

Case Report

Reverse Takotsubo Cardiomyopathy presents as predominantly Dyspnea in a middle-aged female.

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Abstract

Takotsubo cardiomyopathy (TTC) or stress cardiomyopathy, first described in Japan, 1990 (1,10). It was stress-induced and known as broken heart syndrome and by various other synonyms due to its relation to stress (1, 8). The name comes from a device used to catch octopus, known as Tako-tsubo, as the echocardiographic picture of the left ventricle resembles this shape of the device. TTC cardiomyopathy classically is reversible myocardial dysfunction. TTC confirms the apical ballooning pattern on echocardiography and left ventriculogram (1). Reverse Takotsubo cardiomyopathy (rTTC), as the name suggests has a reverse pattern, here apical myocardium is unaffected (6,7). This condition is usually reported in younger aged females (7). They have better-preserved left ventricular systolic function and there is a stronger association with the neurological disease compared to TTC(7). The exact mechanism of rTTC is complex. Postulated mechanisms proposed are, catecholamine-induced cardiotoxicity through cAMP-mediated protein kinase pathway involving free radical-mediated, reversible myocardial dysfunction (8,9). Other mechanisms put forth are multiple coronary artery spasm (9), coronary microvasculature impaired function leading to myocardial dysfunction, and a substrate such as estrogen deficiency.

Patients with rTTC usually present with chest pain, with or without breathlessness. They also have inferior wall ischemia mimicking symptoms like nausea, epigastric pain autonomic symptoms, etc. There is usually a precipitant in the form of emotional or neurological stress in the background. Reported cases have also confirmed the association of rTTC with intracranial hemorrhage, general anesthesia, malnutrition, and drug usage causing catecholamine stress. Diagnosing rTTC requires presence of LV basal hypokinesis or akinesis instead of apical ballooning as in classic Takotsubo cardiomyopathy (TTC)(7). New electrocardiographic (EKG) abnormalities with elevated cardiac troponin in the absence of obstructive coronary disease, pheochromocytoma, or myocarditis. The management of rTTC is like TTC, which is predominantly supportive. The recurrence rate of rTTC has been reported at around 10%. Amongst common complications of rTTC are myocarditis and related arrhythmias, pleural and pericardial effusions, and development of LV thrombi. The predictors of mortality are reduced LVEF, development of atrial fibrillation, and neurologic disease.

Here we present a case of rTTC in a 55-year female, which is a higher age, than usually reported, in literature. She has an atypical presentation, presenting with main dyspnea without any chest pain. She had moderate to severely reduced left ventricular ejection fraction. She presented to the outpatient department of our tertiary care private hospital in Qatar. There was no evident neurological insult suspected. No history of any drug use or malnutrition/anesthetic use recently. She got treatment initially as an acute coronary syndrome and was finally diagnosed as rTTC upon full investigation including cardiac MRI. Treated conservatively, and she made full recovery.

Learning objective:

We present a case of a rare variant of stress-induced cardiomyopathy known as reverse or inverted Takotsubo cardiomyopathy (7), with atypical symptoms. The name is itself descriptive of the finding of basal hypokinesis as opposed to the common variant with apical hypokinesis. This interesting case, selected for case reporting, to highlight yet another phenotype presented by rTTC. Here no intracranial subarachnoid hemorrhage or neurological insult was found. Nor

was there a history of any substance abuse or anesthetic implicated as a cause. The patient had no classic CAD risks. She was older than usually reported cases (7). The patient presented with acute severe left ventricular systolic dysfunction, mainly as breathlessness and mild chest tightness, which is also atypical. Typically, she made full recovery with supportive treatment. The patient also underwent all recommended protocols of investigation and treatment recommended. Readers will be able to ingrain additional information through this case scenario in general.

