

CASE REPORT

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Takotsubo cardiomyopathy in a female presenting with status asthmaticus: a case report and review of literature

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Abstract

Background: Takotsubo cardiomyopathy (TCM) is a non-ischemic syndrome characterized by transient acute left ventricular dysfunction as evident on transthoracic echocardiography. It can often mimic myocardial ischemia and is characterized by the absence of angiographic evidence of obstructive coronary artery disease. Reports of Takotsubo syndrome in elderly with asthma exacerbations have been noted.

Case presentation: We describe a case of TCM in a 68-year-old female who presented with acute shortness of breath secondary to status asthmaticus. Her electrocardiogram showed ST segment elevations in multiple coronary artery distributions and mildly elevated troponin levels. Coronary angiography showed no significant stenosis of the coronary arteries with left ventriculography that showed systolic apical ballooning with a 10% ejection fraction, consistent with TCM.

Conclusions: Takotsubo syndrome should be considered in the differential diagnosis of patients presenting with status asthmaticus and elevated troponin levels on admission. Patients should be asked about the use of beta agonist prior to admission. A thorough literature review including a summary of 11 previously published case reports of TCM with acute asthma exacerbations has been presented.

Keywords: Takotsubo syndrome, Takotsubo cardiomyopathy, Cardiomyopathy, Status asthmaticus, Case report, Review of literature

Background

Takotsubo cardiomyopathy (TCM) is an acute cardiac dysfunction that typically represents hypokinesis of the apical segment of the left ventricle (LV) beyond a single coronary artery territory [1]. It presents with typical features of myocardial ischemia including central tightening chest pain and shortness of breath, electrocardiographic changes which mimic coronary artery disease, and minimal release of myocardial enzymes in the absence of angiographically significant coronary artery

stenosis. The condition is relatively rare and is found in about 1–2% of all patients with suspected acute coronary syndromes (ACS) [2]. It is commonly seen among postmenopausal women [3]. The underlying pathophysiology of this acute cardiac entity remains largely unclear, but is often associated with physical or emotional stress, hence the term “stress cardiomyopathy” [4]. Catecholamine surge-induced cardiomyocyte injury in response to emotional or physical stress has been postulated as its primary pathophysiology [5]. The list of potential triggers associated with TCM continues to expand as the disease gains increasing recognition among internists and cardiologists. The condition is usually benign, and reversible, with nearly full recovery expected in around 6–8 weeks [6]. Rarely, it may be complicated by life-threatening sequelae including acute cardiogenic shock, lethal

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ventricular arrhythmias, or ventricular wall rupture [7]. In this report, we present a case of TCM secondary to asthma exacerbation along with a review of the published case reports (Table 1) [8–18]. This report emphasizes the importance of the awareness of the potential association between status asthmaticus and TCM.

Case presentation

A 68-year-old female presented to the Emergency Department with chief complaint of shortness of breath, wheezing, and cough for past 3 days. Prior to the hospital visit, she was seen by her primary care provider who prescribed her clarithromycin and Medrol dose pack but she had no significant benefit. She denied any episodes of chest pain or fever.

Her medical history was significant for asthma since childhood, hypertension, hypothyroidism, and left lower extremity deep venous thrombosis 15 years back. The patient reported an eight-pack-year smoking history. There was no personal history of coronary artery disease, prior myocardial infarction, or hyperlipidemia. She had no history of unusual emotional stress prior to admission.

On examination, patient was afebrile with temperature of 36.3 °C, heart rate of 116 beats/minute, blood pressure of 102/75 mm Hg, and respiratory rate of 22 breaths/minute. Bilateral wheezes were heard on chest auscultation. In the emergency room, patient was placed on bilevel positive airway pressure (BiPAP) to maintain oxygen saturation. Appropriate management for asthma exacerbation was started and patient received methylprednisolone 125 mg IV one time along with repeated albuterol nebulizers, Ipratropium–albuterol inhalers, and magnesium sulfate. Initial Chest radiograph revealed mild flattening of diaphragm without any acute process, cardiomegaly or effusions. Electrocardiogram (EKG) on admission showed mild ST elevation in the inferior and anterolateral leads as well as a prolonged QT interval (0.486 s) (Fig. 1A). Initial troponins at the time of admission were normal (0.023 ng/ml). Her pro-BNP was 103 pg/ml. Her erythrocyte sedimentation rate was 7 mm/h and her C-reactive protein was 1.34 mg/l.

