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A rare manifestation of Takotsubo Cardiomyopathy associated with non-tuberculous mycobacterium

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ABSTRACT

Background: Takotsubo Cardiomyopathy or broken heart syndrome is a rare cause of non-ischemic cardiomyopathy that produce left ventricular dysfunction with characteristic left ventricular apical ballooning. It rarely caused by infection. We present an atypical manifestation of non-tuberculous mycobacterial (NTM) infection with myocardial involvement and its diagnostic challenge.

Case illustration: A 57-year-old female presented with prolonged fever, fatigue and weight loss for one and half months. General examination was unremarkable with elevated C-Reactive Protein and normal troponin. Electrocardiogram (ECG) showed diffuse T wave inversion with prolonged QTc. Echocardiography showed hypokinetic apical with normal ejection fraction. Angiography showed patent coronary arteries. Ventriculography showed apical ballooning. Workup with ethambutol scan revealed active mycobacterial infection in both lung and mesentery. Sputum polymerase chain reaction (PCR) was positive for non-tuberculous mycobacterium. Follow up ECG and echocardiography showed improvement in QTc interval and left ventricular wall motion abnormalities.

Results: Takotsubo Cardiomyopathy may manifest as asymptomatic ventricular dysfunction following non-tuberculous mycobacterial infection. A thorough investigation will help identify the systemic disease with cardiac involvement which potentially could be fatal.

Conclusion: Takotsubo cardiomyopathy may be triggered by infection. Identification of causal is crucial as a management strategy to restore cardiac function.

1. Introduction

Takotsubo Cardiomyopathy with non-tuberculous mycobacterial (NTM) infection as the aetiology is a rare condition. NTM infection may induce changes in inflammatory cells and cytokines, and maybe increased the risk of a cardiovascular event, including myocardial dysfunction [1].

The prevalence of Non-Tuberculous Mycobacterium (NTM) has increased worldwide in recent decades with incidence rate vary from 1.0 to 1.8 cases per 100.000 persons, higher in the woman and elderly [2,3]. The most common clinical manifestation of NTM is lung disease, followed by lymphatic, skin/ soft tissue, and disseminated disease [1,3]. We described the first case of non-tuberculous mycobacterial infection and transient left ventricular dysfunction known as Takotsubo Cardiomyopathy.

2. Case report

A 57 years old female patient was admitted to the emergency ward with prolonged fever, fatigue and weight loss for one and half months. The patient had a history of smoking and pulmonary tuberculosis at ten years ago. The patient had no history of hypertension, diabetes, hypercholesterolemia, and family history of coronary artery disease. Upon physical examination, the blood pressure was 120/60 mmHg, with heart rate 111 bpm, body temperature was 39 °C. Thoracic, and abdominal examination was normal. Laboratory results showed a haemoglobin 10.7 gr/dl, leucocyte 8.480/mm3 with increase C-reactive protein 9.29 mg/dl. Kalium level was 4.3 mEq/L, and calcium was 4.3 mg/dl. Blood culture result was negative. Chest X-Ray was normal with negative acid-fast bacilli staining for sputum. An electrocardiogram (Fig. 1) showed diffuse T wave inversion with prolonged QTc despite correction for hypocalcemia. The cardiac enzyme was normal.

Trans-thoracic echocardiography (Fig. 2) showed hypokinetic

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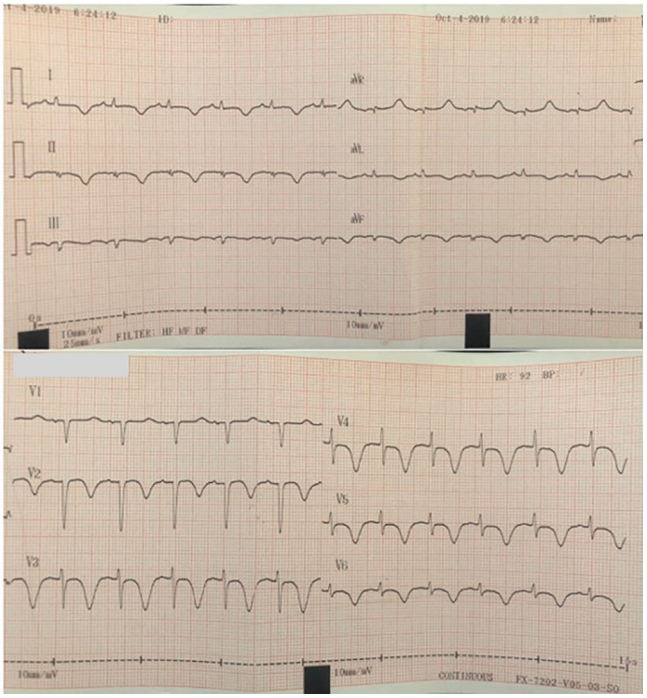

