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CASE REPORT

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"Takotsubo cardiomyopathy presenting with QT prolongation: an atypical presentation."

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ABSTRACT

Takotsubo Cardiomyopathy (TCM), also known as broken heart syndrome, is a syndrome of transient and reversible cardiac dysfunction in the absence of obstructive coronary artery disease following an unpleasant emotional event. TCM commonly presents as chest pain mimicking acute coronary syndrome (ACS) in character. The most common electrocardiogram (EKG) findings associated with TCM are ST-segment elevation or T wave inversion. Herein, we present a case of TCM in an individual who presented with a sudden onset chest pressure following a stressful event. She was found to have QT interval prolongation on EKG and elevated troponins. Initially thought to have non-ST elevation myocardial infarction (NSTEMI). Cardiac catheterization did not reveal coronary artery disease. The ventriculography suggested apical ballooning and the diagnosis of TCM with atypical EKG presentation. Our case is unique as we describe an atypical electrocardiographic presentation of TCM. Our case emphasizes that physicians should refrain from prescribing QT-prolonging drugs to patients with TCM, to avert potential QT prolongation and progression to torsade de pointes (TDP).

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1. Background

TCM is a syndrome characterized by transient and reversible cardiac dysfunction in the absence of obstructive coronary artery disease. The name of the term "Takotasubo" derives from the Japanese name for an octopus trap, which is the typical ballooning appearance of the left ventricle [1]. The usual sequence of EKG changes described in the literature is an initial ST-segment elevation, followed by a T-wave inversion and partial resolution of the ST-segment elevation [2]. We present a case of a 75-year-old female who presented with chest discomfort concerning acute coronary syndrome (ACS), and QT prolongation. Echocardiography led to a diagnosis of TCM. TCM usually presents with ST-segment elevations and other repolarization changes. QT prolongation is a rarely reported electrocardiographic finding in patients that can progress to a life-threatening ventricular tachycardia, like torsade de pointes (TDP).

2. Case description

A 75-year-old female presented to the emergency room for evaluation of chest pain. The patient developed a sudden onset chest discomfort which brought upon following a recent stressful event in when she was trying to help an elderly gentleman who had fallen in the snow. She described the pain to resemble a dull pressure like feeling in the sub-sternal area. The pain was non-radiating and seemed not to be affected by exertion. This pain persisted until she went to bed. Upon awakening, she still had the discomfort, therefore, sought medical attention the next morning. Her past medical history was significant for hypertension and atrial fibrillation for which she had been on apixaban and flecainide. The patient had noninvasive cardiac studies done within the last few months which had not suggested ischemic coronary artery disease.

On presentation, her vitals were: temperature 96.2 F, blood pressure 185/74 mm Hg, heart rate 66 beats per minute (bpm), respiratory rate 20, and oxygen saturation of 98% on room air. An EKG showed sinus rhythm at 74 bpm, QRS duration was 96 milliseconds (ms) with a prolonged QT interval with the corrected interval (QTc) of 641 ms (Figure 1). However, baseline EKG while patient was on flecainide for underlying atrial fibrillation revealed a mild QTc and QRS duration prolongation which was consistent with flecainide use (Figure 2).

Laboratory tests showed leukocytosis of 19200 cells per microliter (μL) of blood with reference range (RR) of 4000–11000 cells/μL, hemoglobin 14.8 gram per

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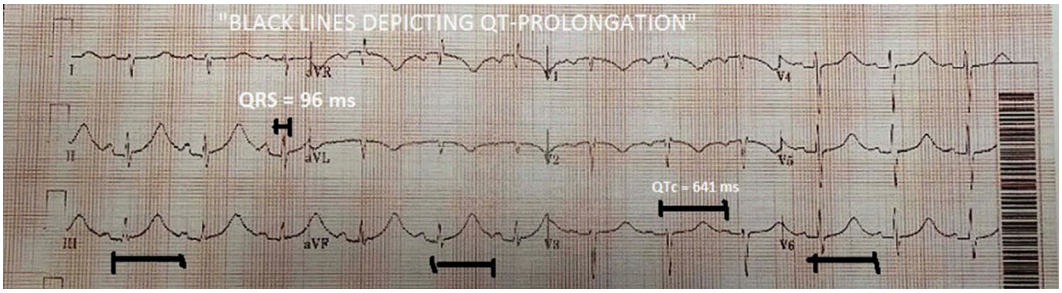

Figure 1. EKG on presentation showing QT prolongation with no ST/T changes.

