Right Ventricle Fatty Infiltration Evaluated by Cardiac-CT Scan in Anderson-Fabry's Disease, A Case Report

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Abstract

Introduction: Anderson Fabry Disease (AFD) is a metabolic storage disorder that leads to a multisystemic accumulation of glycosphingolipids. AFD cardiomyopathy presentation includes left ventricular hypertrophy, tachyarrhythmias and conduction disturbances. Right ventricle impairment is less common, probably underdiagnosed and its prognosis has been barely reported possibly due to technical limitations in cardiac magnetic resonance studies (CMR).

Case presentation: A patient with AFD presented with functional deterioration, moderate left ventricular systolic dysfunction and a new onset lateral segmentary defect. A cardiac CT scan was indicated to rule out significant coronary artery disease and showed myocardial fatty infiltration progression and right ventricle involvement that was not reported in previous cardiac magnetic resonance (CMR).

Conclusions: Although CMR is the gold standard technique to study AFD cardiomyopathy, in some selected cases cardiac CT scan could help to better evaluate disease progression, especially when RV is affected.

Introduction

Anderson Fabry Disease (AFD) is a metabolic storage disorder due to the deficiency of lysosomal α-galactosidase A leading to multisystemic accumulation of glycosphingolipids (1). Its prevalence is estimated at 1 in 40,000 to 170,000 population (2). While patients with the classic severe form of AFD disease have severely reduced or absent α-galactosidase activity leading to the full-blown syndrome, the later-onset cardiac phenotype of AFD usually shows moderately reduced α-galactosidase activity. AFD cardiomyopathy presentation includes LV hypertrophy, myocardial fibrosis, tachyarrhythmias and electrical conduction disturbances (3). RV involvement, mainly with hypertrophy or systolic dysfunction is less common (4) and its cardiovascular prognosis has been barely reported (5), mainly determined by concomitant renal involvement and LV hypertrophy.

Case Presentation

A 65-year-old woman presented with exertional dyspnea during the follow up of Anderson-Fabry's disease (AFD). The patient had a medical history characterized by hypertension, dyslipidemia, primary antiphospholipid syndrome, cutaneous lupus disease, hypothyroidism. She presented to an AFD with scarce angiokeratomas, cornea verticillata and neurosensory hypoacusia that was confirmed by genetic testing (*GLA* DNA variant: p.[I270T + =] (c.[809T>C + =]) and treated with enzyme replacement therapy after diagnosis in 2016 and replaced two years later with migalastat.

She had a hypertrophic cardiomyopathy phenotype with preserved left ventricular ejection fraction (LVEF) and diastolic dysfunction. She also had a permanent bicameral pacemaker from early 2019 due to an unexplained syncope and conduction disturbances that were confirmed on a pathological electrophysiological study. During follow-up the patient also presented paroxysmal atrial fibrillation.

Physical examination noted signs of congestive right heart failure with increased jugular vein engorgement, mild peripheral oedema and no pulmonary crackles. Bedside transthoracic echocardiography showed moderate systolic dysfunction (LVEF 41%) with a new segmentary defect on inferior and lateral basal segments (video 1) as well as left ventricle global longitudinal strain (GLS) (video 2) and free wall right ventricle strain deterioration (video 3).

The main differential diagnosis proposed after the clinical findings, the LVEF deterioration and the new onset segmentary defect were coronary artery disease, recent pulmonary embolism and progression of her cardiomyopathy since inferior and lateral basal segments are usually affected by globotriaosylsphingosine (Lyso-Gb_3) infiltration.

