

Clinical Overlap Between Myopericarditis and Stress Induced Cardiomyopathy: A Diagnostic and Therapeutic Challenge

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

ABCDEF 1 **Toishi Sharma**
ABE 2 **Supriya M. Tigadi**
AE 1 **Jennifer Baldwin**
ABDEF 2 **Sara R. Tabtabai**

1 Department of Internal Medicine, University of Connecticut, Hartford, CT, U.S.A.
2 Department of Cardiovascular Disease, University of Connecticut, Hartford, CT, U.S.A.

Corresponding Author: Toishi Sharma, e-mail: tosharma@uchc.edu
Conflict of interest: None declared

Patient: Female, 47
Final Diagnosis: Stress induced cardiomyopathy
Symptoms: Chest pain
Medication: —
Clinical Procedure: Catch • echo
Specialty: Cardiology

Objective: Challenging differential diagnosis

Background: Stress induced cardiomyopathy (SIC) is characterized by non-obstructive coronary arteries and characteristic ventricular apical ballooning. The exact pathogenesis of SIC is not well recognized. We present an unusual case of SIC that mimicked acute myopericarditis and discuss the effect of this masquerading presentation of SIC in recognizing pathophysiological association between myopericarditis and SIC and limitations of current diagnostic criteria.

Case Report: A 47-year-old female presented with flu-like illness and pleuritic chest pain. An electrocardiogram (ECG) showed diffuse PR depressions and ST elevations, troponin 5 ng/mL, hemoglobin 14.2 mg/dL, leukocytosis (white blood cell count of $15.1 \times 10^3/\mu\text{L}$) and erythrocyte sedimentation rate (ESR) of 22.4 mm/hour. Echocardiogram showed reduced ejection fraction (EF) with apical ballooning. Catheterization showed non-obstructive coronary disease. The patient was given colchicine and ibuprofen for 1 day with symptom resolution over the next 2 days and repeat echocardiogram with preserved EF. Troponin trended down to 3.24 ng/mL and 0.44 ng/mL, 6 hours apart. ECG showed resolution of PR depressions and subsequent T wave inversions in 1, AVI, V1–V6 by day 3. The diagnosis of myopericarditis was favored by viral prodrome, fever, pleuritic pain, pericardial rub, ECG findings, and elevated ESR. History of emotional stress, characteristic ballooning of left ventricle apex with rapid resolution favored SIC.

Conclusions: This case showed that SIC and myocarditis need not be mutually exclusive and differentiating clinically between these 2 entities can be difficult. Alternatively, SIC can accompany other cardiac conditions like myocardial infarction, pericarditis, and myocarditis making diagnosis and management challenging. Clinicians need to be cautious while making this differentiation as duration and type of therapy may be significantly different. SIC can be considered a variant of regional inflammatory myocarditis wherein pericarditis may result secondary to extension of myocardial inflammation to overlying pericardium. The current Mayo Clinic criteria for diagnosis of SIC appears to be outdated, not accounting for such atypical presentations, and therefore needs to be revised.

MeSH Keywords: Myocarditis • Pericarditis • Takotsubo Cardiomyopathy

Full-text PDF: <https://www.amjcaserep.com/abstract/index/idArt/912169>



1342 2 5 40

Background

Stress induced cardiomyopathy (SIC) is a syndrome which can be seen in any age group but most commonly is seen in post-menopausal women that mimics the clinical presentation of acute coronary syndrome (ACS), and is classically triggered by emotional or physical stress. It is characterized by the absence of obstructive coronary disease [1–7], transient left ventricular (LV) dysfunction, ST segment elevation, and T-wave inversions, and elevated cardiac biomarkers. The exact pathogenesis of SIC is not well understood. Proposed mechanisms include catecholamine excess, coronary artery spasm, and microvascular dysfunction [8,9]. A variant of SIC with clinical features similar to pericarditis or myopericarditis has been described rarely in the literature and may shed light on the underlying pathology of SIC. We describe a unique case, highlighting an overlap in the presentation of SIC and myopericarditis.