Patient was transferred to critical care unit for further management, on BiPAP and was treated for acute asthma exacerbation. A repeat EKG obtained 1.5 hours later showed Left axis deviation but no significant changes from the initial EKG (Fig. 1B). Troponins were trended overnight and continued to rise but were moderately elevated (3.97 ng/ml and 4.65 ng/ml). An EKG the following morning 18 hours later showed a new onset Left bundle branch block (LBBB) (Fig. 1C). She came off the BiPAP and was transitioned to Nasal cannula, was feeling improved the morning of the Day 2. That evening, she started to deteriorate again requiring BiPAP.

An echocardiogram (ECHO) was obtained at this time, which revealed an Ejection fraction (EF) of 24%, with severely depressed LV function but normal wall thickness and shape (Additional file 1: Fig. S1). A prior ECHO done eight months back showed an EF of 65%, without any regional wall motion abnormalities. Due to her worsening respiratory status, new EKG changes from that morning and increasing troponin, she was taken to the Cardiac Catheterization lab urgently. Cardiac catheterization revealed normal coronary angiogram, an EF of 10%, and Left Ventricular End Diastolic Pressure of 35 mm Hg. A pro-BNP resulted that time was 20,242 pg/ml. Left ventriculogram showed akinetic apex, anterior and inferior walls with mild dilation of the left ventricle supporting the diagnosis of TCM (Fig. 2). An intra-aortic balloon pump (IABP) was placed for circulatory support, however vasopressors and inotropes were not required.

The patient was started on carvedilol and enalapril and she was monitored in the critical care unit until the IABP was removed. The rest of the hospital course was unremarkable on the medicine floors and she was discharged after being weaned off supplemental oxygen. She opted out of anticoagulation. Follow-up ECHO 9 weeks later revealed normal left ventricular function with EF of 59%.

Discussion

We presented a case of TCM in a 68-year-old female presenting with asthma exacerbation. Within 24 hours of presentation, she developed a new onset LBBB on EKG and had mild troponin elevation. Her respiratory status improved the morning of the day 2, but then deteriorated again the night of day 2. An ECHO showing low EF, increasing troponin, continuing ST changes, and worsening respiratory status prompted an emergent cardiac catheterization for high-risk NSTEMI. The cardiac catheterization revealed findings that were highly suspicious of Takotsubo syndrome.

Currently, the diagnostic criteria adopted by the Heart Failure Association and European Society of Cardiology are the most widely used in the diagnosis of TCM. In addition to the above definition, criteria includes an absence of atherosclerotic disease that would explain the presentation, new and reversible EKG changes (ST elevation/depression, LBBB, and/or QTc prolongation), elevated Brain natriuretic peptide (BNP) or natriuretic-pro-BNP, slightly elevated troponins and recovery of the ventricular function on imaging at 3 to 6 months. The International Takotsubo Diagnostic Criteria has been recently proposed and is similar to the criteria put forth by the Heart Failure Association and European Society of Cardiology with the exception that infectious myocarditis must be ruled out [19]. Myocarditis requires a biopsy for a definitive diagnosis; however a biopsy for this purpose

Table 1 Literature review of cases of Takotsubo cardiomyopathy in patients with asthma exacerbation