Fig. 1. Electrocardiogram showed diffuse T wave inversion at lead I, aVL, II, III, aVF, V2-V6 with prolonged QTc 525 msec.

anterior, anteroseptal (mid to apical), apicolateral, apicoseptal with normal left ventricular ejection fraction (LVEF 55%). These observations resemble apical ballooning, which is a typical characteristic of Takotsubo Cardiomyopathy.

Angiography showed patent coronary arteries. Ventriculography showed apical ballooning (Fig. 3A and B).

Workup with ethambutol scan revealed active mycobacterial infection in both lung and mesentery (Fig. 4). Sputum PCR was positive for non-tuberculous mycobacterium.

Clinically, the patient was asymptomatic, but due to QTc interval prolongation and risk of torsades de pointes, the patient was given bisoprolol titrated to 10 mg and treatment of underlying disease. Follow

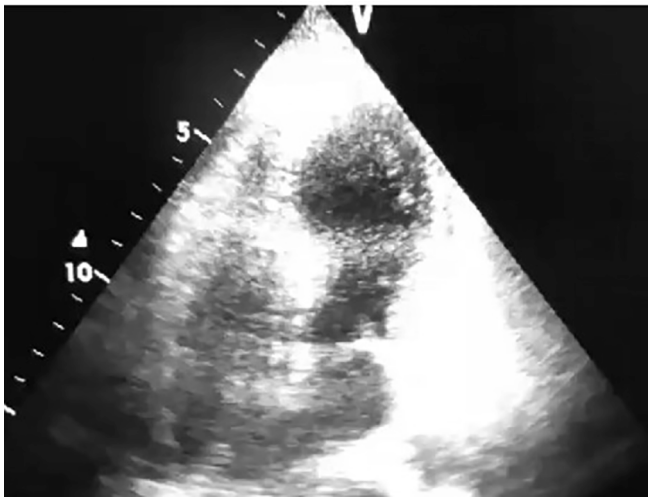

Fig. 2. Echocardiography demonstrated typical apical ballooning of Takotsubo Cardiomyopathy at four-chamber views.

up ECG showed improvement in QTc interval, and echocardiography showed normalized regional wall motion abnormalities. Hence, the diagnosis of Takotsubo Cardiomyopathy was made.

3. Discussion

Takotsubo Cardiomyopathy (TTC), also known as stress-induced cardiomyopathy or apical ballooning syndrome, characterized by temporary wall motion abnormality of the Left Ventricle and shared common feature with acute coronary syndrome [4]. TTC was diagnosed in 0.02% of all hospitalization in United States [5]. Woman older than 55 years old has a fivefold more significant risk of developing TTC than women younger than 55 years old and tenfold greater risk than men [4]. The most common presenting symptom are chest pain, dyspnea, or syncope with the electrocardiogram (ECG) demonstrating ST-segment elevation in 44%, T wave inversion with QT interval prolongation 41%, ST-segment depression in 8%, and left bundle branch block in 5% [6]. However, some patients may be diagnosed incidentally by new ECG changes or elevated cardiac troponin, as in our case [4].

