Basal type Takotsubo Syndrome in the post-ictal period – A case report highlighting the importance of post-ictal cardiac evaluation

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Abstract

Takotsubo syndrome (TTS) is a reversible form of left ventricular dysfunction commonly associated with physical or emotional stress. It is characterised by chest pain and elevated troponin levels, thereby mimicking acute coronary syndrome however there is typically no evidence of obstructive coronary artery disease on invasive angiography. TTS is characterised by apical ballooning or akinesis with basal hyperkinesia. Basal type Takotsubo Syndrome (bTTS) is a less common atypical variant identified by basal akinesis and apical hyperkinesis. Although both forms have been shown to be associated with neurological disease and intracranial haemorrhage or ischaemic stroke, bTTS in the context of epileptiform seizures is relatively rare but an important diagnosis to recognise. We describe a case of a 73-year-old woman who presented to hospital with generalised tonic clonic seizures, followed by centralised chest pain, troponin elevation due to bTTS. This case describes an uncommon presentation of bTTS and highlights the importance of cardiac assessment in patients presenting with generalised tonic-clonic seizures.

Introduction

Takotsubo Syndrome (TTS) also known as Takotsubo cardiomyopathy (TTC) or 'broken heart" syndrome is a reversible form of left ventricular (LV) dysfunction which has become increasingly prevalent since its discovery in 1990 [1]. TTS is characterised by transient left ventricular (LV) impairment involving the apical segments in a non-coronary artery pattern associated non-obstructive coronary artery disease. Clinically, TTS can mimic acute coronary syndrome (ACS) with chest pain, troponin elevation and electrocardiographic (ECG) changes [2, 3]. Although the pathogenesis of the disease remains undefined, a catecholaminergic surge leading to arterial spasm and myocardial injury is hypothesised as the underlying mechanism. Sympathetic overactivation, coronary artery vasospasm, microvascular dysfunction, estrogen deficiency and endothelial dysfunction have also been postulated to contribute [4-7]. Established risk factors for TTS include, but are not limited to hypertension (HTN), diabetes mellitus (DM), hyperlipidaemia, obesity, chronic kidney disease (CKD), female gender and increasing age [8]. Generally, TTS is triggered by emotional stress along with physical triggers, with over 50% of patients presenting with TTS having an acute, former, or chronic neurological or psychiatric disorder. These include epilepsy, subarachnoid haemorrhage, stroke, anxiety, or depression [9-13]. While the apical type is the most common form of TTS, other subtypes exist [14].

Basal Type TTS (bTTS), previously referred to as reverse Takotsubo cardiomyopathy is a rare variant of TTS characterised by basal rather than apical ballooning [15, 16]. From local registry studies, the incidence of the bTTS is variable ranging from 1-23% however, according to the International Takotsubo Registry, only 2.2% of all TTS cases are due to this variant [15, 17]. Most commonly, bTTS has been linked to cases of intracranial haemorrhage and neurological disorders such as multiple sclerosis (MS) and serotonin syndrome but cases following the administration of general anaesthesia have also been reported [18-24]. Although TTS has been reported in cases of epileptic seizures, bTTS is uncommon in this population. In fact, an extensive review performed by Stollberger *et al* described only two cases of bTTS associated with epileptic seizures [25]. Aside from the cases included in this review, only a small number of cases have been published [26-30]. The underlying mechanism linking seizures and TTS is believed to be an acute catecholamine surge resulting in autonomic dysfunction and coronary artery spasm. It is also believed that postictal somnolence or lack of cardiological surveillance play an important role in the pathogenesis of the condition. At this stage, no risk factors have been identified to stratify patients with epilepsy at risk of bTTS.

We present the case of a 73-year-old female who was diagnosed with bTTS after suffering two epileptic seizures presenting to our institution in status epilepticus.

Case Presentation

A 73-year-old female was brought in by ambulance to a metropolitan emergency department after suffering two generalised tonic-clonic seizures at home. Assessment in emergency revealed a recent history of cough, rhinorrhoea, subjective fevers, however the patient denied headache or photophobia.

Her past medical history was significant for epilepsy, atrial fibrillation (AF), ischemic heart disease (IHD), HTN, depression, chronic obstructive pulmonary disease (COPD) and osteoporosis. Her medications included Rivaroxaban 20 mg OD, Metoprolol 25 mg OD, Carbamazepine 100 mg BD, Telmisartan/Hydrochlorothiazide 80 mg/25 mg OD, Budesonide-formoterol 200mcg-6mcg/inhalation 2 puffs BD and Salbutamol as required. She was independent at baseline and smoked cannabis daily.

Further history was difficult to obtain during her preliminary assessment due to intravenous benzodiazepine therapy administered to treat seizure activity and a prolonged post-ictal state.

