Case Report

ANNALS OF MEDICINE & SURGERY

OPEN

Myasthenic crisis-induced Takotsubo cardiomyopathy: a case report

Janak Khadka, MBBS[a,*], Pravesh Bhattarai, MBBS[a], Apsara Adhikari, MBBS[d], Rajat Acharya, MD[c], Parash Rayamajhi, DM, MD[b]

Introduction and importance: Myasthenic crisis (MC) is characterized by severe weakness in the bulbar and respiratory muscles. Takotsubo cardiomyopathy (TC) is a rare clinical entity mainly associated with postmenopausal women. We report a case of both these conditions in a premenopausal woman.

Case presentation: A 31-year-old woman with hypothyroidism presented with dyspnea. Bedside echocardiography in the ICU revealed an apical ballooning with an ejection fraction of 25%, and she was treated with losartan, furosemide, and spironolactone. She was intubated after 2 days as she developed respiratory distress and type II respiratory failure. Upon investigation, the patient tested positive for anti-acetylcholine receptor antibody. Treatment with five doses of IVIG (intravenous immunoglobulin) was given, and she made a remarkable recovery. Repeat echocardiography revealed her ejection fraction is normal and cardiac function is resolved.

Clinical discussion: The association between TC and MC is unusual and not commonly observed. MC can be a natural progression of myasthenia gravis or due to stressors, such as infection, medicine, pregnancy, and surgery. Stressful events can lead to TC. This leads to the possibility of TC, along with other cardiac complications, in patients with MC.

Conclusion: Patients with MC may be at potential risk of developing TC, thus careful cardiac monitoring is necessary while treating them for a better prognosis.

Keywords: case report, echocardiography, myasthenic crisis, Takotsubo cardiomyopathy

Introduction

Myasthenia gravis (MG) is an autoimmune disorder caused by the production of autoantibodies against the nicotinic acetylcholine receptors at the neuromuscular junction[1]. Each year around 4–12 per million people are affected by this disorder[2]. Patients with MG show several cardiac manifestations ranging from asymptomatic electrocardiographic changes to ventricular tachycardia, myocarditis, heart failure, and sudden death[3]. Myasthenic crisis (MC) is defined by the development of neuromuscular respiratory failure from MG that requires mechanical ventilation or endotracheal intubation for airway protection[4]. Among all MG patients, the annual incidence of MC is 2.5%[5].

HIGHLIGHTS

- Myasthenic crisis (MC)-induced Takotsubo cardiomyopathy (TC) is a rare condition.
- Echocardiographic findings in TC show apical ballooning with reduced ejection fraction.
- Both MC and TC are triggered by stressful events.

The crisis may be triggered by physical stressors, infection, emotional stress, surgery, and medication[5].

Takotsubo cardiomyopathy (TC) is characterized by transient motion abnormality of the apex of the left ventricle, but with no obstructive coronary artery disease[6]. The prevalence of TC associated with MC in the nationwide population was 0.3%[7]. Both MC and TC have similar emotional and physical triggers, but TC is a rare and potentially fatal complication of MC[7]. Since the patient's age, in this case, falls in the premenopausal period, it challenges clinicians for a definitive diagnosis of TC, especially those who encountered the disease for the first time. The unavailability of PLEX (plasma exchange) in our settings challenges clinicians in the management of MC. However, we were able to manage successfully with intravenous immunoglobulin (IVIG), which is another mainstay treatment for MC that is considered less effective than PLEX by few previous literature. Early diagnosis and quick treatment are crucial for better outcomes for patients. This is the case report of TC induced by MC, which has been poorly reported so far.

[a]Kathmandu Medical College, [b]Department of Neurology, [c]Department of Internal Medicine, Kathmandu Medical College, Kathmandu, Nepal and [d]Sylhet Women's Medical College, Sylhet, Bangladesh

Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

*Corresponding author. Address: Kathmandu Medical College, Sinamangal, Kathmandu 44600, Nepal. Tel.: +977 984 658 8271. E-mail: janakkhadka345@gmail.com (J. Khadka).

