Case Report

Mucopolysaccharidoses IV and VI: Aspects in Two-dimensional Speckle-tracking Strain Echocardiogram Imaging in a Case Series

Mucopolissacaridoses IV e VI: Aspectos ao Ecocardiograma Bidimensional com Strain pelo Speckle Tracking em uma Série de Casos

João Vitor Tiveron Teodoro[1], Lavínia Ayumi Borges Ribeiro[1], José Marques Ferreira Neto[1], Vinícius Marques Ferreira[1], Carlos Henrique Paiva Grangeiro[1,2], Adriana de Nazaré Miziara Oliveira[1]

[1]Triângulo Mineiro Federal University, Uberaba, MG, Brazil; [2]Hospital Complex of the Federal University of Ceará, Fortaleza, CE, Brazil.

Introduction

Mucopolysaccharidosis (MPS) belongs to the group of lysosomal storage diseases associated with the partial or total deficiency of 11 different lysosomal hydrolases responsible for glycosaminoglycan (GAG) degradation[1]. GAG accumulation may affect the valves, myocardium, and coronary vessels. The forms that accumulate dermatan sulfate (MPS I, II, VI, and VII) are associated with valvular thickening (L > R). MPS is one of the most common causes of mitral annulus thickening in children. Cardiac involvement also includes hypertrophy, tendinous cord shortening, and papillary muscle thickening[2]. Echocardiography is an essential technique used to assess cardiac involvement in MPS. The study of myocardial strain using two-dimensional speckle-tracking echocardiography (2D-STE) provides a more sensitive evaluation of myocardial fiber strain that can reveal early and subclinical myocardial involvement regardless of left ventricular ejection fraction (LVEF) changes[3,4].

This case series reviews relevant echocardiographic aspects of cardiac involvement complemented by 2D-STE in three patients with MPS during outpatient follow-up and taking enzyme replacement therapy (ERT).

Case reports

Patient 1

A 25-year-old woman previously received the biochemical diagnosis of Morquio syndrome (MPS IVA) at 5 years of age due to her short stature and craniofacial dysmorphia. Her parents were consanguineous. At that time, she had a height of 111.5 cm, a weight of 23.6 kg, a body mass index of 18.6 kg/m^2, generalized joint laxity, valgus deformity in the knees, corneal opacity, horizontal nystagmus, tactile and painful glove hypoesthesia, and a mild mesocardial systolic murmur. Transthoracic echocardiography (TTE) revealed a thickened mitral valve and prolapse of the competent posterior cusp. There was also left atrial enlargement, signs of diastolic dysfunction with increased filling pressures (grade II), and aortic valve thickening without dysfunction. A small atrial septal defect (ASD) was observed in the middle third of the septum. The use of 2D-STE showed reduced shortening in the anterior wall and a normal global longitudinal strain (GLS). The patient had been treated with elosulfase alfa (Vimizim®) 2 mg/kg weekly for 6 years (Figure 1).

Patient 2

A 16-year-old female patient previously received the biochemical diagnosis of Maroteaux-Lamy syndrome (MPS VI) at 7 years of age due to craniofacial dysmorphia. At that time, the patient had a height of 110 cm, a weight of 27.4 kg, a body mass index of 22.6 kg/m^2, macrocephaly, infiltrated facies, exophthalmia, gingival hypertrophy, and joint restriction. TTE revealed left atrial enlargement, mild mitral reflux, mitral stenosis (valve area: 1.18 cm^2), a thickened tricuspid valve, a thickened aortic valve with mild insufficiency, and concentric left ventricular (LV) remodeling (relative thickness of 0.6, mass of 83 g/m^2) (Figure 2). The use of 2D-STE revealed reduced longitudinal shortening in the lower and inferolateral basal wall and anterior middle and anteroseptal segment but a normal GLS. The patient had received ERT consisting of galsulfase (Naglazyme®) 1 mg/kg weekly for 8 years.

Patient 3

A 13-year-old male patient previously received the biochemical diagnosis of Maroteaux-Lamy syndrome (MPS VI) at 2 years of age due to craniofacial dysmorphia. At that time, the patient had a height of 126 cm, a weight of 26.6 kg, a body mass index of 16.73 kg/m^2, macrocephaly, and joint stiffness. TTE revealed a thickened mitral valve, a reduced mitral valve opening, a mean gradient of 5 mmHg and maximum gradient of 11 mmHg, an estimated valvar area of 2.27 cm^2, mild reflux (mild double mitral valve lesion), and a thickened aortic valve without dysfunction (Figure 3). The use of 2D-STE showed reduced longitudinal shortening in the anterior wall and a preserved GLS. The patient had received ERT consisting of galsulfase (Naglazyme®) 1 mg/kg weekly for 11 years.

