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GRAND ROUND
Cardiac imaging

Case report: paradoxically reversible perfusion defects on vasodilator stress imaging in a case of metastatic coronary compression

Sara G. Kwiatkowski [1]*, Vikrant S. Aulakh[1], Kunal Kapoor[2], Xin Wei[2], John D. Grizzard[3], W. Gregory Hundley[2], Sarah W. Gordon[4], and Cory R. Trankle[2]

[1]Department of Internal Medicine, Virginia Commonwealth University, Richmond, VA, USA; [2]Division of Cardiology, Pauley Heart Center, Virginia Commonwealth University, Richmond, VA, USA; [3]Department of Radiology, Virginia Commonwealth University, Richmond, VA, USA; and [4]Division of Hematology/Oncology/Palliative Care, Massey Cancer Center, Virginia Commonwealth University, Richmond, VA, USA

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Background Patients with malignancy who experience metastasis to cardiac structures may exhibit ST-segment elevations and acute coronary syndrome (ACS) through poorly understood pathophysiologic mechanisms. We present a case in which vasodilator stress cardiovascular magnetic resonance provides unique insight into one such patient who suffered from recurrent episodes resembling ACS.

Case summary A 58-year-old male with metastatic lung adenocarcinoma presented with refractory angina and dynamic inferior electrocardiogram changes. The patient was referred for adenosine stress cardiovascular magnetic resonance, revealing multiple territories of abnormal perfusion during rest with improvement during adenosine infusion. Subsequent computed tomography displayed tumour encasement of the right coronary artery. Taken together, vasodilator-responsive extrinsic compression of multiple epicardial coronary arteries was suspected. Outpatient oncology follow-up for chemoimmunotherapy initiation was arranged with the hope that reducing tumour burden might alleviate coronary compression. However, in the ensuing months, the patient's disease advanced beyond the point of which his symptoms could be controlled medically, and he was ultimately enrolled in hospice care.

Discussion Encasement of coronary arteries can result in anginal symptoms if their position impairs coronary arterial flow. The presented case highlights the unique manner in which these lesions might behave on stress cardiac magnetic resonance imaging. Clinicians who encounter such unusual findings on vasodilator stress imaging should consider metastatic lesions to the cardiac structures on the differential diagnosis.

Keywords Case report • Cardiac malignancy • Acute coronary syndrome • Cardiac imaging

ESC Curriculum 2.1 Imaging modalities • 2.3 Cardiac magnetic resonance • 3.1 Coronary artery disease • 3.2 Acute coronary syndrome • 6.8 Cardiac tumours

Learning points

- A patient with known malignancy presenting with new cardiovascular symptoms should alert the clinician to the possibility of cardiac metastases.
- Vasodilator stress cardiovascular magnetic resonance evaluation of patients with extrinsic coronary vessel occlusion may reveal a unique pattern of perfusion defects that appear at rest and resolve during stress.

