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Takotsubo Cardiomyopathy after Permanent Pacemaker Implantation: Insights from a Rare Clinical Case

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Abstract

Takotsubo cardiomyopathy is a cardiac syndrome described as a typical form of non-ischemic acute transient left ventricular dysfunction usually associated with a stressful event. We hereby report the case of an 85-year-old frail woman with 2:1 atrio-ventricular nodal block who underwent isoprenaline infusion and permanent pacemaker implantation. After the procedure, she developed an acute left ventricular impairment with typical apical ballooning, not documented on preoperative echocardiography, in the absence of coronary artery stenosis

shown on coronary angiography. The patient was treated with conventional heart failure therapy and completely recovered, confirming our clinical hypothesis. Pre-existing factors on one hand and emerging factors on the other could have favored an anomalous, both endogenous and exogenous, catecholamine release, which could have contributed to precipitate this syndrome. Takotsubo cardiomyopathy should be considered as a rare, but potential complication following permanent pacemaker implantation, that has to be kept in mind by clinicians in order to apply the right diagnostic-therapeutic strategy.

Keywords: Apical ballooning syndrome; Pacemaker implantation; Takotsubo cardiomyopathy

Introduction

Takotsubo cardiomyopathy, also known as apical ballooning syndrome or stress cardiomyopathy, is a form of acute transient left ventricular (LV) dysfunction in the absence of obstructive coronary artery disease. It has been reported since the 1990s and it takes its name from the Japanese octopus-fishing pot for the resemblance with the “stressed” heart shape.(1)

The clinical presentation may mimic acute myocardial infarction, with typical symptoms like chest pain or dyspnea, associated to ST segment elevation or other electrocardiogram (ECG) alterations and mild cardiac enzymes increase. On echocardiography, myocardial dysfunctions are typical, in general with hypokinesia of the middle and distal segments and hyperkinesia of basal portions of the left ventricle. Coronary angiography and left ventriculography help to make differential diagnosis.

The onset of this syndrome has often been associated with stressful triggers, which could be either emotional or physical and the subjects most frequently affected are postmenopausal women.(2,3) Despite it could be associated with serious complications, prognosis is in general favorable. The underlying mechanism has not been established yet; however catecholamine excess has been proposed to explain microvascular dysfunction in the determinism of TCM.(4,5).

We hereby report a rare case of takotsubo cardiomyopathy following permanent pacemaker implantation.

Case

An 85-year-old woman, without significant medical history with the exception of arterial hypertension, was admitted to the emergency department of our hospital with syncope. She

was hemodynamically stable and physical examination was unremarkable. Her ECG showed a new 2:1 atrioventricular nodal (AV) block and old right bundle branch block (RBBB). Routine blood tests for renal and liver function, electrolytes, thyroid function, troponin and brain natriuretic peptide were all within normal ranges. Chest radiography showed no sign of pulmonary congestion.

At echocardiography examination, normal systolic function (left ventricular ejection fraction [LVEF] 55%) was detectable with no wall-motion abnormality. During hospitalization in the Coronary Care Unit, isoprenaline was administered in continuous infusion to support heart rate, without any adverse effects.

After exclusion of reversible causes of AV block, the patient was scheduled for definitive bicameral pacemaker implantation. After local anesthetic lidocaine injection, through cephalic vein, a dual-chamber rate-modulated (DDDR) pacemaker with ventricular lead in the right ventricle was implanted (Medtronic, Minneapolis, MN, USA). The procedure was completed without any complications. During the following hours the patient remained under observation, asymptomatic and with normal parameters.

In the following morning, routine assessment of serum troponin levels showed a significant increase (6908 ng/L [reference range 0-16]). Creatine kinase and creatine kinase-MB levels were also raised (respectively 193 U/L [reference range 0-145] and 10 ng/mL [reference range 0-3.1]). The patient reported no symptoms and ECG showed atrial and ventricular pacing, with ST-segment conditioned by pacemaker activity (**Figure 1**). A pacemaker check was performed, revealing normal electronic parameters. However, repeat transthoracic echocardiography showed akinesia in the apical areas and hypercontractile basal segments, with a moderate reduction of the LVEF (40%). Given the possibility of myocardial ischemia, an urgent coronary angiogram was performed, revealing no significant coronary artery disease (F**igure 2**), while a ventriculogram revealed ballooning of apical regions with typical so-called takotsubo shape.