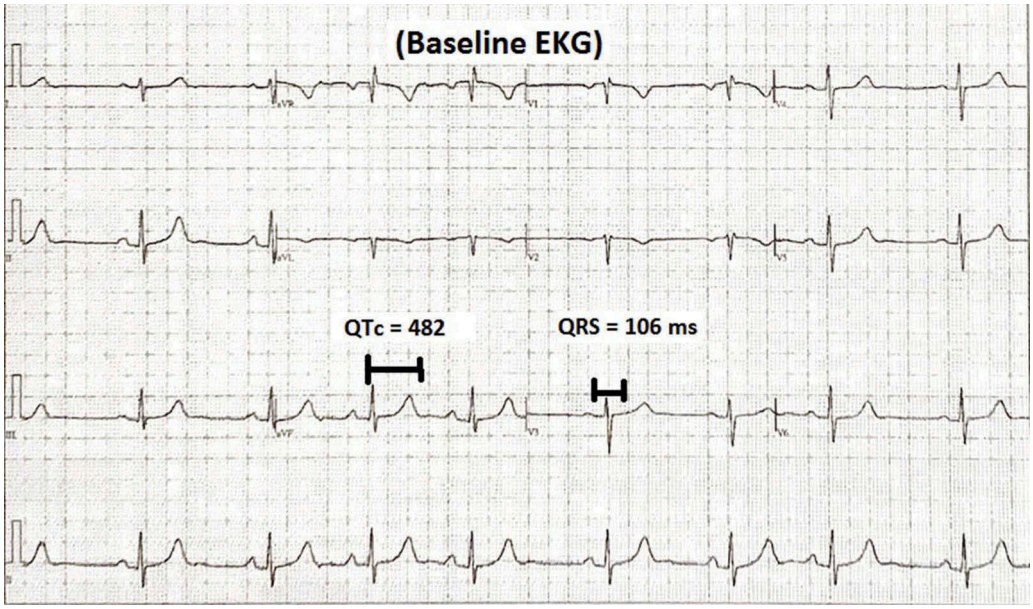

Figure 2. Baseline EKG on flecainide showing mildly raised QTc and QRS interval.

deciliter (g/dL) (RR 12–15.5 g/dL) and platelet count 323000 cells/μL (RR 150000–450000 cells/μL). A comprehensive metabolic panel revealed blood urea nitrogen 12 mg/dL (RR 0–23 mg/dL), creatinine 0.78 mg/dL (RR 0.0–1.11 mg/dl), potassium 3.7 mEq/L (RR 3.5–5.1 mEq/L), corrected calcium 10.1 mg/dL (RR 8.4–10.2 mg/dL), and albumin 4.4 g/dL (RR 3.4–4.8 g/dL). Further investigations included a magnesium 2.0 (RR 1.6–2.6 mg/dl), phosphorus 2.7 (RR 2.3–4.7 mg/dL), Troponin 1.21 (RR <0.10 ng/ml), BNP 708(RR 0–99 pg/mL), CK 128 (RR 68–168 U/L), and D-dimer 715 (RR 0–230 ng/mL). A CT chest done in the ER was unremarkable and ruled out pulmonary embolism.

