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Report of a case with cardiac X syndrome diagnosed by echocardiography

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Key words: coronary flow reserve, coronary microvascular disease, cardiac syndrome X, stress echocardiogram

ABSTRACT

Cardiac syndrome X is a term that describes the association of typical oppressive chest pain, ST segment depression during exercise, and normal coronaries on angiography. It's attributed in most cases to change in coronary microvasculature.

As it is currently known that normal coronaries on angiography are required to diagnose cardiac syndrome X. In the following article, the first cardiac syndrome X to be diagnosed by stress echocardiogram is reported. A coronary angiography done few days later, confirmed the diagnosis.

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INTRODUCTION

The term "cardiac syndrome X" was first introduced to broadly describe patients with typical chest pain and angiographically normal coronary arteries [1].

Currently the use of this term is no longer limited to the old definition introduced by Kemp in 1973. It instead implies the presence of exercise induced chest pain, an ST segment depression during exercise testing, and normal epicardial coronary arteries [1].

The coronary microvasculature consists of the prearterioles and arterioles that use various regulatory mechanisms in order to match coronary blood flow (CBF). Coronary microvascular disease (CMD) occur because of a disruption of endothelial-dependent or endothelial-independent mechanism [2].

As for coronary artery disease, the risk factors for the development of CMD are smoking, diabetes mellitus (DM), hypertension (HTN), hyperlipidemia and systemic inflammation.

CMD can occur alone or in the presence of coronary artery disease (CAD). Studies have shown that 59% of the patients with angina symptoms, but with angiographically normal coronary arteries, were found to have abnormal response to vasodilator agents, adenosine and acetylcholine (Ach) suggestive of CMD [3]. Another large cohort study found no significant difference in the prevalence of CMD between men and women [4]; this is in contrast to epicardial stenosis where women have been consistently found to have less obstructive CAD than men [5;6].

Few decades back, CMD was considered a benign disease with a good prognosis [7]. While this concept was valid for many years, several further studies have showed the complete opposite. CMD is now associated with adverse cardiovascular events including myocardial infarction, stroke, worsening angina and death [8].

The coronary flow reserve (CFR) is the ratio of coronary blood flow (CBF) at maximal dilation to CBF at baseline. CFR is decreased in CMD patients. One study concluded that patients with CFR < 1.5, were associated with a 5-6 fold increase in the risk of cardiac death compared with those with CRF > 2 [9].

CASE REPORT

A 50 year old female, previously healthy, and athletic, presented for 6 months history of typical, pressure-like chest pain, occurring only upon severe exertion and typically at a heart rate of 140-150 bpm. The pain subside progressively when the heart rate decrease.

The patient remained stable until July 2014, when she seeked medical advice and underwent an evaluative exercise test, which showed a diffuse ST segment depression of 2 mm, associated with significant chest pain, oppressive in type which began after few minutes of exercise, and at a heart rate of 140 bpm **(Figures 1 and 2)**.

An echocardiogram was performed immediately after exercise test and showed a rate depending Takotsubu-like hpokinesia (occurring only at a heart rate of 140 bpm and above) **(Figures 3 and 4)**.

During the initial phase of recovery there was a regression of ST segment to normal, decrease in chest pain, and restoration of myocardial wall motion.

To note that her blood pressure was maintained before and during exercise. It was not exaggerated by efforts. Maximum SBP reached at any time was 160 mmHg.

Few days later the patient was hospitalized to perform an elective coronary angiography. It was scheduled for the 30th of July 2014. The absence of coronary artery lesions was determined in the angiographic study performed at the hemodynamic and interventional cardiology unit.

DISCUSSION

Despite all the efforts to directly visualize the coronary microvasculature, no current technique is so far available. Hemodynamic information about coronary microvascular system is often represented by the CFR in response to vasodilators, where CFR < 1.5 is associated with high mortality in CMD patients [10].

Trans-Thoracic Doppler echocardiogram (TTDE) is an easy and cheap technique that measures the distal left anterior descending artery (LAD) CBF velocity (CBFV). CFR is then measured as the ratio of peak CBFV after vasodilator to CBFV at rest [11]. However, TTDE is limited only to LAD.

Cardiovascular Magnetic Resonance (CMR) involves intravenous gadolinium injection. The myocardial perfusion reverse index is then calculated using the ratio of the rates of contrast uptake during stress and at rest [12]. A decrease response to vasodilators is seen in CMD patients [13]. Given its good diagnostic accuracy, CMR seems to be the most promising non-invasive technique.