* Corresponding author. Tel: +1 804 968 8563, Email: sara.kwiatkowski@vcuhealth.org
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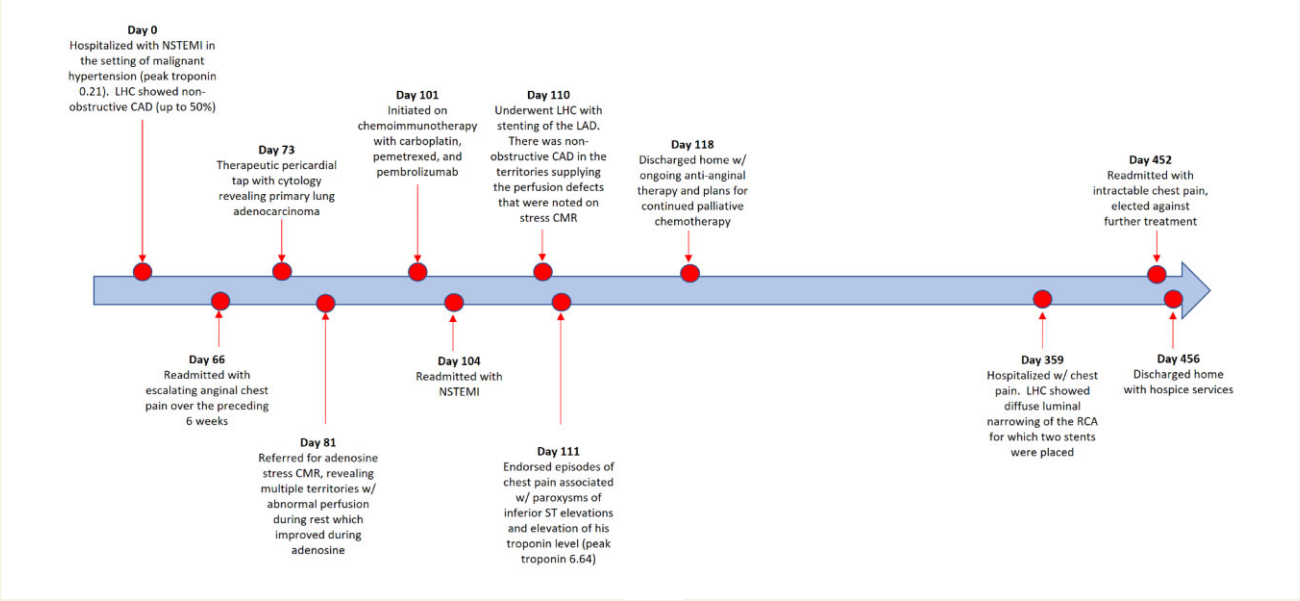
Primary specialities involved other than cardiology

Internal medicine, haematology/oncology, radiology.

Introduction

Malignant cardiac tumours seldom arise from the heart itself and typically represent metastases from other sites.[1] Although these tumours are often clinically silent, symptoms can manifest depending on which structures are involved.[1] For instance, patients with malignancy who experience metastasis to cardiac structures may exhibit ST-segment elevations and acute coronary syndrome (ACS) through poorly understood pathophysiologic mechanisms.[2–5] Herein, we discuss the case of a patient with lung adenocarcinoma who presented with refractory angina and dynamic electrocardiogram (ECG) changes and was found to have metastatic spread to the myocardium and pericardium with tumour encasement of the right coronary artery (RCA). The presented case highlights the unique manner in which such lesions might behave on stress cardiac magnetic resonance imaging.

Timeline



History of presentation

A 58-year-old male with hypertension, hyperlipidaemia, and tobacco dependence presented with recurrent typical angina. He had been hospitalized with malignant hypertension and a non-ST elevation acute myocardial infarction (peak troponin 0.31 ng/mL, reference range ≤0.19) 2 months prior and had undergone coronary angiography, which revealed diffuse non-obstructive lesions (see Supplementary material, Video S1). Presuming his symptoms were related to his hypertensive crisis on a background of small vessel coronary disease, he was medically optimized and discharged home. However, he had escalating symptoms over the following 6 weeks typical for angina aetiology, with abrupt worsening for which he was referred to the emergency department.

On presentation, his temperature was 36.5°C; heart rate, 77 beats/min; blood pressure, 102/74 mmHg; respiratory rate, 12 breaths/min; and pulse oximetry, 100% on room air. His cardiac, pulmonary, and abdominal examinations were without clear abnormal findings. Inspection of his electrocardiogram revealed new inferior T-wave inversions, and serial troponin levels were undetectable. A thoracic computed tomography (CT) study revealed a moderate circumferential, pericardial effusion, and a nodular appearance of the right ventricular free wall with encasement of the RCA in the soft tissue (*Figure 1* and Supplementary material, Video S1). It was also notable for mediastinal adenopathy, diffuse bronchial wall thickening, and pulmonary nodules. This constellation of findings raised concern for an underlying malignancy with metastatic spread to the myocardium and pericardium, as well as tumour encasement of the RCA.