All patients were evaluated by the same echocardiographer. Good quality videos were made in three echocardiographic windows (four-, three-, and two- chamber). The exams were performed using Philips Affiniti 50 equipment. The 2D-STE GLS analysis was performed offline using QLAB software (Figure 4).

Keywords

Echocardiography; Echocardiography, Doppler; Mucopolysaccharidosis IV; Mucopolysaccharidosis VI; Rare diseases.

Mailing Address: João Vitor Tiveron Teodoro •
E-mail: jvitortiveron@gmail.com
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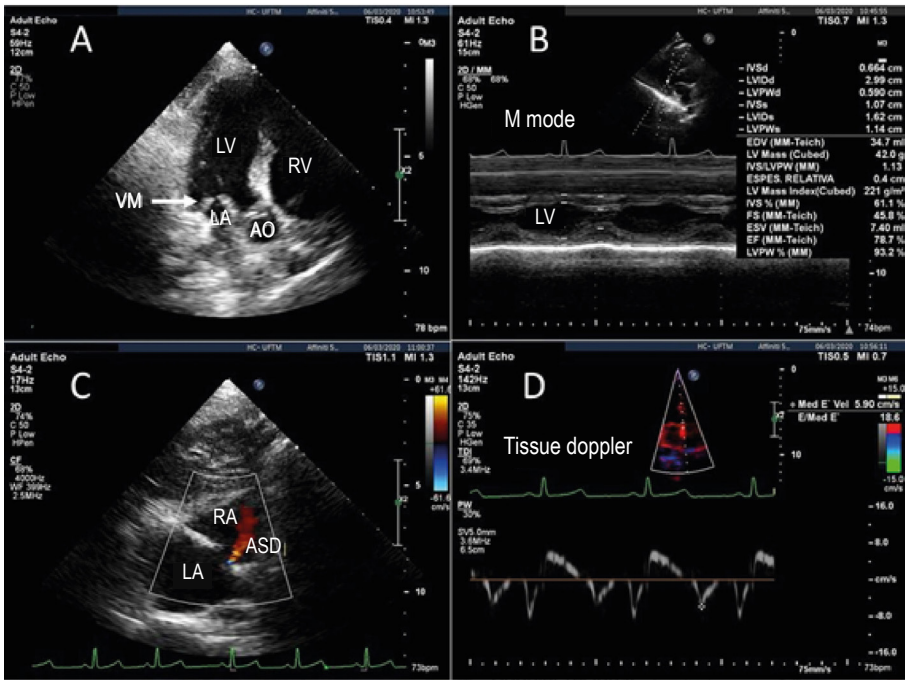
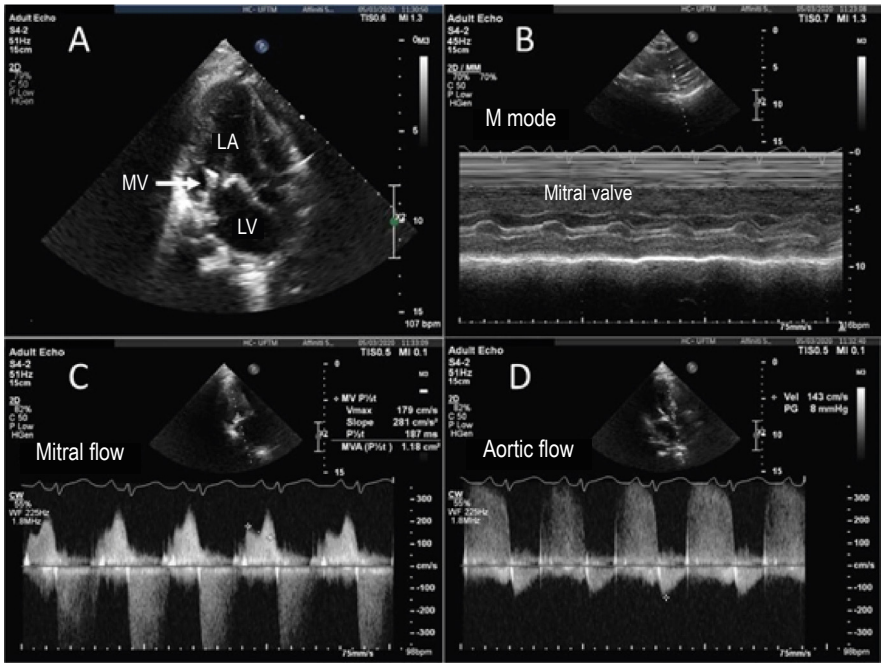