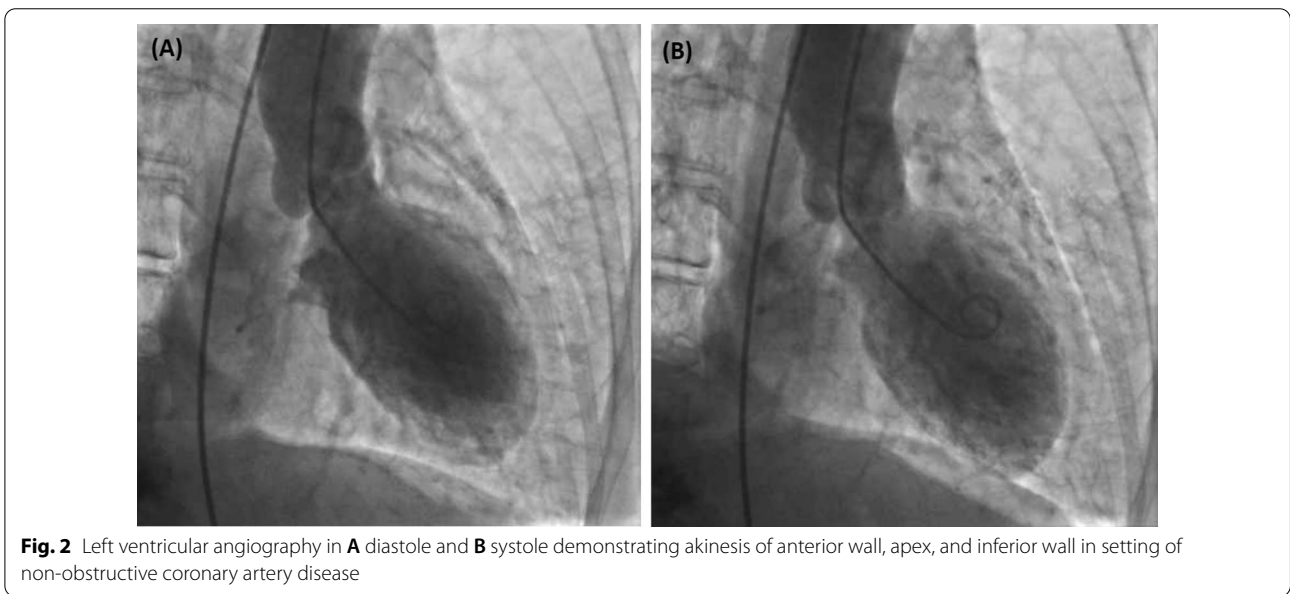
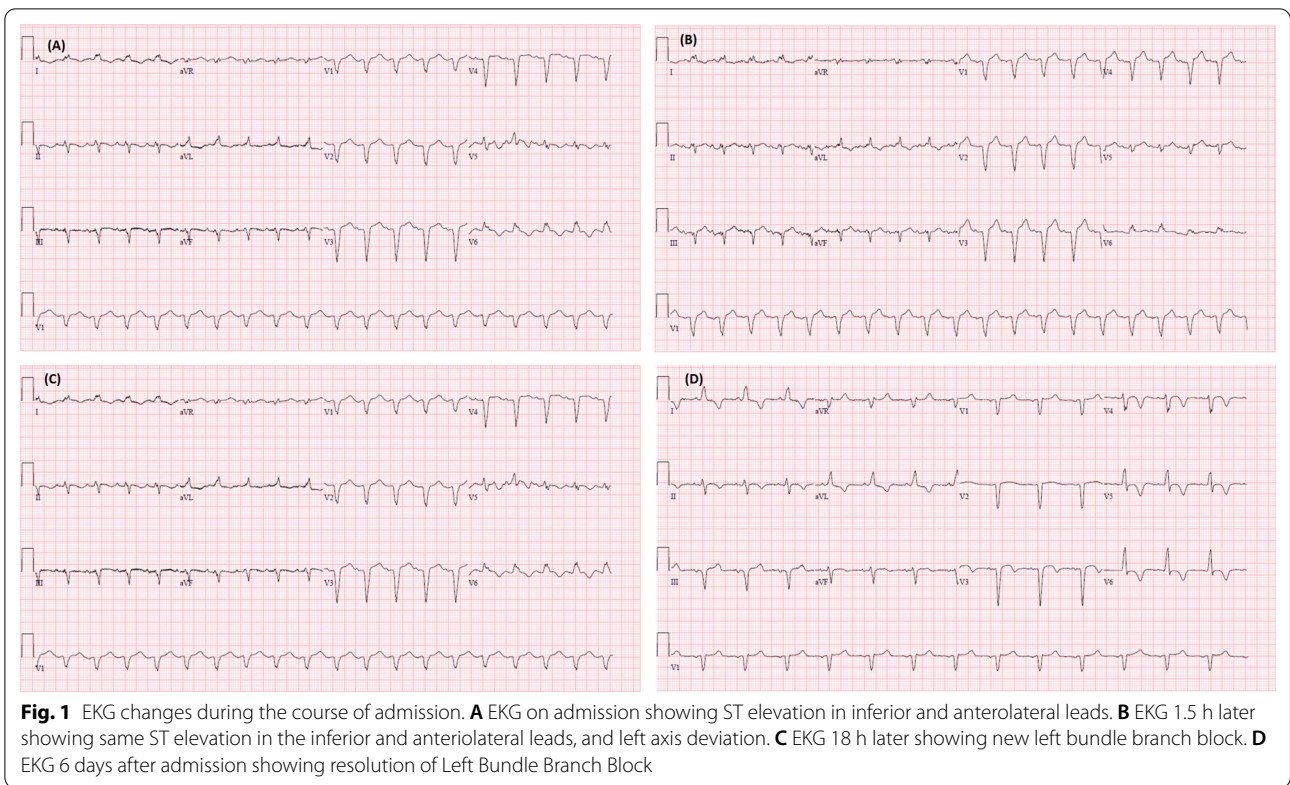
| Study | Age/Gender | Presentation | EKG changes | Peak Troponin levels | BNP levels | Management | Outcome | Possible etiology/preceding stressor |
|--------------------|-----------------|---|--|----------------------|------------|---|--|--|
| Kansara et al. [8] | 58 years/male | Dyspnea, chest pain, wheezing, psychiatric exacerbation | New RBBB plus Left anterior fascicular block | 4.9 ng/ml | Not given | Initial ECHO normal, Repeat ECHO showed LV Apical Ballooning, Patient refused cardiac catheterization | Repeat ECHO 8 weeks later showed resolution of WMA | Agitation due to psychiatric disturbance/ asthma exacerbation |
| Kotsiou et al. [9] | 43 years/female | Chest tightness, dyspnea, dry cough, Salbutamol use 3 times a day prior to admission Stressful family event the day before | TWI in II, III, AVF | 2.2 ng/ml | 345 pg/mL | Nebulized bronchodilators, IV steroids, adrenaline given. Pt intubated; repeated bronchodilators, IV steroids, and Magnesium Sulfate; ECHO showed 45% EF and Apical ballooning Repeat ECHO showed recovery of LV WMA. Cardiac catheterization showed normal coronaries, EF 60%, no WMA | Repeat EKG 2 months after discharge was normal | Epinephrine use, beta agonist in treatment of Status asthmaticus |
| Ozturk et al. [10] | 58 years/female | Dyspnea, chest pain, wheezing | Diffuse ST depression, Precordial TWI | 0.672 ng/ml | Not given | ECHO showed hypokinesis of mid/apical segment of intraventricular septum, LV anteroseptal wall, and hyperkinesia of the basal segment, EF 35% Cardiac catheterization revealed normal coronaries, hypokinesis of LV except bases and apex of LV | Repeat ECHO showed normal EF and no segmental WMA | Physiological stress of asthma exacerbation |

