

How you treat your patients today, affects them tomorrow: Sinus tachycardia-induced cardiomyopathy

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Abstract

Background: Tachycardia-induced cardiomyopathy (TCM) is a reversible form of myocardial dysfunction because of tachyarrhythmias. Therefore, it is essential to identify arrhythmias in patients presenting with myocardial dysfunction without apparent aetiology.

Case: Herein, we present a thirty-seven-year-old male with bouts of prolonged sinus tachycardia and severe mental stress, averaging >130 beats per minute, before abdominal operations more than once in a few months. A notably dynamic ventricular stunning was noted that partially normalized in a few days, once relieving tension and reduced heart rate. Complete normalization of ventricular function was observed after five months of maintaining the average heart rate. Initially, the present case was missed due to its paroxysmal nature. Later, the patient was cured with a maximum tolerated dose of beta-blockers, anti-failure, and small doses of anxiolytic agents. Our case is a rare case report of recurrent TCM the same patient due to episodes of marked sinus tachycardia.

Conclusion: Sinus tachycardia is often considered a physiological response to mental stress that may cause cardiac injury related to a prolonged stress response. Treatment of stress sinus tachycardia-induced cardiomyopathy (sinus tachycardia-ICM) leads to recovery of myocardial function. The literature does not recommend controlling heart rates in patients with persistent sinus tachycardia preoperatively, but it is a therapeutic option for preparing patients for operation. Successfully, beta-blockers were used in our patient and should be considered in similar case scenarios.

Keywords: Tachycardia-Induced Cardiomyopathy; Myocardial Dysfunction; Prolonged Sinus Tachycardia; Case Report

1 Introduction

Tachycardiomyopathy (TCM) is a reversible impairment of ventricular function induced by persistent arrhythmia without other identifiable causes [1]. The diagnosis is usually established retrospectively after demonstrating complete or partial recovery of the left ventricular function with reduced heart rate [2].

2 Case Study

A thirty-seven-year-old male presented to a local hospital on June 3, 2020, with severe loin pain and was diagnosed with multiple renal stones. He was admitted for an abdominal operation. From his medical reports, he was pretty anxious, and his heart rate was 130 beats/min and regular, with a blood pressure of 120/70 mmHg. The gentleman

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reported shortness of breath along with easy fatiguability. His electrocardiogram (ECG) showed marked sinus tachycardia. Echocardiography revealed global left ventricular hypokinesia with markedly reduced systolic function. The left ventricular ejection fraction (LV-EF) was 20-25%. His past medical history was unremarkable, and he took no cardiac medications. The gentleman had no risk factors for coronary artery disease and denied typical chest pain or other angina equivalent symptoms. Coronary angiography revealed normal coronary arteries. He was diagnosed with non-ischemic-cardiomyopathy and started on a beta-blocker and other anti-failure therapies. The gentleman's symptoms had resolved one week later, with partial normalization of his left ventricular function (LV-EF= 45%). He underwent his planned operation, which passed smoothly. The patient had residual renal stones that were managed conservatively with watchful waiting. He defaulted from follow-up, and he took his medication sporadically.

On February 1, 2021, he came to our hospital because of intolerable abdominal pains, and his investigations revealed a collection of pus intra-abdominally. He was arranged to do another abdominal operation. He was highly anxious and frightened from the operation. The patient developed worsening dyspnea (NYHA Class III), palpitations, and cough. His heart rate was regular, at 150 beats/min. His blood pressure was 110/65 mmHg. ECG revealed marked sinus tachycardia. Chest-X ray showed cardiomegaly with an increase in bronchovascular markings. His echocardiogram displayed extensive global hypokinesia with LVEF was approximately 15-20% and grade II/IV functional mitral regurgitation due to tethering, consistent with significant cardiomyopathy.