Clinical and demographic profile of the case:

The present case a 55years female with a good social background. She had not been diagnosed with diabetes, HTN, or dyslipidemia. She had no addiction to smoking or drugs. She presented with predominantly severe acute unusual breathlessness at rest and with the exertion of 4-6 hours, mild pressure like tightness in the chest from the same duration. She had no chest or epigastric pain, nausea, or vomiting. She had no sweating dizziness or lightheadedness. There was no LOC or palpitations. She was attended to and clinically evaluated. Examination findings were suggestive of mild congestive heart failure, presence of bilateral basal crepitation with sinus tachycardia but normal JVP, HJR (hepato-jugular reflux), and no S3. ECG done showed septal QS complexes and left axis deviation with normal sinus rhythm. Her vitals were essentially normal with BP-110/69 mm Hg; HR- 114 / min regular, the temperature was 37.4 degrees Celsius with oxygen saturation at room air of 97%. Her BMI (weight in kg /height square in meter) was 28. On inquiry, she admitted to having stressful experience from her family side in recent 2-4 weeks, and last week especially intense.

She did not recall any recent flu-like illness. She had a distressed and worried look. Her troponin I was reported positive and with a provisional diagnosis of the acute coronary syndrome, was admitted to CCU for further care and investigation.

Timeline of course in hospital/investigations done:

Day 1 at outpatient department. First troponin came – 0.920 mcg/ / L (normal being < 0.040 mcg/L), the troponin repeated after 6 hours at CCU came – 1.443 mcg / L (normal being < 0.040 mcg/L). It was not repeated further, as coronary angiography was done before the next due sample.

Day 1 Serial ECG repeated at CCU did not show any evolution. Vitals remained maintained throughout, the patient received 2L oxygen for the first day by nasal cannula and maintained saturation after day 1 without.

Day 1 CXR (figure 1)-s/o pulmonary edema with the bat-wing distribution pattern is seen.

Day 1 Echocardiography- at admission- showed presence of reduced left ventricular function, ejection fraction 35-40% (normal > 55%) with RWMA (regional wall motion abnormality). Marked anterior mid basal hypokinesis. Valves were normal and there were no clots seen or pulmonary hypertension present. There was no effusion in the pericardium. Repeat echo before discharge (day 4) showed improved LV function, 45-50%. Echo after 3 months at follow-up - showed normalization of left ventricular function and no RWMA.

Day 2 Coronary angiography (figure-2.) done as ACS workup- showed normal coronary anatomy and no atherosclerotic plaques in all coronary artery territory. There was no spasm either.

Left ventricular angiogram (figure -3) showed preserved apical contraction and hypokinetic anterior mid basal segments with reduced ejection fraction.

Day 3 Cardiac MRI (figure 4) done to exclude myocarditis and cardiomyopathy with late gadolinium enhancement – reported to be normal, also excluded cardiomyopathy.(Both magnetic resonance imaging and histopathological findings can differentiate patients with rTTC from those with acute myocardial infarction resulting from coronary arterial occlusion).

ECG monitored at CCU stay for 48 hours – did not show any pauses or significant arrhythmias.

Treatment given Plavix and aspirin was stopped after coronary angiography. Not indicated in normal coronaries. Injection clexane 0.6 mg subcutaneous given twice until the desired INR was achieved. Tablet carvedilol started at a low dose of 3.125 mg twice eventually was bumped up to 25 mg twice daily, over 6 weeks was discontinued after 3 months. Tablet warfarin 5 mg once daily, titrated to INR 2-2.5. This was continued for 3 months to prevent clot formation in the left ventricle. Injection Lasix was given 40 mg stat IV slow push at admission and 20 mg twice x 2 days at CCU and ward. At discharge, she was on Tablet Telmisartan 40 mg once daily. At no point, she needed inotropic support or antiarrhythmic support.

