Histologically Proven Myocardial Carcinoid Metastases: the Value of Multimodality Imaging

Multimodality imaging in carcinoid heart disease

Annina A Studer Bruengger, MD[1,2], Kshama Wechalekar, DNB[3], Rajdeep Khattar, DM[1,3], Stuart D Rosen MD[1,3], Jan Lukas Robertus, PhD[3,4], Ian Chau, MD[5], Daniel Morganstein, PhD[3,5,6], Ulrich Rosendahl, MD[3,7], Alexander Lyon, PhD[1,3], Raad Mohiaddin, PhD[1,3]

1) NIHR Cardiovascular Biomedical Research Unit, Royal Brompton and Harefield NHS Trust, London, UK

2) Department of Cardiology, City Hospital Triemli, Zurich, Switzerland

3) Imperial College London, National Heart and Lung Institute, London, UK

4) Department of Pathology, Royal Brompton and Harefield NHS Trust, London, UK

5) Department of Medicine, Royal Marsden NHS Foundation Trust, London UK

6) Department of Endocrinology, Chelsea and Westminster NHS Trust, London UK

7) Department of Cardiac Surgery, Royal Brompton and Harefield NHS Trust, London UK

Corresponding author:

Dr Annina A Studer Bruengger

Department of Cardiology

City Hospital Triemli

Birmensdorferstrasse 497

8063 Zurich, Switzerland

Phone: +41 (0) 44 416 33 60

Email address: annina.studer@triemli.zuerich.ch

Total word count manuscript: 903

Subject codes: [19], [20], [30], [31], [32]

Abstract:

We present a case of a patient with intramyocardial metastases of a carcinoid tumor. These findings were detected anatomically using cardiovascular magnetic resonance, with functional metabolic activity confirmed using nuclear imaging in vivo, and confirmed by histology at surgical biopsy. The detection of the metastatic lesions changed management of the patient und shows the importance of multimodality imaging.

Manuscript:

A 59-year-old man with known carcinoid tumor of the ileocecal valve with hepatic metastases was referred to our joint cardio-oncology clinic for investigation of bilateral lower limb edema and breathlessness. He had markedly elevated levels of urinary 5-Hydroxyindoleacetic acid (1365µmol/24h). Echocardiography showed the classical features of carcinoid valvular heart disease with thick, fixed and retracted leaflets of the tricuspid valve and free tricuspid regurgitation (figure 1A and B). Doppler pulmonary valve flow profile showed a dense signal with steep deceleration suggesting severe pulmonary valve regurgitation (figure 1C). No left ventricular abnormality was noted. Cardiovascular Magnetic Resonance (CMR) study requested prior to consideration for surgical double valve replacement confirmed the echocardiographic findings of severe regurgitation of both right-sided valves. The right ventricle was dilated (RVEDVi 119ml/m^2) with normal ejection fraction (66%, figure 1D and E). In addition, focal thickening of the mid antero-septal and anterior wall was noted on SSFP cine imaging (figure 2A). The regions of focal thickening showed increased myocardial signal on the T2 weighted Short Tau inversion recovery (STIR) imaging indicating myocardial oedema or increased vascularity in these regions (figure 2B) with subtle patchy enhancement on late gadolinium-enhanced images corresponding to the enlarged extracellular space. These findings were highly suggestive of intramyocardial carcinoid metastases. SPECT-CT with ^{111}Indium-labelled octreotide (somatostatin receptor agonist) performed for confirmation of intramyocardial metastases showed tracer uptake at the site of the primary tumor at the ileocecal region and liver metastases. Furthermore, there was octreotide uptake in the anterior, anterolateral and anteroseptal walls of the left ventricle (figure 2C) corresponding to the CMR findings and confirming the intramyocardial metastases. The patient underwent surgery due to progressing cardiac symptoms related to severe valvular regurgitation one year after the first manifestation of carcinoid heart syndrome. The tricuspid and pulmonary valves were replaced. Further on, tumor tissue obstructing the right ventricular outflow tract was resected and

the outflow tract wasreconstructed. Intraoperative ventricular biopsy at the site of tracer uptake (figure 2D) confirmed intramyocardial carcinoid metastases (figure 2E and F). Despite the extent of the operation the patient had an uneventful recovery after the operation and had made excellent progress at follow-up 12 months post surgery.

Carcinoid tumors are rare neuroendocrine malignancies (incidence of 1.2 to 2.1 in 100000 of the general population). The primary tumour is most often found in the gastrointestinal tract (predominantly the appendix, the terminal ileum and the rectum) and can secrete large amounts of vasoactive substances, including 5-hydroxytryptamine (5-HT), tachykinins and prostaglandins[1]. Neuroendocrine cells typically show strong expression of vascular endothelial growth factor (VEGF) and are therefore highly vascularised. This explains the increased myocardial signal on T2 weighted STIR imaging (CMR). The combination of a carcinoid tumour and symptoms of hormonal hypersecretion is called carcinoid syndrome. This is unlikely to occur in the absence of hepatic or nodal metastases, because the substances are metabolized by the liver. Cardiac valve involvement develops in more than half of the patients with carcinoid syndrome, thought to be mediated by activation of 5HT3 receptors. It is characterized by plaque-like deposits of fibrous tissue, typically on the endocardium of right-sided valvular leaflets and the right atrium and ventricle[2]. The deposits on the valve leaflets cause thickening and retraction and lead to valvular dysfunction. The left-sided cardiac structures are usually not affected unless there is an intracardiac or intrapulmonary shunt as the lungs filter the vasoactive substances.

