

A puzzling case of left ventricular hypertrophy in an elderly man

Shing Ching[✉], Karl Chan

Division of Cardiology, Department of Medicine and Geriatrics, United Christian Hospital, Hong Kong, China

✉ Correspondence to: aj12029@yahoo.com.hk

<https://doi.org/10.26599/1671-5411.2026.08.003>

Diagnosing the cause of left ventricular hypertrophy (LVH) can take a serpiginous route in the geriatric patient. The effects of aging and comorbidities may mask pathognomonic findings that are otherwise recognized in the younger population. We describe a case of late-onset Fabry disease in an elderly man with cardiac and myopathic manifestation.

An 80-year-old man was evaluated for progressive proximal muscle weakness and heart failure for two years. Medical history was significant for permanent atrial fibrillation, hypertension, well-controlled diabetes mellitus and stage 2 chronic kidney disease. He required assistance in ambulation due to leg weakness. He had persistently elevated creatine kinase around 1000 U/L (reference: < 440 U/L). Muscle biopsy did not yield adequate tissue. Myositis autoantibodies and a metabolic panel of inborn errors of metabolism was unrevealing. Nerve conduction study showed sensorimotor axonal neuropathy. Nerve biopsy found amyloid deposition but no lambda/ kappa restriction. Serum electrophoresis showed monoclonal band. Bone marrow examination found no evidence of plasma cell malignancy. Plasma variant transthyretin protein was not identified. Genetic panel for hereditary amyloidosis was negative. Pyrophosphate scan was not suggestive of transthyretin amyloidosis.

The electrocardiogram showed atrial fibrillation, lateral Q wave in leads I and aVL, and pseudo-delta wave in V5 & V6 (Figure 1). Transthoracic echocardiogram found left ventricular ejection fraction of 60%, moderate concentric LVH and mild pulmonary hypertension. Genetic panel for hereditary myopathy and kidney disease, which included the gene of *alpha-galactosidase A* (GLA), was negative.

Cardiac magnetic resonance (CMR) corroborated with the echocardiographic finding of concentric LVH (Figure 2A). Partial thickness infarct in the left circumflex territory was shown (Figure 2B). Fibrosis in the septum (Figure 2C) and the ba-

sal inferolateral segment (Figure 2D) was noted. Native T1 of the non-fibrotic part of the septum was 970 ms (local reference: 900–1035 ms). The patient was re-tested for Fabry disease biochemically. Serum GLA activity was depressed at 0.247 $\mu\text{mol/L/hr}$ (reference: > 1.2 $\mu\text{mol/L/hr}$); serum lyso-Gb3 level was elevated at 8.54 (reference: < 2.5). Targeted sequencing of the *GLA* gene revealed a hemizygous c.640-801 G>A (previously known as IVS4+919G>A) pathogenic mutation, confirming late-onset Fabry disease. Family screening was positive for the patient's younger brother with similar symptoms.

We presented a patient with the heart failure, unexplained LVH, proximal myopathy and amyloid neuropathy. Despite the presence of amyloid in peripheral nerves, no evidence of cardiac amyloidosis was found on pyrophosphate scan and CMR. Two observations point to glycogen storage disease as the unifying diagnosis. On the one hand, the pseudo-delta wave in electrocardiogram was unexpected in hypertrophic cardiomyopathy and amyloidosis, but is well reported in Fabry disease. On the other hand, the native myocardial T1 was below 1000 ms despite septal fibrosis, ageing and a remote myocardial infarct, all of which are associated with elevated T1.

The intracellular accumulation of lipids, which have very short T1, in Fabry disease reduces the myocardial T1. It is typically present before the onset of myocardial fibrosis, which elevates T1 back into the “normal” range in a phenomenon of “pseudo-normalization of T1”.^[1] In our patient, the apparently “normal” native myocardial T1 is attributed to the myocardial fibrosis “balancing out” the T1-lowering effect of intracellular lipids. Indeed, the myocardial T1 slowly increases with age.^[2] It is very unusual for patients in their 80 s to have T1 lower than 1000 ms at 1.5T. Although it would be desirable to have age-specific reference range of T1, T1 reference range is magnet-specific and not directly transferrable. The logistic challenge to establish age-specific reference ranges at