On preliminary examination in the postictal period, the patient was febrile to 38.4 degrees Celsius with a heart rate of 78 beats per minutes and blood pressure of 150/78 mmHg. She was normoxic on room air. She was drowsy on review, however her neurological examination revealed preserved motor function in the upper and lower limbs (5/5) with normal reflexes and no evidence of cranial nerve abnormalities. A thoracic examination demonstrated an expiratory wheeze with a mid-systolic murmur heard over her aortic region consistent with mild to moderate aortic stenosis. On repeat examination, her neurological examination was unremarkable and her Glasgow Coma Scale improved to 15. A 12-lead electrocardiogram (ECG) showed AF with voltage criteria for left ventricular hypertrophy but no evidence of acute ischemia; **Figure 1**. A chest radiograph and computed tomography (CT) of the brain did not demonstrate any acute abnormality. Further history on repeat assessment revealed compliance with anti-epileptic medications.

Admission blood tests demonstrated a mildly elevated creatinine at 95 umol/L (reference range (RR) 45-90 umol/L) and elevated white cell count (15.9 $x10^9$/L) with neutrophilic shift on full blood count assessment. Her carbamazepine level was less than 2 mg/L (RR 6 – 12 mg/L) with a free carbamazepine

level of 0.3 mg/L (RR 1.0 - 3.0 mg/L). The C-reactive protein was 9 mg/L. A venous blood gas demonstrated a pH of 7.02, pCO2 94 mmHg, base excess -9 mmol/L and lactate of 15.7 mmol/L.

The patient was loaded with 1 g of Levetiracetam and commenced on empiric therapy for viral and bacterial meningitis. The carbamazepine dose was also increased to 200 mg twice daily.

On day 1 of admission the patient reported anterior chest wall pain associated with new T-wave inversion in leads V1-V5 on a 12-lead ECG; **Figure 2**. The initial troponin was 64ng/L (RR <14ng/L). The patient was given 300 mg of Aspirin and 300 mg of Clopidogrel, with resolution of pain on repeat review. At four-hours, the serial troponin was 56ng/L. A transthoracic echocardiogram (TTE) demonstrated significant regional wall motion abnormality involving the basal to mid segments with moderate to severe LV systolic dysfunction (LVEF calculated by Simpsons method – 35%). An invasive coronary angiogram and left ventriculogram demonstrated non-obstructive coronary artery disease (CAD) and apical hyperkinesis with basal akinesis; **Figure 3**. Given the ECG, coronary angiogram and ventriculogram, a diagnosis of bTTS precipitated by generalised tonic clonic seizures was postulated.

The patient was commenced on Bisoprolol 2.5 mg OD and Ramipril 2.5 mg OD. The remainder of her inpatient admission was unremarkable, and she was subsequently discharged home with outpatient management and review. On follow-up TTE at 40 days, there was improvement in global LV function particularly in the basal segments (LV EF – 50%).

Discussion

TTS is a transient cardiomyopathy characterised by transient LV dysfunction in a non-coronary artery pattern in the absence of obstructive CAD or plaque rupture [2, 3]. Although seizures are the second most frequent central nervous syndrome disorder linked to TTS, only a few cases of bTTS have been reported [11]. This case highlights the association between the two conditions and emphasises the need for diagnostic pathways in patients with epilepsy who develop chest pain suggestive of TTS.

TTS has been linked to a number of neurological diseases and neuromuscular syndromes however the underlying pathophysiology has not been completely elucidated. It has been hypothesised that, during seizure induction, an acute catecholamine surge is activated leading to autonomic dysfunction and coronary artery spasm, resulting in TTS [31, 32]. This hypothesis is supported by prolonged, increased levels of noradrenaline in patients with prolonged seizures [33]. Compared to the classical form of TTS, bTTS is more frequently associated with cerebrovascular events and more common in younger patients. This has been postulated to be secondary to a higher frequency of adrenoreceptors expressed in the basal LV wall compared to the apical segment in this age group. Only a small number of cases of bTTS have been reported in association with seizure disorders (Table 1) [26-30]. Although TTS largely involves the left ventricle, recent evidence suggests that almost one-third of cases involve both ventricles [34, 35].

Overall, the incidence of the bTTS in patients with seizure related conditions is low with a prevalence rate of about 0.1% [36, 37]. TTS secondary to seizure associated conditions has been shown to have a higher mortality than other causes, suggesting the need for further risk stratification in these patients. Additionally, the mortality rate associated with bTTS is reported to be higher compared typical TTS, however this may be due to the underlying predisposing condition rather than the pattern of myocardial damage [38].

The International Takotsubo Diagnostic Criteria (InterTAK Diagnostic Criteria) has recently published guidelines based on clinical features and ECG characteristics adapted from the first diagnostic criteria developed by Abe *et al.* in 2003 (Table 2) [39, 40]. This diagnostic score can be used to predict the probability of TTS and help distinguish TTS from ACS with good efficacy. Overall, gender and emotional triggers have been shown to have the highest predictive value. Unfortunately, the criteria do not distinguish between the various TTS variants relying on imaging such as ventriculography, TTE or cardiac magnetic resonance (CMR). Historically, echocardiography and ventriculography were the imaging modalities of choice however both modalities have been shown to have low accuracy when compared to CMR as a potential gold standard (sensitivity 57% and 77% and specificity 72% and 95%, respectively)[41]. In particular, CMR is more accurate in cases with concomitant CAD where unlike myocardial infarction or myocarditis, late gadolinium enhancement (LGE) is generally absent in cases of TTS [42, 43]. The value of CMR has been recently demonstrated in the Stockholm Myocardial Infarction With Normal Coronary Arteries 2 (SMINC-2) study. In this study, Sorensson *et al found* 77% of patients with troponin elevation with non-obstructed coronary arteries (MINOCA) were diagnosed with TTS when investigated early with CMR imaging [44]. Overall, the authors found that early CMR imaging strategy (three days) was more accurate for the diagnosis of myocarditis and TTS compared to other imaging modalities and late CMR imaging. This study highlights that early CMR imaging is highly valuable in patients with chest pain, troponin elevation and non-obstructive coronary artery disease.