Discussion

Stress-induced cardiomyopathy or Takotsubo cardiomyopathy, first reported in Japan in 1990 (1,5). It is a form of reversible left ventricular dysfunction. Historically associated with extreme emotional stress, thereby also referred to as the “broken-heart syndrome”. Classically involves the apical region of the heart, thus named apical ballooning syndrome, resembling the Takotsubo device used in Japan to catch octopus. It comprises 1-2% of patients presenting as an acute coronary syndrome. The reverse pattern of left ventricular dysfunction is even rarer. Usually, it is diagnosed in < 10 percent of these cases. Reverse pattern, where the apical region is spared and instead mid/basal segments are involved in reversible systolic dysfunction of the left ventricle (3). There is notably, absence of obstructive coronary artery disease as a cause. Other variations include hypokinesis of the mid ventricle in about 15%, global involvement of the ventricle, and focal involvement of an isolated section of the ventricle in about 1.5%. Variants result possibly from beta-receptor density distribution variation or multivessel spasm intensity and distribution.

Takotsubo or stress-induced cardiomyopathy thought to be the resulting from catecholamine surge induced cardiotoxicity brought on by intense emotional or physical stress.

The rare variants of Takotsubo (6) have been shown to have different clinical presentations (3, 10) and are associated with different triggers of stress (4). There are important features that differentiate reverse Takotsubo from its more classic form. The reverse type of Takotsubo usually presents in a younger population with a mean age of 36 years versus 62 years, seen in classic form (3). rTTC, being almost exclusively found in patients with emotional or physical stress as opposed to other subtypes with no known physiological trigger. According to the International Takotsubo Registry (ITR), physical stress is a more common precipitant than emotional stress, 36% versus 27.7%. Emotional triggers were more common among females as opposed to men who presented with physical triggers. Additionally, troponin levels tend to be higher and ejection fraction lower in reverse Takotsubo with a paradoxical faster recovery as we see in our case. We present a case, admitted as acute coronary syndrome only to be diagnosed as rTTC after further investigation, based on a full-recommended workup by the European society of cardiology. She did not have any complications during recovery and made full recovery on supportive treatment. She is doing well on careful advice to avoid any severe stress and to undertake healthy lifestyle preventive measures to maintain health. Referral to cardiac rehabilitation was done.

She was given a proper directive about reporting if symptoms recurred and planned scheduled follow up. Careful, clinical, and psychosocial assessment in this patient led to the correct diagnosis and obviates the need for unnecessary intervention. Finally, this rare condition can be considered in any patient with known emotional stressors at low risk for atherosclerotic coronary artery disease and moderate to severe acute left ventricular dysfunction.

Outcome:

In this case, we made an uncomplicated and full recovery in 3 months. Confirmed with normal left ventricular function at 3 months echocardiography and clinically. She is following full healthy lifestyle directives and has already been counseled by a psychologist at our center.

Future perspective:

Research into the preventive aspect of this often underdiagnosed and poorly recognized Neuro-cardiogenic condition mandates more research into trials of drugs affecting the autonomic nervous system, targeting alpha-beta receptors, estrogen receptor mechanism. Also, important regulators of nerve pathways, which handle emotions and stabilize them. Developing a sound guideline for evidence-based treatment will need a broader base pool of case data. Public awareness will enhance early and more cases and milder cases, diagnosis and thereby help research and guided treatment. An intensive holistic strategy is needed in preventing recurrence. Frequent case reporting into structured registries will make the spectrum of presentation clearer and enable prognosticating with confidence. Keeping an eager eye to diagnose this rare entity completely and properly is advised. To devise rational treatment and prevention strategies, more attention is paid to not only the myocardium and coronary arteries but also the integration of central neural, autonomic, endocrine, and circulatory systems involved in emotional stress.

