Dilated Cardiomyopathy in Systemic Lupus Erythematosus: A Pediatric Case Report

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Case Report

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Abstract

Background: Systemic lupus erythematosus (SLE) is a chronic inflammatory autoimmune disease that can affect any organ in the body, nonetheless cardiac involvement is frequent. Pericarditis is the most common type of heart attack followed by endocarditis, whereas myocarditis is rare. Despite improvements in the survival and quality of life of children with SLE, morbidity from the disease continues to be a major cause of death. Over the past three decades, lupus-related mortality has declined in all categories except cardiovascular disease. Heart disease is currently recognized as a major cause of death and morbidity in children with SLE. In fact, in the majority of cohort studies, the mean cardiovascular mortality is between 7 and 30%. We report full recovery of a little girl with SLE who developed dilated cardiomyopathy and review the literature.

Case presentation: A 7-year-old girl presented with persistent fever, severe weight loss, alopecia, purpuric spots, positive anti-lupus antibodies, and decreased complement. She was diagnosed with SLE and treated with oral corticosteroids and hydroxychloroquine. On the third day of hospitalization, she developed a macrophage activation syndrome which improved with the methylprednisolone bolus. Additional examinations have been performed, including chest x-ray and echocardiography. They showed respectively marked enlargement of the cardiac silhouette and dilated cardiomyopathy with a left ventricular ejection fraction (LVEF) of approximately 35% associated with low pericardial effusion. She was diagnosed with SLE-related dilated cardiomyopathy and treated with furosemide, captopril, digoxin, spironolactone, and acetyl-salicylic acid. Clinical improvement was observed and the echocardiographic examination after 4 months of evolution was normalized, allowing cardiac treatments to be stopped while maintaining captopril.

Conclusions: It is mandatory to check cardiac involvement in all patients with pediatric lupus to make an early diagnosis and ensure optimal management of cardiomyopathy, which is a rare, severe and silent complication.

Introduction

Systemic lupus erythematosus (SLE) in children, also known as juvenile systemic lupus erythematosus (JSLE), is an autoimmune disease that can affect any organ. It has a multifactorial origin and may be secondary to genetic, immunological and environmental factors [1]. Compared to adults, this condition is relatively rare in children, but it is more severe and is characterized by high clinical polymorphism [1, 2]. The heart is a commonly affected organ in SLE. Indeed, cardiac involvement is currently recognized as a major cause of mortality and morbidity in children with SLE. Pericarditis is the main cardiac complication. At the opposite, cardiomyopathy remains an unusual event [3, 4]. In this article, we report the case of SLE in a 7-year-old girl with exceptional cardiac involvement represented by dilated cardiomyopathy. We also reviewed the literature on cardiac involvement with an emphasis on cardiomyopathy for patients with JSLE in order to raise awareness of this rare and severe complication which can lead to a fatal outcome in case of late diagnosis.

