Ventricular tachycardia revealing an Anderson– Fabry disease , a rare case report

Abstract :

Background

Anderson–Fabry disease is the second most frequent lysosomal storage disorder. It is an inherited rare metabolic disease caused by mutation in the GLA gene, encoding lysosomal enzyme alpha-galactosidase A. The disorder is a systemic disease that manifests as cerebrovascular and cardiac disease, chronic renal failure, skin lesion, peripheral neuropathy, and other abnormalities. Ventricular tachycardia as a Fabry disease presentation is very rare.

Keywords. Fabry disease • Hypertrophic cardiomyopathy • Ventricular tachycardia • Alpha-galactosidase A • Metabolic disease

Introduction

Anderson–Fabry is a X-linked genetic disease secondary to alpha-galactosidase A enzyme deficiency. It is characterized by progressive accumulation of globotriaosylceramide (Gb3) in various organ systems and a wide variety of progressive signs and symptoms. Classical symptoms and organ involvements are acral pain crisis, cornea verticillata, hypertrophic cardiomyopathy, stroke and chronic kidney disease with proteinuria. Nevertheless, organ damages can be missing or pauci-symptomatic and other common symptoms are poorly recognised, such as gastrointestinal or ear involvement. In classical Fabry disease, symptoms first appear during childhood or teenage in males, but later in females. Patients may have non-classical or late-onset Fabry disease with delayed manifestations or with single-organ involvement. Recognition of Fabry disease is important because treatments are available, but it may be challenging. We present a case of unusual cardiac manifestation of Fabry disease.

Case presentation

A 42-year-old man non-smoker, with no past medical history and no regular medication self-presented complaining of sudden episodes of shortness of breath at rest together with unexplainable malaise in the previous 4 months. He reported no episodes of chest pain under any circumstances. On physical examination, he had a regular pulse, with a blood pressure of 150/70 mmHg. The oxygen saturation was 100%. His chest was clear on auscultation. There was no peripheral oedema present. A 12-lead electrocardiogram (ECG) showed sinus rhythm at a rate of 75 b.p.m, There was concave ST segment elevation in leads V1 and V2 and T wave was biphasic in lead III. The precordial leads suggested left ventricular hypertrophy (LVH) according to the Sokolow-Lyon criteria. This ECG prompted a decision to transfer him immediately to a hospital under the suspicion of acute coronary syndrome without ST elevation. Whilst awaiting transport,

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he experienced acute onset of dyspnoea together with non-specific chest heaviness. A repeat ECG showed ventricular tachycardia transforming to ventricular fibrillation. The patient was successfully defibrillated. Coronary angiography was performed upon arrival at the hospital and demonstrated unobstructed coronary arteries.Transthoracic echocardiography revealed concentric left ventricular hypertrophy (LVH) and normal systolic function, with severe diastolic dysfunction. Magnetic resonance imaging (MRI) confirmed the LVH, and did not demonstrate any late gadolinium enhancement. Biochemistry revealed acute on chronic kidney failure (creatinine at 35 g/L , GFR of 17mls/min) . The rest of the biochemistry was within the normal range.The patient stayed on the coronary care unit for 72 h, and then transferred to a monitored bed on the standard cardiology ward. He had no further episodes of ventricular tachycardia during the hospital stay. He was administered bisoprolol 2.5 mg per day and ramipril 2.5 mg per day. The indication for an implantable cardioverter-defibrillator (ICD) therapy was discussed. A cardiac magnetic resonance imaging (MRI) study confirmed the LVH, and did not demonstrate any late gadolinium enhancement. Within the differential diagnoses, we considered Fabry disease as a possible cause of concentric ventricular hypertrophy although the patient had no classical pain symptoms (acroparaesthesia and abdominal pain) or specific signs such as skin changes (angiokeratomas in lower abdomen, groin, gluteal regions, and anhidrosis). The screening dried blood spot test was positive for Fabry disease, confirmed by low plasma activity of alpha-galactosidase A. Genetic counseling and family screening have been offered to the patient and his relatives.

Discussion

Fabry disease is an inherited rare metabolic disease caused by mutation in the GLA gene, encoding lysosomal enzyme alphagalactosidase A. This enzymatic defect results in excessive accumulation of neutral glycosphingolipids in the cellular lysosomes(1).The disorder is a systemic disease that manifests as cerebrovascular and cardiac disease, chronic renal failure, skin lesion, peripheral neuropathy, and other abnormalities (2). Dominant presentations in adulthood are those of renal (chronic kidney disease) followed by cardiac involvement (arrhythmias, heart failure with preserved ejection fraction)(3) and neurologic manifestations (stroke)(4). A ‘variant phenotype’ of Fabry disease is related to patients with reduced alpha-Galactosidase A activity leading to a later onset of the manifestation of renal or cardiac symptoms.

The cardiac presentation of Fabry disease is considered common in the literature. But if cardiac presentation would be defined as the first and the only clinical manifestation of Fabry disease, then there have been only a limited number of reported clinical cases or case series. The exceptions are the cohort studies from international registers established upon the arrival of enzyme replacement therapy. The international Fabry outcome survey(5) reported no patient with exclusively cardiac involvement among 714 patients. The leading symptoms were dyspnoea (23%) and chest pain (22%). The dominant clinical sign of cardiac involvement is LVH. Unexplained LVH serves as an important prompt to consider Fabry disease and if diagnosed to initiate enzyme replacement therapy. Tissue Doppler imaging was found to be able to detect myocardial impairment prior to manifest LVH in Fabry patients with causal mutations without

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LVH14 and in a larger cohort of patients with Fabry disease without LVH.(6) Cardiovascular magnetic resonance (CMR) plays a pivotal role in the non-invasive differential diagnosis of LVH and cardiomyopathy in general.(7) Typical late gadolinium enhancement (LGE) distribution in the inferolateral basal or mid-basal segments(8) low native T1 value,(9) and prolonged T2, particularly in areas of LGE are the hallmarks of Fabry disease on CMR. The amount of myocardial fibrosis assessed using CMR was found to be an independent predictor of incidence of malignant ventricular arrhythmias (non-sustained and sustained ventricular tachycardia, sudden cardiac death) in Fabry disease patients.(10) The clinical manifestation with a possible association to ventricular tachycardia is syncope, showing an incidence of only 3%. Unfortunately, this study does not report the number of patients with ICD therapy. In 2007, the Fabry Registry data reported a 9% incidence of arrhythmia in 2187 enrolled patients of which only 74 were reported to have congestive heart failure (3.4%). (11)Again, there are no data on the number of patients with ICD.

Conclusion Our case report would present one of a rare published case of sustained ventricular tachycardia as the sole manifestation of cardiac involvement of Fabry disease and illustrates the pivotal role of critical clinical thinking in the diagnosis of rare but treatable hereditary cardiomyopathy.

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