TTS often presents with variable ECG patterns however the most common findings are ST-segment elevation involving the anterior leads (V1-V3) with associated T-wave inversion similar to the appearance found in Wellens' syndrome [45-48]. There may also be low-voltage QRS complexes and other Q-wave abnormalities. Although ST-segment depression is rarely observed, it is more commonly found in variants of TTS, including bTTS [49, 50]. J-wave and

fragmented QRS complexes are also observed in those with hyperacute presentations, and the incidence of AF and ventricular fibrillation are reported as 4.7% and 1.8% respectively [51-53].

At present, there are limited guidelines on stratifying patients with seizure associated conditions at risk of TTS. One study however has suggested routine monitoring of blood and urine catecholamine levels in the ictal and post-ictal phases may provide further insight into stratifying patients at risk for developing TTS [7]. Additionally, all patients with a generalised seizure should be evaluated with a 12-lead ECG, given those with diffuse T-wave inversion have a 4-6% 30-day mortality [54].

Similar to TTS, the management of bTTS focuses on the pharmacotherapy of heart failure. During the acute presentation, management is largely supportive and follows guideline directed heart failure therapy such as intravenous diuretic therapy to treat pulmonary oedema and the commencement of long-acting beta-blockers and pre-load optimisation with agents such as angiotensin converting enzyme inhibitor (ACEi) or angiotensin receptor blockers (ARB) [55]. Unfortunately, some cases can be complicated by cardiogenic shock requiring acute intensive management. In fact, up to 10% of patients with TTS have been shown to develop cardiogenic shock, particularly those younger than 65 years of age and those with a physical trigger [56]. Importantly, management is dependent on the presence of left ventricular outflow tract obstruction (LVOTO). In those with LVOTO, vasopressor therapy and inotropic agents are contraindicated with fluid resuscitation and short acting beta-blockers being preferred to help improve cardiac function and improve the obstruction. In those with LVOTO and refractory shock, mechanical circulatory support should be considered [57]. Although the incidence of ventricular thrombus is relatively low in patients with TTS, its presence should be evaluated and treated with anticoagulation [58].

This case highlights an uncommon presentation of bTTS and subsequently reinforces the importance of cardiac evaluation in some patients presenting with seizure disorders. The authors acknowledge the lack of CMR imaging in the presented case as a potential limitation in the diagnosis of bTTS, however given the presenting symptoms, ECG changes, static troponin levels and normalisation of cardiac function on follow-up TTE, a diagnosis of bTTS precipitated by generalised tonic-clonic seizures can be inferred. Moving forward, emphasis should be placed on stratifying patients at risk of bTTS as the condition has been associated with significant complications such as myocardial inflammation, pleural and/or pericardial effusions and left ventricular thrombi [59]. We agree with previous reports that suggest all patients with seizure disorders or other neurological conditions and chest pain should be evaluated with a 12-lead ECG, a serum troponin test and cardiac imaging [60]. Those with T-wave inversion and/or troponin elevation and/or LV systolic impairment function should undergo coronary angiography to assess for obstructive coronary artery disease. Ultimately, in the absence of CAD, patients should be investigated with CMR imaging to help identify TTS or differentiate it from myocardial infarction or myocarditis.

Declarations

Acknowledgement

Nil

Statement of Ethics

Informed consent was obtained from the presented patient for publication of the details of their medical case and any accompanying images.

Conflict of Interest Statement

The authors have no conflicts of interest to declare

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Author Contributions

RO, GF, KC and BM were involved with the care of the patient, the design of the presented manuscript and writing of the presented manuscript. JA was involved with the writing and editing of the presented manuscript, as well as study conceptualization.

Data Availability Statement

The authors confirm that the data supporting the findings of this study are available within the article.

References

1. Sato H, Tateishi H, Uchida T, Dote K, Ishihara M, Kodama K, et al. Clinical aspect of myocardial injury: from ischemia to heart failure. Kagaku Hyoronsha. 1990:55-64.

2. Ojha V, Khurana R, Ganga KP, Kumar S. Advanced cardiac magnetic resonance imaging in takotsubo cardiomyopathy. The British Journal of Radiology. 2020;93(1115):20200514.

3. Medina de Chazal H, Del Buono MG, Keyser-Marcus L, Ma L, Moeller FG, Berrocal D, et al. Stress cardiomyopathy diagnosis and treatment: JACC state-of-the-art review. Journal of the American College of Cardiology. 2018;72(16):1955-71.