So, by exclusion of other diagnoses, pacemaker implantation-induced Takotsubo cardiomyopathy was considered to be the cause of this acute onset of heart failure. Accordingly, the patient was treated conservatively with conventional heart failure therapy, including angiotensin-converting enzyme inhibitors, beta-blockers and diuretics. She was discharged from the hospital after two days in stable condition, asymptomatic, after a gradual normalization of myocardial enzymes, with effective dual-chamber stimulation and predischarge echocardiography substantially comparable to the previous one.

The patient was reevaluated 1 week, 4 weeks and 12 weeks in the cardiology clinic. During this period, she remained free from symptoms and the electronic recheck of the pacemaker was

functionally regular. After 1 month, a transthoracic echocardiography control documented a complete recovery of left ventricular function, with LVEF of 55% and no wall motion abnormalities (**Figure 3**). Heart failure medications was discontinued and she remained well during subsequent follow-up.

Discussion

This clinical vignette is one of few cases reporting an acute episode takotsubo cardiomyopathy following permanent pacemaker implantation.(6,7,8,9)

To date, no definitive consensus has been defined regarding diagnostic criteria of takotsubo cardiomyopathy,(KATO) but the proposed Mayo Clinic definition has been generally accepted.(9,10,11) In our patient, the evidence of transient typical kinesis alterations after a stressful trigger in the absence of obstructive coronary disease and associated with modest elevation in cardiac troponin level, was satisfied; ECG changes were precluded, as it showed ventricularly paced and underlying RBBB; finally, the classical course of gradual and complete resolution of regional wall abnormalities and normalization of the LVEF at follow-up, through a supportive and conservative management, helped to confirm the diagnosis.

Few other previous case studies have been reported in the literature about takotsubo cardiomyopathy following pacemaker insertion. Our case shares these common themes. However, takotsubo cardiomyopathy remains an unrecognized complication of the procedure, and pathophysiologic mechanisms, impact, management and outlook are still debated (**Table 1, Figure 4**). The well known dyssynchronous ventricular activation pattern resulting from the direct right ventricular pacing may promote progressive left ventricular dysfunction and clinical heart failure, but would not account for the typical territory involvement seen in acute takotsubo cardiomyopathy. Therefore, the pathophysiological process of this type of acute myocardial dysfunction needs to be explained in another way.

The exact underlying mechanism of takotsubo cardiomyopathy syndrome is unclear, but it seems mainly related to an excess of circulatory catecholamine release in stressful physical or psychological conditions.(3,5,12). An exaggerated sympathetic response is hypothesized to induce myocardial toxicity leading to myocardial stunning and negative cardiac myocyte inotropy.

With these assumptions, pacemaker implantation, even if uncomplicated, may be sufficiently stressful in individual patients to precipitate this syndrome. In fact, surgical distress adds to the hemodynamic, therefore multisystemic one, induced by the presence of cardiac electrical dysfunction. Furthermore, it has been seen that excess internal adrenergic activation is common

in subjects with complete AV block presumably representing a finalized compensative mechanism.(13) In the same way, authors hypothesize an increased apical adrenoceptor density and responsiveness following AV node ablation; indeed, takotsubo cardiomyopathy has also been reported following.(14) In our case, an external trigger of catecholamine presence can be possibly identified, represented by infusion of Isoprenaline administered before the intervention.

Finally, analyzing the history in detail, we discovered that our old patient has been presenting initial symptoms of senile dementia accompanied by an anxious state in the last months. This is in agreement with Niewinski at al, who showed that patients with cognitive impairment and frailty are at greater risk of takotsubo cardiomyopathy following pacemaker implantation.(15) All these factors may have contributed to the development of this syndrome in our case.

In summary, cardiac pacing is associated with a substantial risk of complications, most of which occur in the perioperative phase (such as pocket hematoma, infection, tricuspid valve interference, pneumothorax, or cardiac perforation), while a sizable risk remains during long-term follow-up (infection, lead-related reintervention, or pacemaker syndrome and dyssynchronous ventricular activation).(16) Takotsubo cardiomyopathy usually occurs after a stressful trigger and is rarely seen as an adverse event after permanent pacemaker implantation, especially in a particular category of patients. This has to be kept in mind by clinicians in order to apply the right diagnostic-therapeutic strategy.

