1. Introduction

Takotsubo cardiomyopathy (TTC) is a transient phenomenon of myocardial hypo-contractionality that occurs in the presence of physical or emotional stressors and involves non-obstructive coronary circulation [1]. Though Takotsubo is a temporary stress-related myocardial dysfunction, clinical presentation of TTC is often alarming as it mimics acute coronary syndrome (ACS), and therefore, necessitates angiography in most of the cases. Angiography not only confirms the diagnosis of TTC but rules out concurrent coronary artery disease (CAD). To date, numerous physical and emotional stressors have been identified as precipitants of TTC [2]. There is a consensus regarding the occurrence of TTC triggered by stressors, but the prompt recognition of these factors is not always possible. Additionally, rare stressors continue to be recognized and complicate the clinical picture. We report on an unusual case of TTC in which an ascending colon mass was identified as the most likely stress trigger in the development of TTC.

2. Case report

An 84-year-old African-American female with diverticulosis and recurrent episodes of diverticulitis was admitted to the hospital for acute sigmoid diverticulitis where she received intravenous (IV) fluids and antibiotics. On the seventh day of admission, she underwent diagnostic colonoscopy which showed diverticulosis with local infection, two sessile polyps in the transverse and sigmoid colon (SC), and a large malignant appearing mass of the proximal ascending colon (Figure 1(a)). Though she had a previous CT of the abdomen showing SC diverticulitis, the ascending colon mass could not be seen since it was done as a non-contrast CT. Because of a possible colon malignancy, a CT with contrast of chest, abdomen and pelvis was performed for staging in which a focal density measuring 4 cm x 2.4 x 3.9 cm was found within the proximal ascending colon (Figure 1(b)). The ascending colon mass was limited to the colon without lymph node or distant metastasis. Tumor markers (CA and CEA) were not elevated. Histopathology was consistent with tubular adenoma polyps and tubulo-villous adenoma with high-grade dysplasia in the ascending colon mass. Diagnostic features of invasive cancer were absent; however, the reliability of biopsy was limited because of the large size of the mass and focal collection of biopsy specimens. Therefore, absence of malignancy could not be completely ruled out and a right robotic hemicolecction was planned. Additional indication for surgical resection in this patient was the likelihood of bowel obstruction in the near future due to the large size of the mass. Elective surgery was scheduled, and the patient was discharged home. Before elective hemicolecction, the patient initiated a bowel preparation with polyethylene glycol. She was readmitted to the hospital within three weeks because of intractable nausea, vomiting, left lower quadrant pain and loose stools, so the hemicolecction was postponed. During admission, her vitals included blood pressure: 146/66 mmHg, pulse: 88/minute, respiratory...
rate: 18 breaths/minute, oxygen saturation: 96% on room air and temperature: 97.7°F (36.7 °C). On examination, she appeared pale and was in moderate distress. Abdomen was soft and mildly tender in left lower quadrant. Hyperactive bowel sounds were present. Cardiopulmonary examination was unremarkable. Labs showed white blood cells 9.3 × 10^3/μL (4.50–11.00), hemoglobin of 9.9 g/dL (12.0–15.7), hematocrit of 29.4% (34.9–46.9), and platelet count 395 × 10^3/μL (150–400). Sodium 135 mmol/L (134–145), potassium 2.6 mmol/L (3.5–5.1), chloride 101 mmol/L (98–112), bicarbonate 24 mmol/L (24–30) and anion gap of 10 mmol/L (6–14) glucose 135 mg/dL (70–105), blood urea nitrogen 20 mg/dL (7–22) and creatinine 0.85 mg/dL (0.50–1.50). Amylase and lipase were normal. Non-contrast CT of abdomen showed inflammatory changes and thickening of the SC, consistent with diverticulitis; there was no abscess. The ascending colon mass could not be appreciated again due to the lack of contrast. Oral diet was restricted, and she was started on IV antiemetics, opiates and IV potassium replacement. Four hours later, she became unresponsive in the emergency room, and rhythm monitor showed ventricular tachycardia (VT) with a rate of 227 beats per minute. The patient became responsive after a precordial thump before receiving any chest compressions and reverted into sinus rhythm. She denied chest pain, dizziness, shortness of breath and vomiting before or after the event; but continued to complain of left lower quadrant pain associated with nausea. During CPR, labs drawn showed a low potassium 3.0 mmol/L and elevated troponin I 0.70 ng/mL (0.00–0.04). Electrocardiogram showed an old right bundle branch block. She was admitted to the coronary care unit and was started on IV piperacillin-tazobactam. She reported no chest pain, but her troponin continued to rise from 0.70 ng/mL to 3.24 ng/mL over the next 16 hours. She was started on IV heparin, oral aspirin, clopidogrel, atorvastatin, and metoprolol for non-ST-segment elevated myocardial infarction (NSTEMI). Transthoracic echocardiogram (TTE) showed mildly increased left ventricle (LV) cavity size, regional wall motion abnormalities (mid to apical akinesis) and an ejection fraction (EF) of 35% decreased from the baseline of 60% reported eight months prior (Figure 1(a)). Because of this NSTEMI and prior VT-arrest, a cardiac catheterization was performed (Figure 2(b)) which ruled out significant CAD. However, left ventriculogram showed typical apical ballooning of the LV, consistent with TTC. After cardiac catheterization, IV heparin and clopidogrel were discontinued, and ACE inhibitor (lisinopril) was added because of reduced EF. She received seven days of IV antibiotics for diverticulitis. She was discharged on the 7th day of admission with a LifeVest®, a wearable defibrillator for prevention of sudden cardiac death. Due to her history of the acute cardiac event, the risk of mortality was high. Therefore, the elective robotic hemicolectomy was postponed. Follow-up TTE was planned for 3–4 weeks after discharge for the assessment of any improvement of cardiac function in preparation for a robotic hemicolec tomy of the colonic mass.

