Could your patient with unexplained heart disease have undiagnosed Fabry disease?

When to Rule Out Fabry

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to order a free screening test.

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Have you considered
Fabry disease as a possible cause?

Fabry disease is an X-linked lysosomal storage disorder, which can affect both men and women.[1]

A mutation of the α-galactosidase A (α-Gal A) gene on the X chromosome causes α-Gal A deficiency.[2]

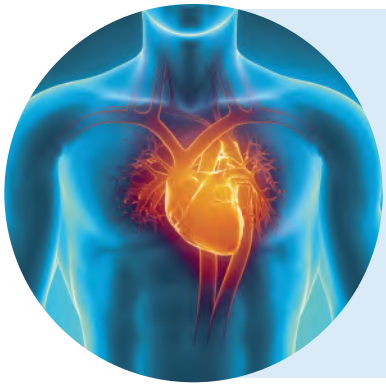
Deficiency in α-Gal A results in progressive accumulation of the glycolipid Gb3 in lysosomes, causing widespread organ damage and premature death.[3,4]

The heart
in Fabry disease

Cardiac involvement is common in Fabry disease, affecting 69% of male and 65% of female patients.[4] Cardiac disease is the leading cause of death in Fabry disease.[5,6]

The prevalence of cardiac signs and symptoms increases with age in patients with Fabry disease.[7]

Of 42 patients enrolled in the Fabry Outcome Survey whose deaths were reported between 2001 and 2007, cardiac disease was the main cause of death (where known) in both male (34%) and female (57%) patients.[6]



Common cardiac manifestations include:[8,9]

> Left ventricular hypertrophy (LVH)
> Hypertrophic cardiomyopathy (HCM)
> Conduction defects
> Arrhythmias
> Valvular abnormalities
> Coronary artery disease
> Heart failure

There are two forms
of cardiac involvement in Fabry disease:

1 Classic

Cardiac manifestations occur alongside other signs and symptoms of Fabry disease.[4]

The predominant symptoms of cardiac involvement are dyspnea as a result of cardiac failure caused by LVH, chest pain, palpitations, and syncope, depending on the cardiac tissue involved.[10]

2 Cardiac variant

Manifestations are predominantely cardiac with residual levels of α-Gal A activity.[11,12]

Cardiac manifestations typically present later in life and are limited to the heart, usually as LVH.[5–7] LVH was reported to begin at a mean age of 28.7 years for men and 34.1 years for women.[6]

1/20–25*

patients with unexplained LVH† or HCM could have Fabry disease[13,14]

LVH is a common
cardiac manifestation of Fabry disease[15]

The international Fabry Outcome Survey of untreated patients observed LVH in:

53%
of males
(mean age of 45 years)[7]

33%
of females
(mean age of 54 years)[7]

Fabry disease
and earlier diagnosis

Fabry disease presents a diagnostic challenge that can be attributed to two main factors:

1 It is rare, affecting approximately 1 in 40,000 males[16] and 1 in 20,000 females.[17]

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1 in 20,000[17]

2 The clinical presentation of Fabry disease is phenotypically heterogeneous: organ involvement can range from a classic clinical picture with multiple organ manifestations to an isolated organ being affected, e.g. the heart.[18]

An analysis of Fabry disease patients revealed that over 25% were initially misdiagnosed, with a mean time of over 13 years‡ between onset of symptoms and diagnosis.[4]

*The prevalence of Fabry disease was 4% (1 in 25) in a cohort of men (N=100) with unexplained LVH[13] and 5% (1 in 20) in a cohort of patients (N=141) with unexplained HCM[14]
†Unexplained = not caused by hypertension/valve disease, etc. Sarcomeric causes were excluded.
‡Mean delay was 13.7 years in males and 16.3 years in females.[4]

Could your HCM patient
have Fabry disease?

Fabry disease is common among patients with LVH, and studies have estimated that 3%–12% of patients with unexplained LVH have Fabry disease.[11,16,19]

Fabry disease should therefore be considered in patients with unexplained LVH, such as those without hypertension or aortic valve pathologies, or in patients with LVH considered disproportionate with treatment-controlled hypertension.[15]

Patients > 30 years of age with LV wall thickness > 12 mm (males) or > 11 mm (females)[15,20–23]

NO

Patient presents with other cardiac signs and symptoms (arrhythmias, angina, valvular abnormalities, or dyspnea), and one or more of the following:[7,15,21,24–33]

- History of stroke/transient ischemic attack < 55 years of age[34]
- Reduced eGFR or proteinuria[15]
- Neuropathic pain, most common in extremities (acroparesthesia)[15,22]
- Family member(s) with end-stage renal disease by the age of 50 years or who died of kidney failure, heart failure, stroke, or sudden cardiac death by the age of 60 years.[15]

YES

YES

Test for Fabry disease

What to do next if you suspect that your patient has Fabry disease:
RULE OUT FABRY.

Refer to your local metabolic/genetics clinic or treatment centre for a comprehensive assessment and/or to order a free screening test.

For more information on Fabry disease and available patient resources, please visit the Canadian Fabry Association at: **www.fabrycanada.com**.

To order your free Fabry disease screening test, visit **dbskit.ca** or contact your local Takeda representative.

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