Table 1 (continued)

| Study | Age/Gender | Presentation | EKG changes | Peak Troponin levels | BNP levels | Management | Outcome | Possible etiology/preceding stressor |
|-----------------------|-----------------|--|--|--|-------------|---|---|--|
| Khwaja et al. [11] | 51 years/female | Dyspnea, wheezing; hospitalized for asthma exacerbation 1.2 days prior | ST elevation in precordial leads + TWI in inferior leads | 5.557 ng/ml | 9490 pg/mL | Salbutamol/ipratropium nebulizer and IV steroids, IV aminophylline, antibiotics, BIPAP. Cardiac catheterization showed normal coronaries, EF 30% and apical akinesia and basal segment and basal segment hyperkinesia | Repeat ECHO showed normal LV systolic function and no segmental WMA | Methylxanthines increase Norepinephrine release and trigger negative inotropic response by way of G-protein signalling |
| Saito et al. [12] | 63 years/male | Dyspnea, wheezing | ST elevation V2-V6 With TWI in II, III, AVF, V2-V6 | 3.45 ng/ml | 703.3 pg/ml | Non-invasive ventilation, IV steroids, continuous SABA nebulizer and inhaled anticholinergic. Cardiac Catheterization showed normal coronaries, EF of 49%, and Apical Ballooning | Repeat EKG normal, ECHO with normal EF | LABA Overdose, stress of asthma attack |
| Marmoush et al. [13] | 80 years/Female | Dyspnea, wheezing, left-sided substernal chest pain | New LBBB | 1.112 ng/ml | Not given | IV steroids, albuterol/ipratropium plus Aspirin, ECHO showed EF 65% with hypokinesia of LV apex and distal septum. Cardiac catheterization showed apical ballooning | Persistent LBBB; repeat ECHO showed normalized EF, resolution of Apical WMA | Increasing beta agonists use in mild asthma exacerbation |
| Salahudin et al. [14] | 50 years/male | Acute respiratory failure requiring mechanical ventilation | ST elevation in precordial leads | 2.29 n/ml | Not given | ECHO showed EF 25–30%, with cardiac catheterization showing normal coronaries, apical dilation and ballooning. | Repeat ECHO showed normal EF and no apical ballooning | Albuterol (total of 50 gm of albuterol daily in the preceding 24 h) plus stress of asthma exacerbation |
| Pontillo et al. [15] | 72 years/male | Dyspnea | ST Elevation in anterior leads | Fourfold rise in troponin (values not given) | Not given | ECHO showing apical ballooning and EF 37% | Repeat ECHO showing normal cardiac function | Physiological stress of Asthma exacerbation |