3. Discussion
TTC is less common than ACS and can mimic any spectrum of ACS including ST-segment elevated MI (STEMI), NSTEMI and unstable angina. Among patients with troponin-positive ACS, TTC accounts for only 1.2% of cases [3]. It occurs mainly in postmenopausal females and elderly individuals. One study documented 89.8% cases of TTC were among females [4]. Etiologically, the high prevalence of TTC in postmenopausal females could be attributed to an estrogen deficiency. Other proposed mechanisms include 1) excessive catecholamine release, 2) microcirculatory
dysfunction, 3) coronary artery dysfunction and 4) direct cardiotoxicity [5,6].

One study reported higher catecholamine levels in Takotsubo patients than in MI patients [5]. Pathologically, catecholamines could cause myocardial stunning because of microvascular spasms or direct myocardial toxicity. Cellularity, histologic changes such as structural alteration of myocytes and intracytoplasmic accumulation of glycogen stores occur in Takotsubo and improve with clinical recovery of cardiac dysfunction [6]. Molecularly, elevated catecholamines are involved in a signalling switch from a stimulatory ionotropic response to an inhibitory ionotropic response [7]. Apart from these, many physical and emotional stressors are considered as the possible precipitants of TTC. A large systemic review of 1109 patients with TTC reported 39% of patients with emotional stressors and 35% with physical stressors [2]. This study reported hypertension (54%), dyslipidaemia (32%), smoking (22%), obesity (17%) and diabetes (17%) as major comorbid conditions [2]. This means the potential role of premorbid conditions in the pathogenesis of TTC, may be due to endothelial dysfunction [2]. In addition to these common disorders, a higher prevalence of psychiatric and neurological disorders has been reported in TTC patients than in ACS [4]. Based on this, it can be speculated that stressful life events play a pivotal role in generating catecholamine surges, and comorbid conditions cause a baseline myocardial dysfunction. Baseline conditions and stress may allow one to achieve a threshold for development of TTC. Our patient developed TTC three weeks after the diagnosis of an ascending colon mass. She underwent a series of stressful events lowering her threshold for the development of TTC. She was scheduled for the right-sided hemicolectomy. However, she ended up in the hospital with severe GI symptoms. She developed VT and required resuscitation for cardiac arrest. She had typical apical ballooning of the LV with normal coronary arteries. Her surgery was postponed due to acute cardiac events. Though our patient had multiple stressors (bowel preparation, diverticulitis, electrolyte imbalance and psychological stress of malignancy), the ascending colon mass was thought to be the most significant stressor in her case. This is based on the increasing evidence in the literature favouring the role of malignancy in TTC. In one study, 38 patients with malignancies including lymphoproliferative disorders (30%), gastrointestinal (15%) and lung cancer (12.5%) developed TTC in a six-year duration [8]. Cancer-related treatments (surgery, chemotherapy and stem cell transplantation) can also precipitate Takotsubo. TTC has been speculated as one of the paraneoplastic phenomena of malignancy [2]. Malignancy-related mechanisms of TTC include 1) neurohormonal changes 2) inflammatory response and 3) altered adrenoceptor sensitivity [9]. Malignancy can lower the threshold for stress stimuli and therefore generate LV systolic dysfunction. Girardey et al. compared patients of TTC with and without malignancy [9]. Takotsubo patients without malignancy had emotional stressors, were mainly females and had hypertension whereas those with malignancy had more often smoking and physical stressors. High-level peaks of B-type natriuretic peptide, leukocyte count and C-reactive protein were also seen in patients with malignancy. Troponins also peaked higher in malignancy but achieved no statistical significance [9]. Our patient had a tubulovillous adenoma with high-grade dysplasia. There was no proven malignancy on biopsy, however the absence of malignancy could not be completely ruled out as the ascending colon mass was not resected. Po-Yen and Po-Ming reported about a Taiwanese woman with TTC [10]. No identifiable trigger was found until she underwent colonoscopy. She had a 20-cm adenocarcinoma mass in SC that required radical sigmoidectomy. Contrary to this, our patient underwent no resection, and therefore, malignancy could not be completely ruled out. Bergdorf et al. followed 50 TTC cases with same number of MI controls. They had a baseline difference of malignancy (18% in TTC versus 6% in MI) [11]. On follow-up, seven new cases of cancer occurred in Takotsubo

