Case Report

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Myocardial bridge: an unrecognized cause of chest pain in pulmonary arterial hypertension

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Abstract

Pulmonary arterial hypertension (PAH) is characterized by an increased pulmonary vascular resistance resulting in progressive right ventricular hypertrophy and failure. While dyspnea on exertion is the leading symptom at diagnosis, the occurrence of chest pain, although less frequently observed, is an alarming symptom that requires immediate diagnostic work-up.

Here we report the case of a 44-year-old woman with severe end-stage group 1 PAH who had repetitive occurrences of chest pain that led to frequent emergency room visits with documented signs of myocardial ischemia on EKG and troponin leaks. A computed tomography (CT) angiogram of the coronary arteries revealed the presence of a myocardial bridge (MB). An invasive coronary angiogram confirmed a MB over the left anterior descending (LAD) artery compressing the lumen of the LAD. As the patient was deteriorating on maximal medical PAH therapy, she was listed for, and subsequently received, a bilateral lung transplantation. Recognizing that the MB would pose a significant risk for ischemia during surgery as well as continuing source for chest pain after lung transplantation, the MB was surgically "unroofed" during the transplant surgery. The patient did well after surgery and did not complain of any residual chest pain.

In conclusion, a MB compressing a segment of the coronary artery could be an under-diagnosed, but potentially not so rare cause of recurrent chest pain in PAH patients, which requires specialized diagnostic evaluation and treatment

Keywords

chest pain, myocardial bridge, pulmonary arterial hypertension

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Case report

A 44-year old woman with severe Group 1 pulmonary arterial hypertension (PAH) due to Hereditary Hemorrhagic Telangiectasia (as defined by nosebleeds, family history of nosebleeds multiple arteriovenous malformations in the gastrointestinal tract, ACVRL1 (ALK1) c.794_799del6 mutation), as well as prior Fenfluramine/ Phentermine exposure, was referred to the pulmonary hypertension service at Stanford University Medical Center.

At presentation, the patient reported New York Heart Association functional class IIIb symptoms, with presyncopal events and chest pain with minimal exertion. A transthoracic echocardiogram demonstrated a severely enlarged right ventricle (RV) and a severely reduced RV function with an RV systolic pressure of 116 mmHg. A right heart catheterization confirmed severe PAH with a pulmonary arterial pressure of 95/41 mmHg (mean = 63 mmHg), a pulmonary capillary wedge pressure of 12 mmHg, a cardiac index of 1.94 L/min/m^2, and a pulmonary vascular resistance

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of 14.5 Wood units. Vasoreactivity testing with inhaled nitric oxide was negative. Despite initiation of triple-PAH therapy (intravenous epoprostenol at 17 ng/kg/min, an endothelin receptor antagonist Ambrisentan at 10 mg, and the phosphodiesterase-5-inhibitor Sildenafil at 20 mg three times daily), her PAH continued to worsen. She was listed for a lung transplantation, given her severe PAH despite maximal medical therapy. Her REVEAL risk score at the time of listing was 13, a score that predicts a one-year survival of <70%. She continued to have chest pain, which varied in intensity, was intermittent, occurred with exertion yet also at rest, and was described as pressure-like and burning, substernal, and radiating to her left jaw and shoulder. The patient presented to the emergency room on multiple occasions, her troponins in the range of 0.2–2.0 ng/mL, the latter in the setting of anemia due to an upper gastrointestinal bleed while her EKG showed right ventricular hypertrophy and ST depressions suggestive of ischemia.

Our differential diagnosis for her chest pain, included severe PAH with RV ischemia, coronary artery disease (CAD), compression of her left main coronary artery from an enlarged pulmonary artery (4.3 cm), a pulmonary embolus, and gastroesophageal reflux disease. A coronary computed tomography angiogram (CCTA) was performed, which demonstrated only mild ostial compression of the left main coronary artery, but also a myocardial bridge (MB) in the mid left anterior descending coronary artery (LAD).