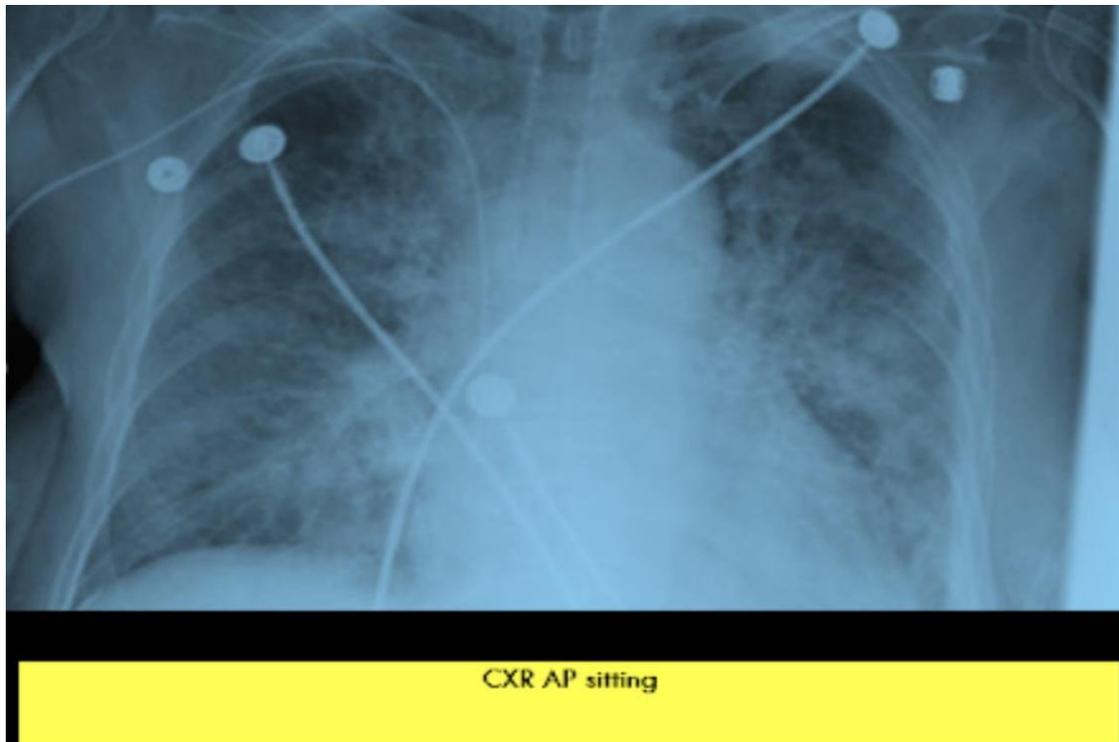


Figure.1. Chest X-ray performed at CCU for breathlessness

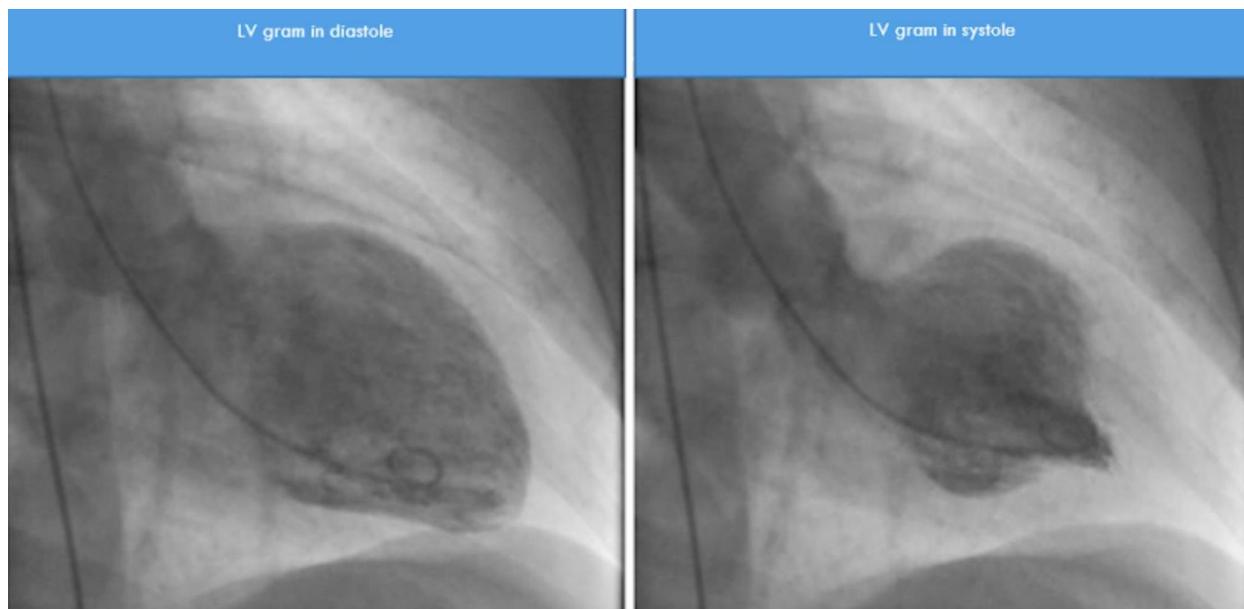


Figure 2. Coronary Angiography