Annals of Medicine & Surgery (2024) 86:1704–1707

Received 5 December 2023; Accepted 5 January 2024

Published online 15 January 2024

http://dx.doi.org/10.1097/MS9.0000000000001723

Case presentation

A 31-year-old married female from Kathmandu presented to the Emergency Department of KMCTH (Kathmandu Medical College and Teaching Hospital) with a 2-day history of dyspnea. The patient has been known to have hypothyroidism for 3 months and is under medication thyroxin 37.5 μg.

On examination, she was alert and oriented to time, place, and person. The blood pressure was 130/100 mmHg, pulse was 130 beats per minute, temperature was 97°F, respiratory rate was 20 breaths per minute, and SpO_2 was 98% on room air. Glasgow Coma Scale had a score of E4V5M6. Cardiovascular and respiratory examinations were unremarkable. The neurological examination revealed bilateral ptosis and general muscular weakness with a power of 4/5 in bilateral upper and lower limbs with no other focal localizing sign.

Electrocardiography demonstrated sinus tachycardia and slight ST elevation in Lead I and aVL with no reciprocal changes and no axis deviation. The cardiac marker was elevated with Troponin I of 3.2 ng/ml. An acute myocardial infarction was suspected, and aspirin 300 mg and clopidogrel 300 mg were given in the emergency department. Then, she was admitted to the ICU. A bedside transthoracic echocardiography showed apical ballooning of the left ventricle with a reduced ejection fraction of 25%. In coronary angiography, no obstruction was seen (Fig.1). This finding was suggestive of TC. She has commenced on losartan 25 mg, furosemide 10 mg, spironolactone 25 mg, low molecular weight heparin, and metoprolol 25 mg.

She was initially kept on non-invasive ventilation for respiratory support and changed to continuous positive airway pressure (CPAP) as saturation of oxygen was not maintained. This did not improve the patient's condition and she developed persistent respiratory distress. So, she was intubated 2 days after her ICU stay and kept in continuous mandatory ventilation (CMV). In arterial blood gas analysis, she was in type II respiratory failure with pH 7.146, partial pressure of carbon dioxide (pCO_2) 97.8 mmHg, partial pressure of oxygen (pO_2) 114.6 mmHg, and bicarbonate (HCO_{3-}) 34 mmol/l. Since she developed type II respiratory failure, we suspected having weakness in her respiratory muscles. On further inquiry, the family members revealed that she had a history of ptosis, dysphagia, and difficulty in speaking with marked diurnal variation for the last 10 years. Based on this history and current clinical presentation, we suspected her of MC, so we sent an investigation for MC. The serum anti-acetylcholine receptor antibody was positive with a value of 7.78 nmol/l. The diagnosis criteria of MC were fulfilled as she had a combination of symptoms and signs, along with positive specific autoantibodies, which require intubation due to respiratory failure[1,4]. Instantly, IVIG was administered at a rate of 2 g/kg for 5 days. As the patient's condition improved, the CMV mode of mechanical ventilation was changed to synchronized intermittent mandatory ventilation (SIMV) and gradually to CPAP. Then, a spontaneous breathing trial was done and she was extubated after 6 days of intubation.

After 2 days of extubation, she developed fever, cough, and crepitation in the inframammary and infra-axillary area. The chest radiograph is shown in Figure 2. As soon as she developed hospital-acquired pneumonia (HAP), we started her on meropenem and linezolid. Her condition was improving. After the acquisition of the microbiological report, *Escherichia coli* was isolated in sputum culture. In the antibiotic susceptibility test, the bacteria were found to be resistant to piperacillin-tazobactam, ceftriaxone, amoxicillin-clavulanic acid, and cefixime. However, it was sensitive to colistin. So, we added colistin nebulization. Since her chest radiograph and condition were improving, we continued the same antibiotics. She was then shifted to the cabin