In conclusion, takotsubo cardiomyopathy should be considered as a rare, but potential complication that can occur after permanent pacemaker implantation, with greater risk of patients with cognitive impairment and frailty.

Declarations

Acknowledgement

The patient described in this case report signed a pertinent written informed consent form. This manuscript was revised with the assistance of artificial intelligence tools, including ChatGPT 4 (OpenAI, San Francisco, CA, USA), in keeping with established best practices (Biondi-Zoccai G, editor. ChatGPT for Medical Research. Torino: Edizioni Minerva Medica; 2024). The final content, including all conclusions and opinions, has been thoroughly revised, edited, and approved by the authors. The authors take full responsibility for the integrity and accuracy of the work and retain full credit for all intellectual contributions. Compliance with ethical standards and guidelines for the use of artificial intelligence in research has been ensured.

Conflict of interest

Giuseppe Biondi-Zoccai has consulted for Abiomed, Advanced Nanotherapies, Aleph, Amarin, Balmed, Cardionovum, Crannmedical, Endocore Lab, Eukon, Guidotti, Innovheart, Meditrial, Menarini, Microport, Opsens Medical, Terumo, and Translumina, outside the present work. All other authors report no conflict of interest.

Table 1

Potential pathophysiologic mechanisms of takotsubo cardiomyopathy cause by cardiac pacing, with ensuing impact, management and outlook.

Mechanism	**Impact**	**Management**	**Outlook**
Autonomic nervous system dysregulation	Pacing disrupts the autonomic balance, increasing sympathetic activity and reducing vagal tone, triggering stress-induced cardiomyopathy.	Sympathetic modulation using beta-blockers and lifestyle modifications.	Potential for long-term autonomic dysfunction; requires tailored pacing strategies.
Catecholamine surge	Excessive catecholamines cause transient myocardial stunning, leading to apical ballooning.	Beta-blockers, supportive therapy, and monitoring for arrhythmias.	Generally reversible with supportive care; recurrence possible in susceptible patients.
Inflammatory response	Pacing-induced myocardial stress triggers inflammatory cytokine release, exacerbating myocardial dysfunction.	Anti-inflammatory treatments, corticosteroids in select cases, and symptom management.	Inflammatory mechanisms may contribute to long-term myocardial vulnerability.
Mechanical stress from pacing	Rapid pacing alters ventricular contractility, causing regional wall motion abnormalities mimicking takotsubo syndrome.	Adjusting pacing parameters to reduce mechanical stress and considering alternative pacing strategies.	Pacing adjustments can mitigate risk; research on safer pacing approaches is ongoing.
Microvascular dysfunction	Impaired coronary microcirculation due to pacing-induced vascular dysfunction leads to ischemia-like myocardial stunning.	Vasodilators, endothelial function improvement, and close cardiac monitoring.	Chronic microvascular dysfunction may predispose to recurrent cardiac events.
Myocardial energy imbalance	Abnormal pacing affects myocardial metabolism, leading to transient dysfunction similar to Takotsubo cardiomyopathy.	Metabolic support with glucose-insulin-potassium infusions and dietary modifications.	Metabolic interventions may enhance recovery; further research needed.
Pre-existing electrical abnormalities and drug triggers	Pre-existing conduction system diseases (e.g., atrio-ventricular block) and adrenergic drug exposure (e.g., isoprenaline) may heighten susceptibility to takotsubo cardiomyopathy.	Monitoring and gradual titration of adrenergic agents; cautious use of isoprenaline in predisposed patients.	Better identification of high-risk patients may improve outcomes and reduce the incidence of takotsubo cardiomyopathy.
Psychological stress and cognitive impairment	Elderly patients with cognitive impairment and frailty may experience exaggerated sympathetic responses, increasing susceptibility to takotsubo cardiomyopathy.	Careful pre-procedural assessment of frailty and cognitive function; minimizing perioperative stressors.	Increased risk in frail and elderly patients necessitates proactive monitoring and preventive strategies.