Positron Emission Tomography (PET), uses a radioactive tracer to calculate regional blood flow in addition to global flow [14]. This modality has the advantage of assessing all three coronary distributions, thus allowing a more accurate assessment of microvascular dysfunction [15].

Invasive testing consists of insertion of a doppler guided wire in the LAD artery and injection of vasodilators. CMD patients can be expected to have a possibly decrease CBF to these substances [16].

All the above listed modalities can be used to diagnose CMD.

But in this special case, the diagnosis of CMD was established using only a stress echocardiogram, that showed a global myocardial hypokinesia post treadmill stress test.

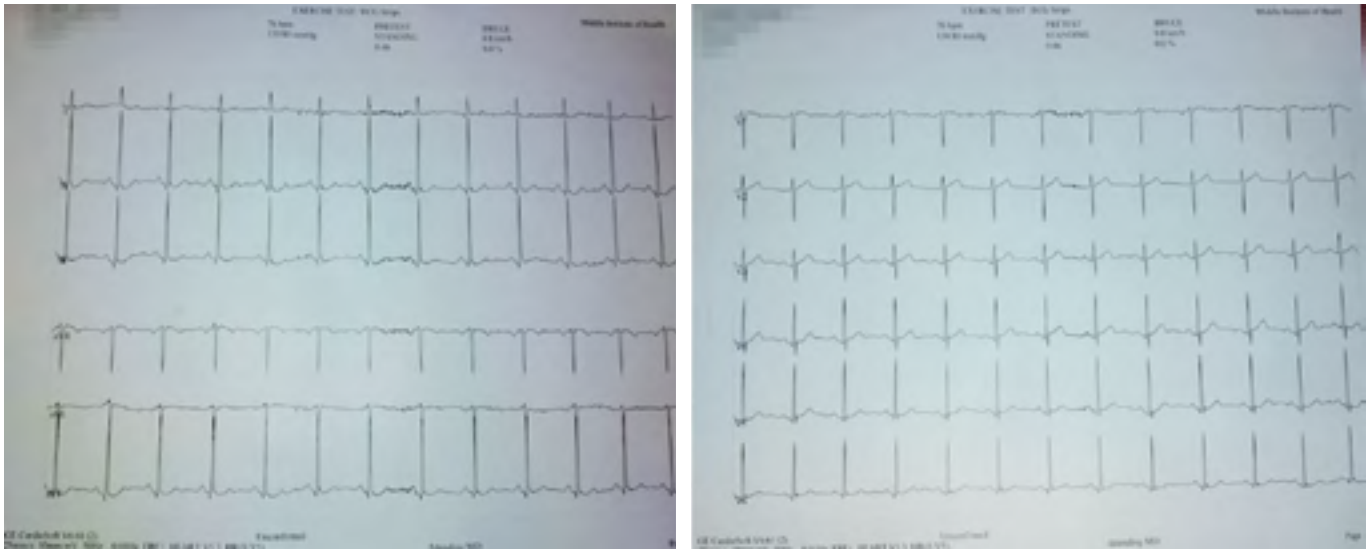

Figure 1: Resting Electrocardiogram ©EKaram

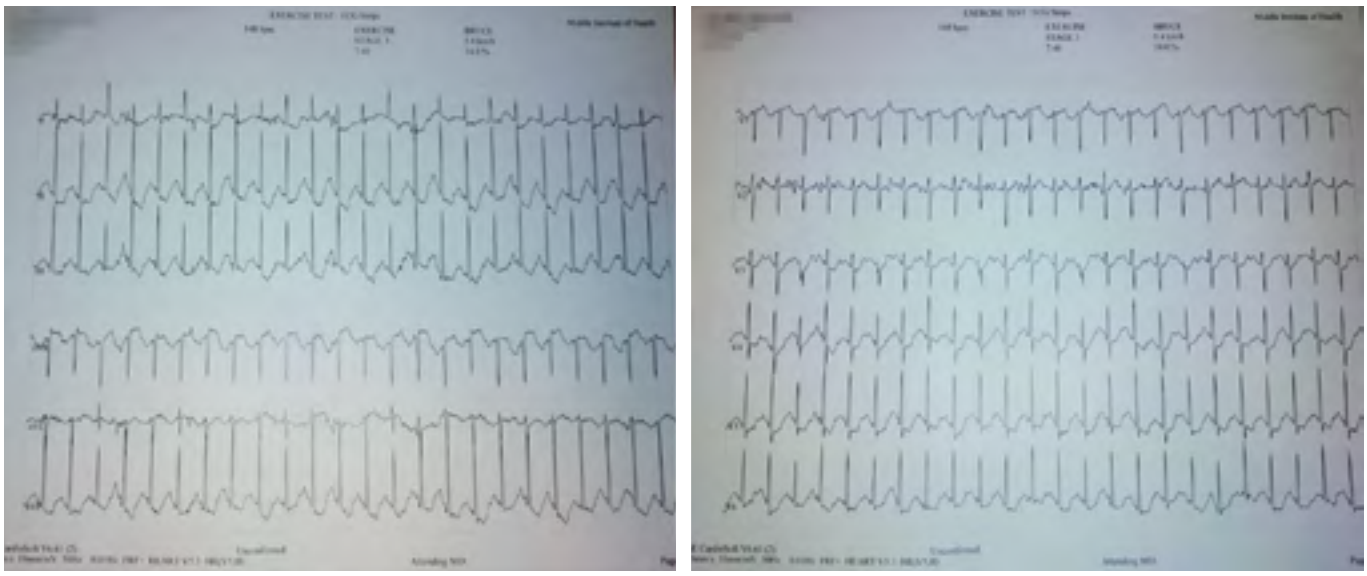

Figure 2: Post exercise Electrocardiogram, showing diffuse ST segment depression of 2 mm, at a heart rate of 148 bpm ©EKaram

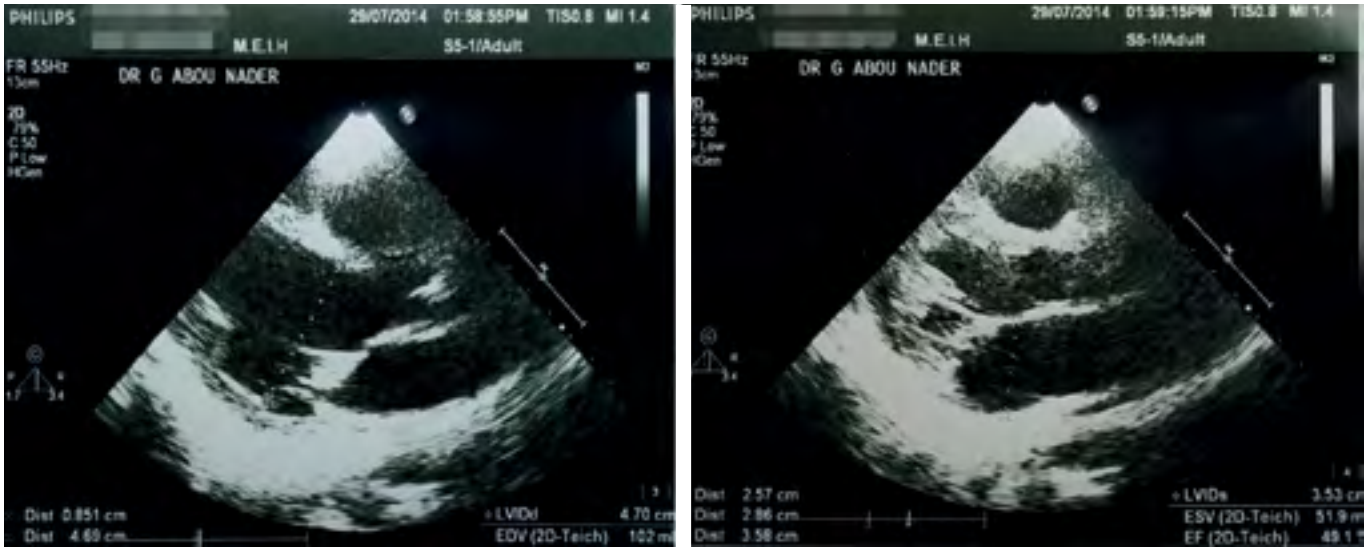

Figure 3: Left parasternal long axis view of the resting Echocardiogram, showing a good contractility of the myocardium with an Ejection Fraction (EF) of 49.1%, and a Left Ventricular Internal Diameter end systole (LVIDs) of 3.53 cm ©EKaram