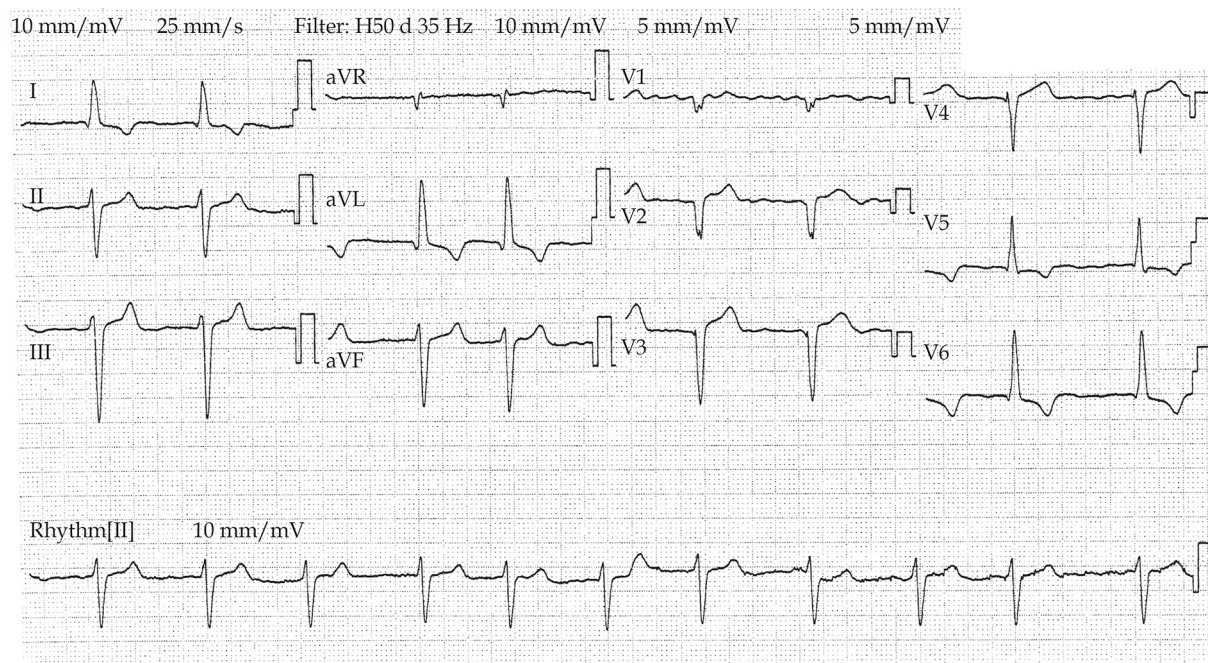


Figure 1 Electrocardiogram showed atrial fibrillation, lateral Q wave in leads I and aVL, and pseudo-delta wave in V5 & V6.

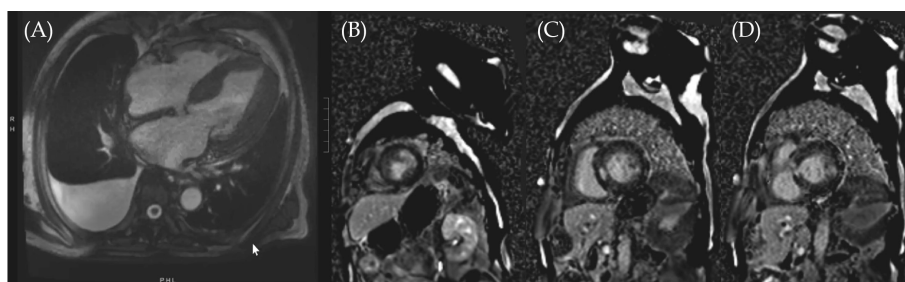


Figure 2 Cine four-chamber view in cardiac magnetic resonance showed concentric left ventricular hypertrophy and right pleural effusion (A); and late gadolinium enhancement showed subendocardial infarct in the left circumflex artery territory (B), fibrosis in the septum (C) and the basal inferolateral segment (D).

every center is overwhelming and impractical. Notwithstanding, interpretation of T1 should step beyond a simple dichotomization into “normal” and “abnormal”; it should take into account the patient’s age, comorbidities and the presence of myocardial substrates that favor fibrosis.

The genetic basis of late-onset Fabry disease is variable. Genetic panels cover common mutations that are implicated in classic Fabry disease, but may overlook less frequent ones. For example, our patient, despite a negative genetic panel including the *GLA* gene, harbored the c.640-801G>A mutation, which is implicated in most cases of late-onset Fabry disease in southern China, Japan and southeast Asia, presumably due to a founder effect originating in China around 800 years ago.^[3] Cardiac manifestation is prominent with this mutation. Unlike mutations in classic Fabry disease affecting the exons, c. 640-801G>A falls in the introns causing alternative splicing of

messenger RNA^[4] and reduced, but not absent expression of *GLA*. Carriers of this mutation have lower levels of lysoGb3, accounting for the late-onset phenotype. Due to the complex mutation landscape, testing the *GLA* activity in men and lysoGb3 level in women should be starting point to diagnose Fabry disease instead of genetic panels.

In summary, we presented a case of very late-onset cardiac variant of Fabry disease, and demonstrated the pitfalls of interpreting CMR parametric mapping and genetic panels.

ACKNOWLEDGMENTS

This research did not receive any specific grant from funding agencies. All authors had no conflicts of interest to disclose.



REFERENCES

- [1] Aida H, Nishikawa R, Yano T, *et al.* Pathological analysis of T1 pseudonormalization in the advanced stage of female Fabry cardiomyopathy. *Circ Heart Fail* 2025; 18: e012234.
- [2] Corpataux N, Haider A, Fuentes Artiles R, *et al.* Effect of age and sex on cardiac magnetic resonance native T1 mapping and synthetic extracellular volume. *Int J Cardiol* 2026; 442: 133818.
- [3] Liang KH, Lu YH, Niu CW, *et al.* The Fabry disease-causing mutation, GLA IVS4+919G>A, originated in Mainland China more than 800 years ago. *J Hum Genet* 2020; 65: 619–625.
- [4] Chang WH, Niu DM, Lu CY, *et al.* Modulation the alternative splicing of GLA (IVS4+919G>A) in Fabry disease. *PLoS One* 2017; 12: e0175929.

Please cite this article as: Chi S, Chan K. A puzzling case of left ventricular hypertrophy in an elderly man. *J Geriatr Cardiol* 2026; 23(8): 529–531. DOI: 10.26599/1671-5411.2026.08.003