Figure 1

ECG recording at 25 mm/s showing atrial and ventricular pacing; ST-segment is conditioned by pacemaker activity.

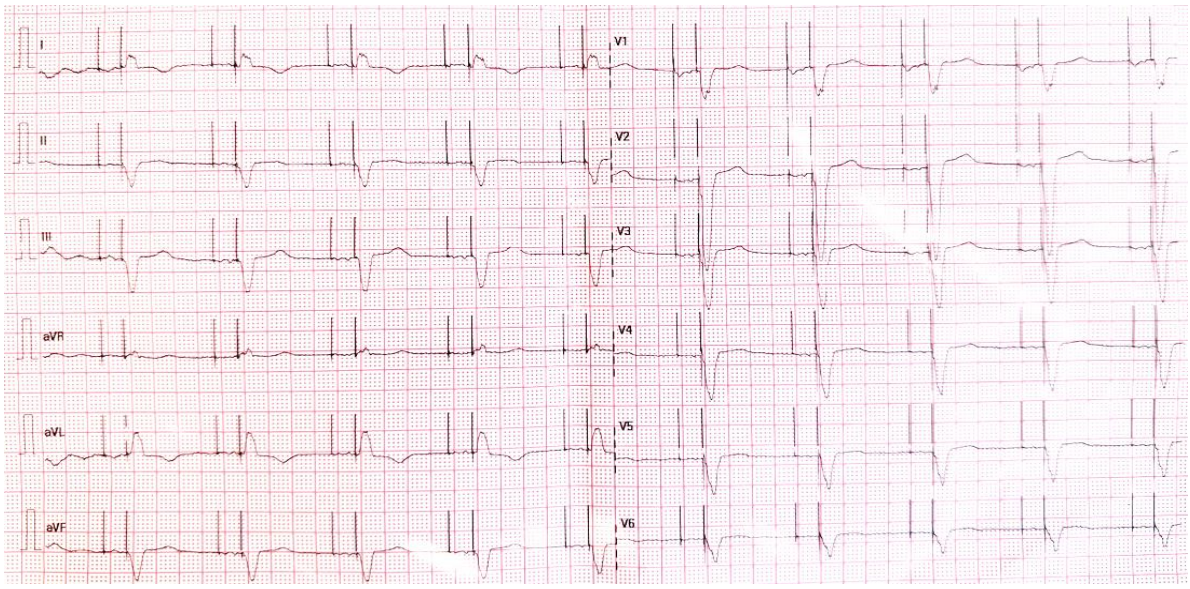


Figure 2

Coronary angiogram revealing no significant coronary artery disease (top panels: left coronary angiograms; bottom panel: right coronary angiogram).