Case Report

A 47-year-old female with a history of hypertension, bipolar disorder, and chronic low back pain status post lumbar fusion, presented with a 1-week history of flu-like illness and pleuritic chest pain. Her only home medications were amlodipine 5 mg daily and she was not currently on treatment for bipolar disorder. Physical examination at presentation revealed a fever 38.5°C (101.3°F) and a pericardial rub. An electrocardiogram (ECG) showed diffuse PR depressions and ST elevations (Figure 1). The patient's troponin was elevated at 5 ng/mL (<0.05 ng/mL), hemoglobin was 14.2 mg/dL (normal range 12–14 mg/dL), an elevated white blood cell count of $15.1 \times 10^3/\mu\text{L}$ (normal range 4000–11 000/ μL) and erythrocyte sedimentation rate (ESR) of 22.4 mm/hour (0–29 mm/hour). Procalcitonin and C-reactive protein were not measured. Echocardiogram revealed LV ejection fraction (EF) 35–40% and hypokinesis of mid, apical, anteroapical, anterior and lateral, inferior and apical myocardium with apical ballooning. The patient was admitted for further evaluation with a differential diagnosis of ACS versus myopericarditis. She was taken urgently for ventriculography and coronary angiogram, which revealed characteristic apical ballooning (Figure 2) and non-obstructive coronary artery disease (Figures 3, 4). Subsequent troponin downtrended (Table 1) and ECG evolved into T wave inversions with resolution of PR depressions over the next 2 days (Figure 5A, 5B) She was given colchicine and ibuprofen for 1 day. She was unable to undergo cardiac magnetic resonance imaging (cMRI) due to metallic lumbar implant. Her symptoms resolved over the next 2 days and repeat echocardiogram revealed an EF of 50–55% and resolution of apical and anterior wall motion abnormality. On repeat questioning, she reported an acute emotional stress 1 day prior to presentation during an encounter with the police. She was discharged in improved condition on a low dose of beta blocker.

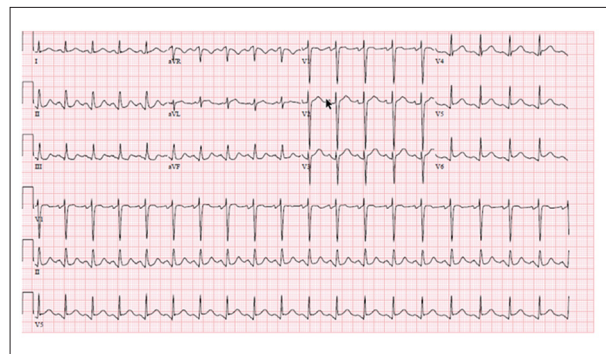


Figure 1. Electrocardiogram at admission showing diffuse PR depressions suggesting pericarditis.



Figure 2. Ventriculography showing apical ballooning of heart characteristic of stress induced cardiomyopathy.

Discussion

This case describes a clinical syndrome with overlap of myopericarditis and SIC. The diagnosis of pericarditis was initially favored due to pleuritic chest pain, pericardial rub, diffuse PR depressions on ECG, elevated inflammatory markers, and leukocytosis. Myocardial involvement suggesting myopericarditis was indicated after identification of hypokinesis. Interestingly, the wall motion involved the anterior wall and apex, without a culprit left anterior descending (LAD) lesion, suggesting SIC or myocarditis with a coincidental wall motion abnormality mimicking Takotsubo cardiomyopathy. Furthermore, a history of emotional stress prior to the onset of chest pain, complete resolution of symptoms and LV dysfunction within 3 days of onset favors the diagnosis of SIC. Rare similar cases have been described in the literature of a “myopericarditis variant” of SIC.

Classic SIC has been described in post-menopausal women with a mean age of 66 years [10]. However, since initial description in 1990, there have been multiple case reports recognizing the



Figure 3. Normal right coronary circulation without evidence of obstructive disease.