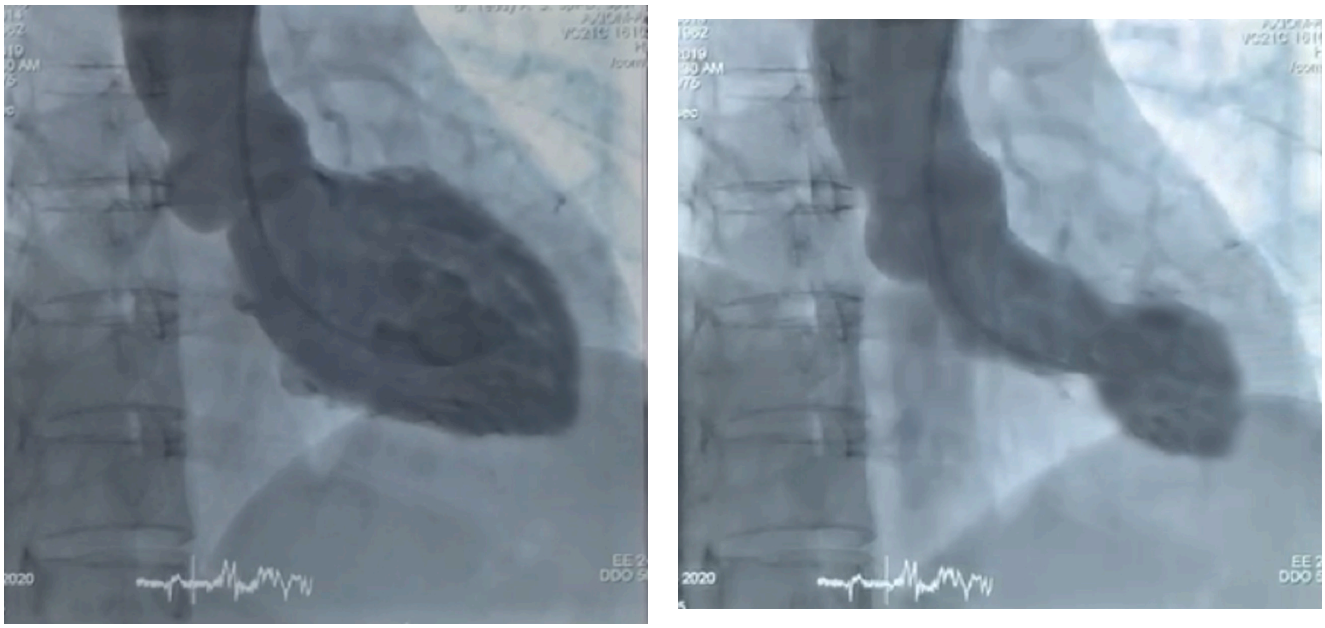

Fig. 3. A: Left ventriculography during the diastolic phase. B: Left ventriculography showed apical ballooning during the systolic phase.