Careful review of the CCTA showed a deep and complete MB of the LAD starting 2.5 cm from the origin of the LAD and spanning 13 mm of the conus muscle of the right ventricle (Fig. 1). Because MBs are quite common in the general population and may simply be an incidental finding, we attempted to determine the hemodynamic significance of the MB by calculating the MB muscle index (MMI) by CCTA. Developed at Stanford University, this is a non-invasive index of hemodynamic compromise of an MB, which is defined by the product of the length and depth of the MB.[1] The MMI of our patient was 39. An MMI of $\geq$31 indicates a 71% sensitivity and a 62% specificity for detecting a hemodynamically significant MB, as determined by an invasive assessment of diastolic fractional flow reserve (dFFR) of < 0.76.[1] An invasive coronary angiogram was then performed, which excluded atherosclerotic CAD and confirmed the CT finding of an MB in the mid LAD. Invasive stress testing with dobutamine to determine the dFFR was not undertaken, albeit the risk of such an evaluation in patients with severe PAH and the development of hypotension and arrhythmias is relatively low. Intracoronary imaging, such as intra-vascular ultrasound (IVUS) or optical coherence tomography (OCT), would also have been an alternative diagnostic tool to document the minimal lumen area and thereby receive some more anatomic information about the MB; while a possible correlation of the anatomic findings with the hemodynamic significance of the MB is controversially discussed in the field. We did not pursue this route, given the potentially additional risk of instrumenting the LAD with an imaging catheter (i.e. intravascular ultrasound or optical coherence tomography). It was our suspicion that, because the MB was imbedded in the conus muscle of the RV in close vicinity to the dilated pulmonary artery, her severe PAH with a severely dilated RV and severely reduced RV function as well as low cardiac output most likely limited coronary flow through the MB leading to progressive myocardial ischemia and chest pain.

Treatment options were subsequently discussed by a multidisciplinary team consisting of colleagues from cardiology, pulmonary, lung transplantation, and thoracic

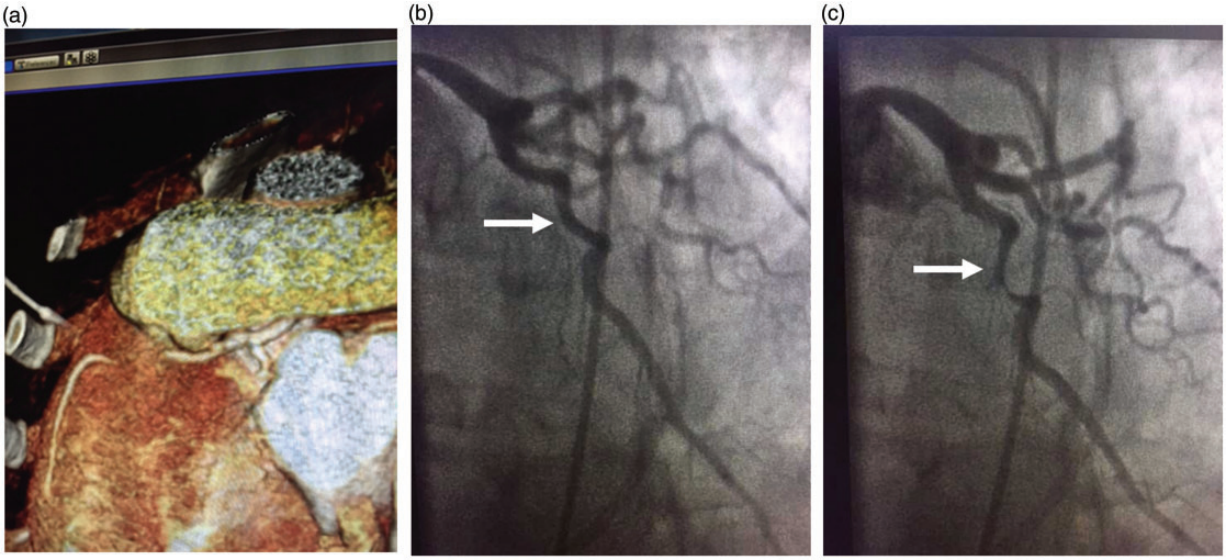

Fig. 1. (a) CT angiogram showing the epicardial left anterior descending coronary artery (LAD) being bridged by the myocardium over a length of 13 mm. (b, c) Angiography (still frame) in end-diastole (b) and systole (c) showing a dynamic narrowing of the mid LAD (arrows).

surgery, with the goal of alleviating the chest pain by reducing the compression of the LAD. First, medical management with calcium channel blockers or beta-blockers was deemed not feasible since the patient was already hypotensive. Second, stenting of the MB was considered too risky since it carried the inherent complication of stent fracture, stent compression, and/or laceration of the LAD through unabated compression by the MB. Third, surgical unroofing was thought to be an option, yet only possible at the time of transplantation as the patient was too sick for an elective unroofing surgery. Finally, coronary artery bypass grafting (CABG) of the MB at the time of transplantation was not recommended due to observations of early closure of bypass grafts, likely due to competitive flow through the bridged segment at rest (unpublished data).

Given that the MB could pose a risk for ischemia during the transplantation surgery, as well as serve as a potential continued source of chest pain after transplantation, it was decided that surgically unroofing the bridged segment of the LAD at the time of lung transplantation was the best option. The patient subsequently underwent a successful bilateral lung transplantation with MB unroofing of the LAD, along with tricuspid valve ring annuloplasty. Immediately post-transplantation, the patient reported feeling better, denying any chest pain, shortness of breath, or palpitations, an effect that has been sustained three years after transplantation. Follow-up EKGs did not show any residual ST depressions and her troponins normalized, although this of course could be due to the resolution of the right ventricular after transplantation and not necessarily due to the surgical treatment of the MB.