Myocardial metastases from carcinoid tumors are rare. They may present clinically with breathlessness, arrhythmias, or angina if coronary flow is compromised. A retrospective study by the Mayo clinic investigating metastatic carcinoid tumour to the heart found 11 cases of pathologically confirmed myocardial metastases between 1985 and 1999, representing 4% of all referred patients with carcinoid heart disease[3]. In 5 of these 11 cases, the diagnosis of myocardial metastases was first made on autopsy, and these tumours were significantly smaller than the ones detected on echocardiography, highlighting the difficulty of echocardiographic diagnosis especially in small metastases. CMR is useful in assessing carcinoid heart disease providing accurate ventricular volumes measurements, quantification of the severity of valvular involvement and tissue characterization for assessment of myocardial carcinoid metastases in a single examination which is complimentary to echocardiography particularly in patients with poor echocardiographic images.

Somatostatin receptors are present in the majority of neuroendocrine tumors and are activated by somatostatin analogs such as octreotide to reduce the symptoms caused by hormonal hypersecretion. SPECT-CT with ^{111}-Indium-labelled octreotide also targets these receptors to visualise the primary tumour and metastases with high sensitivity (80-90%) and specificity (88-97%)[4]. PET-CT with ^{68}-Gallium-labelled octreotide is known to have even higher sensitivity (82-100%) and specificity (92-100%). Due to local availability at the time of presentation, nuclear imaging was in our case performed by SPECT-CT. This modality is known to have the ability to diagnose myocardial metastases but case reports are very rare as the prevalence of the disease itself is very low. Unlike echocardiography and CMR this method uses radiation and requires imaging at 4 and 24 hours, but has the advantage of confirming the neuroendocrine origin of the lesions.

Carcinoid heart disease is uncommon and myocardial metastasis is extremely rare. In addition to the more widely recognized complication of right-sided valvular heart disease, assessment for myocardial metastases is appropriate to help guide optimal surgical management. Cardiac imaging is crucial in the management of patients and this case report highlights the value of multimodality imaging approach in the management of our patient.

Fundings sources

The work was not financially supported.

Disclosures

The authors declare that they have no conflicts of interest.

Acknowledgements

IC and DM would like to thank National Health Service funding to the National Institute for Health Research Biomedical Research Centre at the Royal Marsden NHS Foundation Trust and the Institute of Cancer Research.

Contributors

All authors contributed to patient care and writing of the report. Written consent to publication was obtained.

References

1. Ha J, Tan WA. Gastrointestinal Carcinoid Tumours: A Review. J Gastroint Dig Syst. 2012;2:107. doi: 10.4172/2161-069X.1000107.

2. Bernheim AM, Connolly HM, Hobday TJ, Abel MD, Pellikka PA. Carcinoid Heart Disease. Prog Cardiovasc Dis. 2007;49(6):439-51.

3. Pandya UH, Pellikka PA, Enriquez-Sarano M, Edwards WD, Schaff HV, Connolly HM. Metastatic Carcinoid Tumor to the Heart: Echocardiographic-Pathologic Study of 11 Patients. J Am Coll Cardiol. 2002;40:1328-32.

4. Wong KK, Waterfield RT, Marzola MC, Scarsbrook AF, Chowdhury FU, Gross MD, Rubello D. Contemporary nuclear medicine imaging of neuroendocrine tumours. Clin Radiol. 2012;67:1035-50.

Figure legends

Figure 1. Echocardiographic images of the right ventricular (RV) inflow view in systole showing thickened, fixed and retracted tricuspid valve leaflets (white arrows in A) with severe free tricuspid regurgitation on colour flow imaging (B). Continuous-wave Doppler flow profile of the pulmonary valve shows a steep deceleration (white bold arrow) of the diastolic pulmonary regurgitant velocity with early termination of flow due to early equalization of pulmonary artery and RV pressures indicating severe pulmonary regurgitation (C). CMR SSFP images show a dilated RV with normal ejection fraction and severe free tricuspid regurgitation (end-diastolic and end-systolic images of four-chamber view in D and E). RA = right atrium. RV = right ventricle.

Figure 2. CMR SSFP images show focal thickening (asterisk) in the mid anterior and septal walls (A) with increased myocardial signal on corresponding T2 weighted STIR images (B). Fused SPECT-CT with ^{111}Indium-labelled octreotide uptake in coronal (C) view shows low-grade uptake in the antero-lateral and antero-septal walls of the left ventricle (dotted white arrow). Intraoperative view of the lesions in the anterior/anterolateral wall after pericardiotomy (black arrows, D). Haematoxylin and eosin stained slide of the right ventricular wall shows cohesive nests of tumor cells with monotonous nuclei, speckled chromatin and granular cytoplasm. No necrosis or mitosis is seen (E). Chromogranin A shows strong positive cytoplasmic staining in the tumor cells confirming the neuroendocrine origin of the tumor (F). (Original magnification x 200).