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Research paper

Paradoxical coronary vasospasm and transient apical ballooning in a post-menopausal woman: An imaging case report of an unusual INOCA presentation

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ABSTRACT

Ischemia with non-obstructive coronary artery disease (INOCA), a common cause of angina, can occur due to coronary vasospasm, microvascular dysfunction, endothelial dysfunction, atherosclerosis or a combination of these mechanisms. We describe a case of adenosine-associated paradoxical coronary vasospasm and Takotsubo-like apical ballooning in a postmenopausal woman with underlying mild coronary atherosclerosis and microvascular dysfunction.

1. Introduction

Adenosine, a coronary vasodilator, is generally used to treat supraventricular tachycardia, and also used as a pharmacological agent in stress myocardial perfusion imaging studies. Adenosine is occasionally associated with paradoxical coronary vasospasm [1–5]. We describe a case of transient left ventricular apical ballooning mimicking Takotsubo-like syndrome in a postmenopausal woman after adenosine withdrawal during stress perfusion cardiac magnetic resonance imaging (CMR).

2. Case description

A 64-year-old obese, Caucasian woman with hypertension and paroxysmal atrial fibrillation presented with recurrent episodes of severe debilitating chest pain for six months. The episodes were cramping in nature without clear triggers and were relieved with rest and deep breathing. She had significant fatigue, dizziness and near syncope during the episodes. Her medications included apixaban, olmesartan and atenolol. The patient had recently discontinued hormone replacement therapy. She also reported ongoing emotional stress.

Echocardiography and nuclear stress testing were unremarkable. A coronary computed tomography (CT) angiogram revealed non-obstructive disease in the right coronary artery and a wrap-around left anterior descending artery (LAD) with mild diffuse narrowing in the mid to distal LAD (Fig. 1). Adenosine stress perfusion CMR was performed as part of a research protocol. Six minutes post adenosine infusion, the patient developed severe chest pain similar to her presenting symptoms. Cine imaging during this episode revealed marked left ventricular dysfunction with extensive thinning and dyskinesis of the mid to distal anterior wall and apex (Fig. 2, Video 2). ST segment elevation was noted on telemetry. Quantitative myocardial perfusion assessment on the stress CMR images demonstrated severely reduced stress myocardial blood flow (1.2 ml/g/min; normal >2.3 ml/g/min).

The symptoms and wall motion abnormalities were reversed with sublingual nitroglycerin. Based on her clinical picture, she was diagnosed with vasospastic (Prinzmetal's) angina. The patient had complete relief of her chest pain symptoms with high dose diltiazem during two years of outpatient follow up.

3. Discussion

Ischemia with non-obstructive coronary artery disease (INOCA) is an under recognized cause of chest pain in women [6] and can result in

Abbreviations: MRI, Magnetic resonance imaging; LAD, Left anterior descending artery; INOCA, Ischemia with non-obstructive coronary artery disease.

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significant morbidity and mortality [7,8]. INOCA predominantly affects women more than men. Women often develop ischemia in response to mental, emotional, and psychological triggers relative to men who generally have physical triggers [9]. Women, when compared to men, have a different activation of their limbic system and hypothalamic-adrenocortical axis that can explain their increased cardiovascular susceptibility to emotional stress [9]. Stress activates the sympathetic nervous system and induces a catecholamine surge that can result in coronary spasm and direct myocardial injury [10]. Our patient did not report anxiety or claustrophobia during the stress test.

Our patient had minimal coronary artery disease, however she developed extensive wall motion abnormalities and apical ballooning during stress testing. Apical ballooning with coronary macrovascular spasm has been reported on occasion [11]. The perfect match between the segmental dysfunction in the anterior wall and apex and the wrap-around LAD along with the transient ST elevation suggests that macrovascular spasm in the LAD was the likely culprit. According to the INTERTAK consensus document, classic apical ballooning phenotype is rare but possible if the wall motion abnormality is in the territory of a single epicardial coronary artery such as the wrap-around LAD in our case [12]. Our patient's symptoms were consistent with coronary spasm and were immediately relieved with sublingual nitroglycerin. Although our patient did not undergo invasive angiography and provocative testing to confirm epicardial coronary artery spasm, the quick recovery with nitroglycerin is consistent with vasospastic angina.