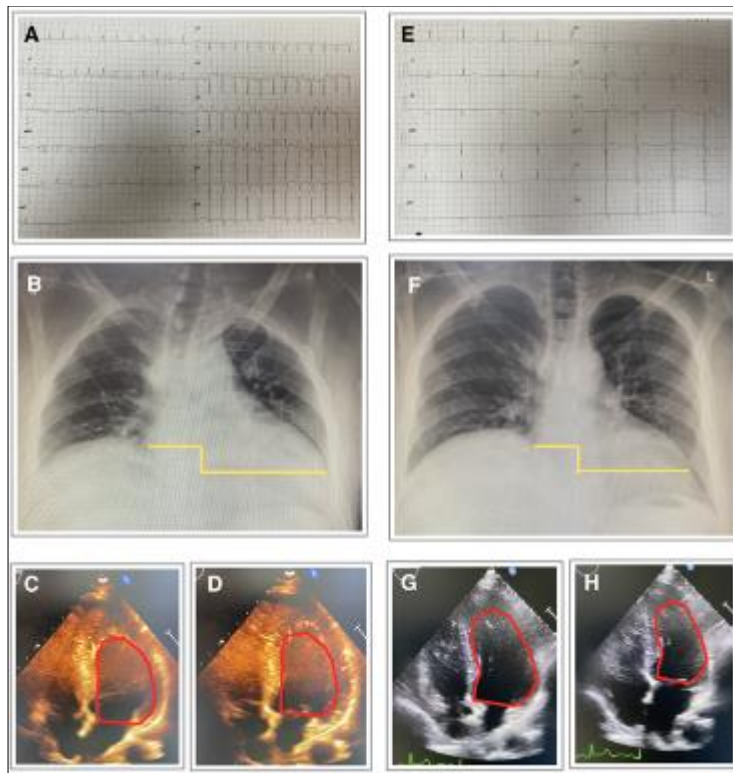


Figure 1 On admission: A) Twelve lead electrocardiogram (ECG) recordings demonstrated sinus tachycardia with heart rate (HR) around 130/min. B) Chest X-ray revealed cardiac enlargement with an increase in apical bronchovascular markings (BVM). C) Echocardiogram in apical four-chamber view during the diastolic phase and D) systolic phase recording during marked sinus tachycardia, demonstrated mildly dilated LV cavity, global LV hypokinesia with a marked drop in LV systolic function.

Haematological and biochemical investigations were within average values apart from elevated ESR and C reactive protein (90 and 24 mg/L, respectively). Also, his BNP was elevated. Cardiac enzymes and thyroid profile were unremarkable. The patient was given good antibiotics, anxiolytic agents, carvedilol, sacubitril/valsartan, spironolactone, and frusemide. One day later, his ECG showed sinus rhythm with a heart rate of 70 beats/min. The patient's symptoms resolved, and his clinical condition quickly improved. Two days later, echocardiography revealed partial recovery of the left ventricular function with LV-EF= 45%. He went to do his operation without any complications.

We were stuck in a dilemma, which came first? We needed to answer whether dilated cardiomyopathy causes persistent sinus tachycardia or prolonged sinus tachycardia causes cardiomyopathy? Our patient had persistent sinus tachycardia with worsening myocardial dysfunction without coronary artery disease, and myocardial dysfunction was finally reversed; hence we highlighted the possibility of sinus tachycardia-induced cardiomyopathy (Sinus tachycardia-ICM). We performed thorough investigations to detect any underlying diseases causing this LV stunning; however, all results were inconclusive. At that time, we were satisfied with the thought that our patient had a resolved stress sinus tachycardia-ICM and was treated with the maximum tolerated doses of beta-blockers and small doses of anxiolytic and anti-failure medications.

The gentleman was discharged in normal sinus rhythm four days later and was in good health. Two months later, he came for a follow-up, and his left ventricular systolic function was 45-50%, with partial resolution of all previous wall motion abnormalities and mitral regurgitation.