Figure 4. Normal left coronary circulation without obstructive disease.

incidence in other age groups [11–15], as well as atypical clinical presentations [16–18]. There have been 9 reported cases of clinical association between SIC and acute pericarditis. In 3 of these cases, the course of SIC was complicated by pericarditis [19–21] and in the other 6 cases, an acute pericarditis picture preceded the development of SIC [22–26]. To explain the confounding clinical picture, we support the “inflammatory hypothesis”. According to this proposed mechanism, SIC can be considered a variant of regional inflammatory myocarditis

with extension of the myocardial inflammation to the overlying pericardium, leading to pericarditis [27–29]. The evidence of inflammation of the myocardium has been previously reported

Table 1. Cardiac biomarker pattern.

Cardiac marker	Reference value	Day 1	After 6 hours	After 12 hours
Troponin	<0.05 ng/mL	5.02 ng/mL	3.24 ng/mL	0.44 ng/mL
Creatinine kinase- MB	0–8 ng/mL	25 ng/mL	18 ng/mL	
Creatinine kinase	22–269 IU/L	1709 IU/L	1591 IU/L	

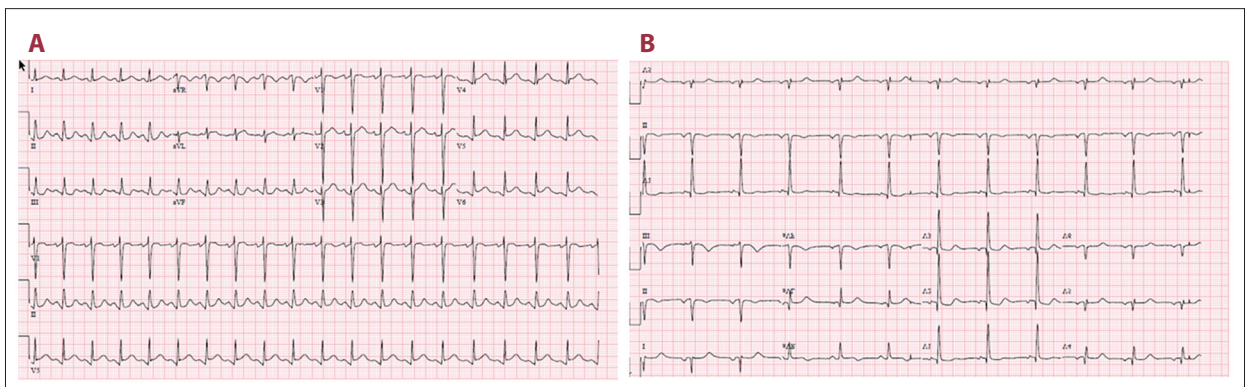


Figure 5. (A, B) Electrocardiogram taken 6 hours later showing rapid progression to T wave inversion favoring stress induced cardiomyopathy over myocarditis.

Table 2. Comparing characteristics of myocarditis, Takotsubo cardiomyopathy, and their combined variant.

Clinical features	Myopericarditis	Takotsubo cardiomyopathy (TCM)	Combined variant
Viral prodrome, fever, pleuritic chest pain	Present	Absent	Present
History of emotional stressor	Absent	Present	May be present
Cardiac enzymes	Elevated	Elevated	Elevated
Typical ECG findings	Diffuse PR depressions	Non-specific: Most common ST elevations in anterior leads	Diffuse PR depressions
Most common echocardiographic findings	Left ventricular dilation, development of a more spheroid shape	Characteristic ballooning of apex	Apical ballooning similar to TCM
Cardiac MRI	Patchy LGE1	LGE usually absent, may be present in some cases2	Suggested when the amount of LGE cannot reliably explain the WMA
Coronary angiogram	No obstructive coronary disease	No obstructive coronary disease	No obstructive coronary disease
Duration of illness/time to recovery	3–6 months	Days to weeks	Days to weeks
Duration of therapy	3–6 months of GDMT for HFrEF, avoidance of strenuous physical activity	Days to weeks until resolution; no proven role of therapy to prevent recurrence	Days to weeks: similar to TCM

ECG – electrocardiogram; MRI – magnetic resonance imaging; LGE – late gadolinium enhancement; GDMT – guideline-directed medical therapy.

both on endomyocardial biopsy [27,30] and on cMRI [31]. The role of intense catecholamine surge secondary to the chest pain caused by pericardial inflammation has also been proposed and may explain how pericarditis can trigger SIC [27,32]. Given the overlap described, the disease processes may represent a spectrum of inflammation and be viewed as myopericarditis-variant SIC (Table 2).