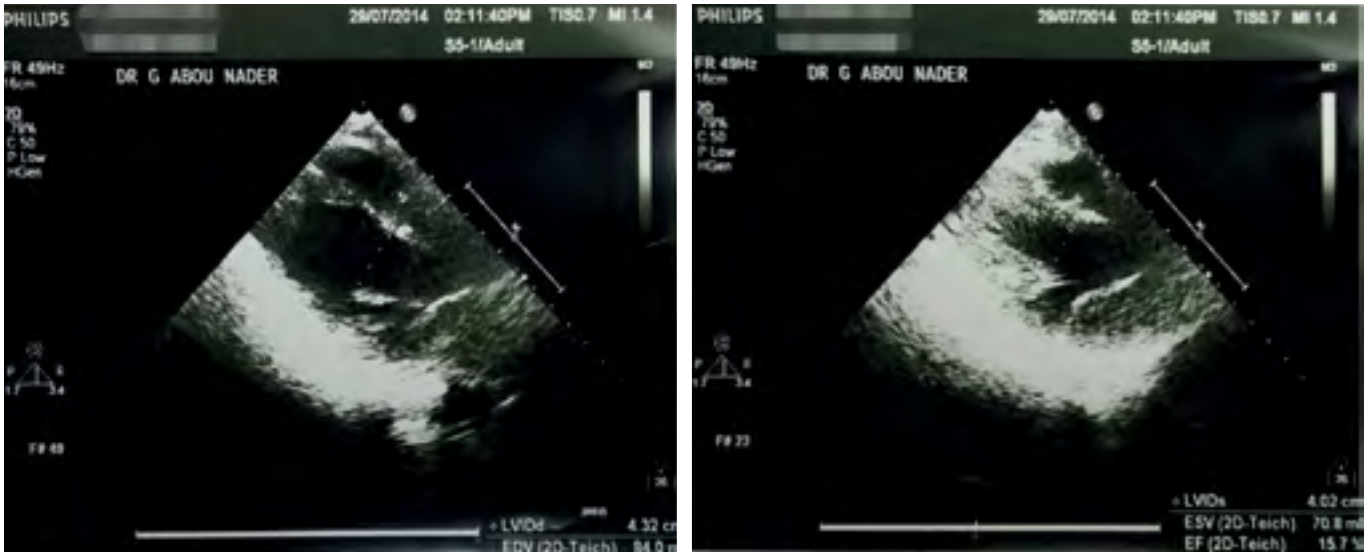

Figure 4: Left parasternal long axis view of the stress Echocardiogram, showing a diffuse hypokinesia of the myocardium with an Ejection Fraction (EF) of 15.7%, and Left Ventricular Internal Diameter end systole (LVIDs) of 4.02 cm ©EKaram

The stress echocardiography is a high sensitivity (88%) and specificity (83%) test, for the detection of significant coronary artery stenosis, defined as > 50% diameter stenosis on coronary angiogram [17]. In fact, compared to nuclear perfusion imaging, studies have shown that stress echocardiography have similar sensitivity and higher sensitivity for detection of coronary artery disease [17]. But despite the high specificity and sensitivity, a subset of patients were found to have a false positive echocardiogram defined as < 50% diameter coronary stenosis on the subsequent angiogram, in the absence of left bundle branch morphology, right ventricular pacing, prior cardiac surgery, or abnormal wall tethering at baseline [18]. In this particular group of patients, studies have concluded that a significant rise in blood pressure during exercise could be related to a higher chance of a false positive echocardiography [18]. So coming back to our patient, we re-insist on the fact that blood pressure has remained constant at rest and was not abnormally exaggerated by stress test (maximum systolic blood pressure at any time was 160 mmHg). This proves that the global hypokinesia observed on stress echocardiography was not related to a hypertensive response.

One other possible diagnosis is Takotsubo cardiomyopathy (TTC), which can also cause myocardial wall hypokinesia. In fact coronary microvascular integrity is impaired in patients with TTC, but what is not yet clear is the fact that myocardial stunning is consequence of metabolic disorder or CMD [19]. About 90% of patients are postmenopausal women, with a mean age of 70 years, presenting with resting angina that is by far the most common symptom (59%), and is usually triggered by unexpected emotional stress situations [20;21]. Typical form of TTC affects the mid and apical segments of the left ventricle with compensatory hyperkinesis of the basal segments [21]. As opposed to the history and echo findings of our patients, the diagnosis of TTC is easily eliminated. Moreover, ST segment depression is the least frequent ECG abnormality on TTC, and is very uncommon compared with ACS [22].

Finally, a study published in fall 2016 concluded that the evidence is insufficient to state that false-positive stress echocardiography in the absence of obstructive coronary artery disease portends a poor outcome, but considerable evidence shows that some of these patients have microvascular abnormalities and endothelial dysfunction [18]. Subsequent multivariate analysis showed that this particular group of patients were most likely non diabetic, non hypertensive, younger females, without prior history of CAD as is the case of our patient.

CONCLUSION

A young healthy lady with complaints of exertional chest pain was found to have positive stress test and a global myocardial hypokinesia on stress echocardiogram. After eliminating other possibilities, she was diagnosed with cardiac X syndrome. An angiogram confirmed the diagnosis few days later.

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