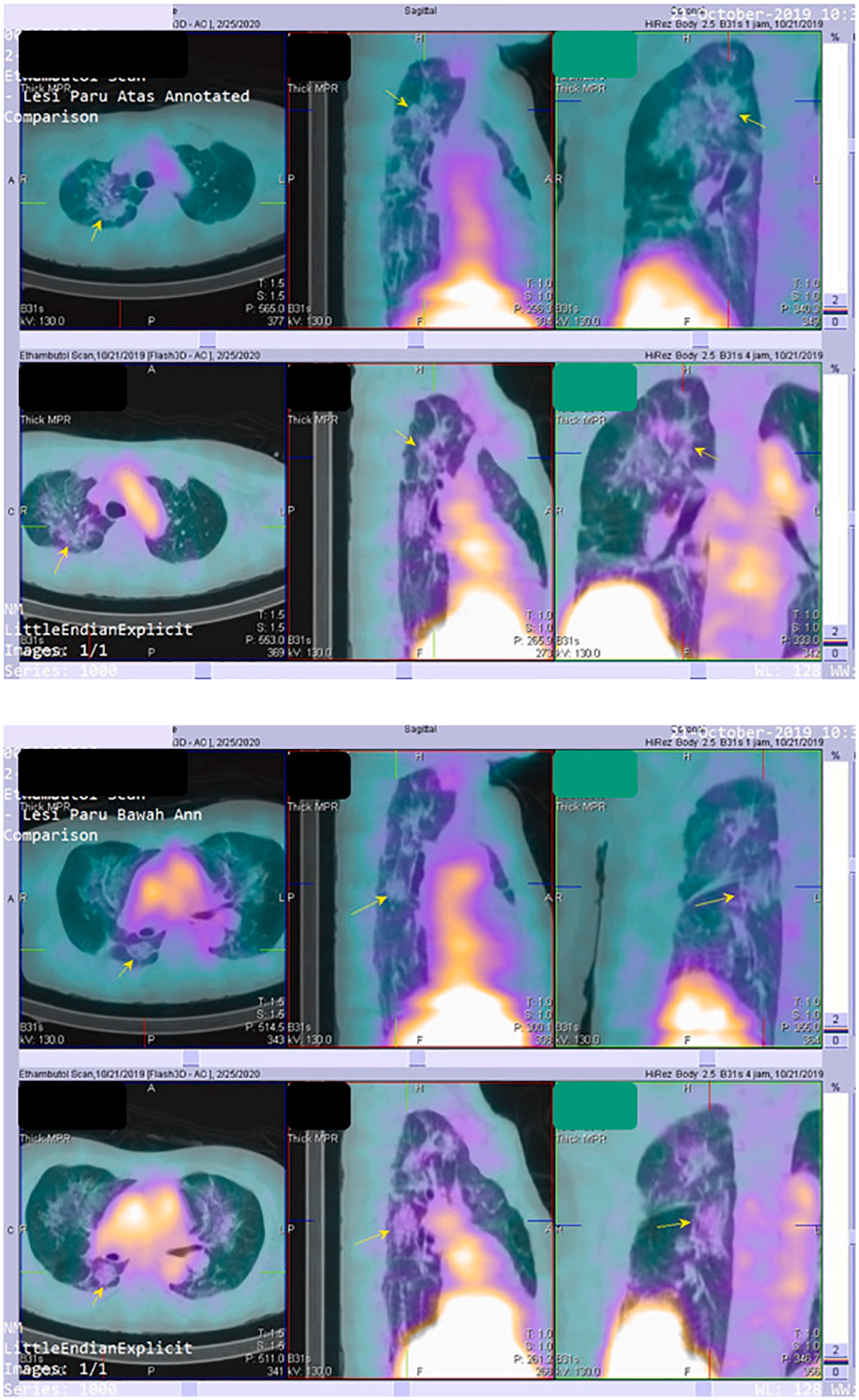

Fig. 4. Ethambutol scan showed active and sustained uptake of Tc-99m Ethambutol, revealed active infection of mycobacterium in both lung and mesenterium.

Pathophysiology of TCC remains poorly understood. Several hypotheses have been proposed, including sympathetic stimulation, multivessel epicardial spasm, microcirculatory dysfunction, catecholamine toxicity, neurogenically mediated myocardial stunning, and focal myocarditis [7]. Takotsubo cardiomyopathy may be induced by a physical or emotional stressor. Rarely, an infection may be the cause. Severe infection can cause above-mentioned physiological response and theoretically may precipitate TTC in susceptible individuals [8]. In this case, we did not find any emotional stressor. Hence we suggest non-tuberculous mycobacterial infection as a precipitant.

Prior studied have linked several infections to TTC, including pulmonary infection and upper respiratory tract infection [9,10]. De Giorgi et al. reviewed 27 reported case related to acute infection-induced TTC, found that it most frequently affects female and caused by bacterial infections. The proposed mechanisms responsible for infection-induced TTC could be alteration in intracellular of the myocardium, such as calcium transport, myofibrillar or mitochondrial dysfunction and activation of cellular apoptosis. Besides, extracellular factors of

myocardium such as alteration in metabolism and microcirculation, dysregulation of the autonomic nervous system, the release of inflammatory cytokines including tumor necrosis factor (TNF) α, interleukin (IL) 1β, IL-6, until vasoactive substances such as nitric oxide, endothelin 1, and catecholamines may also contribute [11].