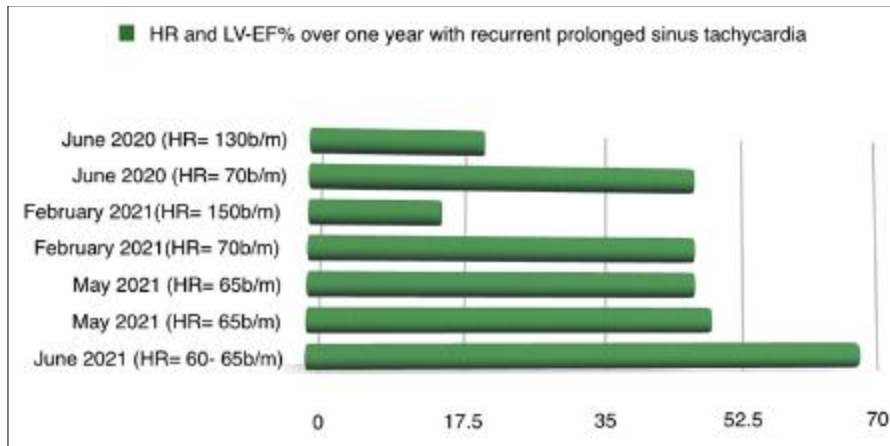


Figure 2 The summary of changes in the left ventricular ejection fraction (LV-EF) seen in our patient with episodes of prolonged sinus tachycardia over one year. When the patient was on a beta-blocker before and after the last operation, he did not develop marked sinus tachycardia, and his LV-EF was nearly unchanged. A few months after maintaining and sustaining controlled heart rate (HR), complete recovery of LV systolic function was detected.

Table 1 Heart rate (HR) and Left ventricular ejection fraction (LVEF) at the presentation of each episode of sinus tachycardia before abdominal operations in June 2020 and February 2021, with subsequent partial recovery of EF after correction of heart rate. Also, unchanged LVEF in May 2021 before and after the surgical operation (The patient was maintained on beta-blocker). Finally, in June 2021, complete recovery of LVEF could be appreciated during regular follow-up.

Date	HR (BPM)	LVEF%
June 2020 (Preoperative)	130	20
June 2020 (Post-operative)	70	45
February 2021 (Preoperative)	150	15
February 2021 (Post-operative)	70	45
May 2021 (Preoperative)	65	45
May 2021 (Post-operative)	65	45-50
June 2021 (Regular follow up)	60-65	65

On May 5, 2021, he underwent another operation with reasonable heart rate control. This time, the operation passed smoothly with no ventricular dysfunction.

During his follow-up visits, his heart rate was controlled and maintained around the 60s. In June 2021, a complete recovery of his LV-EF was documented with an EF of 65-70% and no mitral regurgitation (Figure 1). The patient's symptoms ultimately resolved, consistent with his cardiomyopathy's complete resolution. The summary of changes in LV-EF is shown in Table 1 and Figure 2. Our patient has been followed monthly without symptoms, and he will continue to receive follow-ups to monitor any recurrence of sinus tachycardia-ICM.

After controlling HR: E) Twelve lead ECG showed normal sinus rhythm with HR around 70 beats/min F) Chest X-ray revealed normal cardiac shadow with a decrease in apical BVM G) Echocardiogram in apical four-chamber view during the diastolic phase and H) systolic phase recording with controlling HR; demonstrated normal LV cavity size with a resolution of LV systolic function.

3 Discussion

Long-standing tachycardia is a well-known cause of cardiomyopathy and has led to TCM. TCM was described for the first time in 1913 in a young male who presented with manifestations of congestive heart failure and atrial fibrillation (AF) with a rapid ventricular response [3]. The goal of reporting our case was to advance the knowledge of prolonged stress and sinus tachycardia as a cause of a reversible form of cardiomyopathy.

3.1 Pathophysiology of Tachycardiomyopathy

Our understanding of the pathophysiology of TCM remains not fully explained despite wide-ranging work more than a decade after the first reported case.

Various mechanisms can be considered for the pathophysiology of TCM. The close association between the stress-induced prolonged sinus tachycardia and the rapid onset of symptoms suggests that stress hormone was the trigger for TCM development. The psychosocial stress strikes normal neurohormonal cardiac regulation. It reduces vagal tone combined with activation of sympathetic pathways leading to a surge in catecholamines, endothelin, and cortisol, causing metabolic myocardial stunning [4]. Also, catecholamines and endothelin are powerful vasoconstrictors of the coronary microvasculature, and vasodilators such as nitric oxide are impaired. Hence, blow-up of catecholamines may induce myocardial injury directly via cyclic AMP-mediated calcium overload or indirectly due to catecholamine-induced endothelial dysfunction and associated damage to the underlying myocytes [5].