A cardiac CT scan was performed, ruling out significant coronary artery disease and pulmonary embolism. It confirmed an eccentric left ventricle (LV) myocardial hypertrophy (113 g/m^2) with bi-ventricular systolic dysfunction (LVEF 38% and RVEF 42%). A mesocardial hypodense area was noted in the basal inferolateral segment of the LV consistent with the segments previously described as hypokinetic by echocardiography and a previous CMR study (figure 1). Likewise, in the present CT scan a right ventricle (RV) free wall thickening and an extensive subendo-mesocardial hypodensity of the RV free wall, basal inferior segment and RV outflow tract were observed (figure 2a). Those hypodense segments had very low attenuation Hounsfield Units (HU), leading to the suspicion of fatty infiltration in those areas. No previous RV involvement was reported in the CRM performed one year before (figure 2b).

Since ischemic or thromboembolic triggers for the functional class deterioration were ruled out disease progression was the main diagnosis. CT scan findings also explained the new segmentary defect on inferior and lateral basal LV segments as well as LV global longitudinal strain (GLS) and RV free wall strain deterioration. During hospitalization she received intravenous diuretic treatment with good response and migalastat treatment was maintained.

Discussion

In this case we presented an AFD patient with an extensive fatty infiltration of the RV described in a cardiac CT that was performed to rule out coronary artery disease and pulmonary embolism. Although RV fatty infiltration has been observed in 1 out of 3 to 4 healthy subjects without RV dysfunction (6), association with depressed free wall strain as well as mild reduction of RVEF in the context of AFD suggests that this is a pathological finding.

CMR is the gold standard technique in AFD cardiomyopathy to study left ventricular mass, functional assessment, myocardial tissue and fibrosis characterization, the latter even in patients with only mild ventricular hypertrophy (7). Even so, RV tissue characterization with CMR has not been reported consistently even in series where right ventricular hypertrophy was specifically studied (8). This may be due to the fact that CMR has some limitations at describing fatty infiltration in the RV free wall due to low spatial resolution of LGE sequences, partial-volume effects, breathing/motion artifacts and suboptimal

time interval following the inversion pulse (TI) which can produce a black rim artifact darkening RV myocardium.

In addition to patients with contraindication for CMR, cardiac CT scan has some advantages at describing fatty infiltration compared to CMR: it is easier and faster to perform, has a submillimeter collimation and has less breathing artifacts and operator dependency. Although images are acquired only in the axial plane, the acquisition of a 3-dimensional dataset allows relocating in any desirable plane with a good tissue differentiation between fat and myocardium due to their different densities (-190 to -30 HU in fat tissue vs 20 to 50 HU in myocardium). In this case, the double rule-out CT protocol helped to delineate the RV wall better compared to the usual cardiac CT systemic arterial phase.

Conclusion

Although CMR is the gold standard technique to study AFD cardiomyopathy in some selected cases cardiac CT scan could help to evaluate disease progression, especially when RV is affected. RV myocardial infiltration may be underdiagnosed in CMR studies and its prognostic impact is unclear. Nowadays, new treatment options are changing the management of AFD and multimodality imaging may bring the opportunity to better define the prognosis of these patients in the future.

Declarations

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CONFLICT OF INTERESTS: On behalf of all authors, the corresponding author states that there is no conflict of interest.

ETHICS APPROVAL: The authors confirm this work has been approved by the local ethics committee

CONSENT TO PARTICIPATE AND PUBLICATION: The authors confirm that written consent for submission and publication of this case report including images and associated text has been obtained from the patient.

AVAILABILITY OF DATA: Not applicable

CODE AVAILABILITY: Not applicable

AUTHORS CONTRIBUTIONS: The authors confirm that have equally contribute to this work