4. Galiuto L, De Caterina AR, Porfidia A, Paraggio L, Barchetta S, Locorotondo G, et al. Reversible coronary microvascular dysfunction: a common pathogenetic mechanism in Apical Ballooning or Tako-Tsubo Syndrome. European heart journal. 2010;31(11):1319-27.

5. Naegele M, Flammer A, Enseleit F, Roas S, Frank M, Hirt A, et al. Endothelial function and sympathetic nervous system activity in patients with Takotsubo syndrome. International journal of cardiology. 2016;224:226-30.

6. Williams R, Arri S, Prasad A. Current concepts in the pathogenesis of Takotsubo syndrome. Heart failure clinics. 2016;12(4):473-84.

7. Pelliccia F, Kaski JC, Crea F, Camici PG. Pathophysiology of Takotsubo Syndrome. Circulation. 2017;135(24):2426-41.

8. Liang J, Zhang J, Xu Y, Teng C, Lu X, Wang Y, et al. Conventional cardiovascular risk factors associated with Takotsubo cardiomyopathy: A comprehensive review. Clin Cardiol. 2021.

9. Templin C, Ghadri JR, Diekmann J, Napp LC, Bataiosu DR, Jaguszewski M, et al. Clinical Features and Outcomes of Takotsubo (Stress) Cardiomyopathy. N Engl J Med. 2015;373(10):929-38.

10. Lee VH, Connolly HM, Fulgham JR, Manno EM, Brown RD, Jr., Wijdicks EF. Tako-tsubo cardiomyopathy in aneurysmal subarachnoid hemorrhage: an underappreciated ventricular dysfunction. J Neurosurg. 2006;105(2):264-70.

11. Le Ven F, Pennec PY, Timsit S, Blanc JJ. Takotsubo syndrome associated with seizures: an underestimated cause of sudden death in epilepsy? Int J Cardiol. 2011;146(3):475-9.

12. Yoshimura S, Toyoda K, Ohara T, Nagasawa H, Ohtani N, Kuwashiro T, et al. Takotsubo cardiomyopathy in acute ischemic stroke. Ann Neurol. 2008;64(5):547-54.

13. Summers MR, Lennon RJ, Prasad A. Pre-morbid psychiatric and cardiovascular diseases in apical ballooning syndrome (tako-tsubo/stress-induced cardiomyopathy): potential pre-disposing factors? J Am Coll Cardiol. 2010;55(7):700-1.

14. Ghadri JR, Wittstein IS, Prasad A, Sharkey S, Dote K, Akashi YJ, et al. International Expert Consensus Document on Takotsubo Syndrome (Part I): Clinical Characteristics, Diagnostic Criteria, and Pathophysiology. Eur Heart J. 2018;39(22):2032-46.

15. Ghadri JR, Cammann VL, Napp LC, Jurisic S, Diekmann J, Bataiosu DR, et al. Differences in the Clinical Profile and Outcomes of Typical and Atypical Takotsubo Syndrome: Data From the International Takotsubo Registry. JAMA Cardiol. 2016;1(3):335-40.

16. Sharkey SW, Maron BJ. Epidemiology and clinical profile of Takotsubo cardiomyopathy. Circ J. 2014;78(9):2119-28.

17. Ramaraj R, Movahed MR. Reverse or inverted takotsubo cardiomyopathy (reverse left ventricular apical ballooning syndrome) presents at a younger age compared with the mid or apical variant and is always associated with triggering stress. Congest Heart Fail. 2010;16(6):284-6.

18. Kumai T, Inamasu J, Watanabe E, Sugimoto K, Hirose Y. Differences between Takotsubo cardiomyopathy and reverse Takotsubo cardiomyopathy associated with subarachnoid hemorrhage. Int J Cardiol Heart Vasc. 2016;11:99-103.

19. Gobeske KT, Sarano ME, Fugate JE, Wijdicks EF. Medulla Oblongata Hemorrhage and Reverse Takotsubo Cardiomyopathy. Neurocrit Care. 2018;29(3):508-11.

20. Elikowski W, Małek-Elikowska M, Kudliński B, Skrzywanek P, Smól S, Rzymski S. ECG pattern in reverse takotsubo cardiomyopathy demonstrated in 5 cases with intracranial hemorrhage. Pol Merkur Lekarski. 2016;41(243):136-40.

21. Lee CH, Son JW, Kim U. Reverse Takotsubo Cardiomyopathy following Inadvertent Intrathecal Injection during Percutaneous Epidural Neuroplasty. Heart Lung Circ. 2015;24(9):e148-51.

22. Açar B, Kırbaş Ö, Ünal S, Gölbaşı Z, Aydoğdu S. Reverse Takotsubo cardiomyopathy following intra-abdominal surgery. Turk Kardiyol Dern Ars. 2016;44(6):514-6.

23. Mehta NK, Aurigemma G, Rafeq Z, Starobin O. Reverse takotsubo cardiomyopathy: after an episode of serotonin syndrome. Tex Heart Inst J. 2011;38(5):568-72.