In 2007 Calo et al., stated that the pathophysiology of ventricular dysfunction in TCM is related to abnormal calcium handling in the myocardium, decreasing cellular energy stores with an abnormal utilization of energy which affects the myocardial remodelling causing maladaptive remodelling [6]. Abnormal calcium homeostasis in TCM is assumed to be responsible for impaired excitation-contraction coupling and ventricular dysfunction. In 2004, Deshmukh et al. reported that an angiotensin-converting enzyme polymorphism increases serum angiotensin-converting enzyme levels, more common in patients with TCM than in patients with tachycardia but with no LV dysfunction [7].

There was complete resolution of heart failure manifestations in our patient with the recovery of ventricular dysfunction after controlling and maintaining heart rate for a long time. This can be explained by subclinical myocardial ischemia with prolonged sinus tachycardia resulting in decreased myocardial blood flow and significant remodelling of the coronary capillary vasculature. Hibernation of the myocardium due to ischemia may develop, explaining the reversed remodelling of the myocardium after cessation of the tachycardia [8]. Martin, in 2017, stated that subclinical ischaemia takes part in the pathogenesis of TCM [1].

The mechanical ventricular performance is produced by interactions between myocytes, the basement membrane and the extracellular matrix. Consequently, any changes lead to ventricular dilation and contractile dysfunction that affect mechanical ventricular performance [9]. The pathologic effects of tachyarrhythmias on ventricular morphology initially include cellular changes that are characterized by cardiomyocytes elongation and hyperplasia, reduction in the extracellular matrix, which has a role in myocyte alignment that disrupts the basement membrane-sarcolemmal interface leading to loss of sarcomere register, myocardial fibrosis, myofibril misalignment, and apoptosis. It is essential to clarify that in cases of TCM, some changes such as ventricular fibrosis persist even with reversal of the tachycardia and normalization of LV systolic function [10].

Therefore, early pathologic changes in TCM differ from late changes. In the first days, prolonged rapid heart rate leads to dilatation and dysfunction of the left ventricle. These changes are insufficient to affect cardiac output or systemic perfusion pressures [11]. After the first week, later pathologic changes include neurohormonal changes following hemodynamic alternans. The neurohormonal system is upregulated in response to these structural changes in TCM

[12]. Also, LV dilatation and dysfunction are accompanied by increased central venous and pulmonary capillary wedge pressure and systemic vascular resistance that affect intrinsic myocardial contractility. Therefore, although initial HF manifestations are adaptive, constant rapid heart rate affects LV load-ejection relationships [13].

3.2 Categories of Tachycardiomyopathy

3.2.1 Pure Type

Arrhythmia can cause LV dysfunction in a normal heart that completely recovers after tachycardia termination (*Arrhythmia-induced CM*).

3.2.2 Impure Type

Arrhythmia can exacerbate or worsen a pre-existing LV dysfunction in a patient with structural heart disease that incompletely recovers after tachycardia termination (*Arrhythmia-mediated CM*) [1].

3.3 Diagnosis of Tachycardiomyopathy

As a clinical diagnosis, it may be challenging to decide whether the fast heart rate is the cause or result of cardiomyopathy?

There are no clear criteria for the diagnosis of TCM, but it is highly suspected after demonstrating recovery of left ventricular systolic function with lower heart rate without an obvious aetiology. The diagnosis of the present case was initially missed, but finally, we considered an arrhythmic aetiology as a factor contributing to cardiac dysfunction, confirmed by recurrent marked sinus tachycardia with worsening/reversible myocardial dysfunction.

TCM can be caused by supraventricular, ventricular tachycardia and other less common types, such as sinus tachycardia associated with thyrotoxicosis [11]. Our patient can be considered a less common type of cardiomyopathy induced by persistent sinus tachycardia as reports on prolonged sinus tachycardia-complicated TCM are scarce.

The classic presentation of TCM is symptoms and signs of heart failure [1]. It is essential to exclude other aetiologies of cardiomyopathy by a thorough history, physical, laboratory, echocardiography and coronary angiography to suggest TCM diagnosis. TCM in our patient was mistaken for acute coronary syndrome in his first presentation as typically present with progressive dyspnea, with echocardiographic changes suggesting myocardial injury/ischemia. Coronary angiography added important supportive clues for TCM diagnosis. Okada and others 2016 [13] submitted that coronary angiography is recommended to exclude coronary artery disease as a cause of ventricular dysfunction in patients with persistent tachycardia and cardiomyopathy.