Investigations

Pericardiocentesis was performed with cytology revealing malignant cells of lung origin, with transbronchial needle aspiration of the mediastinal lymph nodes subsequently confirming the diagnosis of metastatic lung adenocarcinoma. Immunochemistry showed 10% PD-L1 protein expression, whereas all other tumour biomarkers —including EGFR, ALK, ROS, RET, BRAF, NTRK—were negative. His presenting symptoms were ascribed to pericarditis, and he was further treated with anti-inflammatory agents. However, he continued to experience episodic chest pain with anginal characteristics. To confirm that the coronary arterial lesions identified on angiography were indeed non-flow-limiting, he was referred for an adenosine stress cardiovascular magnetic resonance (CMR) scan.

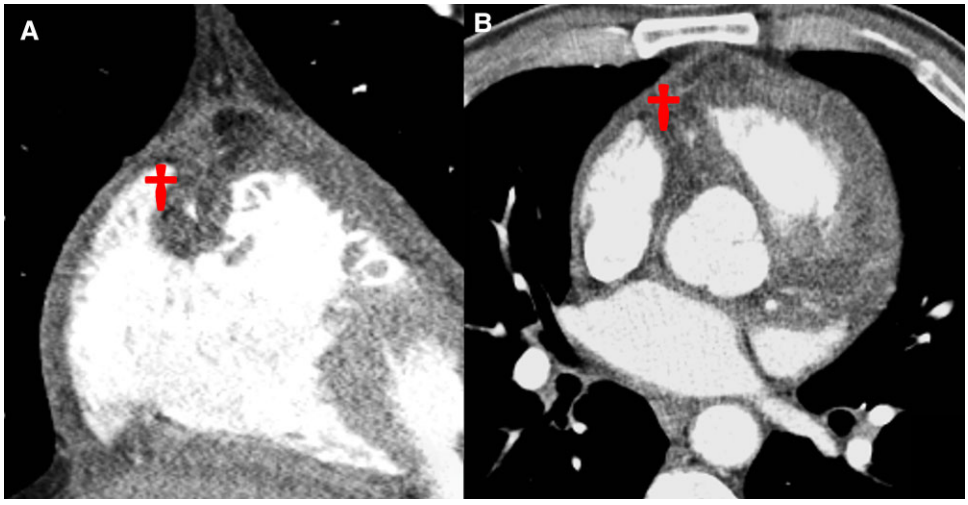


Figure 1 Computed tomography. Coronal (*A*) and axial (*B*) contrast-enhanced CT images demonstrate abnormal soft tissue (due to metastatic disease) encasement and narrowing of the RCA†.