Differentiating clinically between the 2 entities can be difficult [27–36]. Sequential ECG may be helpful in differentiating myopericarditis-variant SIC from classic myopericarditis. The general evolution of T wave changes is similar between the 2 entities, though it tends to occur at different rates. Rapid development of T wave inversions following ST elevation, as in our case, favors SIC [27,32]. Whereas classic pericarditis tends to have a slower progression to T wave inversion. Late gadolinium enhancement (LGE) on cMRI may also be useful. Myocarditis is characterized by patchy LGE on cMRI. However, when a low threshold for LGE is used (e.g., 3 standard deviations above the mean signal intensity of remote myocardium), LGE can occasionally be detected in stress cardiomyopathy, leading to erroneous diagnosis of myocarditis [37]. Despite this potential confusion, one can consider if the degree of wall motion abnormality is not explained by the amount of LGE present, this would support myopericarditis-variant SIC [26]. While a widely

established non-invasive tool allowing a rapid and reliable diagnosis of Takotsubo syndrome is currently lacking, according to the International Expert Consensus Document on Takotsubo Syndrome [33,34], coronary angiography with left ventriculography is considered the gold standard diagnostic tool to exclude or confirm TTS. However, cMRI is essential to exclude infectious myocarditis. In addition to the aforementioned discussed limitations of MRI in diagnosing myocarditis, MRI is not always feasible in these cases, due to lack of availability, patient factors (presence of a permanent pacemaker, or metallic implant as in our patient), or prohibitive cost.

Clarification of diagnosis has important treatment implications. Non-steroidal anti-inflammatory agents are the treatment of choice in acute pericarditis, but can be harmful in myocarditis and SIC [47–40]. In either case, if reduced EF is present, guideline-directed medical therapy (GDMT) is indicated. However, the recommended duration of therapy differs greatly. In myopericarditis, 3–6 months of GDMT is usually recommended after resolution of symptoms. However, for cases of SIC, GDMT is generally discontinued following normalization of EF, which occurs rapidly over days to weeks. Although routine use of beta blocker therapy to prevent recurrence of SIC has been proposed, literature has not supported decreased recurrence [10,40]. Patients with myopericarditis-variant SIC

tend to have a better overall prognosis and need to avoid strenuous activity for 3–6 months as in cases of pure myocarditis. In certain patient populations, the 3–6 months of GDMT can have a significant impact, including for women of child-bearing age, young men known to be particularly sensitive to beta blocker side effects, or cases where antihypertensives or those without blood pressure indications for antihypertensives.

Finally, although we support a shared myocardial inflammatory process for both entities, the question of why inflammation in myopericarditis-variant SIC resolves rapidly compared to inflammation associated with pure myocarditis remains unanswered. Additionally, since SIC has been shown to accompany other cardiac conditions like myocardial infarction, it is possible that this entity is capable of accompanying pericarditis and myocarditis as well.

References:

