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Reply to Letter to the Editor: "Pheochromocytoma and Takotsubo Syndrome: An Ominous Duo"

LETTER TO THE EDITOR REPLY

To the Editor,

We thank the authors for their great interest in this topic and thoughtful comments on our case report.[1] We appreciate the authors' important observations on the implications of the pheochromocytoma–Takotsubo syndrome (TTS) coexistence and we would like to respond to their concerns.

Firstly, we agree with the authors that in this case, the diagnosis of atypical TTS was difficult because of the non-specific electrocardiographic findings and the lack of a classical echocardiographic apical ballooning pattern.

In our patient, no emotional or physical triggers had been detected and pheochromocytoma–TTS coexistence was considered only when echocardiography was incidentally extended to the abdominal upper quadrants and showed a suspected right suprarenal mass.

The prevalence of TTS in patients with pheochromocytoma may be up to 3%[2]; in all cases described in the review of Gagnon et al[2], the diagnosis of pheochromocytoma in the clinical setting of Takotsubo-like catecholamine cardiomyopathy was performed following the incidental finding of radiologic mass. Anyway, the real prevalence of pheochromocytoma in TTS remains to be determined.

Interestingly, Eisenhofer et al[3] have demonstrated that patients with hereditary pheochromocytoma are younger at the moment of the diagnosis than sporadic cases. Furthermore, the reported mean age of the population in pheochromocytoma-induced TTS is about 46 ± 15.6 years, which is almost 20 years younger than the emotionally induced TTS population.[4] However, the suspect of pheochromocytoma should not be based only on age criteria.

In our case, the coronary angiography did not report coronary slow flow, as well as malignant arrhythmias were not documented during hospitalization.

Secondly, as mentioned by the authors, in atypical TTS cases, subclinical myocardial dysfunction may persist and cause exercise intolerance.[5] In our patient, no symptoms were referred at post-discharge, and unfortunately left ventricular (LV) global longitudinal strain at follow-up was not available.

Thirdly, we have already published a case[6] in which TTS-like LV dysfunction led us to suspect a pheochromocytoma precipitating adrenergic myocarditis.

It is known that catecholaminergic crisis may be complicated not only by transient and reversible LV dysfunction but also by progressive patchy necrosis and irreversible fibrosis related to a cardiac chronic catecholamine exposure which was reported to persist even after tumor resection.[7-9]

Interestingly, we observed a markedly elevated troponin value with a peak of 9739 ng/dL (normal value of hs-troponin T < 20 ng/dL), differently from emotionally induced TTS in which typically the increase of serum troponin is disproportionately low compared with the wide extent of regional wall motion abnormalities.[10]

Maria Vincenza Polito[1]
Elena De Angelis[2]
Amelia Ravera[1]

[1]*Department of Cardiology, A.O.U. "San Giovanni di Dio e Ruggi D'Aragona", Salerno, Italy*
[2]*Department of Cardiology and Intensive Care Unit, San Luca Hospital, Vallo della Lucania, Salerno, Italy*

Corresponding author:
Maria Vincenza Polito
✉ mvpolito@hotmail.it

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Furthermore, we prescribed to the patient a cardiac magnetic resonance after discharge for more detailed tissue characterization, but it was not performed.

Fourth, we underline that dobutamine was started in order to improve cardiac output and tissue perfusion in the context of cardiogenic shock (CS), and only when pheochromocytoma was hypothesized, it was titrated off.

Templin et al[11] have reported that in TTS patients treated with catecholamines, the mortality was 20% and that inotropic support should be considered at the lowest possible dose and for the shortest time.

Only recently, levosimendan has been proposed as a valid alternative agent in this setting, but its use may be controversial in the case of severe hemodynamic collapse.

To date, no robust data regarding the treatment of TTS patients with CS are available, and standard treatment of adrenergic shock is not well established.

Finally, the authors asked if LV outflow tract obstruction (LVOTO) was present and if the transition of wall motion abnormalities (from basal to apical pattern) was detected.