The patient's clinical presentation was concerning for ACS. She started on aspirin and a heparin infusion for NSTEMI management. Given the significant QT prolongation and risk for torsade de pointes (TDP), the serial EKGs were followed up. The patient underwent diagnostic left heart catheterization and coronary angiography along with left ventriculography. The angiography did not reveal any significant obstructive coronary disease. However, the ventriculography showed an ejection fraction of 40–45%

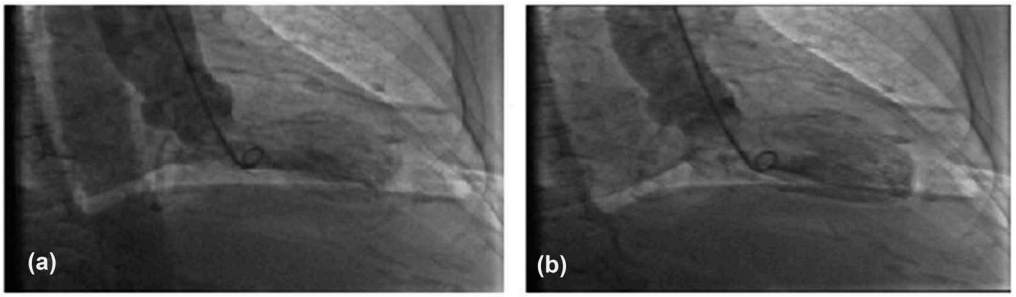

Figure 3. Left ventriculogram suggestive of of mild-to-moderate anterior, apical, and inferior apical hypokinesis during systole (a) and diastole (b).

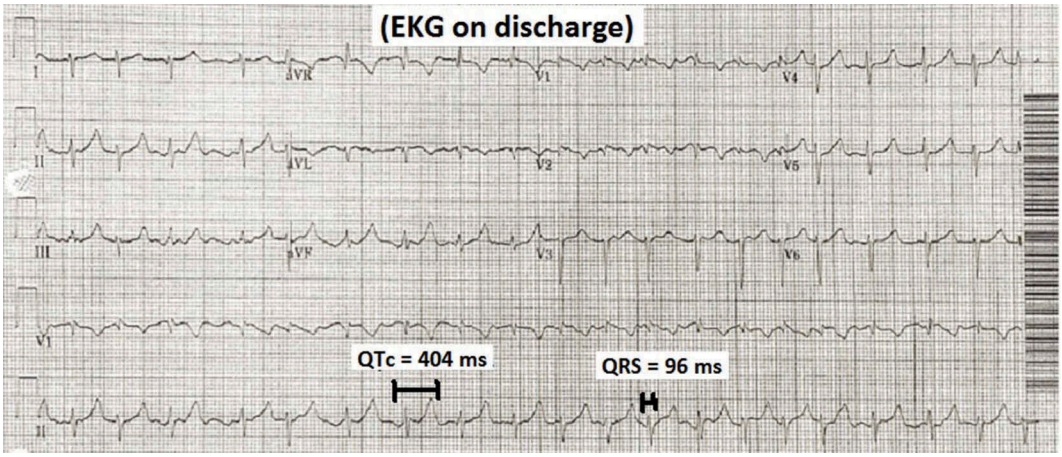

Figure 4. EKG on discharge showing normal QTc interval.

with the evidence of mild-to-moderate anterolateral, anterior, apical and inferior apical hypokinesis on systole (Figure 3(a)), consistent with TCM. The depolarization changes and the QT prolongation were attributed to the TCM. Serial EKGs that proceeded showed a sequential decrease in the corrected QT, to the point where it completely normalized. Troponin trended down during the hospitalization. During hospitalization, she had intermittent runs of atrial fibrillation with a rapid ventricular response and bradycardia. The patient symptoms resolved and she was discharged to home, with follow up. Her EKG at discharge showed a normal QT interval (Figure 4).

3. Discussion

Dote et al. described the transient myocardial dysfunction and named it "Takotasubo" because the shape of the left ventricle resembled a Japanese octopus trap [3]. TCM predominantly occurs in post-menopausal females following, but not always, a recent emotional or physical stress [4]. TCM is characterized by transient but reversible ventricular dysfunction with the resolution of ventricular dysfunction within a few days to weeks. Patients typically present with chest pain (70% of cases) mimicking ACS, acute dyspnea (20%), hypotension and or cardiogenic shock [3]. Conversely, a small number of cases may be asymptomatic and are incidentally based on ST segment or T wave changes on EKG, minor elevation of cardiac enzymes or cardiac echocardiography. The exact prevalence of this syndrome is still unknown, but literature indicates the prevalence to be between 1.0–2.5% [3].