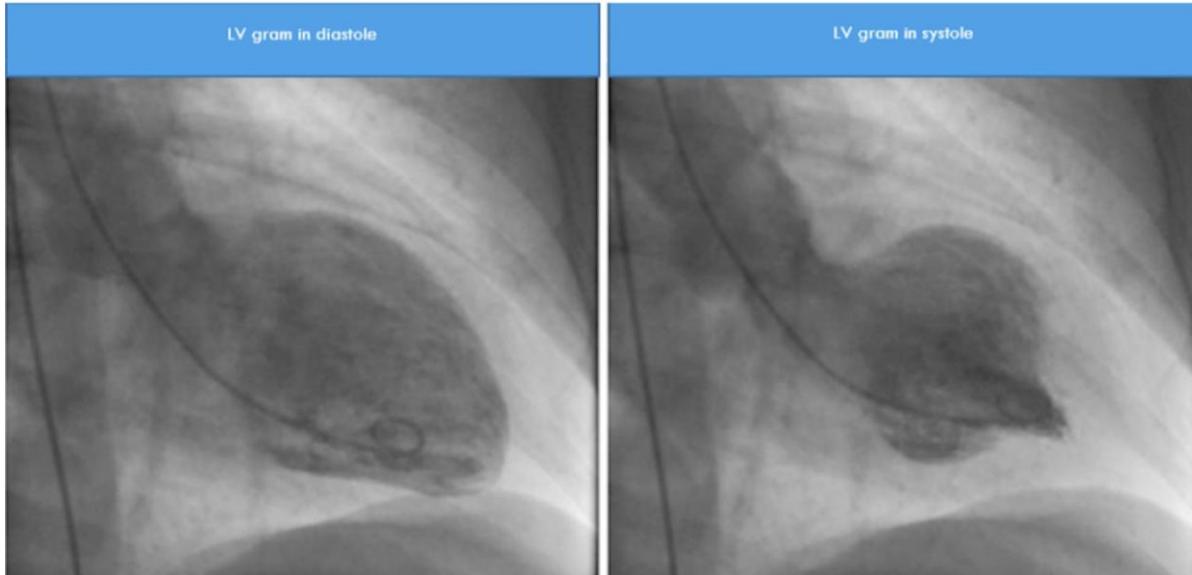


Figure 3. Left Ventriculogram

Left ventriculogram shows preserved apical contractility and mid basal ballooning

