipidus in children. *Pediatrics.* 1978;33(8):757-765. [French]
- Pisani A, Petruzzelli Annichiarico L, Pellegrino A, et al. Parapelvic cysts, a distinguishing feature of renal Fabry disease. *Nephrol Dial Transplant.* 2017 March 28. (ePub ahead of print)
- Politei JM, Bouhassira D, Germain DP, et al. Pain in Fabry disease: practical recommendations for diagnosis and treatment. *CNS Neurosci Ther.* 2016;22(7):568-576.
- Politei J, Remondino G, Heguilen R, Wallace E, Durand C, Schenone A. When arthralgia is not arthritis. *Eur J Rheumatol.* 2016;3(4):182-184.
- Sack KE. When vasculitis is not vasculitis. *Hosp Practice.* 1993;28(7):94-103.