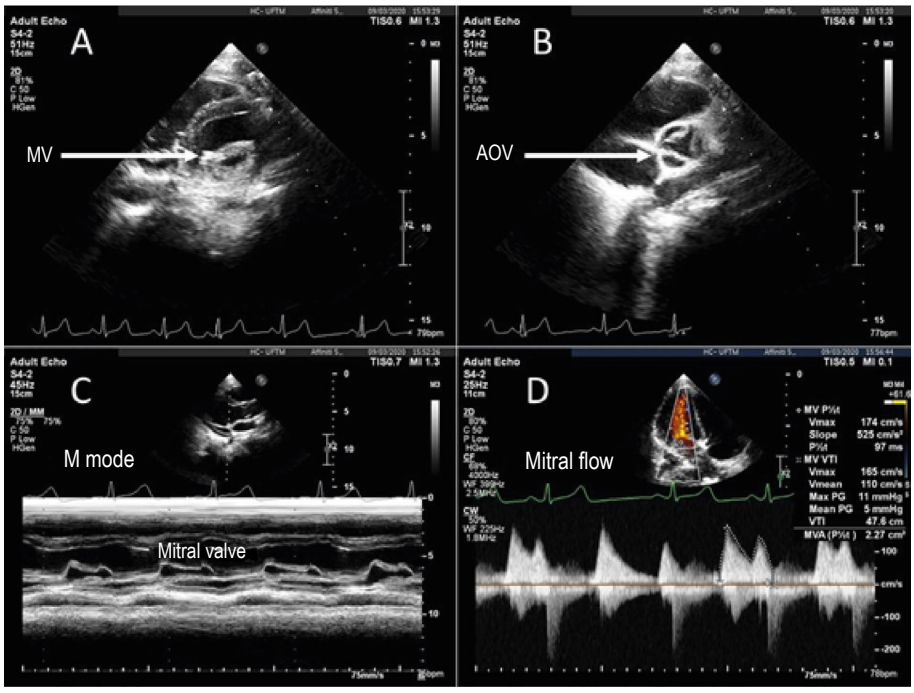
AO, aorta; ASD, atrial septal defect LA, left atrium; LV, left ventricle; MV, mitral valve; RA, right atrium; RV, right ventricle.

Figure 1 – *Echocardiogram of patient 1. (A) Five-chamber apical view showing mitral and aortic valve thickening. (B) M mode demonstrating preserved left ventricular systolic function. (C) Atrial septal defect with no repercussion. (D) Tissue Doppler showing increased left ventricular filling pressures with a decreased E-wave.*



LA, left atrium; LV, left ventricle; MV, mitral valve.

Figure 2 – *Echocardiogram of patient 2. (A) Tree-chamber apical view showing a thickened mitral valve. (B) M-mode showing a reduced mitral valve opening. (C) Continuous Doppler showing mitral valve stenosis and reflux. (D) Continuous Doppler showing aortic insufficiency.*



AOV, aortic valve; MV, mitral valve.

Figure 3 – *Echocardiogram of patient 3. (A) Transverse parasternal view showing thickening and a reduced mitral valve opening. (B) Transverse parasternal view of base vessels showing a thickened aortic valve. (C) M-mode showing thickening and a reduced mitral valve opening. (D) Continuous Doppler showing mitral valve insufficiency and an increased mean gradient.*