Case Report

A 7-years-old girl from a consanguineous union with history of familial lupus and incident seizures was admitted in our tertiary care pediatric rheumatology department. She presented with a long-lasting fever and a significant weight loss. Clinical examination revealed fever about 40°, alopecia, purpuric spots and a turgor in the jugular veins with burst of B2. Investigations revealed normochromic normocytic anaemia with haemoglobin at 6.9 g/dl, leukopenia at 2270/µl, lymphopaenia at 590/µl, thrombocytopenia at 108 000/µl, normal inflammatory markers with an erythrocyte sedimentation rate (ESR) of 4mm/first hr. and c-reactive protein (CRP) of 1.1mg/l and normal renal function with urea 6.16mmol/l (normal range=2.16-7.16), creatinine 41.5µmol/l (normal range=50.4-98.1). Coagulation screen was normal with prothrombine rate at 135%. Albumin was normal at 33g/l (normal range=36-50g/l) and liver function tests were normal. Antinuclear antibody titres were strongly positive at 1:640 IU, anti double-stranded DNA was positive with a titres more than 80 IU and there was marked hypo- complementaemia with C3 at 0.28 g/l (normal range= 0,8-1.93) and C4 at 0.06 g/l (normal range=0.13-0.57), without biological syndrome of anti-phospholipids (anti β2 glycoproteins 1 antibodies and anti cardiolipine antibodies were negative) neither anti SSA/Ro nor antibodies. The diagnosis of JSLE was confirmed after 3 days of hospitalization with an estimated duration of the disease of 8 months. After a transient renal failure (urea at 18.93mmol/l and creatinine at 176.6µmol/l) corrected by filling, no renal involvement associated with lupus was found based on normal rates of blood pressure at 100/60 mmHg, negative urine sediment, normal urine albumin:creatinine ratio of 5,52 mg/mmol (normal < 3.4 mg/mmol) and proteinuria of 24 hours at 5.52 mg/kg/day. During the third day of hospitalization, a macrophage activation syndrome was diagnosed with pancytopenia (polynuclear neutrophils at 560/µl), hyperferritinemia at 15368 ng/ml, hepatic cytolysis (ALT at 973 IU/l and AST at 136 IU/l), elevated LDH level at 2000 IU/L, triglycerides increased to 4.77g/l and hyponatremia at 128 mEq/l, without hemophagocytes on the myelogram. As part of the evaluation of the lesions, a brain MRI revealed a cortico-subcortical atrophy at the supratentorial level, with hyper-signals of non-specific periventricular white matter, without parenchymal or vascular involvement related to lupus, the electroencephalogram (EEG) did not show any abnormalities. A chest x-ray showed marked enlargement of the cardiac silhouette with a cardio-thoracic ratio of 0.6 [figure1], transthoracic echocardiography showed primary-looking dilated cardiomyopathy with a 35% left ventricular ejection fraction (LVEF), enlarged left ventricle and pulmonary arterial hypertension, pulmonary arterial pressure at 25 mmHg, associated with pericardial effusion [figure2]. Faced with this unusual cardiac ultrasound appearance in JSLE, assays of calcium, thyroid hormones and L-carnitine were performed excluding other causes of dilated cardiomyopathy and linking this aspect to lupus. The electrocardiogram (ECG) did not show any rhythm or conduction disturbance. The patient was treated with hydroxychloroquine 5 mg/kg/day, infusions of methyl-prednisolone 1g/1.73 m²/day, followed by oral corticosteroid therapy at 2mg/kg/day and furosemide 10 mg/ kg/day, captopril 2.5 mg/kg/day, digoxin 0.1 ml/kg/day, spironolactone 10 mg/kg/day and acetyl-salicylic acid 5 mg/kg/day. The evolution was marked by a clear clinical improvement, normalization of C3 and C4 levels (C3=0.91 g/l, C4= 0.35 g/l) after 2 months, normal echocardiographic imaging after 4 months [photo 3], allowing cardiac treatments to be stopped while maintaining captopril.

Discussion

SLE is a chronic autoimmune disease that can lead to organ damages. JSLE counts for 15-20% of all lupus [5]. It is usually diagnosed during adolescence and remains rare before the age of 5, with the average age of diagnosis being around 11 to 12 years [6]. The incidence of this disease varies between 0.36 and 0.60 per 100,000 children and its prevalence is estimated between 1 and 6 per 100,000 children with a higher frequency in non-Caucasian populations [1, 7].

The initial manifestations are variable with an insidious and progressive onset. Non-specific symptoms are fever, anorexia, weight loss and asthenia [2]. At the onset of the disease, only one organ may be affected, but systemic involvement is the usual presenting feature [1]. Joint, mucocutaneous, haematological and renal damages are the most frequent manifestations of JSLE [8].