The exact mechanism of adenosine associated vasospasm is not fully understood. Coronary spasm from adenosine is rare but has been reported previously during stress testing and during treatment of supraventricular tachycardia [1–5]. Adenosine binds to A2A receptors on vascular smooth muscle that results in coronary vasodilation with a negative chronotropic effect [2]. One possible mechanism of paradoxical coronary vasospasm is the abrupt withdrawal of the short acting vasodilator effect of adenosine [13]. Patients with Prinzmetal's angina may have increased susceptibility to vasospasm with the withdrawal of adenosine [3]. Additionally, adenosine stimulates baroreceptors by the vasodilator and hypotensive effect, which leads to sympathetic activation and increased plasma catecholamine concentration and this can further contribute to coronary spasm [4].

Patients with vasospastic angina have abnormal vasoreactivity and potentially have increased susceptibility to vasospasm with adenosine withdrawal [3]. Concomitant atherosclerosis, as seen in this patient, is not uncommon in vasospasm. Other contributing factors are her postmenopausal status and recent cessation of hormone replacement therapy. The decreased estrogen level in postmenopausal women has been known to contribute to endothelial dysfunction and abnormal coronary vasoreactivity [14].

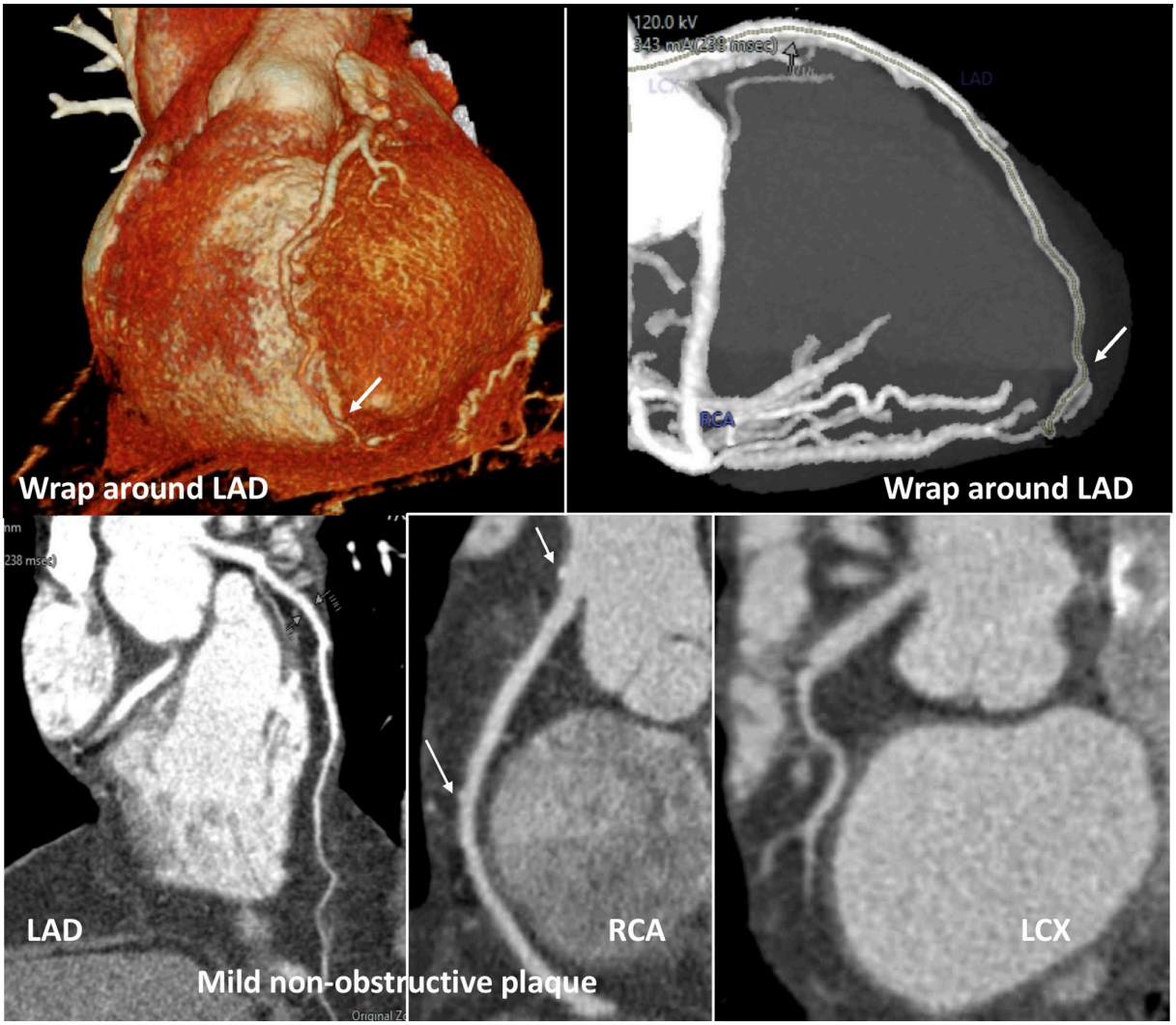

Fig. 1. Minimal non obstructive coronary artery disease on Coronary CT Angiography, Multiplanar reformatted views of the right coronary artery (RCA), left anterior descending (LAD) and left circumflex (LCX). The coronary angiogram reveals minimal non-obstructive disease in the RCA and a wrap-around LAD with mild diffuse narrowing in the mid to distal LAD.

Coronary vasospasm (micro or macro) is an important mechanism causing INOCA. Positron emission tomography is the most validated modality to evaluate microvascular dysfunction with robust prognostic data. Quantitative myocardial perfusion by CMR has an emerging role in the diagnosis of microvascular disease. In the absence of regional perfusion abnormalities, a globally reduced stress myocardial blood flow can be due to obstructive three vessel