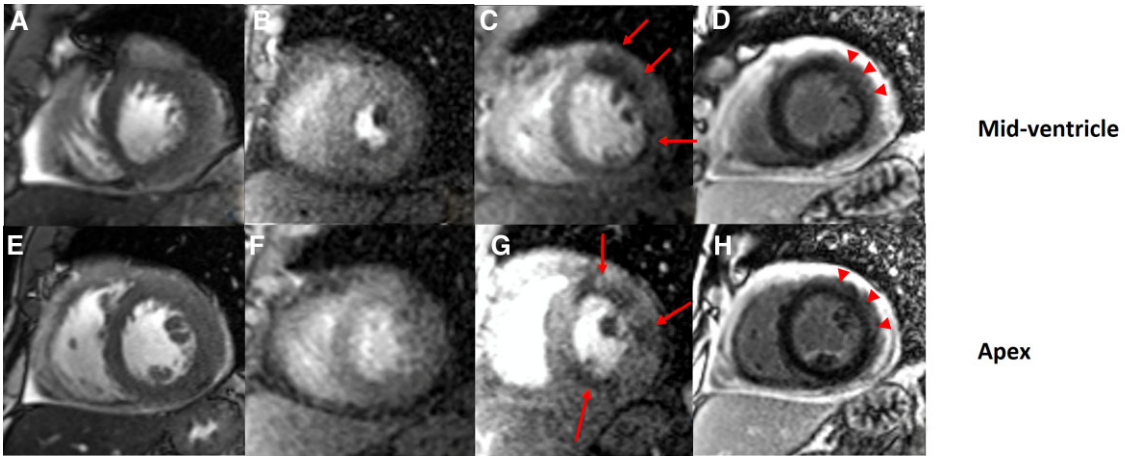


Figure 2 Stress cardiac magnetic resonance. Short-axis cinematic sequences (*A* and *E*) and delayed gadolinium enhancement (*D* and *H*) of the mid-ventricle revealed abnormal heterogeneous thickening of the right ventricular free wall with focal enhancement concerning for tumour infiltration (arrowheads). Vasodilator perfusion (*B* and *F*) did not demonstrate relative perfusion defects, whereas the rest perfusion (*C* and *G*) paradoxically showed multiple territories of abnormal perfusion (arrows).

The vasodilator stress CMR revealed a highly atypical pattern of perfusion defects (*Figure 2* and Supplementary material, Video S1). First-pass perfusion of gadolinium during peak vasodilation (adenosine 140 μg/kg/min for 3 min) revealed a small perfusion defect involving the apical segment of the lateral wall. However, subsequent first-pass perfusion images during rest (following adenosine washout) displayed several areas of severe perfusion defects involving the inferior, inferolateral, anterolateral, and anterior walls. Inspection of the cinematic series and delayed gadolinium enhanced images revealed a nodular appearance of the right ventricular free wall with heterogeneous enhancement (*Figure 2* and Supplementary material, Video S1).

Ordinarily, in the presence of luminal obstruction from coronary thrombosis, flow heterogeneity would be expected to manifest under conditions of stress. The observed pattern of resting ischaemia resolved by administration of a coronary dilator suggests the patient's symptoms were instead caused by *extraluminal* compression of coronary vessels—either the macrovasculature (in the case of the encased RCA) or the microvasculature from direct tumour invasion of the myocardium. Regardless of the mechanism, we suspect that the mechanical compression imposed by the tumour was transiently surmounted by the vasodilatory effects of adenosine, thereby restoring myocardial blood flow.