1. Sato H, Taiteishi H, Uchida T: Takotsubo-type cardiomyopathy due to multivessel spasm. In: Clinical aspect of myocardial injury: In Ischemia to Heart Failure, Kodama K, Haze K, Hon M (eds.), Kagakuhyoronsha, Tokyo, Japan 1990; 56
2. Dote K, Sato H, Tateishi H et al: Myocardial stunning due to simultaneous multivessel coronary spasms: A review of 5 cases. *J Cardiol*, 1991; 21: 203–14
3. Bybee KA, Kara T, Prasad A et al: Systematic review: transient left ventricular apical ballooning: A syndrome that mimics ST-segment elevation myocardial infarction. *Ann Intern Med*, 2004; 141: 858–65
4. Tsuchihashi K, Ueshima K, Uchida T et al: Transient left ventricular apical ballooning without coronary artery stenosis: A novel heart syndrome mimicking acute myocardial infarction. *Angina Pectoris-Myocardial Infarction Investigations in Japan*. *J Am Coll Cardiol*, 2001; 38: 11–18
5. Abe Y, Kondo M, Matsuoka R et al: Assessment of clinical features in transient left ventricular apical ballooning. *J Am Coll Cardiol*, 2003; 41: 737–42
6. Hachamovitch R, Chang JD, Kuntz RE et al: Recurrent reversible cardiogenic shock triggered by emotional distress with no obstructive coronary disease. *Am Heart J*, 1995; 129: 1026–28
7. Sharkey SW, Lesser JR, Zenovich AG et al: Acute and reversible cardiomyopathy provoked by stress in women from the United States. *Circulation*, 2005; 111: 472–79
8. Wittstein IS, Thiemann DR, Lima JA et al: Neurohumoral features of myocardial stunning due to sudden emotional stress. *N Engl J Med*, 2005; 352: 539–48
9. Paur H, Wright PT, Sikkil MB et al: High levels of circulating epinephrine trigger apical cardiodepression in a β_2 -adrenergic receptor/Gi-dependent manner: A new model of Takotsubo cardiomyopathy. *Circulation*, 2012; 126: 697–706
10. Templin C, Ghadri JR, Diekmann J et al: Clinical features and outcomes of Takotsubo (stress) cardiomyopathy. *N Engl J Med*, 2015; 373: 929–38
11. Sato H, Taiteishi H, Uchida T et al: Tako-tsubo-like left ventricular dysfunction due to multivessel coronary spasm. In: Kodama K, Haze K, Hori M (eds.), Clinical Aspect of Myocardial Injury: From Ischemia to Heart Failure. Tokyo, Japan: Kagakuhyoronsha Publishing, 1990; 56–64
12. Ramakrishna G, Ravi BS, Chandrasekaran K: Apical ballooning syndrome in a postoperative patient with normal microvascular perfusion by myocardial contrast echocardiography. *Echocardiography*, 2005; 22(7): 606–10
13. Vultaggio A, Matucci A, Del Pace S et al: Tako-Tsubo-like syndrome during anaphylactic reaction. *Eur J Heart Fail*, 2007; 9(2): 209–11
14. Ohwada R, Hotta M, Kimura H et al: Ampulla cardiomyopathy after hypoglycemia in three young female patients with anorexia nervosa. *Internal Medicine*, 2005; 44(3): 228–33
15. Lee SY, Lee SE, Choi JW et al: A case of transient left ventricular apical ballooning syndrome in a child: clinical features and imaging findings. *Int J Cardiovasc Imaging*, 2010; 26(2): 345–51
16. Dorfman TA, Iskandrian AE, Aqel R: An unusual manifestation of tako-tsubo cardiomyopathy. *Clin Cardiol*, 2008; 31(5): 194–200
17. Fortunato G, Ceresa F, Sansone F et al: Acute ischemia of right superior arm: An unusual presentation of Takotsubo cardiomyopathy? *Minerva Cardioangiologica*, 2010; 58(1): 156–57
18. Mathew B, Villarreal D: Two unusual cases of Takotsubo cardiomyopathy presenting with sudden cardiac death. *Am J Med Sci*, 2009; 337(6): 473–75
19. Maruyama T, Hanaoka T, Nakajima H: Acute pericarditis in the recovery phase of transient left ventricular apical ballooning syndrome (Takotsubo cardiomyopathy). *Internal Medicine*, 2007; 46(22): 1857–60
20. Guevara R, Aguinaga-Meza M, Hazin MI et al: Takotsubo cardiomyopathy complicated with acute pericarditis and cardiogenic shock. *J Natl Med Assoc*, 2007; 99(3): 281–83
21. Le EJ, Hendriks R, Whelan AP: Takotsubo cardiomyopathy complicated by Dressler's syndrome. *Med J Aust*, 2008; 188(12): 725–27
22. Lee SY, Lee SE, Choi JW et al: A case of transient left ventricular apical ballooning syndrome in a child: Clinical features and imaging findings. *Int J Cardiovasc Imaging*, 2010; 26(2): 345–51
23. Li JW, Nanda S, Longo S: Acute pericarditis induced stress cardiomyopathy. *Acta Cardiologica*, 2010; 65(3): 361–64
24. Cambronerio F, Peñafiel P, Moreno V et al: An atypical presentation of Tako-Tsubo cardiomyopathy. *Int J Cardiol*, 2010; 138(3): e53–55
25. Jimmy HO, Foo D: An unusual electrocardiographic manifestation of Takotsubo cardiomyopathy. *Am J Emerg Med*, 2012; 30(7): 1323.e1–e4
26. Chhabra L, Khalid N, Kluger J et al: Lupus myopericarditis as a preceding stressor for takotsubo cardiomyopathy. *Proc (Bayl Univ Med Cent)*, 2014; 27(4): 327–30
27. Sezavar SH, Toofaninejad N, Hajsadeghi S et al: Takotsubo cardiomyopathy coexisting with acute pericarditis and myocardial bridge. *Case Rep Cardiol*, 2016; 2016: 5189741

