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IMAGING VIGNETTE

Many Faces of Fabry Cardiomyopathy

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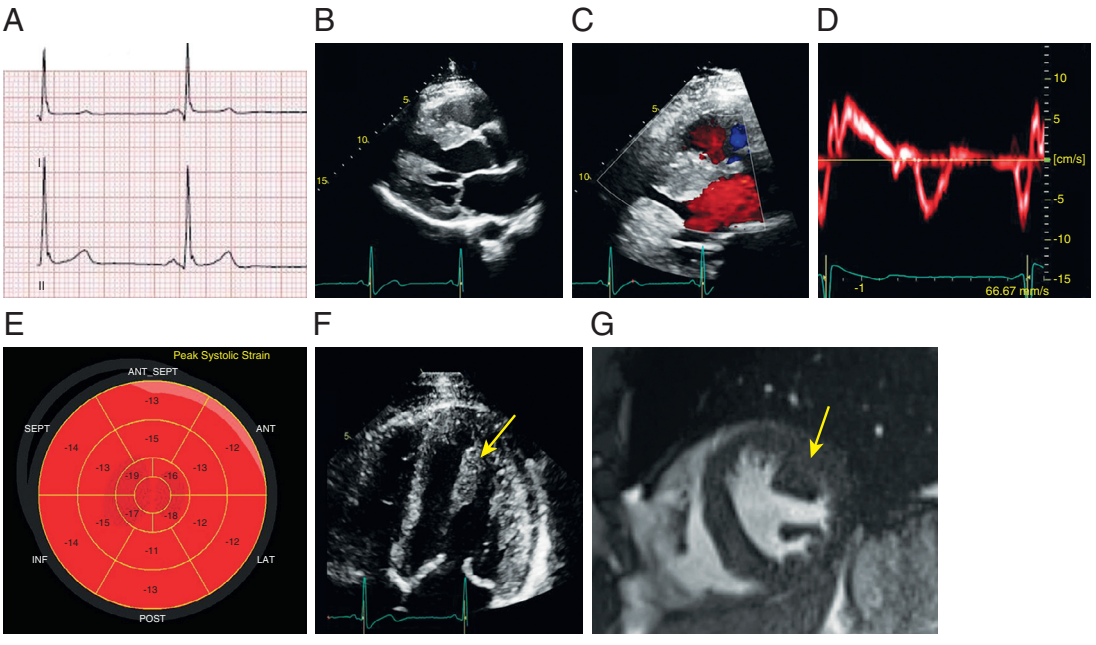
ANDERSON-FABRY DISEASE, AN X-LINKED INHERITED DEFICIENCY OF ALPHA-GALACTOSIDASE A (*GLA* gene) with a birth frequency of 1 in 100,000, results in systemic sphingolipid accumulation with characteristic clinical findings. The predominant causes of significant morbidity and mortality are renal, cerebrovascular, and cardiac.

FIGURE 1 Fabry Cardiomyopathy Presenting as Hypertrophic Nonobstructive Phenotype



On electrocardiography, this 45-year-old man demonstrated a short PR interval (132 ms)–characteristic of Fabry disease—and left ventricular hypertrophy **(A)**. Transthoracic echocardiography demonstrated hypertrophic nonobstructive cardiomyopathy; maximum septal wall thickness was 20 mm **(B)**. No left ventricular outflow gradient was present at rest **(C),** during Valsalva maneuver, or during amyl nitrite inhalation. The patient had diastolic dysfunction (grade II); septal e′ measured 7.6 cm/s **(D).** Global longitudinal strain **(E)** was reduced (–14.3%) with preserved left ventricular ejection fraction (61%). Note the hypertrophic papillary muscle **(arrows)** and that the anterior papillary muscle measures 2.1 cm and is more hypertrophic than the posterior papillary muscle; apical displacement of papillary muscles is seen on echocardiography **(F)** and cardiac magnetic resonance **(G)**. Hypertrophied papillary muscles are characteristic of Fabry disease compared with other hypertrophic cardiomyopathy phenotypes (1). No delayed enhancement of gadolinium, which would suggest myocardial fibrosis, was noted. ANT = anterior; ANT_SEPT = anteroseptal; INF = inferior; LAT = lateral; POST = posterior; SEPT = septal.