coronary artery disease or microvascular disease or both [15]. In our patient, coronary CT angiography did not demonstrate obstructive three vessel disease. The global stress myocardial blood flow however was significantly reduced (1.2 ml/g/min), suggesting underlying microvascular dysfunction. The extensive wall motion abnormalities after adenosine withdrawal are consistent with epicardial vasospasm superimposed on microvascular dysfunction.

Coronary vasospasm and Takotsubo-like apical ballooning from adenosine withdrawal has not been previously reported. It is possible that adenosine withdrawal potentially unmasked the coronary vasospasm in our patient. Further studies are needed to understand the interplay between emotional stress, hormonal status, coronary plaque burden, epicardial and microvascular coronary flow and physiology in the evaluation of INOCA.

In conclusion, we report an unusual case of INOCA, where coronary vasospasm during adenosine stress CMR resulted in severe left ventricular dysfunction and Takotsubo-like apical ballooning in a postmenopausal woman after recent cessation of hormone replacement therapy. Additionally, the patient also had mild coronary atherosclerosis and microvascular dysfunction. Microvascular dysfunction was diagnosed based on quantitation of stress myocardial blood flow on CMR. This case illustrates the multifactorial etiology of INOCA that included non-obstructive atherosclerosis, coronary vasospasm and microvascular dysfunction. Quantitative stress perfusion CMR has an emerging role in elucidating the mechanisms of INOCA.

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Disclosures

Drs. Kadiyala, Patibandla, and Michos have no relevant relationships with industry to disclose. Unrelated to this topic area, Dr. Michos reports advisory boards for Astra Zeneca, Amarin, Bayer, Boehringer Ingelheim, Esperion, Novarits, and Novo Nordisk.

CRediT authorship contribution statement

Madhavi Kadiyala: Conceptualization, Supervision, Roles/Writing - original draft, Writing - review & editing.

Saikrishna Patibandla: Roles/Writing - original draft, Writing - review & editing.

Nathaniel Reichek (posthumous): Writing - review & editing.