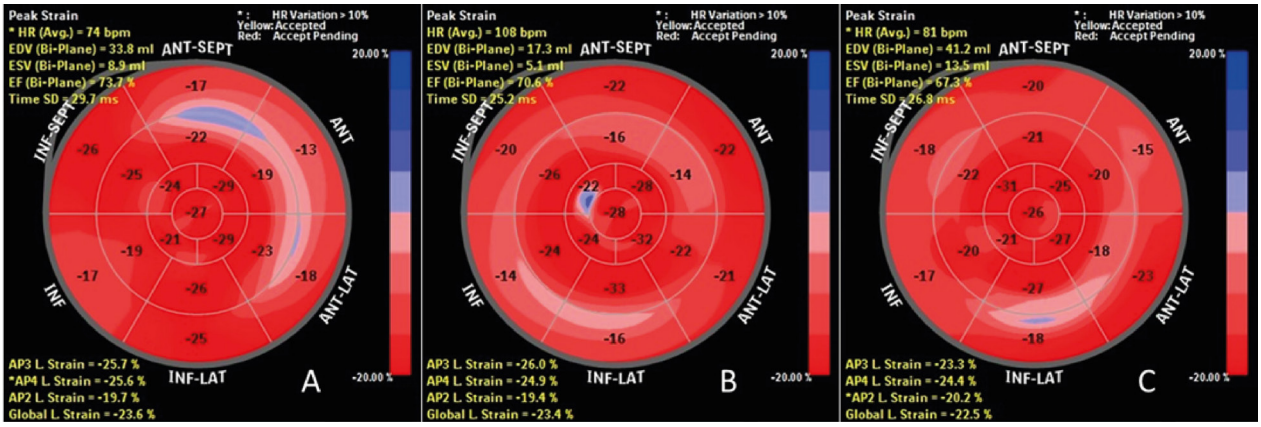


Figure 4 – *The 2D-STE longitudinal strain bullseye. (A) Patient 1: Reduced shortening of the anterior wall without repercussion on the global longitudinal strain. (B) Patient 2: Reduced longitudinal shortening of the lower and inferolateral basal wall of the anterior middle and anteroseptal segment without repercussion on the global longitudinal strain. (C) Patient 3: Reduction anterior and inferior wall strain without repercussion on the global longitudinal strain.*

Discussion

The global MPS incidence is 1 per 25 live births[3], making it a rare disease. The specific prevalence of MPS IV (Morquio syndrome) is 0.15–1.3 cases per 100,000 inhabitants, whereas MPS VI (Marateaux-Lamy syndrome), although rarer, represents around 20% of all MPP cases in Brazil[5]. Cardiac involvement in PSS is progressive and among the main causes of early morbidity and mortality. The main causes of death are heart failure, severe arrhythmia leading to sudden death, and coronary occlusion[4]. The use of 2D-STE has become important for MPS patients due to the possibility of early cardiac involvement detection and more accurate follow-up[3].

The most common echocardiography findings of these analyzed patients were mitral and aortic valve thickening with different degrees of valve dysfunction. Other studies reported

this characteristic in all MPS VI patients except in cases with slower progression[6] and almost half of MPS IV patients[4].

LV involvement was observed in patient 1, who presented signs of grade II diastolic dysfunction, and patient 2, who presented slightly increased myocardial thickness, which may be related to increased ventricular mass and/or decreased compliance due to intra- and intercellular storage. There are reports of hypertrophy regression after about 1 year of ERT (if started promptly).

The patients analyzed in this study showed no significant LV GLS changes, which primarily reflects subendocardial fiber strain[7] with normal overall values for their age groups[3,7]. However, some studies reported circumferential and radial GLS changes in MPS patients involving the middle and subepicardial layer fibers, respectively[7]. Reports on Fabry disease, another multisystemic storage disorder, demonstrated myocardial strain changes in the three directions evaluated using 2D-STE, i.e., longitudinal, circumferential, and radial[7]. This report also showed regional changes in a heterogeneous pattern that occurred more frequently in the anterior and inferolateral basal wall segments. Although this case series included a small number of patients that precludes any higher statistical inferences in the analysis of rare diseases, it provides important data for future research.

Although the use of 2D-STE in clinical practice is not universal, several studies have established its accuracy and reliability. One aspect that interferes with its potential routine use is the possibility of GLS variability, and, although it presented good intra- and interobserver reproducibility and a small learning curve, it involves factors that may limit the accuracy of our findings, such as inter-device variability, which can reach ±5%, and image quality[8].

Finally, 2D-STE is a useful and important tool in the early detection of myocardial diseases, particularly in patients with storage diseases who can benefit from an early diagnosis and the introduction of specific treatment in addition to the use of cardioprotective therapeutic interventions. However, further studies on the prognostic and progressive control aspects of the use of 2D-STE are necessary.

Authors' contributions

Research conception and design: Oliveira ANMO and Grangeiro CHP; data collection: Teodoro JVTT, Ribeiro LAB, Oliveira ANMO, and Grangeiro CHP; data analysis and interpretation: Teodoro JVTT, Ribeiro LAB, Ferreira Neto JM, Ferreira VM, Oliveira ANMO, and Grangeiro CHP; manuscript writing: Teodoro JVTT, Ribeiro LAB, Ferreira Neto JM, Ferreira VM, Oliveira ANMO, and Grangeiro CHP; critical review of the manuscript for important intellectual content: Teodoro JVTT, Ribeiro LAB, Ferreira Neto JM, Ferreira VM, Oliveira ANMO, and Grangeiro CHP.

Conflict of interest

The authors have declared that they have no conflict of interest.

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