24. Peller M, Balsam P, Budnik M, Marchel M, Opolski G. Reverse Takotsubo syndrome in a patient with diagnosed multiple sclerosis. Kardiol Pol. 2016;74(9):1029.

25. Stöllberger C, Sauerberg M, Finsterer J. Immediate versus delayed detection of Takotsubo syndrome after epileptic seizures. J Neurol Sci. 2019;397:42-7.

26. Shin S-W, Baek S-H, Choi B-S, Lee H-J, Kim K-H, Kim E-S. Takotsubo cardiomyopathy associated with nonepileptic seizure after percutaneous endoscopic lumbar discectomy under general anesthesia. Journal of anesthesia. 2010;24(3):460-3.

27. Binaghi G, Congia D, Cossa S, Ganga R, Giardina G, Matta G, et al. Seizures and recurrence of Takotsubo syndrome: one clinical presentation and trigger, but two different anatomical variants in the same patient. A case to meditate on. Seizure-European Journal of Epilepsy. 2018;63:37-9.

28. Nash E, Roberts DM, Jamshidi N. Reverse Takotsubo Cardiomyopathy Precipitated by Chronic Cocaine and Cannabis Use. Cardiovascular Toxicology. 2021:1-7.

29. Dupuis M, Van Rijckevorsel K, Evrard F, Dubuisson N, Dupuis F, Van Robays P. Takotsubo syndrome (TKS): a possible mechanism of sudden unexplained death in epilepsy (SUDEP). Seizure. 2012;21(1):51-4.

30. Ennezat PV, Pesenti-Rossi D, Aubert JM, Rachenne V, Bauchart JJ, Auffray JL, et al. Transient left ventricular basal dysfunction without coronary stenosis in acute cerebral disorders: a novel heart syndrome (inverted Takotsubo). Echocardiography: A Journal of Cardiovascular Ultrasound and Allied Techniques. 2005;22(7):599-602.

31. Samuels MA. The brain–heart connection. Circulation. 2007;116(1):77-84.

32. Narayanan A, Russell MD, Sundararaman S, Shankar KK, Artman B. Takotsubo cardiomyopathy following electroconvulsive therapy: an increasingly recognised phenomenon. BMJ Case Rep. 2014;2014.

33. Finsterer J, Wahbi K. CNS disease triggering Takotsubo stress cardiomyopathy. Int J Cardiol. 2014;177(2):322-9.

34. Singh K, Neil CJ, Nguyen TH, Stansborough J, Chong C-R, Dawson D, et al. Dissociation of early shock in takotsubo cardiomyopathy from either right or left ventricular systolic dysfunction. Heart, Lung and Circulation. 2014;23(12):1141-8.

35. Citro R, Lyon AR, Meimoun P, Omerovic E, Redfors B, Buck T, et al. Standard and advanced echocardiography in takotsubo (stress) cardiomyopathy: clinical and prognostic implications. Journal of the American Society of Echocardiography. 2015;28(1):57-74.

36. Stöllberger C, Wegner C, Finsterer J. Seizure-associated Takotsubo cardiomyopathy. Epilepsia. 2011;52(11):e160-7.

37. Desai R, Singh S, Patel U, Fong HK, Kaur VP, Varma Y, et al. Frequency of takotsubo cardiomyopathy in epilepsy-related hospitalizations among adults and its impact on in-hospital outcomes: A national standpoint. Int J Cardiol. 2020;299:67-70.

38. Rosu D, Askandar S, Khouzam RN. Why Is Reverse Takotsubo "Reverse"? South Med J. 2017;110(5):381-5.

39. Abe Y, Kondo M, Matsuoka R, Araki M, Dohyama K, Tanio H. Assessment of clinical features in transient left ventricular apical ballooning. Journal of the American College of Cardiology. 2003;41(5):737-42.

40. Ghadri J-R, Wittstein IS, Prasad A, Sharkey S, Dote K, Akashi YJ, et al. International expert consensus document on Takotsubo syndrome (part I): clinical characteristics, diagnostic criteria, and pathophysiology. European heart journal. 2018;39(22):2032-46.

41. Ghadri J-R, Templin C. The InterTAK Registry for takotsubo syndrome. European heart journal. 2016;37(37):2806-8.

42. Eitel I, von Knobelsdorff-Brenkenhoff F, Bernhardt P, Carbone I, Muellerleile K, Aldrovandi A, et al. Clinical characteristics and cardiovascular magnetic resonance findings in stress (takotsubo) cardiomyopathy. Jama. 2011;306(3):277-86.

43. Eitel I, Behrendt F, Schindler K, Kivelitz D, Gutberlet M, Schuler G, et al. Differential diagnosis of suspected apical ballooning syndrome using contrast-enhanced magnetic resonance imaging. Eur Heart J. 2008;29(21):2651-9.

44. Sörensson P, Ekenbäck C, Lundin M, Agewall S, Brolin EB, Caidahl K, et al. Early Comprehensive Cardiovascular Magnetic Resonance Imaging in Patients With Myocardial Infarction With Nonobstructive Coronary Arteries. JACC: Cardiovascular Imaging. 2021.