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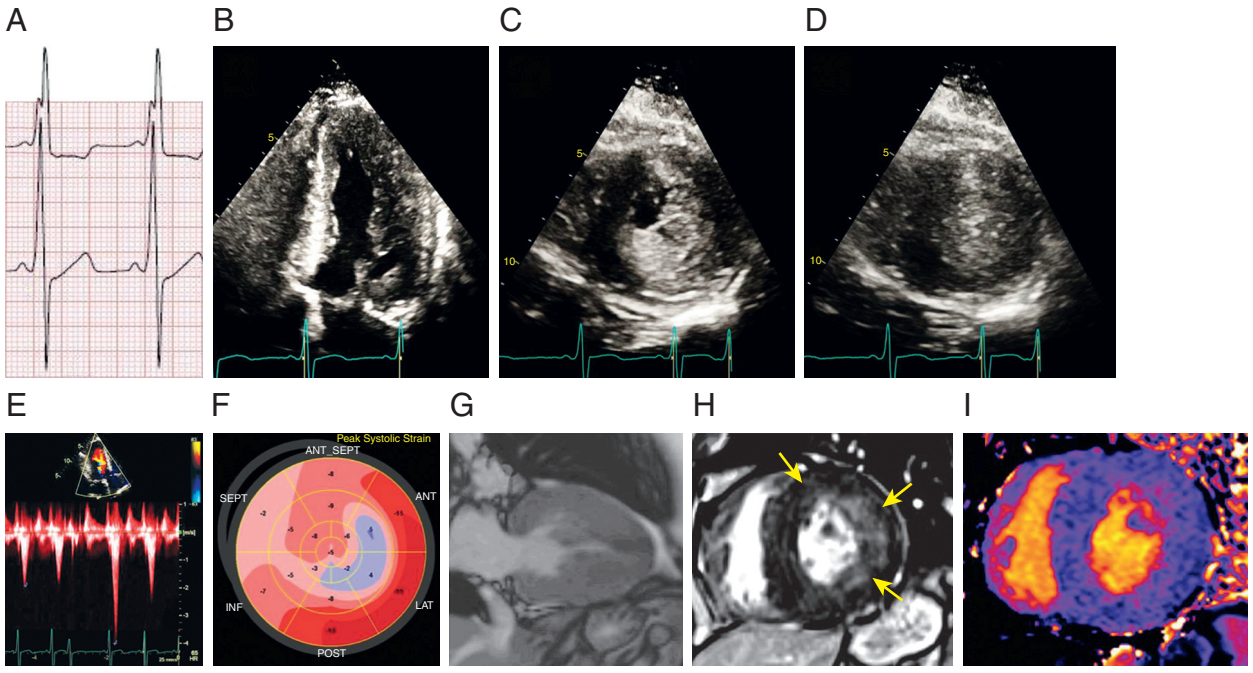
FIGURE 2 Fabry Cardiomyopathy Presenting as Apical-Septal Hypertrophic Phenotype With Midventricular Obstruction



This 61-year-old woman demonstrated a short PR interval (138 ms) and left ventricular hypertrophy on electrocardiogram **(A)**. Transthoracic echocardiography showed the phenotypic appearance of apical hypertrophic cardiomyopathy **(B)**, with severe apical thickening in diastole **(C)** and apical obliteration in systole **(D)**. Midventricular obstruction was present: 15 mm Hg (rest); 65 mm Hg (beat after premature ventricular contraction) **(E)**. Diastolic dysfunction was noted, and global longitudinal strain was abnormal (-7.0%) **(F)**. Cardiac magnetic resonance demonstrated apical thickening **(G)** and delayed gadolinium enhancement in a patchy distribution **(arrows, H)**. Due to the lack of alpha-galactosidase enzyme, excess glycosphingolipids deposit in the myocardium **(I)**. Fat has a lower T_1 value, leading to a shortening of T_1 relaxation; in this patient, the mean T_1 value was 859 ms (our laboratory's abnormal T_1 relaxation time is <920 ms). T_1 mapping can be assessed without administration of gadolinium contrast, which is attractive in patients who often have coexisting renal insufficiency. An apical aneurysm phenotype also has been reported (Patient #5 in Table 1) (2). Abbreviations as in Figure 1.

Cardiac involvement in the disease phenotypically mimics hypertrophic cardiomyopathy, commonly presenting in the echocardiography laboratory as a male patient with concentric left ventricular hypertrophy. However, as we describe, the spectrum of Fabry cardiomyopathy encompasses all hypertrophic cardiomyopathy phenotypes. Also, due to selective X-inactivation, both sexes can be severely affected—women are not merely genetic "carriers."

Certain imaging features are more likely to be seen in Fabry disease than other hypertrophic cardiomyopathy phenotypes. In this case series (Figures 1 to 4, Table 1), we highlight the characteristic findings on multimodality imaging that heighten the probability of a diagnosis of Fabry cardiomyopathy—the echocardiographic, electrocardiographic, and cardiac magnetic resonance findings that are unique to the disease.