Patients may be diagnosed through echocardiography, which helps in excluding other causes. In echocardiography, a dilated left ventricle characterizes TCM with moderate to severe biventricular systolic dysfunction and no hypertrophy. Mitral regurgitation may be due to LV and mitral annular dilatation, lacking leaflet coaptation (tethering effect) [10]. Echocardiographic parameters of our patient, including ejection fraction, improved partially after treatment (from 15% increased to 45%). Following up our patient by echocardiography after a few months of maintaining heart rate control revealed that the LV-EF normalized to 65% with no mitral regurgitation. This is concordant with Martin and Lambiase in 2017 [1]; they concluded that patients presenting the progress of at least one NYHA class and the LV-EF recovery during the follow-up were diagnosed with arrhythmia-induced CM.

The clinical diagnosis of TCM is not always straightforward. Clinical suspicion should come to light in all patients presenting with new and rapidly worsening symptoms of heart failure, a low overall cardiovascular risk profile and recent evidence of high-rate arrhythmia. In these cases, a specific and early reduction of the heart rate (either through rate or rhythm control) should be performed, possibly even while the diagnostic workup for excluding structural heart disease is still ongoing [12].

Differential diagnoses in our case scenario included dilated cardiomyopathy, myocarditis, and cardiac sarcoidosis. Ventricular systolic function improved relatively quickly; therefore, dilated cardiomyopathy and cardiac sarcoidosis were ruled out. There were no symptoms suggestive of viral infection, no inflammatory responses apart from that in the second operation, and no abnormal findings in ECG other than sinus tachycardia, so myocarditis was unlikely. TCM was diagnosed based on LV-EF improvement shortly after the termination of tachycardia and maintaining a controlled heart rate. TCM can be considered one of the stress-mediated syndromes resulting from catecholamine storm-induced metabolic myocardial stunning. Although there are no well-established diagnostic criteria to discriminate Takotsubo

cardiomyopathy from TCM patients, the key diagnostic clues in TCM are the presence of persistent tachyarrhythmia in the absence of other etiologies with the progressive restoration of LV function.

3.4 Recovery and Recurrence of Tachycardiomyopathy

After restoring sinus rhythm or slowing down the ventricular rate, recovery of ventricular function is highly variable, complete or partial and varies from days to several months [13].

Our patient's recovery duration was partial in the first few weeks and then returned to normal after a few months of controlling and maintaining a low heart rate that consistent with Huizar et al. in 2019 [14].

In our case, we noted that; there is an inverse relationship between the heart rate and LV systolic function; a faster rate was associated with a more decrease in LV-EF. Our finding is discordant with Gopinathannair et al. 2015 [9], who declared that; the duration of tachyarrhythmia appears to be a more risk factor than the ventricular rate.

The recurrence of TCM is a latent problem if the arrhythmia recurs; hence maintaining therapy focusing on suppressing the tachyarrhythmia and controlling the heart rate should be considered [15]. In a cohort of 24 patients with TCM in 2004 by Nerheim and others [16], five patients were noted to have recurrent tachycardia. All five patients developed clinical HF with an abrupt drop in their ejection fraction. Recurrent tachycardia in our patient leads to recurrent cardiomyopathy. Our patient underwent a surgical operation three times within eight months and was severely anxious before each one. Before the first two operations without preoperative medications to control his heart rate, he developed clinical HF. Heart failure was reversed over days once established an adequate rate control. Smoothly, his third operation passed, as he was well prepared preoperatively to control his heart rate with beta-blockers.

Complete recovery of TCM is not always the case. The histopathological abnormalities, diastolic dysfunction, and ventricular dilatation in patients with TCM might persist despite the normalisation of LVEF [13]. These histopathological abnormalities are likely responsible for recurrent cardiomyopathy [17].

3.5 Treatment of Tachycardiomyopathy

Management of patients with suspected TCM is directed toward heart rate control and treating heart failure [18]. Shah, in 2018 [19], stated that in tachycardiomyopathy, a rapid clinical improvement and full recovery are usually seen with beta-blockers and conventional treatment for congestive heart failure.