45. Looi J-L, Poppe K, Lee M, Gilmore J, Webster M, To A, et al. A Score to differentiate Takotsubo syndrome from non-ST-elevation myocardial nfarction in women at the bedside. Open heart. 2020;7(1):e001197.

46. Piackova E, Kaufmann CC, Weihs V, El-Razek A, Geppert A, Nürnberg M, et al. ECG Changes and Their Prognostic Impact in Patients With Takotsubo Syndrome. Cardiology and Cardiovascular Medicine. 2019;3(6):438-49.

47. Bybee KA, Prasad A, Barsness GW, Lerman A, Jaffe AS, Murphy JG, et al. Clinical characteristics and thrombolysis in myocardial infarction frame counts in women with transient left ventricular apical ballooning syndrome. The American journal of cardiology. 2004;94(3):343-6.

48. Migliore F, Zorzi A, Marra MP, Basso C, Corbetti F, De Lazzari M, 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.

49. Song BG, Chun WJ, Park YH, Kang GH, Oh J, Lee SC, et al. The clinical characteristics, laboratory parameters, electrocardiographic, and echocardiographic findings of reverse or inverted takotsubo cardiomyopathy: comparison with mid or apical variant. Clinical cardiology. 2011;34(11):693-9.

50. Ghadri JR, Cammann VL, Napp LC, Jurisic S, Diekmann J, Bataiosu DR, et al. Differences in the clinical profile and outcomes of typical and atypical Takotsubo syndrome: data from the International Takotsubo Registry. JAMA cardiology. 2016;1(3):335-40.

51. Shimizu M, Nishizaki M, Yamawake N, Fujii H, Sakurada H, Isobe M, et al. J Wave and Fragmented QRS Formation During the Hyperacute Phase in Takotsubo Cardiomyopathy–Possible Markers for Severity of Myocardial Damage–. Circulation Journal. 2014:CJ-13-1296.

52. Chhabra L, Butt N, Ahmad SA, Kayani WT, Sangong A, Patel V, et al. Electrocardiographic changes in Takotsubo cardiomyopathy. Journal of Electrocardiology. 2021;65:28-33.

53. Syed FF, Asirvatham SJ, Francis J. Arrhythmia occurrence with takotsubo cardiomyopathy: a literature review. Europace. 2011;13(6):780-8.

54. Stiermaier T, Thiele H, Eitel I. Prognosis in Patients With Takotsubo Cardiomyopathy. JACC Heart Fail. 2016;4(6):519-20.

55. Villareal RP, Achari A, Wilansky S, Wilson JM. Anteroapical stunning and left ventricular outflow tract obstruction. Mayo Clinic Proceedings, 2001. Elsevier: 79-83.

56. Vallabhajosyula S, Barsness GW, Herrmann J, Anavekar NS, Gulati R, Prasad A. Comparison of Complications and In-Hospital Mortality in Takotsubo (Apical Ballooning/Stress) Cardiomyopathy Versus Acute Myocardial Infarction. The American Journal of Cardiology. 2020;132:29-35.

57. Sharkey SW, Lesser JR, Zenovich AG, Maron MS, Lindberg J, Longe TF, et al. Acute and reversible cardiomyopathy provoked by stress in women from the United States. Circulation. 2005;111(4):472-9.

58. Templin C, Ghadri JR, Diekmann J, Napp LC, Bataiosu DR, Jaguszewski M, et al. Clinical features and outcomes of takotsubo (stress) cardiomyopathy. New England Journal of Medicine. 2015;373(10):929-38.

59. Elesber AA, Prasad A, Lennon RJ, Wright RS, Lerman A, Rihal CS. Four-year recurrence rate and prognosis of the apical ballooning syndrome. J Am Coll Cardiol. 2007;50(5):448-52.

60. Surges R, Shmuely S, Dietze C, Ryvlin P, Thijs RD. Identifying patients with epilepsy at high risk of cardiac death: signs, risk factors and initial management of high risk of cardiac death. Epileptic Disorders. 2021;23(1):17-39.

Tables

Table 1 – Cases published detailed bTTS in the context of a seizure or seizure related disorder.

Author	Age (years)	Sex	PMHx	Seizure type	Trop (ng/mL)	ECG	TTE	Ventriculogram	CMRI	EEG	Neu
Dupuis et al.	50	F	Psychiatric disorder	GM	7.51	Antero-septal Q waves	Transient antero-infero-apical hypokinesia; EF 36%	Basal hypokinesis	NP	Normal	Nor
Ennezat et al.	39	M	Resected cerebral cavernoma	Epileptic	10	ST elevation V2 and V3	EF 40%; LV akinesis; apex sparing	Basal hypokinesis	NP	NP	CTE fron hyp
Shin et al.	67	F	HTN HCL L3-4 disc herniation	GM	0.09	ST depression II, V1 and V2	Basal-inferior LV hypokinesia; anterolateral wall akinesia.	Basal hypokinesis	NP	Normal	Nor
Binaghi et al.	67	F	HTN HCL alcohol use disorder anxiety disorder pAF TIA Metastatic breast ca	GM	34.9	Diffuse T wave inversion	LV dysfunction; EF 20%; basal akinesia and apical hyperkinesia	NP	Normal with complete recovery of LVEF (68%)	NCSE	MRI pon mye and hyp in ri hipp tem
Nash et al.	31	M	Depression polysubstance use	GM	126#	Anterior-Inferior ST segment depression	Severe LV systolic function impairment; EF 15-20%; hypokinesis of septum, anterior wall, postero-lateral wall and inferior wall. Apex sparing.	NP	Basal hypocontractility and dilation; Severe LV functional impairment. T2 hyperintensity consistent with myocardial oedema and bTTS.	NP	Nor