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Figures

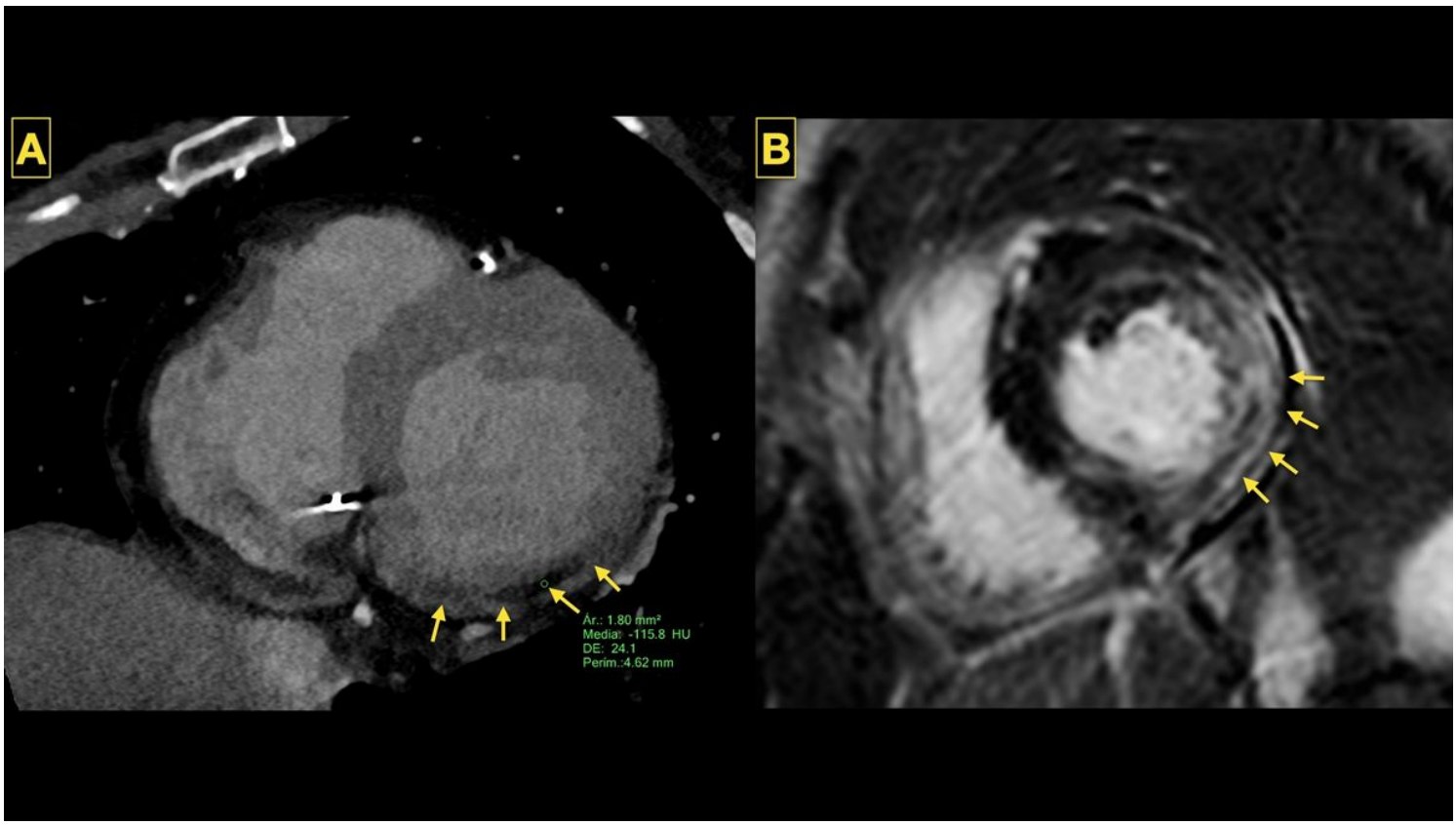

Figure 1

Short axis of LV showing mesocardial fatty infiltration in the LV inferolateral basal segment (see yellow arrows) in cardiac CT (2a) and previous CMR (2b).