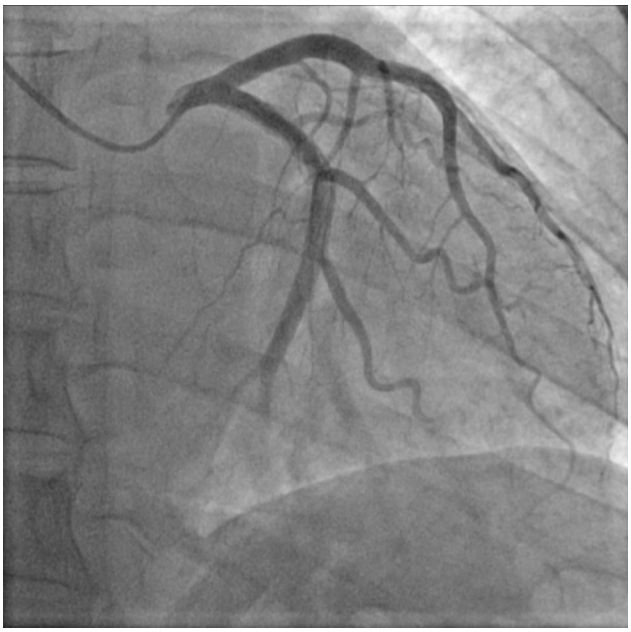

Figure 1. Coronary angiography showing non-obstructive disease in the left anterior descending artery.

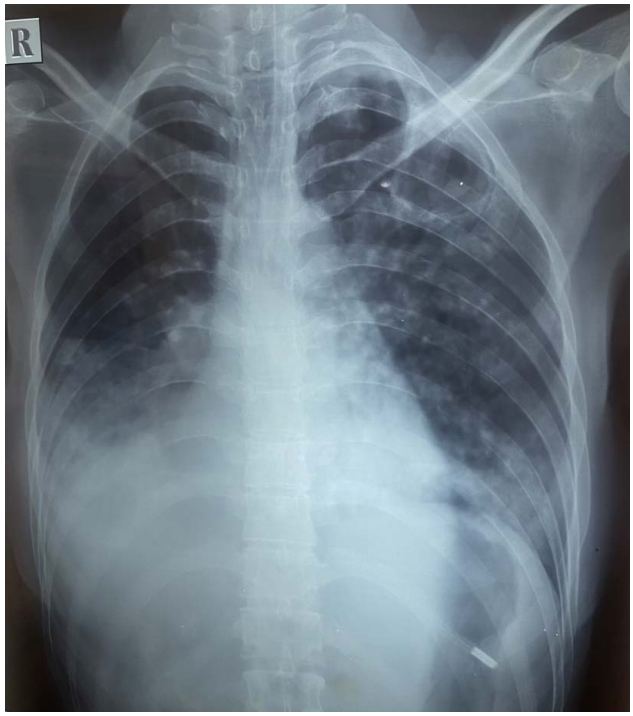

Figure 2. Chest radiograph showing homogenous consolidation in the right lower zone of the lungs.