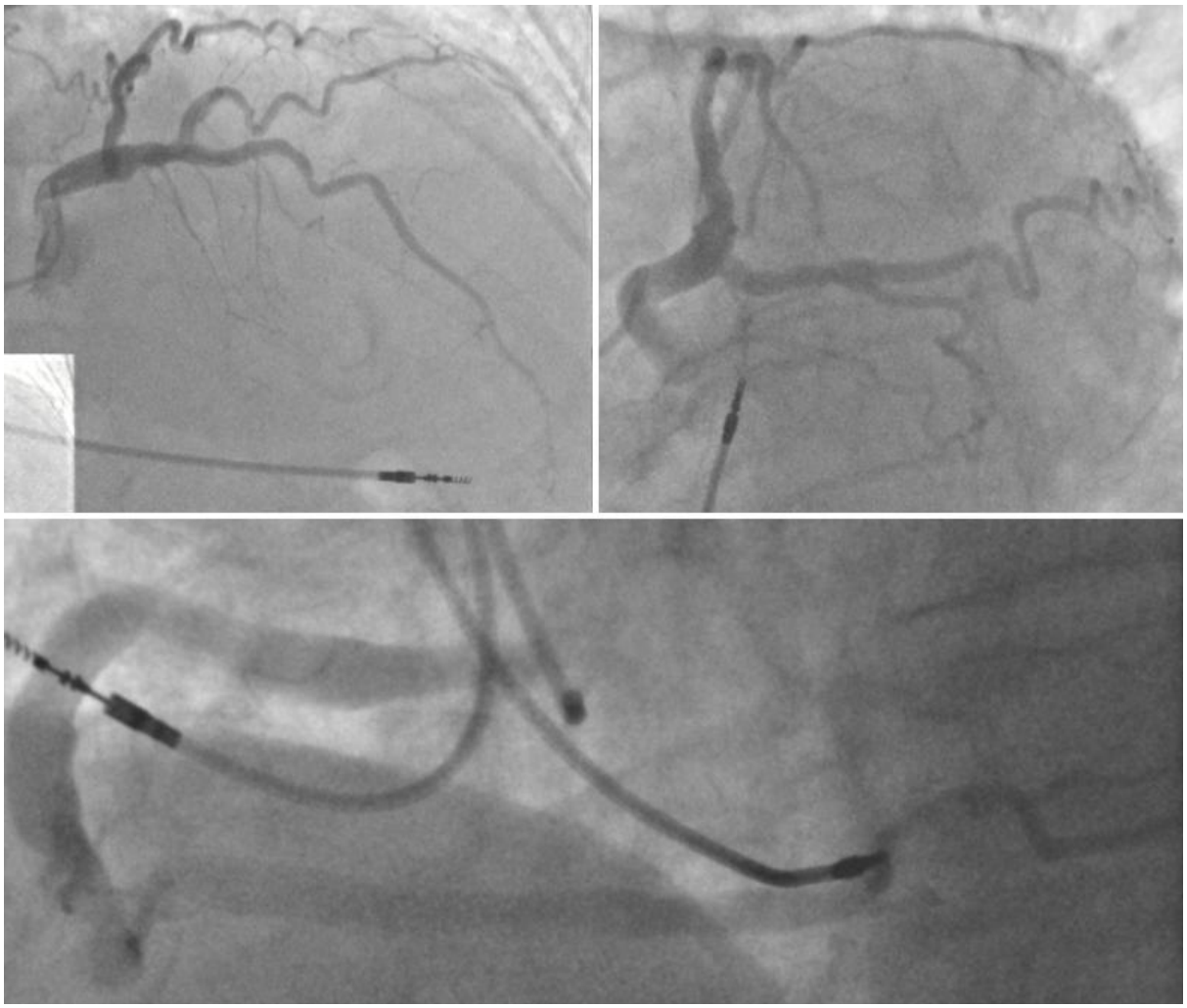


Figure 3

Transthoracic echocardiogram at follow-up showing normal systolic function (left panel: end-diastole; right panel: end-systole).

