Author’s response to reviews

Title: Takotsubo cardiomyopathy after an Upper and Lower Endoscopy: A Case Report and Review of Literature

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Author’s response to reviews:

Reviewer #1: 1. Do you believe the case report is authentic? Yes

2. Do you have any ethical concerns? Please consider if local Institutional Review Board approval or ethical approval was obtained (if appropriate) and if the patient (or their parent or guardian in the case of children under 18) gave written, informed consent to publish this case and any accompanying images. A statement to this effect should appear in the manuscript.

Comments: None

3. Does the Introduction explain the relevance of the case to the medical literature?

Yes- But needs to improve
4. Does the article report the following information? Where information is missing, please specify.

a. The relevant patient information, including:

- De-identified demographic information (age, gender, ethnicity)-yes
- Main symptoms of the patient-yes
- Medical, family and psychosocial history- No

Please see the addition below:

The patient’s medications on presentation included: oxybutynin 10 mg oral tablet extended release once a day for urinary symptoms; omeprazole 40 mg oral tablet once a day for GERD; amlodipine 10 mg oral tablet once a day for HTN; bupropion 300 mg oral tablet extended release once a day for depression; escitalopram 20 mg oral tablet once a day for depression; topiramate 100 mg oral tablet once a day for neuropathy; tramadol 50 mg oral tablet as needed every four hours for pain; and fenofibric acid 135 mg oral tablet delayed release once a day for HLD. She did not have any known allergies. Family history was significant for myocardial infarction in her father and cerebrovascular accident in her mother. She lives in Manhattan with her husband, is retired, but used to work for an advertising agency. She smoked one pack of cigarettes per day for 30 years and occasionally drinks alcohol.

- Relevant past interventions and their outcomes-yes

b. The relevant physical examination findings. The following has been added:

Physical exam was non-significant.

c. Important dates and times in this case (if appropriate, organized as a timeline via a figure or table); if specific dates could lead to patient identification, consider including time relevant to initial presentation, i.e. initial presentation at T = 0, follow up at T = 1 month.

Not-applicable
d. Diagnostic assessments, including:

- Diagnostic methods – please note: upper and lower endoscopies explained in further detail throughout the report

- Challenges (e.g., financial, language/cultural) – not applicable, patient social history is reported

- Reasoning and prognostic characteristics (e.g., staging), where applicable – not applicable

e. Types and mechanism of intervention

not applicable

f. A summary of the clinical course of all follow-up visits

Comments: Yes

5. Is the interpretation (discussion and conclusion) well balanced and supported by the case presented?

Comments: Yes-Needs to improve. Additions have been made regarding diagnostic criteria for stress cardiomyopathy

6. Is the anonymity of the patient protected? Please consider any identifying information in images such as facial features or nametags, whether the patient is named etc. If not, please detail below.

Yes

7. Is the Abstract representative of the case presented?

Comments: yes
8. Does the case represent a useful contribution to the medical literature?

Comments: Yes

9. Additional comments for the author(s)?

Following are my comments and suggestions to the authors

1. Background:

Authors wrote 'While widely considered safe, adverse cardiovascular events can occur in high-risk patients undergoing endoscopy'. This statement needs some evidence and citations. Advice to elaborate on the topic for the reader to understand the potential cardiovascular events and it is important to diagnose the Takotsubo cardiomyopathy.

This sentence has been removed, as there is very limited literature out there on high risk patients undergoing endoscopy and cardiovascular events in the setting of cardiomyopathy. We describe the cases in the report, but there are not much data out there besides what we reported.

Authors wrote 'To date, there have only been six reported cases of stress cardiomyopathy in patients post-endoscopy. We present the second reported case of Takotsubo cardiomyopathy following an upper and lower endoscopy'. They say 6 reported cases and then mention their case is the second reported case. Confusing and needs clarification.

Please note: we added “both” upper and lower endoscopy to help clarify that there are two cases that include both.
2. Case presentation:

- Please mention patients’ current medications, allergy, social and brief family history.

The patient’s medications on presentation included: oxybutynin 10 mg oral tablet extended release once a day for urinary symptoms; omeprazole 40 mg oral tablet once a day for GERD; amlodipine 10 mg oral tablet once a day for HTN; bupropion 300 mg oral tablet extended release once a day for depression; escitalopram 20 mg oral tablet once a day for depression; topiramate 100 mg oral tablet once a day for neuropathy; tramadol 50 mg oral tablet as needed every four hours for pain; and fenofibric acid 135 mg oral tablet delayed release once a day for HLD. She did not have any known allergies. Family history was significant for myocardial infarction in her father and cerebrovascular accident in her mother. She lives in Manhattan with her husband, is retired, but used to work for an advertising agency. She smoked one pack of cigarettes per day for 30 years and occasionally drinks alcohol. Physical exam was non-significant.

