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The path from detection to personalized long-term care for Fabry disease

Practice aid for the management of people living with Fabry disease

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Importance of early recognition of Fabry disease and its multisystem manifestations

Timeline of manifestations in hemizygous male patients[1,2]

~Age of onset		
1st decade onwards	Angiokeratomas, hypohidrosis	• Exercise intolerance
	Gastrointestinal symptoms	• Diarrhoea • Abdominal pain
	Pain, febrile crises	• Exercise intolerance • Socioeconomic impacts, depression
2nd decade onwards	Proteinuria, renal failure	• Haemodialysis
	Cardiomyopathy	• Dyspnoea • Palpitations, angina
3rd decade onwards	Stroke	• Tinnitus, vertigo • Stroke sequelae

Phenotypic variation in Fabry disease

More than one disease?

Clinical[1]
- Age of onset
- Affected organs

Genetic[2]
- Spectrum of phenotypic variants
  benign polymorphisms, variants of unknown significance, pathogenic variants

Biochemical[3,4]
- Levels of lyso-Gb_3
- Residual α-Gal A activity

Considerations for individualized treatment and monitoring

Treatment[5]

Patient with confirmed Fabry disease diagnosis

Identify genotype and refer for HEK amenability assay

Fabry gene mutation type

Discuss options with patients and family/caregivers

Not amenable

- ERT
  - Agalsidase alfa
  - Agalsidase beta
  - Pegunigalsidase alfa

Amenable

Absolute ↑ α-Gal A activity ≥3.0% of wild-type and relative ↑ ≥1.2-fold over baseline

- OCT
  - Migalastat
- ERT

Currently available ERTs are associated with infusion-site reactions and development of anti-drug antibodies[6]

Monitoring[2,5,7]

Management and monitoring of Fabry-related symptoms, organ involvement and effects on QoL require effective interdisciplinary collaboration[5]

Patient needs

- Cardiac
- Pain
- Renal
- Gastrointestinal
- Neurological
- Mental health

Emerging role of telemedicine may:[7]

- Support home-based management and patient preferences
- Reduce travel burden and costs
- Improve access to care

Pathology

- Lyso-Gb_3
- α-Gal A activity

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Recommendations for monitoring organ involvement in adults are available[2]

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Abbreviations and references

Abbreviations

α-Gal A, alpha-galactosidase A; ERT, enzyme replacement therapy; HEK, human embryo kidney; lyso-Gb_3, globotriaosylsphingosine; OCT, oral chaperone therapy; QoL, quality of life.

References

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