* Readmitted after one week with TTS (apical akinesia) secondary to epileptic seizure; #Denotes troponin-T; HTN = Hypertension; HCL = Hypercholesterolaemia; F = female; M = male; GM = generalised motor; EF = ejection fraction; LV = left ventricle; NP = not performed; CTB = computed tomography brain; D/C = discharge; CMRI = cardiac MRI; TTE = transthoracic echocardiogram; Trop = troponin-I; EEG = electroencephalogram; NCSE = non-convulsive status epilepticus; TIA = transient ischaemic attack.

Table 2 - International Takotsubo (InterTAK) Diagnostic Criteria (14)

International Takotsubo Diagnostic Criteria (InterTAK Diagnostic Criteria)
1. Patients show transient left ventricular dysfunction (hypokinesia, akinesia, or dyskinesia) presenting as apical ballooning or midventricular, basal, or focal wall motion abnormalities. Right ventricular involvement can be present. Besides these regional wall motion patterns, transitions between all types can exist. The regional wall motion abnormality usually extends beyond a single epicardial vascular distribution; however, rare cases can exist where the regional wall motion abnormality is present in the subtended myocardial territory of a single coronary artery (focal TTS).[b]
2. An emotional, physical, or combined trigger can precede the takotsubo syndrome event, but this is not obligatory.
3. Neurologic disorders (e.g., subarachnoid haemorrhage, stroke/transient ischaemic attack, or seizures) as well as pheochromocytoma may serve as triggers for takotsubo syndrome.
4. New ECG abnormalities are present (ST-segment elevation, ST-segment depression, T-wave inversion, and QTc prolongation); however, rare cases exist without any ECG changes.
5. Levels of cardiac biomarkers (troponin and creatine kinase) are moderately elevated in most cases; significant elevation of brain natriuretic peptide is common.
6. Significant coronary artery disease is not a contradiction in takotsubo syndrome.
7. Patients have no evidence of infectious myocarditis.[b]
8. Postmenopausal women are predominantly affected.
[a]Wall motion abnormalities may remain for a prolonged period of time or documentation of recovery may not be possible. For example, death before evidence of recovery is captured. [b]Cardiac magnetic resonance imaging is recommended to exclude infectious myocarditis and diagnosis confirmation of takotsubo syndrome.

Figures

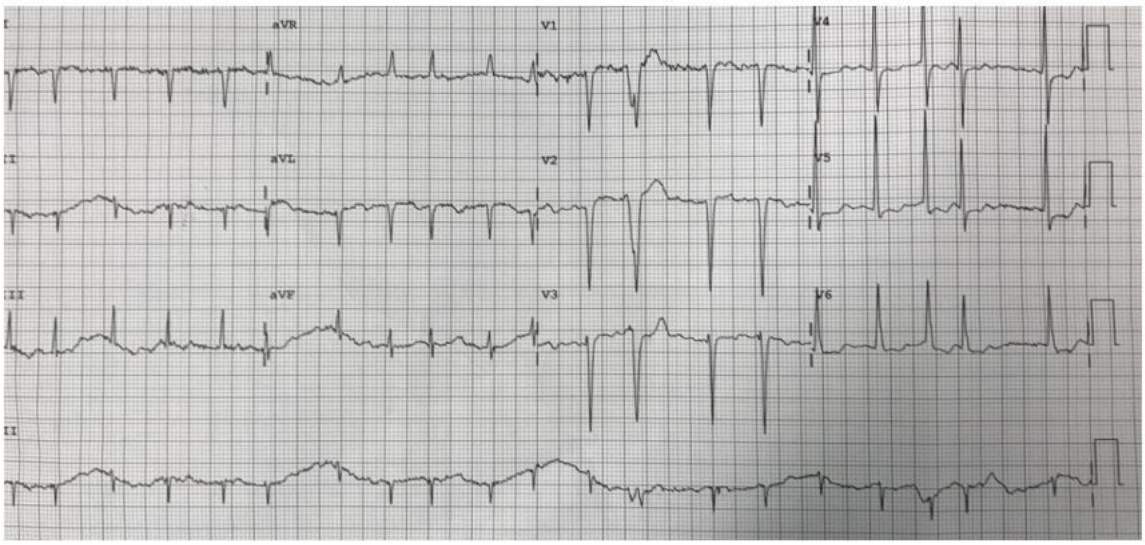

Figure 1

Admission ECG demonstrating atrial fibrillation.