Cardiac involvement was first described by Libman and Sacks in 1924. The frequency of cardiac manifestations varies from 4 to 78% according to literature [9, 10, 11, 12]. Most studies of the cardiac manifestations of SLE are reported in adult patients and describe various types of abnormalities affecting all the layers of the heart with a predilection for the pericardium [3]. Few reports have investigated cardiac manifestations of lupus in children. Guevara et al. found a point prevalence of cardiac abnormalities on the ECG and / or echocardiography in 32% of children with JSLE [13], while Harrison et al. report a 31% prevalence of cardiac involvement in a study of 93 cases of juvenile lupus [14]. A study comparing a pediatric cohort (n = 297) to an adult cohort (n = 6927) of early stage SLE showed an incidence and prevalence of the occurrence of pericarditis and myocarditis at least 4 times higher in the pediatric population compared to the adult one [15]. The classic damage is **pericarditis**, which is observed in a quarter to a third of JSLE's cases and which counts for 83% of heart involvement, in some rare cases it could be fatal due to the risk of tamponade [3,12,14]. **Valvular involvement** (Libman-Sacks endocarditis) is exceptional and generally subclinical; it is often described with positive anti-phopholipid antibodies [9]. **Coronary artery** damage has also been reported; it can be secondary to lesions of coronary artery disease and / or atherosclerosis, of premature onset given to the inflammation and dyslipidemia. They expose to a high risk of mortality [3]. Few cases of myocardial infarction explained by coronary lesions of vasculitis or thrombosis in the context of antiphospholipid antibody syndrome have been reported in children [3, 13].

Cardiomyopathy is reported with an estimated prevalence of 10%. Its clinical expression in JSLE is most of the time silent. In the absence of early diagnosis and management, the progression can lead to a heart failure, that may be irreversible [3, 15, 16]. In a study from Thailand of 26 patients, global left ventricular dysfunction was found to be common in patients with active JSLE, possibly reflecting myocardial involvement [17]. In addition, a longitudinal study of 92 patients with JSLE who never had developed cardiac symptoms, showed a decrease in ventricular diastolic function over time, suggesting a cardiac morbidity linked to the disease [18]. This myocardial involvement can be related to a lupus flare, 3 anecdotal cases of SLE (2 adults and a 15-year-old adolescent) have been reported [19], similarly to the case we reported above. To definitely confirm the diagnosis of cardiomyopathy of lupus origin,

hypertensive cardiomyopathy, toxicity due to hydroxychloroquine, viral, metabolic causes and atherosclerosis although rare in JSLE, must be excluded and the active disease must be proven by complement's comsuption. Although the myocardial biopsy is considered as the gold standard for diagnostic confirmation, this aggressive test is performed exceptionally or even post-mortem [20]. Currently, cardiac MRI remains the best non-invasive test to confirm the presence of myocarditis in JSLE but does not allow its origin to be specified [21]. The outcome is usually satisfactory allowing an improvement after early initiation of immunosuppressive therapy combined with symptomatic measures of heart failure, as we have seen in our patient who had both pericarditis and cardiomyopathy. Inaugural pancarditis in JSLE has been reported, although the patient had recovered with corticosteroids, there is no clear recommendation for treating this condition [22].

Conclusion

Only rare cases of lupus myocarditis in childrenhave been published. Cardiomyopathy is a serious and life-threatening complication of lupus that can go silent for a long time. Its detection and early treatment are the only guarantees of better survival. It seems essential to look for cardiac involvement in juvenile lupus by systematically performing a cardiac ultrasound.

Abbreviations

SLE
Systemic lupus erythematosus
LVEF
Left ventricular ejection fraction
JSLE
Juvenile systemic lupus erythematosus
ESR
Erythrocyte sedimentation rate
CRP
C-reactive protein
DNA
Deoxyribo nucleic acid
ALT
Alanine aminotransferase
AST
Aspartate aminotransferase
LDH
Lactate dehydrogenase
MRI
Magnetic resonance imaging

EEG
Electroencephalogram
ECG
Electrocardiogram

Declarations

Ethic approval and consent: Ethic approval was obtained from the local committee of Hôpital Mère Enfant A Harouchi, Casablanca, Morocco

Consent for publication: Informed consent was obtained from the patient

Availability of data and materials: No applicable

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Authors' contributions:

TF and KB were major contributors in writing the manuscript. KB is the referent rheumatologist of the patient. AD and AB performed cardiac ultrasonography and did the cardiac follow up. AS is a permanent pediatric rheumatologist in the Pediatric Rheumatology unit.