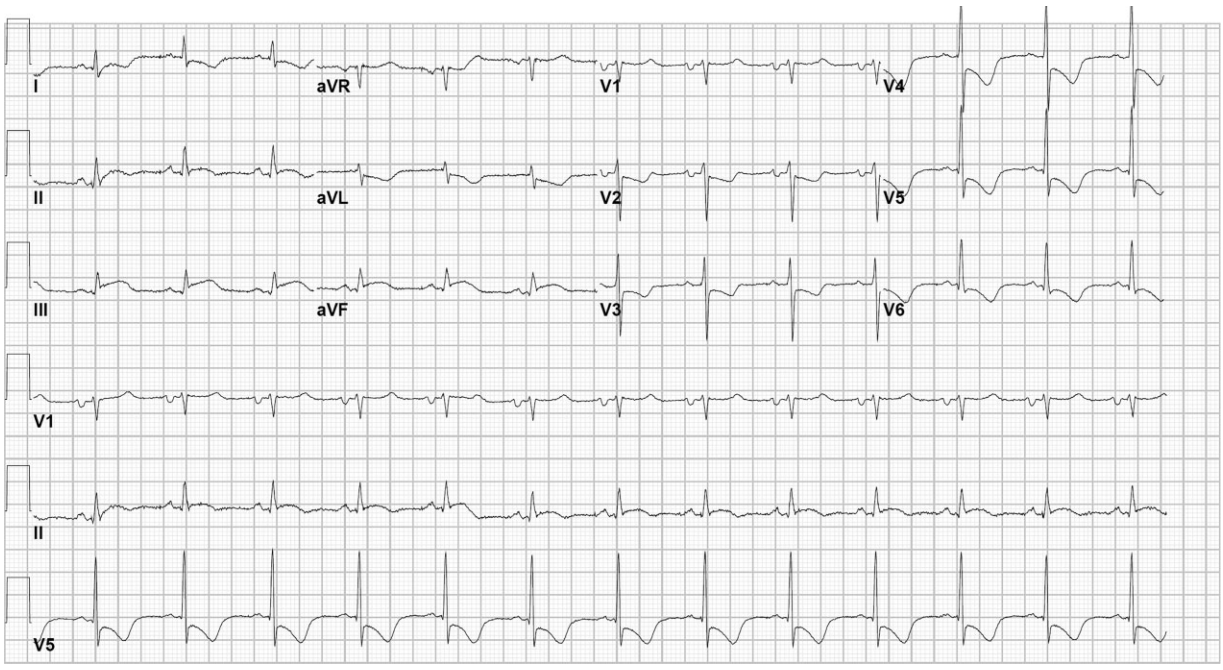


Figure 3 Electrocardiogram obtained during an episode of angina captured paroxysmal inferior ST-segment elevations.

Management

Outpatient oncology follow-up for palliative chemoimmunotherapy initiation was arranged with the hope that reducing tumour burden would alleviate his symptoms. Three days after initiating chemoimmunotherapy (carboplatin, pemetrexed, and pembrolizumab), he was readmitted with non-ST elevation myocardial infarction. Repeat coronary angiography demonstrated progression of a lesion within the distal left anterior descending artery, now 70% in severity, for which a drug-eluting stent was deployed. Notably, he had continued non-obstructive stenoses elsewhere, including in territories supplying the perfusion defects noted on his stress CMR.

In the subsequent 3 days, the patient had stuttering intense chest pain with paroxysms of inferior ST elevations (*Figure 3*). His troponin values rose markedly, to a peak of 6.64 ng/mL. Each episode of chest pain and ST elevations were treated with a nitroglycerin drip with complete resolution. Eventually, the episodes subsided, and the patient was discharged home with ongoing anti-anginal therapy and plans for continued palliative chemoimmunotherapy. The patient tolerated further chemoimmunotherapy treatments over the following 8 months without further cardiac events. Subsequent scans showed a partial response to his systemic therapy, which correlated with a decrease in the patient's anginal symptoms.

Discussion

Malignant cardiac tumours seldom arise within the heart itself and are more commonly metastatic in nature. Regardless of their origin, cardiac malignancies are understood to be exceedingly rare, albeit likely underestimated in incidence due to the fact that they are often clinically silent and first identified post-mortem.[1] When symptoms do manifest, presentation is widely variable depending on the extent of disease and structures involved. If coronary vessels are affected, the clinical presentation may mimic ACS. Indeed, there have been reported cases of ischaemic chest pain and ECG changes incited by cardiac metastases.[2–6]

The pathophysiology of these cardiac findings in patients with metastases to cardiac structures is not well understood, given their rarity. Several mechanisms have been proposed to explain the ECG changes observed in these patients, including tumour-driven cytokine production and inflammation, potassium efflux from necrotic tissue, and peritumour myocardial fibre stretch. The very presence of cardiac metastases can cause ST-segment elevations in the absence of true ACS.

Alternatively, the presence of cardiac metastases can promote ACS due to extrinsic compression of coronary vasculature.[3,4] Malignancy may not initially be considered in the case of bystander coronary artery disease, but a distribution of ST elevations discordant with angiographic findings may alert the clinician to consider an aetiology other than typical atherosclerotic disease. Although not performed in this case, clinicians may consider additional intracoronary diagnostic techniques to aid in elucidating the mechanism of myocardial infarction with non-obstructive coronary arteries.

Others have reported similar cases of cardiac malignancy masquerading as ACS with new ST-segment changes. Salik *et al.* identified a patient with known metastatic squamous cell carcinoma who developed progressive exertional dyspnoea and was found to have anteroseptal ST-segment elevations on ECG without chest pain or elevation in cardiac biomarkers. Although coronary

angiography revealed no clinically significant intraluminal abnormalities, the patient was discovered on imaging to have a new left ventricular mass, suggesting that his electrocardiographic abnormalities were caused by metastatic invasion of the left ventricular myocardium.[5] Chen *et al.*[3] similarly published a case of anteroseptal elevations suspected to be caused by neoplastic infiltration of the right ventricle. Rodrigues *et al*. described a patient who presented in cardiogenic shock with acute-onset typical chest pain and associated lateral ST-segment elevations. On postmortem examination, the patient had complete encasement of the heart by metastatic tumour.[6]

Our case is unprecedented in that it highlights the unique manner in which these lesions might behave on stress CMR. Not only do these findings provide unique insight into the potential pathophysiology behind this phenomenon—creating flow limitations on the macrovascular or microvascular scale that can be overcome with potent vasodilators—but it might have also been a harbinger of things to come for our patient. He poorly tolerated the initial phase of chemotherapy, with paroxysms of inferior ST elevations and repeated episodes of myocardial injury.