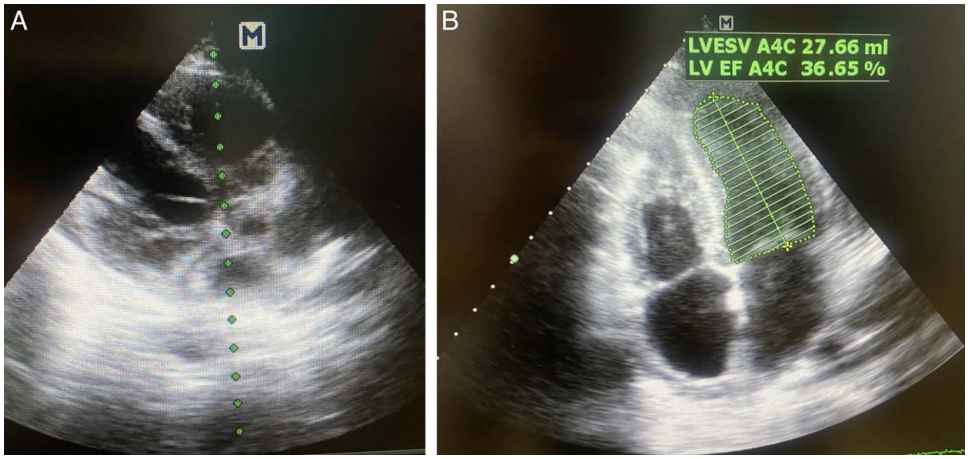

Figure 3. Two-dimensional echocardiograph. (A) Parasternal long axis view showing apical ballooning; (B) four chamber view showing ejection fraction.

for isolation. To prevent HAP, we performed oral care, deep breathing exercises, patient mobility, and timely ICU fumigation.

Formal transthoracic echocardiography was performed after the improvement of the patient's clinical condition, which confirmed the finding of bedside echocardiography and revealed an ejection fraction of 36.65%(Fig.3). She was discharged on medication prednisolone 40 mg, losartan25 mg, furosemide 10 mg, spironolactone 25 mg, aspirin 75 mg, clopidogrel 75 mg, and alprazolam 0.25 mg.

Upon follow-up, she made a remarkable recovery, and her echocardiography showed resolved cardiac function with an ejection fraction of 58%.

Clinical discussion

MC is an uncommon life-threatening disease. MC-induced TC is a rare and deadly combination[7]. The majority of cases (88%) were contributed from the Western Pacific, American, and European regions[8]. No cases from Nepal and Southern Asia are described in published literature. TC is a disease of mostly postmenopausal women[9]. However, this case is unique because our patient's presentation is in the premenopausal period, and it was challenging for us to diagnose MC-induced TC in resource-limited settings.

The exact pathophysiology of TC has not yet been determined, but there is supporting evidence, given sympathetic over-activation and excess catecholamine-induced cardiac dysfunction[10]. Emotional and physical stressors, pheochromocytoma, and alpha and beta agonists that activate catecholamine surge are associated with TC[10]. There is a higher density and sensitivity of beta-2 adrenergic receptors in the apical myocardium than in the basal myocardium[11].

During a catecholamine surge, there is a switching of the G-protein signaling pathway from stimulatory to inhibitory, called ligand-directed trafficking[12]. It is the reason that leads to regional hypokinesia in the apex of the left ventricle in TC, which will also recover quickly as the catecholamine level normalizes[12]. In our case, events leading to MC cause physiological stress that results in catecholamine surge and precipitated TC[13].

Myocarditis is one of the important differential diagnoses, as 97% of thymoma-associated MG and 48% of all MG cases have antibodies directed toward the heart[14]. The presence of apical motion abnormality instead of global hypokinesia in echocardiography suggests this case is less likely to have myocarditis. Acute myocardial infarction mimics TC[15]. However, our case meets the diagnostic modified Mayo Clinic criteria for TC, which includes (a) transient left ventricular dysfunction, (b) absence of obstructive coronary disease or acute plaque rupture, (c) ECG abnormalities or increased cardiac troponin, and (d) absence of pheochromocytoma[12].

The management of MC is mainly a supportive measure for respiratory failure. IVIG is equally effective, but few studies suggest PLEX is more effective and works quickly[16]. In our patient since PLEX was not available in our setting, we treated her with IVIG. Pyridostigmine was not initiated for MG because she was in crisis. So, she was treated with IVIG followed by corticosteroids.

Conclusions

In conclusion, clinicians must be vigilant about the possibility of rare cardiac complications like TC in MC patients. An ST elevation in the ECG and raised cardiac troponin levels led us to suspect myocardial infarction. However, the presence of classical findings in the echocardiography of apical ballooning and reduced ejection fraction led to the diagnosis of TC. We recommend that once a patient presents with MC, continuous cardiac monitoring, such as electrocardiography, echocardiography, and cardiac marker measurement, is of paramount importance. This makes it possible to quickly start the appropriate treatment and improve patient outcomes.