Mycobacterial infections are one of the causes of prolonged fever [12]. In developing countries, the high incidence of tuberculous infection (TB) overshadows the occurrence of non-tuberculous mycobacterial (NTM) infections. NTM infections are the most challenging cases due to their diagnostic difficulty and require prolonged antibiotic regimens. Unlike TB, NTM infection is not a reportable disease in the majority of countries which limits the quality and reliability data collection [13]. NTM infection may induce changes in inflammatory cells and cytokines, that sustain prolonged inflammation may be associated with an increased risk of CV events, including heart failure [1,14]. According to our knowledge, this is the first case of NTM infection associated with TTC.

Mayo clinic proposed diagnostic criteria of TTC in 2004, which have been modified recently: (1) transient hypokinesis, akinesis, or dyskinesis in the left ventricular mid-segment with or without apical involvement; regional wall motion abnormalities that extend beyond single epicardial vascular distribution; and frequently, not always, a stressful trigger; (2) the absence of obstructive coronary disease or angiographic evidence of acute plaque rupture; (3) new ECG abnormalities (ST-segment elevation and/ T wave inversion) or modest elevation in cardiac troponin.; and (4) absence of pheochromocytoma and myocarditis [15]. Our patient meets all the criteria. However, due to instrument limitation, it was not possible to perform cardiac magnetic resonance imaging. Based on the aforementioned criteria, our patient was diagnosed as Takotsubo Cardiomyopathy.

Although TTC is generally considered as benign and reversible conditions, it may cause life-threatening complications, such as acute heart failure, cardiogenic shock, arrhythmia and cardiac arrest [6]. Most of the life-threatening arrhythmia coincide with anterolateral T wave inversion and QT-interval prolongation, as in our case. QT prolongation >500 ms is associated with malignant arrhythmia with pause dependent torsades de pointes degenerating into ventricular fibrillation. Therefore, one of mainstay treatment in TTC is beta-blocker [6]. It acts by minimizing the adrenergic stimulation that results in rapid changes in heart rate with dispersion of depolarization across the myocardium and after depolarization that is believed to be the inciting events for torsades de pointes [16]. Besides, despite the highest density of beta-adrenoreceptors in the apical myocardium, its negative inotropy after exposure to a high level of circulating catecholamines makes beta-blocker as a reasonable supportive treatment [17]. But, it should be used with caution when bradycardia and QTc > 500 ms due to the potential risk of pause-dependent torsades de pointes [6]. In our case, bisoprolol was given titrated to maximal dose and the resulting improvement of QTc interval and left ventricular contractility.

Finally, management of this patient mainly focuses on the treatment of underlying disease. Interestingly, identify the trigger was challenging in this case due to normal chest x-ray and negative acid-fast bacilli staining for sputum specimen. But, due to the high index of suspicious, the ethambutol scan was performed and revealed active mycobacterial infection in both lung and mesentery. Later, the sputum PCR was performed and came out with non-tuberculous mycobacterium. Hence, ethambutol scan and sputum PCR play a pivotal rule in identifying the non-tuberculous mycobacteria as the causal of the prolonged fever and TTC in this patient.

4. Limitation

We did not perform cardiac magnetic resonance imaging.

5. Conclusion

Identify and management of the trigger cause of Takotsubo Cardiomyopathy are crucial due to its reversibility.

Ethical statement

Sources of funding: This research received no specific grant from any funding agency, commercial or not-for-profit sectors.

Informed consent: Informed consent was obtained from each individual participant involved in this study.

Statement of human rights: This study was conducted in accordance with the 1964 Declaration of Helsinki and its subsequent amendments.

Statement of animal welfare: We do not involve animals in our study.

Credit authorship contribution statement

Aninka Saboe: Conceptualization, Investigation, Validation, Methodology, Supervision, Writing - review & editing. **Minsy Titi Sari:** Data curation, Writing - original draft, Software. **Mega Febrianora:** Visualization, Writing - review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

[1] Park CS, Choi E, Kim B, et al. Association between atrial fibrillation, myocardial infarction, heart failure and mortality in patients with non-tuberculous mycobacterial infection: a nationwide population-based study. Sci Rep 2019. https://doi.org/10.1038/s41598-019-51801-w.