Follow-up

After 8 months of chemotherapy, the patient reported a recurrence of exertional chest pain. His ECG was non-ischaemic and unchanged compared with prior studies, and cardiac enzymes were undetectable. He was referred for elective coronary angiography, revealing progression of his RCA luminal narrowing (now 70–80% stenosed) requiring placement of two additional stents (Supplementary material, Video S2). We suspect that advancing malignant compression of the vessel may have been the reason for such rapidly progressive luminal stenosis as opposed to atherosclerosis but are unable to confirm this as intracoronary imaging was not performed. Notably, there was severe spasm of the vessel upon wiring, requiring intracoronary nitroglycerin; this further supports the idea that tumour encasement and its reaction to antineoplastic agents may have provoked the paroxysms of inferior ST elevations observed soon after chemoimmunotherapy initiation. Ultimately, the patient's disease advanced beyond the point of which his symptoms could be controlled with medical management, and he elected to enrol in hospice care.

Conclusions

Cardiac metastases may present with anginal symptoms if their position impairs coronary arterial flow. Our case highlights the highly atypical appearance this may have on adenosine stress CMR and the possibility of rapidly progressing coronary arterial stenoses by angiography. Clinicians should be aware of this unique appearance on vasodilator myocardial perfusion studies and consider metastatic lesions on the differential diagnosis.

Lead author biography

Sara G. Kwiatkowski earned her medical degree from Campbell University School of Osteopathic Medicine in 2020. She is currently an Internal Medicine resident at the Virginia Commonwealth University Health System in Richmond, VA, USA. She plans to pursue a Cardiology fellowship.

Supplementary material

Supplementary material is available at the *European Heart Journal – Case Reports* online.

Slide sets: A fully edited slide set detailing these cases and suitable for local presentation is available online as Supplementary data.

Consent: The authors attest that the patient described in this case signed a standard institutional consent form which included permission to publish their case report. Every effort has been made to anonymize the details of this case. This has been discussed with the editors.

Conflict of interest: None declared.

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References

1. Lichtenberger JP, Reynolds DA, Keung J, Keung E, Carter BW. Metastasis to the heart: a radiologic approach to diagnosis with pathologic correlation. *Am J Roentgenol* 2016;**207**:764–772.
2. Marra MP, Thiene G, De Lazzari M, Calabrese F, Lacognata C, Rizzo S, Cacciavillani L, Tona F, Corbetti F, Iliceto S, Basso C. Concealed metastatic lung carcinoma presenting as acute coronary syndrome with progressive conduction abnormalities. *Circulation* 2012;**125**:e499–e502.
3. Chen T. Persistent ST-segment elevation due to cardiac metastasis. *BMJ Case Rep* 2017;**2017**:bcr2017220621.
4. Salik JR, Parisi EJ, Sakhuja R. ST segment elevation in a patient with myocardial metastases what is up with that? *JAMA Intern Med* 2021;**181**:695–696.
5. Rodrigues ACT, Abreu E, DeMarchi LM, Mathias W, Leal SMB, Andrade JL. Lung neoplasm mimicking an acute lateral myocardial infarction. *J Am Soc Echocardiogr* 2003;**16**:1198–1200.
6. Kasai T, Kishi K, Kawabata M, Narui K, Momomura SI, Yoshimura K. Cardiac metastasis from lung adenocarcinoma causing atrioventricular block and left ventricular outflow tract obstruction. *Chest* 2007;**131**:1569–1572.