Table 1 (continued)

| Study | Age/Gender | Presentation | EKG changes | Peak Troponin levels | BNP levels | Management | Outcome | Possible etiology/preceding stressor |
|------------------------|--------------------|---|--|---|--------------|---|---|--|
| Rennyson et al. [16] | 66-year old/female | Dyspnea; hypoxia, substernal chest pain | ST Elevation in V1-V4 | Initial—normal, second mildly elevated (values not given) | Not given | Emergent cardiac catheterization which showed normal coronaries/EF 15% | Repeat admission 6 months later with same complaints and cardiac findings | High dose beta agonists with continued use, with repeat presentation again at 6 months |
| Stanojevic et al. [17] | 71 years/female | Worsening dyspnea requiring mechanical ventilation | Mild ST Elevation in V2-V3 and prolonged corrected QTc | 2.6 ng/ml | Not given | ECHO showed EF of 35% with severe hypokinesis of basal segments; refused cardiac catheterization | 4-weeks later EF of 55% and complete resolution of the RWMA | Excessive albuterol use for worsening asthma 5 days prior to admission |
| Osorjji et al. [18] | 46 years/female | Worsening dyspnea requiring mechanical ventilation | ST elevation in inferior and lateral leads | 9.56 ng/ml | Not given | Received ketamine and epinephrine to treat bronchoconstriction and developed ST Elevation; Coronaries normal; placed on IABP | Repeat ECHO 3 days later showed normal EF (55%) (Initial EF 10%) | IV epinephrine and ketamine use and status asthmaticus |
| This study | 68 years/female | Dyspnea for 3 days requiring BIPAP, sputum production | LBBS | 9.55 ng/mL | 20,242 pg/mL | ECHO showed EF 24%; severely depressed LV function, no RWMA Cardiac Catheterization showed EF 10%, LV, normal coronaries, akinesis of anterior/inferior wall and apex; IABP placed | Repeat ECHO 9 weeks showing normal EF | Status asthmaticus |



is not commonly done in our facility. Clinically, myocarditis presents with chest pain, which our patient did not report. Other findings suggestive of myocarditis include global dilation on ECHO, elevated inflammatory markers (ESR, C-reactive protein, etc.), and non-specific changes on EKG, which were not seen in our patient. A LBBB is

associated with a worse prognosis in patients diagnosed with myocarditis.

Given its similarity in presentation to ACS, it is imperative to differentiate TCM from ACS. There are certain findings on EKG and imaging that can help differentiate TCM from ACS, although are not definitive.

One finding on EKG that is 100% specific for TCM is ST elevation in AVR combined with ST elevation in more than 2–3 anteroseptal leads (V1–V6). This finding has been reported to have a positive predictive value of 100%, a negative predictive value of 52%, and a sensitivity of 12% [20]. Another finding that may suggest TCM as opposed to ACS is the differences in elevation of cardiac troponins. In TCM, troponins are typically elevated less than 10 ng/ml. BNP and natriuretic-BNP are typically much higher in TCM as compared to ACS. An ECHO may be able to demonstrate the classic apical ballooning form, however, it cannot be differentiated from ischemia involving the apex. Cardiac magnetic resonance imaging has also been used to differentiate TCM from ACS [21]. Delayed gadolinium enhancement, which helps to demonstrate myocardial edema, tends to match the area of akinesis in TCM during the acute phase of illness while it is more localized to the involved coronary artery in ACS.