Ethical approval

This is a case report that does not require formal ethical committee approval.

Consent

Written informed consent was obtained from the patients for the publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Sources of funding

None.

Author contribution

J.K. and P.B.: collected all the required case information, images, and reports, reviewed the literature, and contributed to writing the manuscript; A.A.: literature review, writing the manuscript, and final approval of the manuscript; P.R. and R.A.: were involved in diagnosing the case, counseling, treatment of the patient, and editing of the manuscript.

Conflicts of interest discloure

The authors report no conflicts of interest.

Research registration unique identifying number (UIN)

Janak Khadka (2023), 'Myasthenic crisis-induced Takotsubo cardiomyopathy: a case report', Mendeley Data, V1, doi: 10.17632/t3cs5r2jtm.1.

Guarantor

Janak Khadka.

Data availability statement

The corresponding author confirms the availability of data upon request.

Provenance and peer review

Not commissioned, externally peer-reviewed.

Acknowledgements

None.

References

[1] Gilhus NE. Myasthenia gravis. N Engl J Med 2016;375:2570–81.
[2] Gilhus NE, Verschuuren JJ. Myasthenia gravis: subgroup classification and therapeutic strategies. Lancet Neurol 2015;14:1023–36.
[3] Kumagai S, Kato T, Ozaki A, *et al*. Serial measurements of cardiac troponin I in patients with myasthenia gravis-related cardiomyopathy. Int J Cardiol 2013;168:e79–80.
[4] Seneviratne J, Mandrekar J, Wijdicks EF, *et al*. Predictors of extubation failure in myasthenic crisis. Arch Neurol 2008;65:929–33.
[5] Claytor B, Cho SM, Li Y. Myasthenic crisis. Muscle Nerve 2023;68:8–19.
[6] Pilgrim TM, Wyss TR. Takotsubo cardiomyopathy or transient left ventricular apical ballooning syndrome: a systematic review. Int J Cardiol 2008;124:283–92.
[7] Desai R, Abbas SA, Fong HK, *et al*. Burden and impact of Takotsubo syndrome in myasthenic crisis: a national inpatient perspective on the under-recognized but potentially fatal association. Int J Cardiol 2020;299:63–6.
[8] Rathish D, Karalliyadda M. Takotsubo syndrome in patients with myasthenia gravis: a systematic review of previously reported cases. BMC Neurol 2019;19:281.
[9] Gianni M, Dentali F, Grandi AM, *et al*. Apical ballooning syndrome or Takotsubo cardiomyopathy: a systematic review. Eur Heart J 2006;27:1523–9.
[10] Ranellone A, Abraham MG. Takotsubo cardiomyopathy in the setting of a myasthenic crisis. Int J Neurosci 2022;132:89–94.
[11] Paur H, Wright PT, Sikkel MB, *et al*. High levels of circulating epinephrine trigger apical cardiodepression in a β2-adrenergic receptor/Gi-dependent manner: a new model of Takotsubo cardiomyopathy. Circulation 2012;126:697–706.
[12] Ramrattan A, Gonzalez I, Abdullah H, *et al*. A myasthenic crisis complicated by a Takotsubo cardiomyopathy. Cureus 2022;14:e21067.
[13] Ho RYJ, Chern ZRB, Kristanto W. Takotsubo cardiomyopathy, or 'broken-heart syndrome', with concomitant myasthenic crisis. Singapore Med J 2019;60:267–9.
[14] Shivamurthy P, Parker MW. Cardiac manifestation of myasthenia gravis: a systematic review. IJC MetabEndocr 2014;5:3–6.
[15] 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;38:11–8.
[16] Sanders DB, Wolfe GI, Benatar M, *et al*. International consensus guidance for management of myasthenia gravis: executive summary. Neurology 2016;87:419–25.