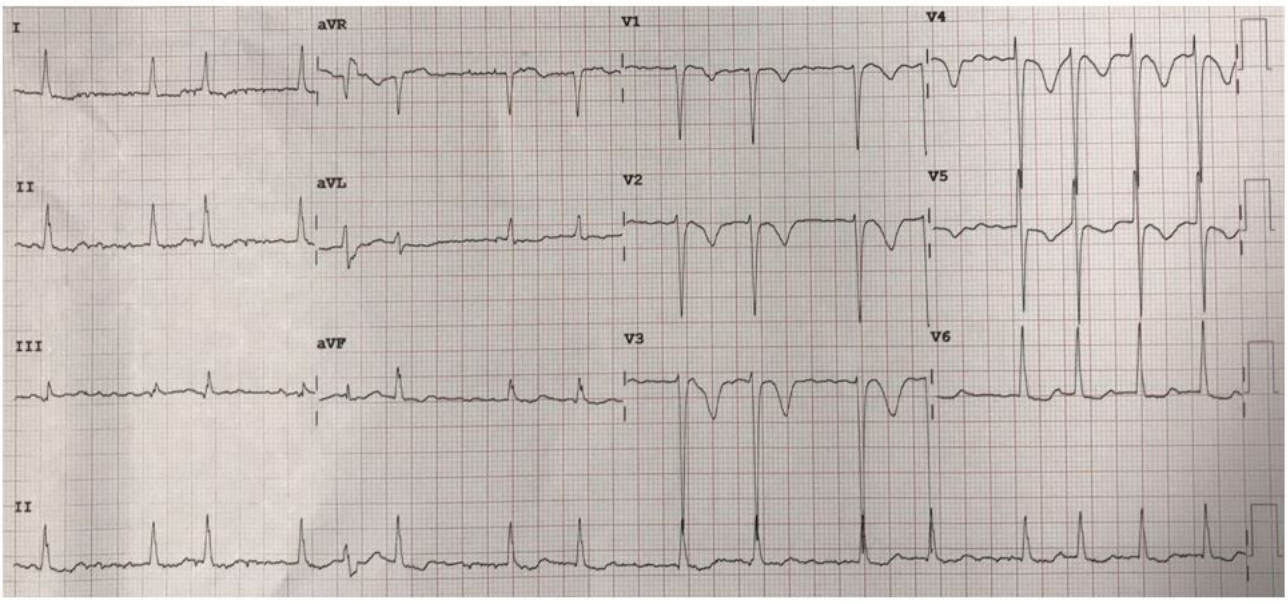

Figure 2

ECG at the time of review on day 1 of admission demonstrating atrial fibrillation and T-wave inversion in leads V1-V5

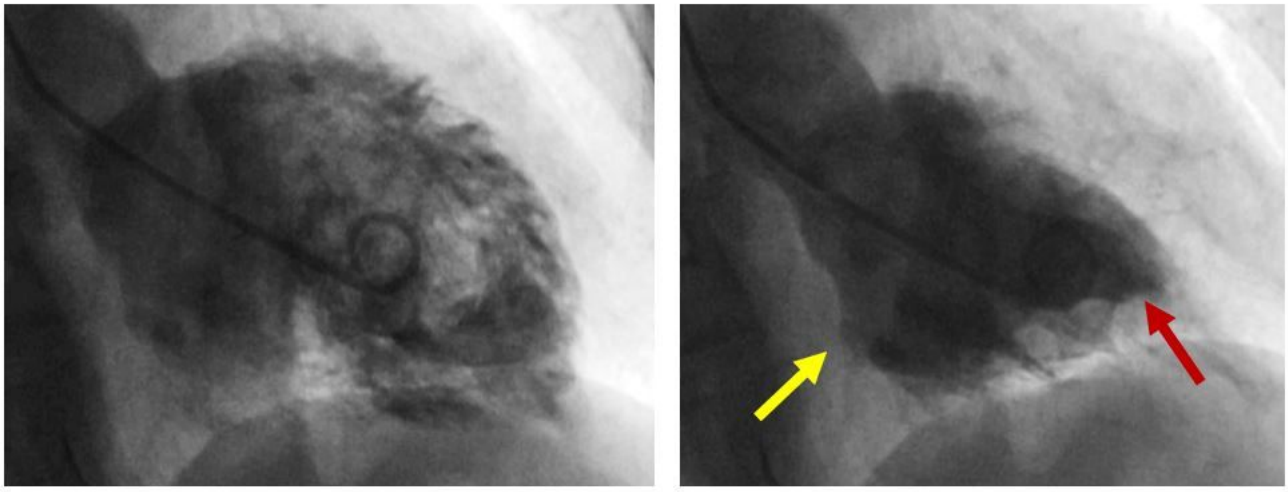

Figure 3

Left ventriculogram in the right anterior oblique position. A) Diastole; B) Systole – demonstrating apical hyperkinesis (red arrow) and basal akinesis (yellow arrow).