Conclusions

Takotsubo cardiomyopathy and myopericarditis may comprise a clinical spectrum of myocardial inflammation (Table 1). This case describes a case of “myopericarditis-variant TC”, the underlying pathophysiologic mechanism of which needs to be further elucidated. Current diagnostic criteria need to be updated to account for atypical presentations of Takotsubo cardiomyopathy which may have therapeutic implications [26,28,29].

Acknowledgements

We would like to acknowledge the providers and nurses from the Departments of Internal Medicine and Cardiology who helped in taking care of the patient and the administration for providing various tools for research.

Conflicts of interests

None.

28. Omar HR: Takotsubo-pericarditis association. *Am J Emerg Med*, 2012; 30(2): 382–83
29. Li JW, Nanda S, Longo S: Acute pericarditis induced stress cardiomyopathy. *Acta Cardiol*, 2010; 65(3): 361–64
30. Nef HM, Möllmann H, Kostin S et al: Tako-Tsubo cardiomyopathy: Intraindividual structural analysis in the acute phase and after functional recovery. *Eur Heart J*, 2007; 28(20): 2456–64
31. Abdel-Aty H, Cocker M, Friedrich MG: Myocardial edema is a feature of Tako-Tsubo cardiomyopathy and is related to the severity of systolic dysfunction: Insights from T2-weighted cardiovascular magnetic resonance. *Int J Cardiol*, 2009; 132(2): 291–93
32. Migliore F, Zorzi A, Marra MP et al: Myocardial edema underlies dynamic T-wave inversion (Wellens' ECG pattern) in patients with reversible left ventricular dysfunction. *Heart Rhythm*, 2011; 8(10): 1629–34
33. Madias JE: Why the current diagnostic criteria of Takotsubo syndrome are outmoded: A proposal for new criteria. *Int J Cardiol*, 2014; 174(3): 468–70
34. Madias JE: Acute myocardial infarction triggering Takotsubo syndrome, and the need to search for its prevalence. *J Geriatr Cardiol*, 2014; 11(3): 278
35. Chhabra L: Myopericarditis and Takotsubo cardiomyopathy association. *Int J Cardiol*, 2015; 186: 143
36. Kuruvilla S, Adenaw N, Katwal AB et al: Late gadolinium enhancement on cardiac magnetic resonance predicts adverse cardiovascular outcomes in nonischemic cardiomyopathy. A systematic review and meta-analysis. *Circ Cardiovasc Imaging*, 2014; 7(2): 250–58
37. Costanzo-Nordin MR, Reap EA, O'Connell JB et al: A nonsteroid anti-inflammatory drug exacerbates Coxsackie B3 murine myocarditis. *J Am Coll Cardiol*, 1985; 6: 1078–82
38. Rezkalla S, Khatib G, Khatib R: Coxsackievirus B3 murine myocarditis: Deleterious effects of nonsteroidal anti-inflammatory agents. *J Lab Clin Med*, 1986; 107: 393–95
39. Khatib R, Reyes MP, Smith F et al: Enhancement of coxsackievirus B4 virulence by indomethacin. *J Lab Clin Med*, 1990; 116: 116–20
40. Singh K, Carson K, Usmani Z et al: Systematic review and meta-analysis of incidence and correlates of recurrence of takotsubo cardiomyopathy. *Int J Cardiol*, 2014; 174: 696–701