It is well known that sinus tachycardia is a physiological stress response, and clinicians may try to manage stress but not hurry to control the rate of patients with a prolonged stress response. Although the risk of the prolonged stress response is well appreciated in patients before any major surgery, there is a deficiency of literature on the effect of sinus tachycardia in the development of TCM in those populations perioperatively [20]. Also, no current guidelines recommend rate control in those patients with prolonged preoperative stress-induced sinus tachycardia. Although theoretically, long-term beta-blockers might prevent TCM recurrence, data are lacking.

Continuing standard HF management is advised as the adverse myocardial remodelling is persistent even after normalization of ventricular systolic function [21]. Hence, patients with partial resolution should continue to be monitored and treated with small doses of anxiolytic and anti-reverse remodelling drugs.

In patients with TCM, a triple-way approach is required to treat arrhythmia and cardiac dysfunction and prevent recurrence (Figure 3). This approach should include heart rate and rhythm control by drug therapy and/ or catheter ablation. Early initiation of optimal medical treatment for heart failure is essential to reverse adverse remodelling and relieve symptoms. The main pillars of anti-failure medications include angiotensin-converting enzyme inhibitors or angiotensin receptor-Nepriylsin inhibitors (ARNi), diuretic agents, beta-blockers, mineralocorticoid receptor antagonists (MRAs), and sodium-glucose cotransporter-2 inhibitor (SGLT2i) [22]. Close monitoring of heart rate, rhythm, and ventricular systolic function with frequent clinic visits, Holter monitoring, and echocardiography. Monitor every 3-6 months in the outpatient clinics for up to one to two years following the initial clinical improvement is essential.

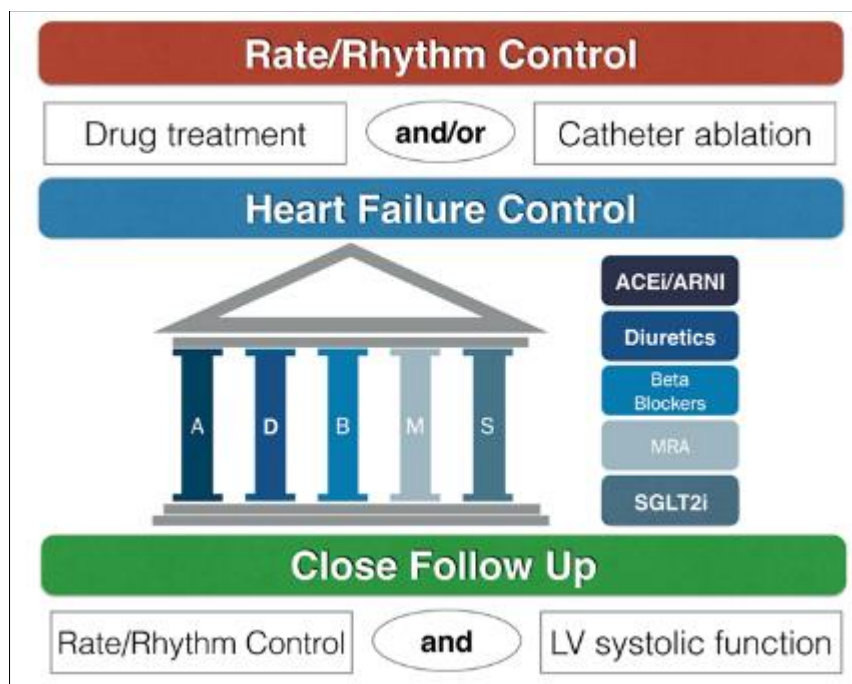


Figure 3 Triple-way approach for treatment of tachycardiomyopathy and prevent recurrence

4 Conclusion

Tachycardiomyopathy is a condition that deserves attention and requires a high index of suspicion to be diagnosed by the treating clinicians. Managing stress and controlling heart rate resulted in remarkable improvement of cardiac dysfunction and could prevent recurrent cardiomyopathy. Appropriate treatment of TCM will likely improve quality of life and clinical outcomes and reduce hospital admission and healthcare spending.

Compliance with ethical standards

Disclosure of conflict of interest

The authors have no conflict of interest.

Statement of informed consent

Informed consent was obtained from our patient.

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