The exact pathophysiology of TCM is yet to be fully understood. Wittstein et al. reported a significantly raised levels of catecholamines during an acute episode of TCM [5]. The possible mechanisms postulated include catecholamine-mediated cardiac toxicity, LV outflow tract obstruction, aborted MI caused by transient left anterior descending artery (LAD) occlusion, multivessel coronary spasm, and microvascular dysfunction [3]. Our patient had a recent stressful event which was thought to be responsible for sympathetic overdrive. An extensive literature review suggests that sympathetic overdrive may play a role in the development of myocardial dysfunction associated with TCM. Elevated levels of catecholamines indicated the linkage with beta$_1$-adrenergic and beta$_2$-adrenergic receptor downregulation with resultant blunted myocardial adrenergic stimulation and LV apex stunning [6]. The higher density of beta-adrenergic receptors in the LV apex than in the base, thus accounting for the apical myocardium being more susceptible, particularly to epinephrine than the basal segments [6,7]. Animal models have shown that elevated levels of catecholamines can cause extensive myocytes necrosis and apoptosis due to oxidative stress [8]. Other proposed mechanism are estrogen deficiency, transient coronary artery spasm or genetic predisposition [3].

The most commonly used diagnostic criteria to define the pathology is the Mayo clinic criteria. This criterion suggests transient hypokinesis, akinesis, or dyskinesis in the left ventricular mid segments with or without apical involvement and regional wall motion abnormalities extending beyond a single epicardial vascular distribution; with frequently, but not necessarily, a new stressful trigger. Pheochromocytoma and myocarditis should be excluded per the Mayo criteria to classify it as 'Takotasubo cardiomyopathy.' [9] The other criteria include the absence of obstructive coronary disease or angiographic evidence of acute plaque rupture, with ECG abnormalities usually ST-segment elevation and or T-wave inversion or modest elevations in cardiac troponins [9]. Although our patient had regional wall motion abnormalities including apical involvement and elevated troponins levels instead of classical ST-segment elevation or T wave inversion on EKG, QT interval prolongation was evident. Previtali et al. described prevalence of variant

EKG findings such as ST-segment elevation were present in 56% of patients, T wave inversion in 39% of cases and a very few had QT interval prolongation [10].

The QT prolongation in TCM is postulated to result from the reduced repolarization reserve and intramyocyte calcium overload. The mechanisms described as pause-dependent, a long-short sequence that characteristically triggers QT prolongation [11]. The patient was taking flecainide for atrial fibrillation for several years before her presentation. Although cases have been reported about QT prolongation with flecainide use, it usually prolongs QT intervals minimally, via increasing action potential duration. The effect mediates via selective Ikr channel-blocking properties, the mechanism of this QT prolongation is typically an increase in QRS complex duration, which was not the case in our patient, as she had a normal QRS duration on electrocardiography [12]. Kinori et al. reported that patients with TCM-associated QT prolongation were at a higher risk for TDP and mortality than TCM patients without QT prolongation [13].

Classically, coronaries are seen as normal or with non-flow limiting coronary artery disease (CAD) upon angiographic evaluation. Recently, cardiac MRI has been used to differentiate the TCM from myocardial infarction in a small subset of the patient who has abnormal coronary artery obstruction [14].

Treatment is mainly supportive. However, beta-blocker and angiotensin-converting enzyme inhibitor or angiotensin II receptor blocking agent are routinely prescribed to counter catecholamine excess and ventricular dysfunction and volume overload [3]. Our patient was put on metoprolol tartrate, amiodarone, and apixaban due to underlying history of atrial fibrillation.

In conclusion, it is essential that clinicians should be aware of this atypical presentation of TCM so that it can be picked up early on before QT prolongation deteriorates into TDP which is associated with higher risk for mortality. Physicians should try to avoid QT-prolonging drugs in patients with TCM to prevent adverse outcomes.

Disclosure statement

No potential conflict of interest was reported by the authors.

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