Left ventricular outflow tract obstruction is a mechanical complication, often dynamic, with a prevalence in large series of TTS patients up to 25%, potentially involved in hemodynamic instability in TTS patients with CS.[12] Despite the absence of specific recommendations, mechanic cardiac support devices have been proposed in cases of dynamic LVOTO as a bridge to recovery.[13] Furthermore, a wandering pattern of LV dysfunction has been observed in some cases of TTS patients,[14] and this may suggest the opportunity for repeated echocardiographic examinations.[15]

In our patient, both at admission and at serial transthoracic echocardiography evaluations, neither significant LVOT gradient nor alternating TTS pattern was documented.

REFERENCES

1. Vincenza Polito M, De Angelis E, Hagendorff A, Puzziello A, Vigorito F, Ravera A. Adrenergic shock presenting with atypical takotsubo syndrome: the alliance between levosimendan and intraaortic balloon pump against the pheochromocytoma. *Anatol J Cardiol*. 2022;26(4):325-327. [CrossRef]
2. Gagnon N, Mansour S, Bitton Y, Bourdeau I. Takotsubo-like cardiomyopathy in a large cohort of patients with pheochromocytoma and paraganglioma. *Endocr Pract*. 2017;23(10):1178-1192. [CrossRef]
3. Eisenhofer G, Timmers HJ, Lenders JW, et al. Age at diagnosis of pheochromocytoma differs according to catecholamine phenotype and tumor location. *J Clin Endocrinol Metab*. 2011;96(2):375-384. [CrossRef]
4. Y-Hassan S. Clinical features and outcome of pheochromo cytoma-induced takotsubo syndrome: analysis of 80 published cases. *Am J Cardiol*. 2016;117(11):1836-1844. [CrossRef]
5. Yalta K, Ozturk C, Yalta T, Yetkin E. Basal takotsubo syndrome: A multifaceted entity with potential implications. *Rev Port Cardiol (Engl Ed)*. 2021;40(8):625-626. [CrossRef]
6. Polito MV, Ravera A, Silverio A, et al. A peculiar etiology of acute heart failure: adrenergic myocarditis. *Am J Emerg Med*. 2015;33(10):1545:e3-e6. [CrossRef]
7. Park JH, Kim KS, Sul JY, et al. Prevalence and patterns of left ventricular dysfunction in patients with pheochromocytoma. *J Cardiovasc Ultrasound*. 2011;19(2):76-82. [CrossRef]
8. Karch SB, Billingham ME. Myocardial contraction bands revisited. *Hum Pathol*. 1986;17(1):9-13. [CrossRef]
9. De Miguel V, Arias A, Paissan A, et al. Catecholamine-induced myocarditis in pheochromocytoma. *Circulation*. 2014;129(12): 1348-1349. [CrossRef]
10. Khan H, Gamble D, Mezincescu A, Abbas H, Rudd A, Dawson D. A systematic review of biomarkers in takotsubo syndrome: A focus on better understanding the pathophysiology. *Int J Cardiol Heart Vasc*. 2021;34:100795. [CrossRef]
11. Templin C, Ghadri JR, Diekmann J, et al. Clinical features and outcomes of takotsubo (stress) cardiomyopathy. *N Engl J Med*. 2015;373(10):929-938. [CrossRef]
12. De Backer O, Debonnaire P, Gevaert S, Missault L, Gheeraert P, Muyldermans L. Prevalence, associated factors and management implications of left ventricular outflow tract obstruction in takotsubo cardiomyopathy: A two-year, two-center experience. *BMC Cardiovasc Disord*. 2014;14(1):147. [CrossRef]
13. Battimelli A, Polito MV, Di Maio M, et al. Stress-related cardiomyopathy, ventricular dysfunction, artery thrombosis: a hidden pheochromocytoma. *Am J Emerg Med*. 2014;32(3):286.e5-286. e9. [CrossRef]
14. Casavecchia G, Zicchino S, Gravina M, et al. Fast 'wandering' takotsubo syndrome: atypical mixed evolution from apical to mid-ventricular ballooning. *Future Cardiol*. 2017;13(6):529-532. [CrossRef]
15. Di Maio M, Polito MV, Citro R, Piscione F. Stress-induced cardiomyopathy in pheochromocytoma: the way we treat and the way we think. *Am J Emerg Med*. 2014;32(8):940-941. [CrossRef]