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Infections precipitating Takotsubo cardiomyopathy, an uncommon complication of a common infection

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Abstract

Takotsubo cardiomyopathy (TTC) is a non-ischemic cardiomyopathy precipitated by stress. Various infections are reported to precipitate this form of cardiomyopathy. We report a patient presenting with TTC secondary to influenza. In this article, we also discuss the various infections reported to precipitate this form of reversible cardiomyopathy in literature. We have also included the recent reports of TTC among patients with COVID-19.

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Introduction

Takotsubo cardiomyopathy (TTC) also known as stress-induced cardiomyopathy usually occurs in the background of episodes of extreme physical, emotional stress. Patients usually present with acute onset chest pain, shortness of breath mimicking acute coronary syndrome. On evaluation, these patients are noted to have elevated cardiac enzymes, electrocardiogram abnormalities, and typical wall motion abnormalities in the echocardiogram. This form of acute cardiomyopathy is nonischemic and reversible with optimal medical management. Though mostly precipitated by emotional stress, many infections have also been reported to precipitate TTC. In this report we described a patient with influenza A, presenting with TTC.

Case Report

A 52-year-old lady with a history of hypertension, asthma, breast cancer in remission, presented with a history of fever, fatigability, loss of appetite, nausea, vomiting, and worsening shortness of breath. At presentation, she was febrile with a temperature of 37.9°C, and the remainder of her vitals were stable. On examination, she was found to have wheeze bilaterally, and decreased breath sounds over the left infrascapular area. Her chest X-ray was unremarkable at presentation. Initial EKG as shown in Figure 1 showed sinus tachycardia. On the subsequent day, her breathlessness worsened. On examination she was found to be tachycardic with a heart rate of 104/min, tachypneic with a respiratory rate of 24/min, saturating 96% on 6 L oxygen, and her blood pressure was 118/78 mmHg. Her EKG showed mild ST elevation across V3 to V6 as shown in Figure 1. Her troponin was raised (113 pg/mL). Her complete blood count and metabolic panel were within normal limits. Computed tomography (CT) of the chest showed increased basilar consolidation in the dependent portion of the left upper lobe (Figure 1). In view of worsening respiratory distress, and hypotension she was intubated and ventilated in the intensive care unit. At this point, her transthoracic echocardiogram (TTE) with Perflutren Lipid Microsphere contrast showed mid ventricular hypokinesia, hyperkinetic basal segment, along with normal contractility of the left ventricular apex (Figure 2). She was also noted to have a severely reduced ejection fraction of 30%. Her catheterization revealed normal coronaries. She was treated with oseltamivir because of positive influenza A. With multidisciplinary medical management, her clinical condition improved. Gradually she was weaned off vasopressors and got extubated. While in the hospital she was started on metoprolol and valsartan. Following

significant clinical improvement, she was discharged and a repeat TTE after 2 weeks showed normal ejection fraction with normal left ventricular wall motion.