a- Diastolic

b- Systolic

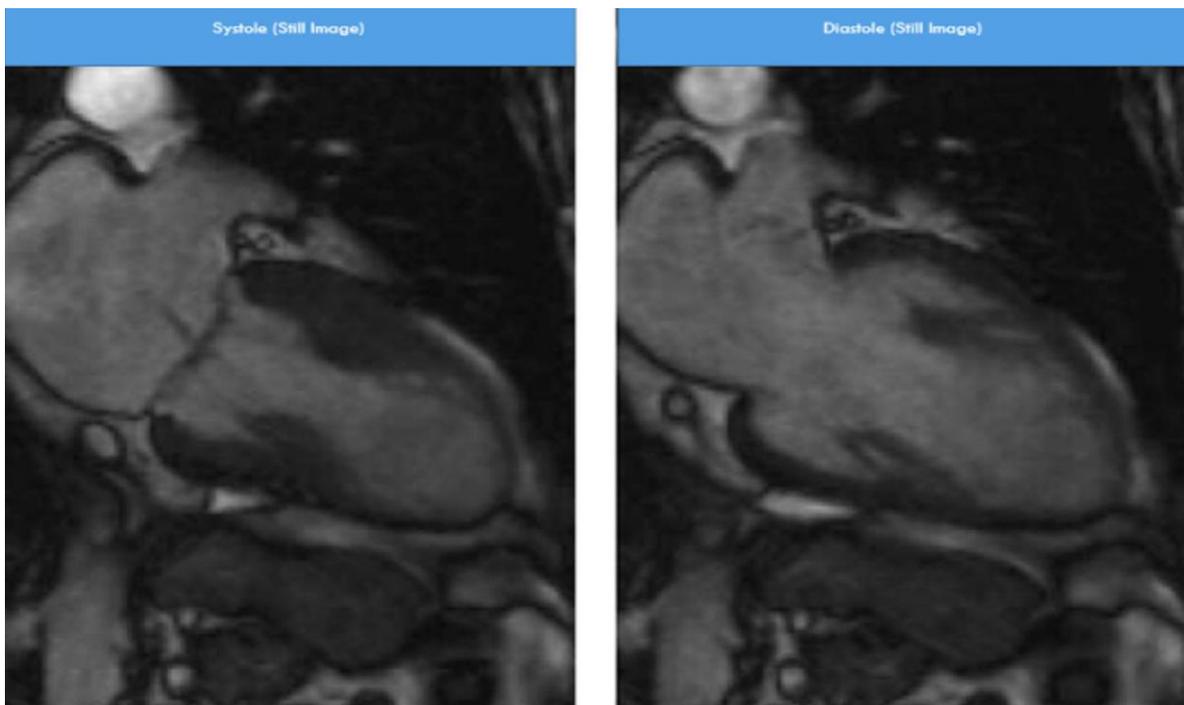


Figure 4. Cardiac MRI, Early, And Late After Contrast

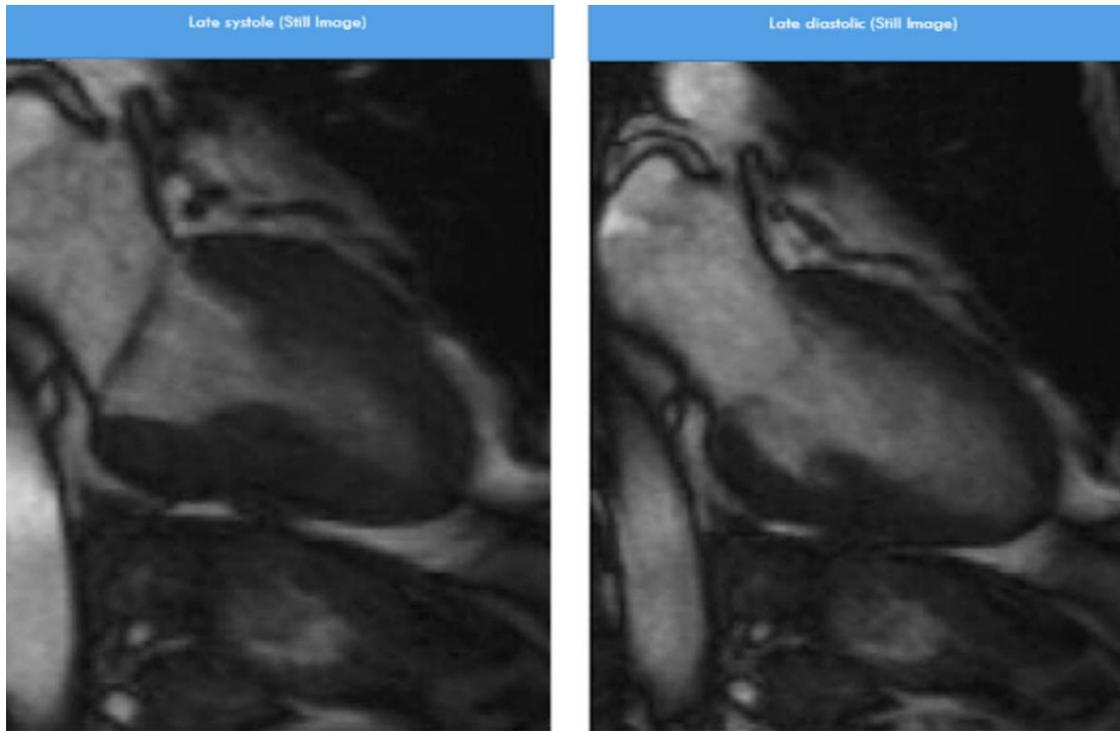


Figure-5

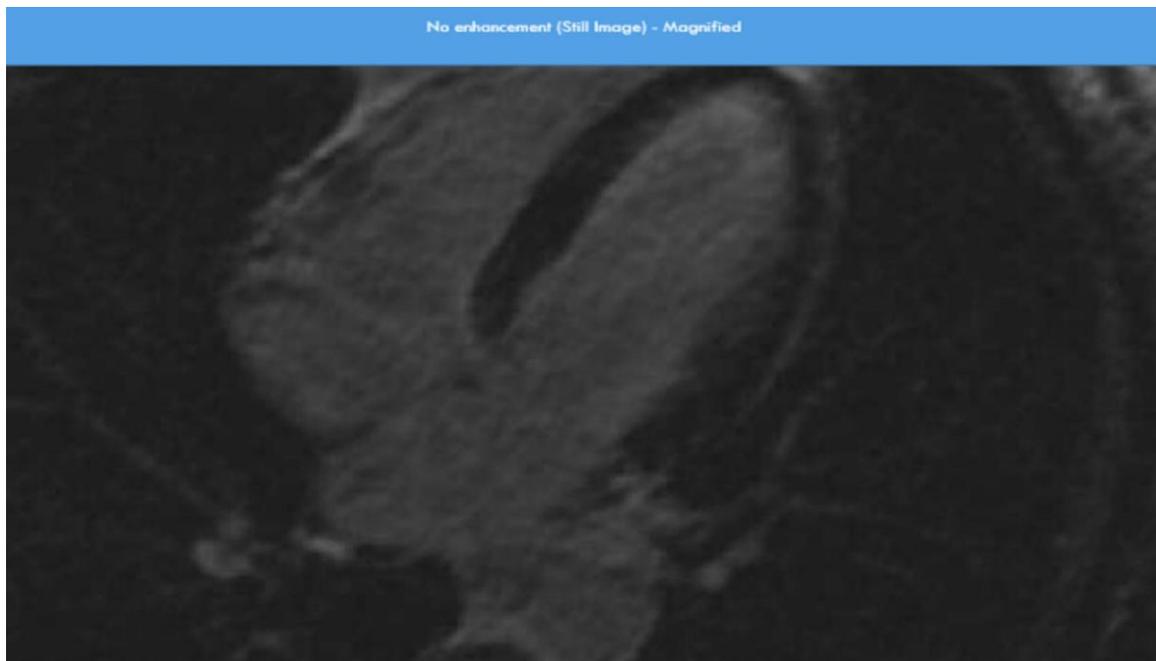


Figure-6: MRI showed negative finding for delayed hyper enhancement with contrast

Conflict of interest

The authors have no conflict of interest.

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