The pathophysiology of asthma-induced TCM is not well understood. It is hypothesized that the asthma attack itself leads to excessive production of catecholamines and Neuropeptide Y, and it may trigger apical cardio-depression precipitating TCM [22]. However, it is not clear if elevated levels of these substrates are a reflection of the pathophysiology or if this is the cause. However, direct exposure of myocardium to catecholamine is deemed to be highly toxic and may cause cellular damage, altered cellular metabolism, and contraction band necrosis [23, 24]. Further, there is evidence to suggest that selective beta-2-agonists may induce apoptosis of cardiac myocytes due to production of reactive oxygen species [25, 26]. Other possible mechanisms proposed include the possibility of increased beta receptors in certain areas of the myocardium (9), changes in G-protein signaling from Gs (stimulatory) to Gi (inhibitory) leading to negative inotropic response (11), and in the event of increasing beta agonist use, the loss of selectivity of these drugs to lung tissue leading to vascular spasm in the myocardium (13).

The main complication of TCM is cardiogenic shock resulting in circulatory failure. The management is supportive, with severe cases requiring Mechanical Circulatory Support with Bridge to Recovery. It is important to determine if a left ventricular outflow tract obstruction (LVOTO) is present (as determined by ECHO). In the case of LVOTO, the obstruction must be relieved prior to treating the heart failure. Given risk of arrhythmias, continuous EKG monitoring is recommended for at least 48 h.

We performed a review of literature and found 11 other cases that describe asthma exacerbation as a trigger for TCM (Table 1). Six out of the 11 cases we reviewed were post-menopausal females. None of the cases, including

ours, exhibited the specific EKG finding for this syndrome. However, there is only one other case to our knowledge that presented with a new LBBB [13]. All cases were treated with a loading dose of steroids and inhaled bronchodilators for management of asthma exacerbation. In our study, additionally, repeated doses of magnesium sulfate were used for the management of status asthmaticus. Other notable treatments used in prior reports included combinations of epinephrine/ketamine and aminophylline. Our case presented with similar troponin elevations, ECHO findings, and cardiac catheterization findings as seen in previous reports.

We suspect that our case of TCM was induced by the physiological stress of an asthma exacerbation or possibly by the administration of beta agonistic drugs. However, the former seems more likely as our patient had EKG changes (ST Elevations in the inferior and anterior–lateral leads) on admission that were not present on a prior EKG and she did not report any chronic and excessive use of inhaled beta agonists. We came to the conclusion that her asthma exacerbation lead to the development of TCM immediately on or prior to admission. The new LBBB on day 2 prompted the cardiac catheterization. The ST elevations and LBBB resolved completely after the catheterization.

Conclusions

This case highlights the importance of maintaining a high suspicion for TCM in post-menopausal women with asthma exacerbations, who have persistent symptoms despite treatment with bronchodilators and steroids, even in the absence of an emotional trigger.

Abbreviations

TCM: Takotsubo cardiomyopathy; LV: Left ventricle; ACS: Acute coronary syndromes; EKG: Electrocardiogram; LBBB: Left bundle branch block; ECHO: Echocardiogram; EF: Ejection fraction; IABP: Intra-aortic balloon pump; BNP: Brain natriuretic peptide; LVOTO: Left ventricular outflow tract obstruction; RBBB: Right bundle branch block; WMA: Wall motion abnormalities; TWI: T-wave inversion.

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s43044-022-00310-9>.

Additional file 1: Fig. S1. Echocardiogram with demonstration of hypokinesis of entire septal area, apex, and lateral areas. On the base contracts (arrow).

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Author contributions

LC and AK were involved in study design, data collection, and original draft preparation. WA contributed to manuscript reviewing and editing. All authors have read and approved the manuscript.

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Availability of data and materials

Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

Declarations**Ethics approval and consent to participate**

Written consent for participation was obtained from the patient. No ethics approval was required as per policy.

Consent for publication

Informed written consent was obtained from the patient for their anonymized information to be published in this paper.

Competing interests

All authors declare that there is no competing interest.

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