While the strategy of unroofing the MB at the time of transplant was appropriate and reasonable, a degree of uncertainty remains of course whether the improvement in chest pain was due to the unroofing or the correction of the severe PAH.

Discussion

The differential diagnosis of chest pain in a PAH patient includes RV ischemia due to progressive PAH, CAD and myocardial infarction, pulmonary embolism, and compression of the left main coronary artery by an enlarged pulmonary artery, as well as musculoskeletal pain and gastroesophageal reflux disease.[2] Though not uncommon, a MB is not routinely considered in the differential diagnosis of chest pain, especially in patients with severe PAH.

A MB is a congenital variant that is defined as an intramyocardial segment of an epicardial coronary artery.[3] MBs have been documented in about 26% of autopsy cases, 88% of which involve the LAD,[4] and in 0.5–16% of invasive angiographic series.[5,6] Most MBs are asymptomatic, but a small portion of patients develop chest pain, as well as exertional dyspnea, secondary to dynamic ischemia in the myocardial territory of septal branches embedded within the bridged segment.[3]

The diagnostic evaluation and treatment of patients with a symptomatic MB includes a variety of non-invasive and invasive modalities with the goal to anatomically identify and functionally assess the MB. Most recently, a novel non-invasive diagnostic technique during stress echocardiography has been shown to identify MBs.[7] Specifically, one sees a unique wall motion abnormality of mid-septal buckling during peak stress, which distinguishes itself from a fixed LAD stenosis by not involving the apex.[8] The presence of focal septal buckling with apical sparing on stress echo is an accurate predictor of an MB in patients with angina in the absence of obstructive CAD. This echo pattern can reliably be used to screen patients who may benefit from advanced non-invasive/invasive testing for an MB as a cause of their angina. In a retrospective cohort, focal septal buckling with apical sparing during stress echo identified the presence of an MB by CCTA with a sensitivity and specificity of 93.3% and 70.6%, respectively.[9] In a prospectively recruited patient cohort, focal septal buckling with apical sparing identified an MB by CCTA with a sensitivity and specificity of 90% and 83%, respectively.[9] The accuracy of this echo pattern in identifying an MB is similar to the accuracy with which we can detect obstructive atherosclerotic CAD by identifying a new wall motion abnormality during stress echo testing.[9]

CCTA allows visualization of both the coronary artery lumen and the myocardium, and can provide MMI, which correlates well with invasive dFFR, and therefore offers a non-invasive way of differentiating an incidental from hemodynamically significant MB, albeit we do agree that the specificity and sensitivity for detecting a hemodynamically significant MB is modest.[1] It has become clear from our work and that of others that traditional adenosine fractional flow reserve (FFR) is inadequate in testing the hemodynamic significance of a MB. Myocardial bridging creates a dynamic stenosis brought on by chronotropic and inotropic stimulation. MBs cause significant diastolic pressure gradients, but normal or negative systolic pressure overshooting. This produces artificial elevation in mean pressure used by traditional (mean) FFR, again causing an underestimation of hemodynamic significance. Therefore, diastolic FFR with dobutamine challenge is currently the technique of choice to evaluate for hemodynamically significant myocardial bridging.[1,7]

The medical management of hemodynamically significant MBs consists primarily of beta blockers and calcium channel blockers, which reduce contractility, increase diastolic filling time, and can contribute vasodilatory properties.[10] It is well-known that patients with MBs can develop coronary endothelial dysfunction, which may further contribute to symptoms. Therefore, vasodilators, including nitrates, may be helpful. Statins and aspirin may also be beneficial given that an atherosclerotic plaque is nearly universally identified proximal to the MB and is prone to rupture.[3,8,11]

When medical therapy is insufficient, surgical treatment of the MB in the form of unroofing (myotomy) is the preferred treatment strategy in the absence of concomitant

obstructive CAD in the LAD.[12] Surgical unroofing of a LAD MB is thought to be superior to CABG or stenting of the coronary artery because of the risk of graft failure due to competitive flow through the MB or stent fracture from unabated compression, respectively.[10,13,14]

Conclusion

A MB compressing a segment of the coronary artery could be an under-diagnosed, but potentially not so rare, cause of recurrent chest pain in PAH patients, which requires specialized diagnostic evaluation and treatment. Surgical unroofing of the LAD MB was an appropriate treatment in our patient with recurrent chest pain and PAH.

Conflict of interest

The authors declare that there is no conflict of interest.

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