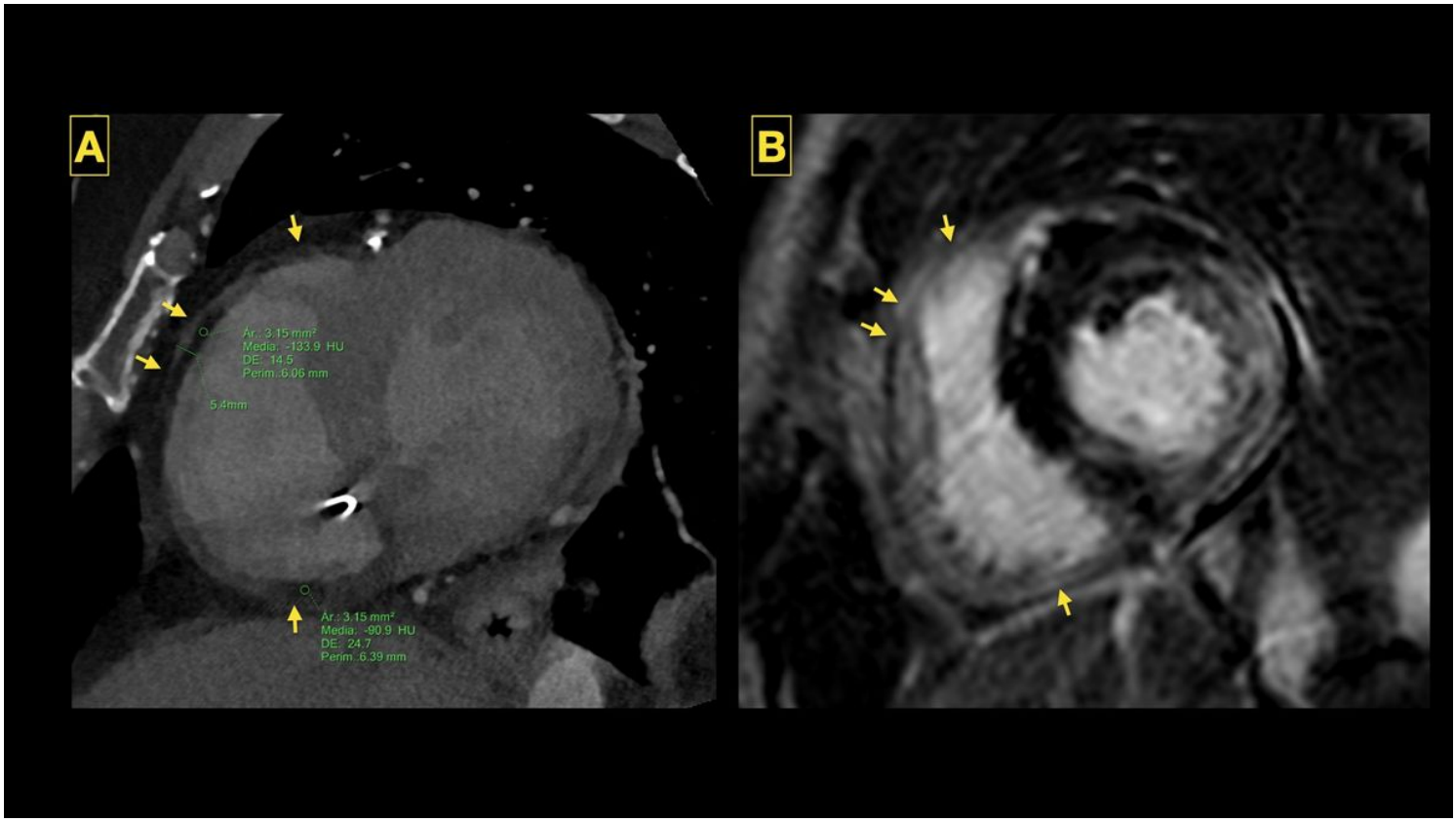

Figure 2

Short axis of RV showing subendo-mesocardial fatty infiltration in proximal outflow tract, free wall and basal inferior segment (see yellow arrows) in cardiac CT (2a) and previous CMR (2b).

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Carechecklist.pdf
- Video1.mp4
- Video2.mp4
- Video3.mp4