- Patient has a diagnosis of Lymphocytic colitis. Has she had any prior endoscopies? If she did then how was she during those procedures?

- Why did she have the procedures scheduled?

- What anesthetic agents and pre-procedural medications were used? Eg: There are reports on meperidine (used for pre-colonoscopy sedation) causing the takotsubo syndrome (1) – please note, meperidine was not used for our patient

Prior to presentation, the patient had three endoscopies, where she was found to be stable post-procedure without any issues. Upper and/or lower endoscopies took place on 03/11/2013, 05/29/2014, and 12/03/2015 for epigastric abdominal pain, periumbilical abdominal pain, and chronic diarrhea, respectively. Pre-procedural medications included the Prepopik prescription medicine, which is a combination of sodium picosulfate (a stimulant laxative) and magnesium citrate (an osmotic laxative), used to prepare for a colonoscopy. The anesthetic agents she received during the procedure included: 50 mcg of fentanyl; 1 mg of midazolam; and 280 mg of propofol.
- Please provide reference ranges for all the laboratory parameters. All normal ranges have been added throughout the report.

- Provide images of the 2D ECHO. This has been added as figure 2.

3. Discussion and Conclusions:

This sentence has been removed, as there is very limited literature out there on high risk patients undergoing endoscopy and cardiovascular events in the setting of cardiomyopathy. We describe the cases in the report, but there are not much data out there besides what we reported.

- Table 1. Needs to provide references. References are listed as subheadings and also within the column of the table.

- Please discuss any available literature on how to evaluate and prevent the Takotsubo before the endoscopies. Any evidence on post-procedure care or monitoring in patients.

There is very limited literature on preventing takotsubo in patients before an endoscopy due to the rarity of the two presenting together.

- If possible, please provide the diagnostic criteria for the takotsubo syndrome:

It can be diagnosed in several ways, including one or more of these criteria: “transient left ventricular dysfunction presenting as apical ballooning or with focal wall motion abnormalities; an emotional, physical, or combined trigger; triggers of neurologic disorders; new ECG abnormalities; elevated cardiac biomarker (troponin and creatine kinase) levels; no evidence of infectious myocarditis; and/or postmenopausal women.”8
- Authors wrote' Myocardial infarction has a similar clinical presentation to that of Takotsubo cardiomyopathy; however, they have significant differences in treatment, prognosis, and complications'. Needs a reference. References have been added.

The case report should include social, environmental, family and employment history.

Did the patient smoke, and/or consume alcohol?

She was married with two children She was retired, previously worked for an advertising agency, and resided in Manhattan. She smoked one pack of cigarettes per day for 30 years and quit in 2001. She drank two alcoholic drinks per night.

Give detailed neurological examination on admission. What was the pulse, blood pressure and temperature, on admission?

Physical exam was non-significant. Vitals at the time were: afebrile (36.8⁰C); heart rate of 101, blood pressure of 116/59, respiratory rate of 16, and oxygen saturation of 93% on room air.

Give the doses of all medications that were given:

Medications given during hospitalization included: oxybutynin 10 mg oral tablet extended release once a day for urinary symptoms; omeprazole 40 mg oral tablet once a day for GERD; amlodipine 10 mg oral tablet once a day for HTN; bupropion 300 mg oral tablet extended release once a day for depression; escitalopram 20 mg oral tablet once a day for depression; topiramate 100 mg oral tablet once a day for neuropathy; tramadol 50 mg oral tablet as needed every four hours for pain; and fenofibric acid 135 mg oral tablet delayed release once a day for HLD.

Give all results of laboratory findings (i.e. electrolytes, calcium, mag, CBC, liver and renal functions), urinalysis, serology etc).

Other laboratory findings, including electrolytes, liver function, renal function, complete blood counts, serology and urinalysis were all within normal limits.
Give information about follow-up for at least 6 months.

Nine months post-discharge, she was admitted for worsening lower extremity edema. A transthoracic echocardiogram (TTE) at the time was significant for a high left ventricular outflow tract (LVOT) gradient (peak LVOT gradient of 42 mmHg at rest and 122 mm Hg with Valsalva). Ejection fraction (EF) (normal range: 55-70%) at the time was 81% and pertinent results from TTE included: fibrocalcific changes of the aortic valve with mildly reduced opening; moderate mitral annular calcification; systolic anterior motion of the anterior mitral valve leaflet; and normal functioning left atrium, right ventricle, tricuspid valve, and pulmonic valve. She was discharged with instructions on avoiding diuresis and beginning initiation of metoprolol (6.25 mg every 6 hours) for negative inotropy and to decrease systolic anterior motion.