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Figures

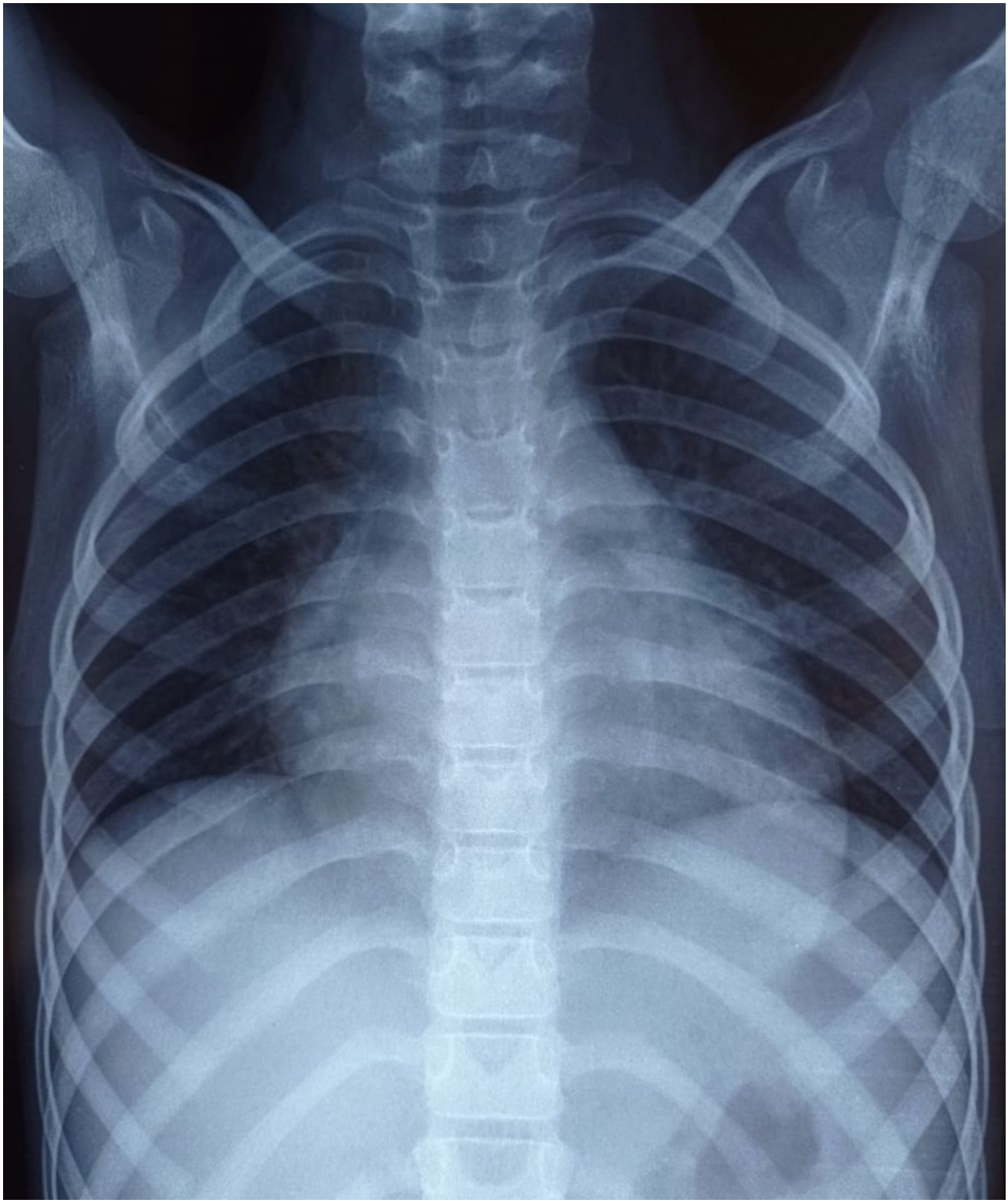

Figure 1

Chest X ray showed cardiomegaly with cardio-thoracic ratio = 0.6.