Erin Michos: Writing - review & editing.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Madhavi Kadiyala reports financial support was provided by American Heart Association. Madhavi Kadiyala reports a relationship with National Institutes of Health that includes: funding grants. This case is part

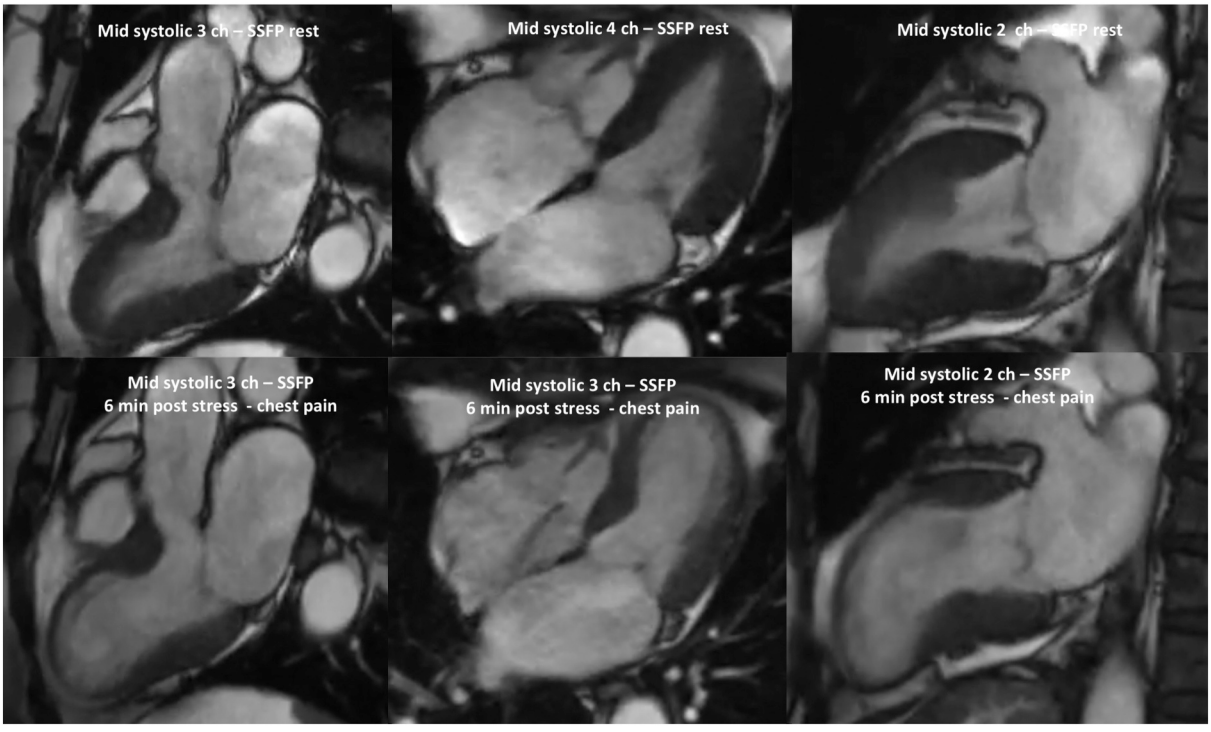

Fig. 2. Apical ballooning 6 min post Adenosine stress CMR. Top panel: Long axis SSFP images of the left ventricle at rest demonstrate normal thickness of the left ventricle with normal systolic contraction at rest (mid systolic frame). Bottom panel: Long axis SSFP images obtained during an episode of chest pain 6 min post Adenosine stress demonstrate marked thinning and dyskinesis of the mid to apical anterior and antero-septal segments with apical ballooning. The marked apical ballooning was reversed after sublingual nitroglycerine as seen in the accompanying video (Video 2).

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References

[1] H.C. Quevedo, J. Munoz-Mendoza, V. Pinto Miranda, R.F. Sequeira, Coronary vasospasm while treating supraventricular tachycardia: is adenosine really to blame? Case Rep. Cardiol. 2013 (2013) 1–5, https://doi.org/10.1155/2013/897813.