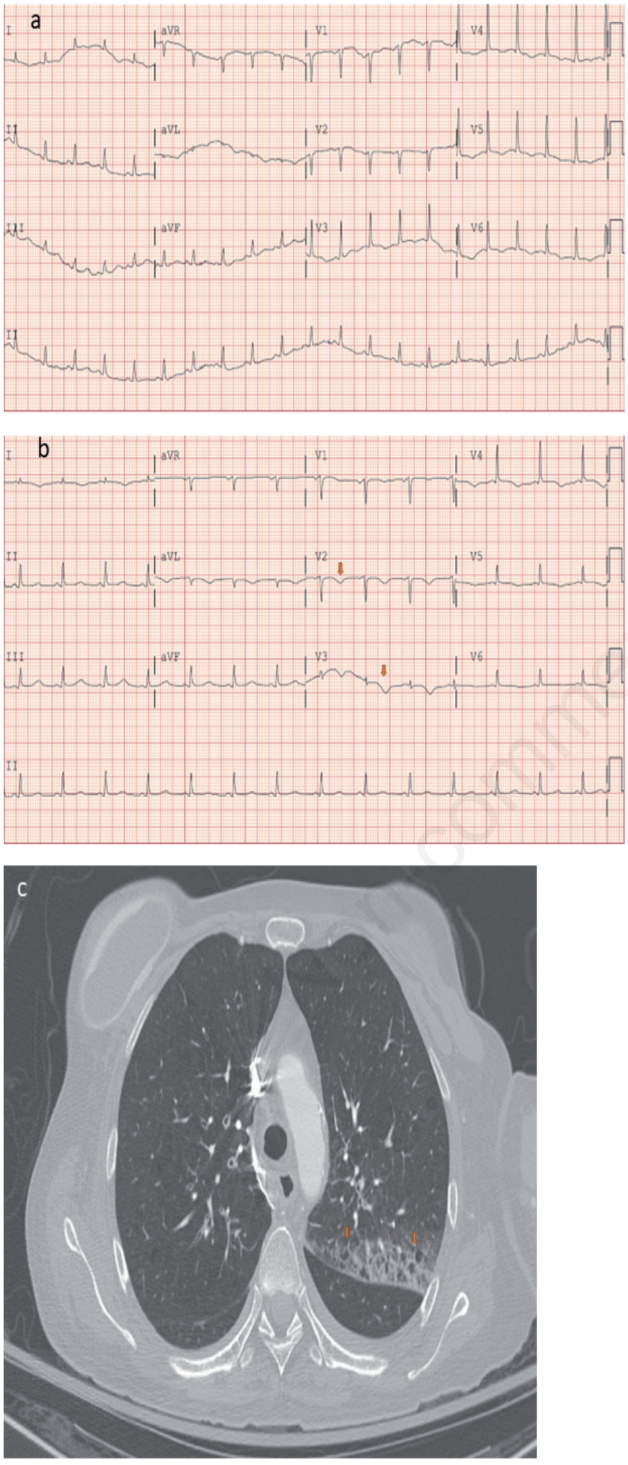

Figure 1. a) EKG showing sinus tachycardia. b) EKG showing ST elevation. c) Chest CT showing left lung infiltrates.

Discussion

TTC, also known as stress-induced cardiomyopathy was initially reported in 1990. At present, the prevalence of TTC is 0.2%, with 90% of events reported in women over the age of 50s [1]. Most often patients presented with clinical features of acute coronary syndrome, or cardiogenic shock precipitated by stress [2]. Revised Mayo Criteria is used to establish the diagnosis of TTC. Physical and emotional stress resulting in excessive sympathetic stimulation contributes to the development of TTC. It is postulated that variable expression of beta receptor densities contributes to differential involvement of the myocardium resulting in apical ballooning in response to catecholamine surge [3.] A systemic review by Nyman *et al*. on potential triggers of TTC reported that physical factors are more common as compared to emotional factors. The common physical factors reported by them were physical illness (60%), procedure, and surgery simultaneously [4]. TTC has been reported secondary to multiple physical conditions including chronic obstructive pulmonary disease, subarachnoid hemorrhage, thyrotoxicosis, Addisonian crisis, autoimmune disease, hypomagnesemia, hypocalcemia, and multiple drugs [4,5].

Infections are a commonly reported precipitator of TTC [3,6]. With an increase in literature on TTC, a vast number of infectious agents are reported to precipitate the same [6-28]. Table 1 summarizes the various bacterial, viral, and parasitic organisms reported to precipitate TTC in literature [6,9-12]. Multiple studies have reported the precipitation of TTC following sepsis and septic shock as well [6,13]. Multiple mechanisms including sepsis, excessive inflammatory response, coronary microvascular injury have been postulated to precipitate TTC in patients with infections.