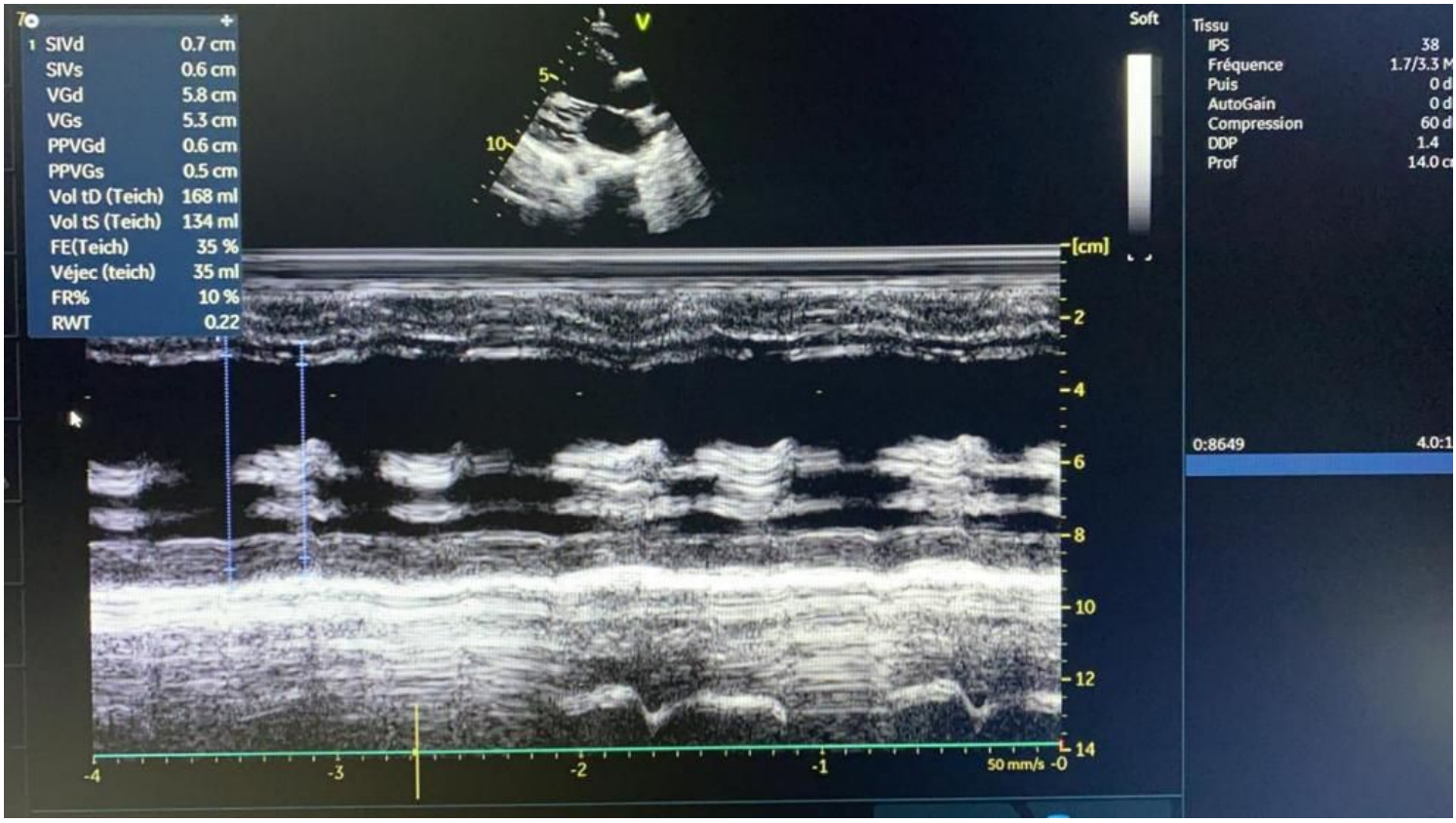

Figure 2

Transthoracic echocardiography N°1 showed enlarged left ventricle with LVEF at 35%, pulmonary arterial pressure at 25 mmHg with pericardial effusion concluding to dilated cardiomyopathy with pulmonary arterial hypertension.