[2] J. Golzar, S.J. Mustafa, A. Movahed, Chest pain and ST-segment elevation 3 minutes after completion of adenosine pharmacologic stress testing, J. Nucl. Cardiol. 11 (6) (2004) 744–746, https://doi.org/10.1016/j.nuclcard.2004.08.003.

[3] P. Arora, V. Bhatia, M. Arora, U. Kaul, Adenosine induced coronary spasm-a rare presentation, Indian Heart J. 66 (1) (2014) 87–90, https://doi.org/10.1016/j.ihj.2013.12.043.

[4] M. Ismail, N. Asaad, J. Al-Suwaidi, Adenosine-induced coronary artery spasm: a case report, Med. Princ. Pract. 21 (1) (2012) 82–85, https://doi.org/10.1159/000331809.

[5] G. Weissman, R.M. Scandrett, C.J. Howes, R.R. Russell, Coronary vasospasm during an adenosine stress test, J. Nucl. Cardiol. 11 (6) (2004) 747–750, https://doi.org/10.1016/j.nuclcard.2004.09.004.

[6] B. Sharaf, T. Wood, L. Shaw, et al., Adverse outcomes among women presenting with signs and symptoms of ischemia and no obstructive coronary artery disease: findings from the National Heart, Lung, and Blood Institute-sponsored Women's ischemia syndrome evaluation (WISE) angiographic core lab, Am. Heart J. 166 (1) (2013) 134–141, https://doi.org/10.1016/j.ahj.2013.04.002.

[7] B.-K. Lee, H.-S. Lim, W.F. Fearon, et al., Invasive evaluation of patients with angina in the absence of obstructive coronary artery disease, Circulation 131 (12) (2015) 1054–1060, https://doi.org/10.1161/CIRCULATIONAHA.114.012636.

[8] C. Noel Bairey Merz, C.J. Pepine, M.N. Walsh, J.L. Fleg, Ischemia and no obstructive coronary artery disease (INOCA): developing evidence-based therapies and research agenda for the next decade, Circulation 135 (11) (2017) 1075–1092, https://doi.org/10.1161/CIRCULATIONAHA.116.024534.

[9] A. Haider, S. Bengs, J. Luu, et al., Sex and gender in cardiovascular medicine: presentation and outcomes of acute coronary syndrome, Eur. Heart J. (2019), https://doi.org/10.1093/eurheartj/ehz898. Published online December 26.

[10] F. Pelliccia, J.C. Kaski, F. Crea, P.G. Camici, Pathophysiology of takotsubo syndrome, Circulation 135 (24) (2017) 2426–2441, https://doi.org/10.1161/CIRCULATIONAHA.116.027121.

[11] A. Brennan, H. Adams, J. Galligan, R. Whitbourn, Coronary vasospasm and concurrent takotsubo cardiomyopathy, Br. J. Cardiol. (2019), https://doi.org/10.5837/bjc.2019.011. Published online.

[12] J.-R. Ghadri, I.S. Wittstein, A. Prasad, et al., International expert consensus document on Takotsubo syndrome (Part I): clinical characteristics, diagnostic criteria, and pathophysiology, Eur. Heart J. 39 (22) (2018) 2032–2046, https://doi.org/10.1093/eurheartj/ehy076.

[13] T. Rosenberg, R. Perdrisot, Coronary spasm after adenosine stress test: an adverse effect of a vasodilator, Acta Cardiol. 63 (2008) 401–404.

[14] J.L. Meadows, D.E. Vaughan, Endothelial biology in the post-menopausal obese woman, Maturitas 69 (2) (2011) 120–125, https://doi.org/10.1016/j.maturitas.2011.03.012. Epub 2011 May 6.

[15] T. Kotecha, M. Fontana, Automated pixel-wise quantitative myocardial perfusion mapping by CMR to detect obstructive coronary artery disease and coronary microvascular dysfunction: validation against invasive coronary physiology, JACC Cardiovasc. Imaging 12 (10) (2019 Oct) 1958–1969.