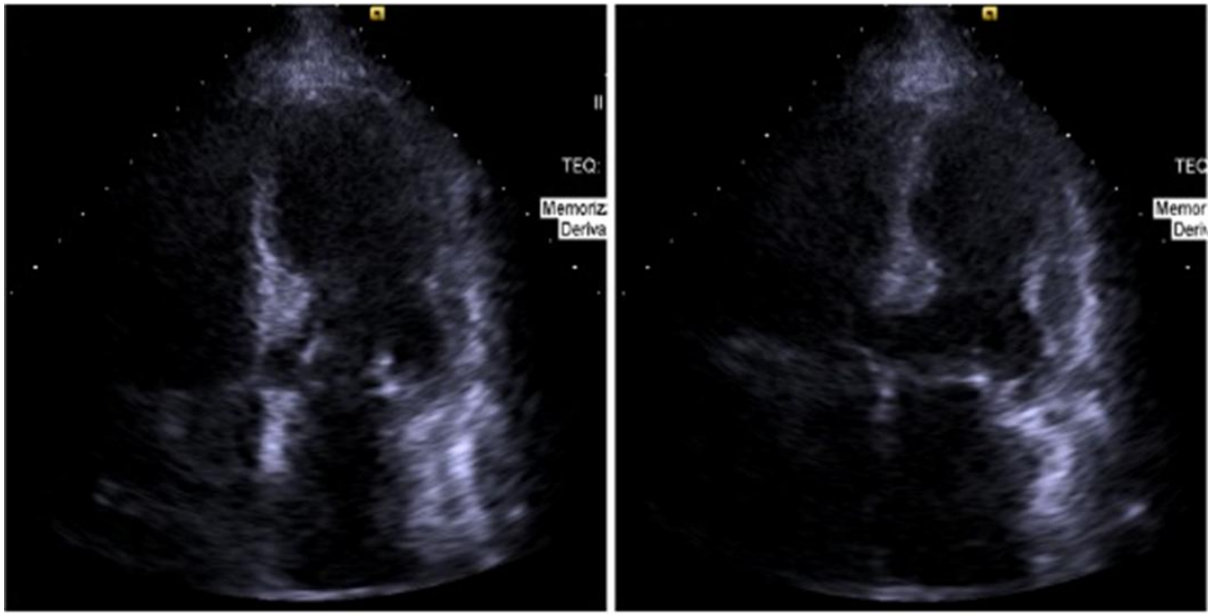
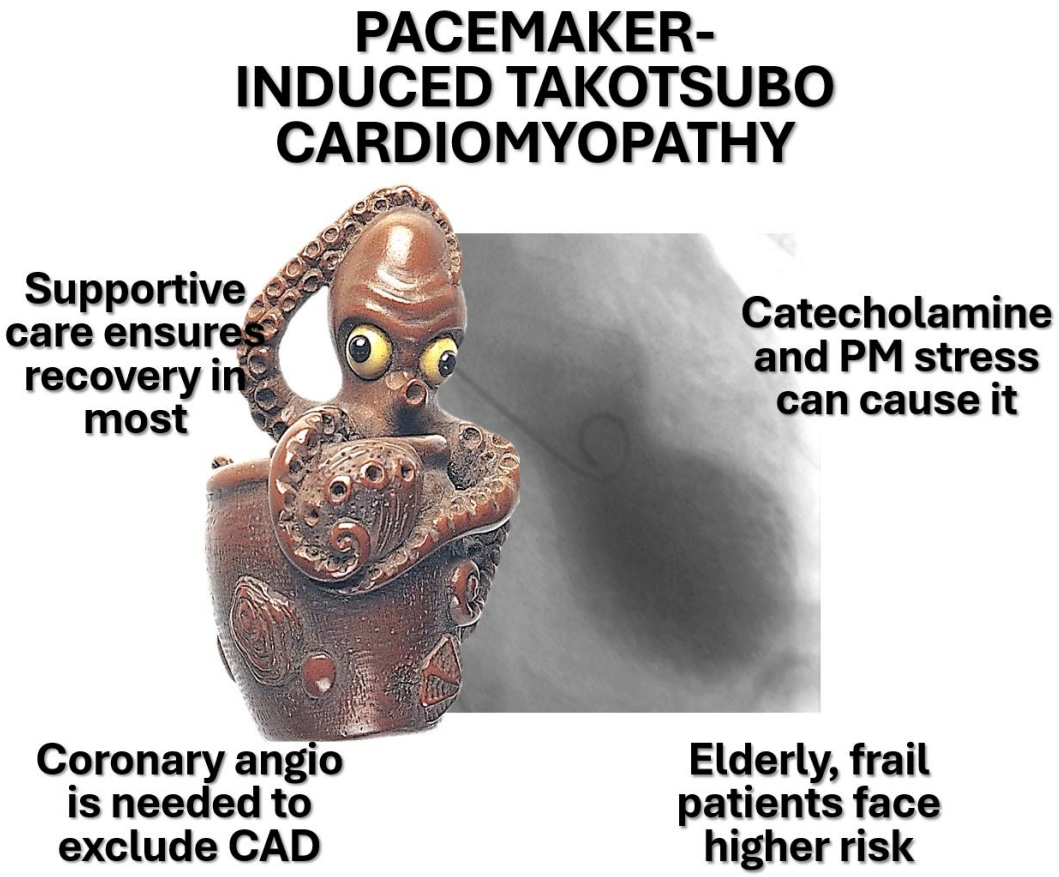


Figure 4

Graphical summary of key highlights of pacemaker-induced takotsubo cardiomyopathy (the image on the left represents a netsuke shaped as an octopus entering a takotsubo; the image on the right a left ventriculogram of a patient with takotsubo cardiomyopathy). CAD=coronary artery disease; PM=pacemaker.



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