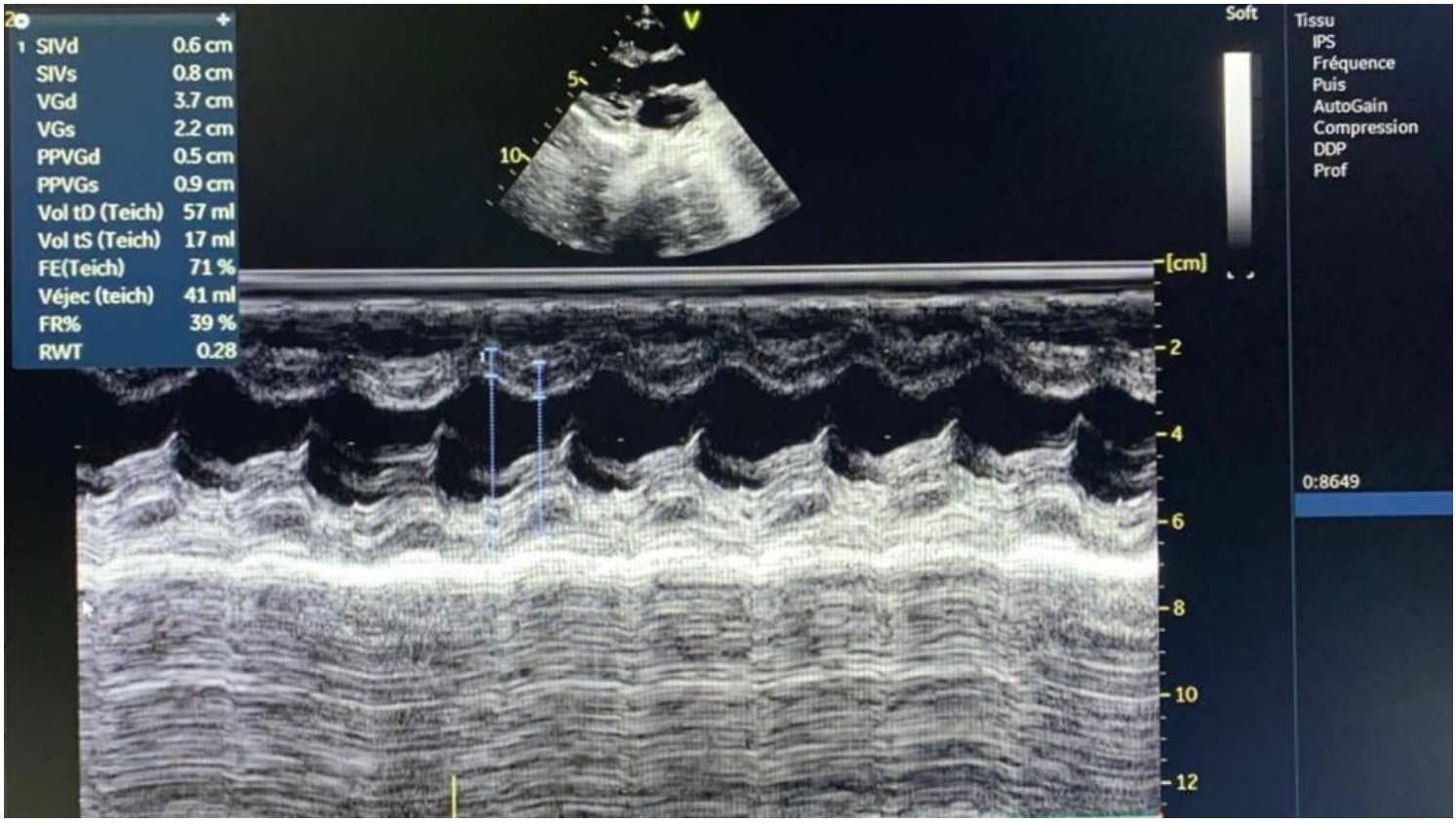

Figure 3

Transthoracic echocardiography N°2 after 4 months showed full recovery.