[2] Park SC, Kang MJ, Han CH, et al. Prevalence, incidence, and mortality of non-tuberculous mycobacterial infection in Korea: a nationwide population-based study. BMC Pulm Med 2019;19:140. https://doi.org/10.1186/s12890-019-0901-z.

[3] Griffith DE, Aksamit T, et al. An official ATS/IDSA statement: diagnosis, treatment, and prevention of nontuberculous mycobacterial diseases. Am J Respir Crit Care Med 2007;175:367–416. https://doi.org/10.1164/rccm.200604-571ST.

[4] Ghadri JM, Wittstein IS, et al. International expert consensus document on Takotsubo Syndrome (Part I): clinical characteristics, diagnostic criteria, and pathophysiology. Eur Heart J 2018;39:2032–46. https://doi.org/10.1093/eurheartj/ehy076.

[5] Deshmukh A, Kumar G, et al. Prevalence of Takotsubo cardiomyopathy in the United States. Am Heart J 2012;164(1):66–71. https://doi.org/10.1016/j.ahj.2012.03.020.

[6] Ghadri JM, Wittstein IS, et al. International expert consensus document on Takotsubo Syndrome (Part II): diagnosis workup, outcome and management. Eur Heart J 2018;39:2047–62. https://doi.org/10.1093/eurheartj/ehy077.

[7] Morel O, Sauer F, et al. Importance of inflammation and neurohormonal activation in Takotsubo cardiomyopathy. J Cardiac Failure 2009;15(3):206–13.

[8] Sun TK. Infection-related stress phenomenon induced takotsubo cardiomyopathy mimicking ST-elevation myocardial infarction. J Clin Gerontol Geriatr 2015;6:106–9.

[9] Brunetti ND, Leva R, Passero T, Correale M, Dioguardi E, Montrone D, et al. Transient apical ballooning accompanying respiratory infection. Acute Card Care 2012;14:96–8. https://doi.org/10.3109/17482941.2012.682070.

[10] Ha JH, Lee H, Park YJ, Kang HH, Lee SH, Moon HS. Takotsubo cardiomyopathy caused by pulmonary tuberculosis: a case report. Tuberc Respir Dis 2014;77(1):24–7. https://doi.org/10.4046/trd.2014.77.1.24.

[11] Giorgi AD, Fabbian F, Pala M, Parisi C, et al. Takotsubo cardiomyopathy and acute infectious diseases: a mini-review of case reports. Angiology 2015;66(3):257–61. https://doi.org/10.1177/0003319714523673.

[12] Bjerrum S, Commey JO, Kenu E, Lartey M, et al. Tuberculosis and non-tuberculous mycobacteria among HIV-infected individuals in Ghana. Trop Med Int Health 2016;21(9):1181–90. https://doi.org/10.1111/tmi.12749.

[13] Chalmers JD, Aksamit T, et al. Non-tuberculous mycobacterial pulmonary infections. Pulmonol J 2018;24(2):120–31. https://doi.org/10.1016/j.pulmoe.2017.12.005.

[14] Varjabedian L, Merchant S, Danek M. Advanced systolic heart failure and Mycobacterium avium complex (MAC) infection: proposed immunologic mechanism, diagnostic dilemma and treatment considerations. Case Rep Int Med 2015;2(3):89–94. https://doi.org/10.5430/crim.v.2n3p89.

[15] Akashi YJ, Goldstein DS, Barbaro G, Ueyama T. Takotsubo cardiomyopathy: a new form of acute, reversible heart failure. Circulation 2008;118:2754–62.

[16] Shah M, Carter C. Long QT syndrome: a therapeutic challenge. Ann Pediatr Cardiol 2008;1(1):18–26. https://doi.org/10.4103/0974-2069.41051.

[17] Wright PT, Tranter MH, Morley-Smith AC, Lyon AR. Pathophysiology of Takotsubo syndrome. Circul J 2014;78(7):1550–8. https://doi.org/10.1253/circj.CJ-14-0623.