Figure 2. Takotsubo cardiomyopathy-triggered by the ascending colon mass. A) Mid to distal apical ballooning of the left ventricle on transthoracic echocardiogram. B) Angiography showing non-obstructive coronary arteries.
whereas none occurred in the MI cohort. The odds of malignancy were significantly higher in TTC than in MI. Notably, TTC had occurred in non-malignant GI causes as well. This could be due to vagal stimulus withdrawal in the presence of elevated catecholamines leading to LV systolic dysfunction. Mohammad et al. reported a 60-year-old female with syncope and GI bleed who underwent colonoscopy [12]. The day after colonoscopy she developed TTC. They speculated the role of a vagal reaction in the presence of intrabdominal processes leading to TTC. The patient might be recovering from the hyper-vagal reaction; however, the concurrent stress of colonoscopy in the presence of vagal withdrawal might have led her to develop TTC. Kurisu et al. reported another non-malignant GI cause of TTC [13]. Their patient presented with a STEMI one hour after receiving an oral contrast for GI examination; cardiac catheterization revealed TTC. In this case, barium swallow might have caused a vagal response leading to the development of TTC. The profile of our patient fits the demographic profile of a typical Takotsubo patient, an 84-year-old postmenopausal female with comorbid conditions. She had active intra-abdominal processes in the form of an ascending colon mass. The stress of a new diagnosis of malignancy might have led her to develop TTC. Kurisu et al. reported another non-malignant GI cause of TTC [13]. Their patient presented with a STEMI one hour after receiving an oral contrast for GI examination; cardiac catheterization revealed TTC. In this case, barium swallow might have caused a vagal response leading to the development of TTC. The profile of our patient fits the demographic profile of a typical Takotsubo patient, an 84-year-old postmenopausal female with comorbid conditions. She had active intra-abdominal processes in the form of an ascending colon mass. The stress of a new diagnosis of malignancy might have led her to develop TTC.

4. Conclusion

- We propose that postmenopausal women with a new or possible diagnosis of GI malignancy are at high-risk for the development of TTC.
- Acute intra-abdominal processes including diagnostic testing or bowel preparations might further lower the threshold for TTC. Therefore, malignancy in the presence of intrabdominal processes should be cautiously handled in an elderly female.
- The development of TTC could postpone the definitive treatment in such cases whereas the optimal preventive strategies could lead to favourable outcomes.
- Future studies are needed to further support this association.

Disclosure statement

No potential conflict of interest was reported by the authors.

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