Over the past 2 years, multiple studies have described cases of TCM secondary to COVID-19 [14]. Among patients with COVID-19, both primary and secondary precipitators of TTC have been reported. The intense emotional stress associated with this pandemic has been attributed to causing primary TTC and physiological response to infection, cytokine storm, microvascular coronary impairments and use of inotropes have been attributed to causing secondary TTC.

Episodes of precipitations of TTC have been reported following hypothyroidism, and malnutrition in the background of sepsis [30,31]. The outcome following Takotsubo cardiomyopathy is mostly thought to be benign with reversal of cardiac functions being common [3,16]. There have been reports of recurrence of

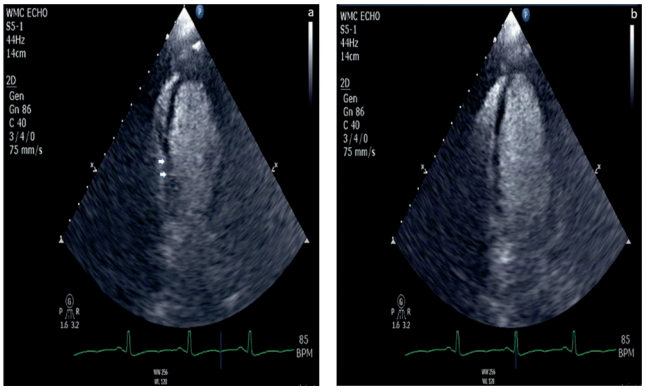

Figure 2. Contrast TTE showing mid-ventricular hypokinesia. a) End systole. b) End diastole.

TTC in around 5 to 6% of patients [3,6,17]. Complications like ventricular arrhythmia and cardiogenic shock have been rarely reported [3,18]. TTC has been reported to recur rarely and has occurred following cardiac transplantation [32,33].

In conclusion, physical illness is a common precipitator of TTC. Infections secondary to multiple bacterial, viral, parasitic, fungal agents and sepsis are known to precipitate TTC. With increasing literature on TTC, multiple other infections will be identified as potential contributors. There has been an increase in reports of the occurrence of TTC among COVID-19 patients in this pandemic. While recurrence, complications are reported outcome following TTC precipitated by infections continues to be benign like our patient.

Table 1. Infections causing Takotsubo cardiomyopathy.

Bacterial	
Gram positive	Cocci *Staphylococcus aureus* (MRSA) [6] *Staphylococcus gallinarum* [6] *Streptococcus pneumoniae* [6] *Streptococcus* group B [6] Bacilli *Clostridium tetani* [6] *Clostridium difficile* [6] *Clostridium botulinum* [6] *Listeria monocytogenes* [18]
Gram negative	Bacilli *Haemophilus influenzae* [20] *L. pneumophila* [22] *Salmonella* [22] *Escherichia coli* [6] *Pseudomonas aeruginosa* [6] *Klebsiella pneumoniae* [6] *Klebsiella oxytoca* [6] *Francisella tularensis* [23] *Aeromonas hydrophila* [6]
Rickettsia	*Orientia tsutsugamushi* [29]
Miscellaneous bacteria	*Nocardia cyriacigeorgica* [24]
Acid fast stain	*Mycobacterium tuberculosis* [10] Nontuberculous *Mycobacterium* [19]
Viral	
Retrovirus	HIV (human immunodeficiency virus) [11]
DNA virus	Cytomegalovirus [6] Hepatitis C [25] Parvovirus B19 [26] Herpes virus [6] Varicella zoster [7]
RNA virus	Influenza AInfluenza B [9] Dengue virus [8] Enterovirus [27] Hepatitis A [17] Norovirus [16] SARS-CoV-2 (COVID-19) [12]
Fungal	*Candida glabrata* [6] *Cryptococcus neoformans* [28]
Parasites	
Protozoa	Babesia [6]
Helminth	*Paragonimiasis westermani* [12] *Taenia solium* [6]

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