Solitary neuroendocrine carcinoma of the heart: a case report

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Background
Cardiac tumours are of rare incidence and usually occur in the form of secondary tumours. Most metastatic tumours are melanomas, sarcomas, lung, and haematological malignancies. Neuroendocrine carcinomas (NECs) of the heart are extremely unusual. This case report demonstrates a solitary high-grade NEC of the heart with an individual therapy strategy and follow-up.

Case summary
A 50-year-old gentleman presented with a 2 days history of recurrent episodes of chest pain. Echocardiography, computed tomography, and magnetic resonance imaging revealed tumorous lesions of the ventricles and aortic valve with large circular pericardial effusion. Histopathology results of the biopsy revealed a poorly differentiated small cell tumour of the neuroendocrine type. Despite further investigations with multiple imaging modalities and laboratory, no primary was found. Chemotherapy was initiated but size progression of the tumour was detected. As no other tumorous lesions were detected and resection was not possible because of the tumour complexity, decision on heart transplantation was made. However, due to the necessary immunosuppression after the heart transplantation, multiple metastasis where discovered in the course of treatment.

Discussion
The presence of a NEC in the heart without evidence of any other metastasis or evidence of primary tumour in other organs is clinically unique. For this individual case, heart transplantation was the therapy of choice due to tumour progression under chemotherapy and lacking possibility of resection, as no other suspect lesion was found other than the ones found in the heart. However, the risk of exacerbation of undiscovered micrometastases under necessary immunosuppression following the heart transplantation should be considered.

Keywords
Case report • Neuroendocrine carcinoma • Primary heart tumours • Heart transplantation

Learning points
• Solitary neuroendocrine carcinoma of the heart is very rare.
• Even with large malignant tumours of the heart, diagnostic assessment of pericardial effusion may be inconclusive.
• Individual treatment strategies have to be decided following multidisciplinary team discussion; chemotherapy and resection of the tumour have to be considered in these cases.
• Heart transplantation for cardiac tumours should be undertaken with caution due to the risk of immunosuppression exacerbating undiagnosed micrometastases.

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Introduction

Cardiac tumours are relatively rare and often challenging to diagnose. Cardiac metastases are more common than primary cardiac tumours. They were detected in autopsy studies of cancer patients in up to 15% of cases.\(^1\) If a primary malignant cardiac tumour is detected, metastasis is already present in 75% of cases.\(^2\)

Neuroendocrine carcinomas (NECs) of the heart are extremely rare and usually occur in the form of secondary tumours. The majority originates from NEC of the gastrointestinal tract or the broncho-pulmonary system.\(^3\) However, in some cases the primary tumour remains unknown. They are often associated with carcinoid syndrome. Their occurrence in the absence of liver involvement is exceedingly rare. Evidence of a NEC as a solitary cardiac tumour has been described in literature only once before.

Timeline

| Day 1        | Patient presentation in emergency room with recurrent chest pain in the last 2 days. Computed tomography (CT) angiography and transthoracic echocardiography revealed cardiac tumour in left ventricle and pericardial effusion. |
|--------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Day 2–15     | Further examinations could diagnose a NEC of the heart. For tumour characterization: transoesophageal echocardiography and cardiac magnetic resonance imaging (revealed another two foci in right ventricle and on the right aortic cusp) pericardiocentesis and tumour biopsy staging: CT-chest/neck/abdomen dermatological examination somatostatin receptor scintigraphy no other suspect lesions than cardiac were detected. |
| Day 16       | Chemotherapy was initiated. |
| Month 5      | Re-staging (CT-chest/abdomen, scintigraphy, PET-CT) showed tumour progression and still no evidence of secondary lesions. |
| Month 6      | Heart transplantation. |
| Month 11     | CT, magnetic resonance imaging: multiple metastases. |

Case presentation

A previously healthy 50-year-old gentleman presented in the emergency room with recurrent episodes of chest pain for the last 2 days. The intensity of the retrosternal localized chest pain varied during respiration and was associated with a ear throb.

The lungs were clear to auscultation bilaterally. Cardiovascular examination showed regular heart rate and rhythm, normal sounds, no murmurs or rubs, and no peripheral oedema.

An electrocardiogram was carried out and showed unspecific abnormalities (T-inversion in the posterolateral leads) (Figure 1).

An acute myocardial infarction was ruled out by negative troponin. The D-Dimer test was positive, so a computed tomography angiography (CTA) was carried out. Pulmonary embolism as well as lung malignancy could be ruled out. However, the scan revealed a large homogeneous intramural mass of the inferolateral wall of the left ventricle with an intracavitary component and presence of pericardial effusion. These findings correlated with the transthoracic echocardiography performed after CTA. Left ventricular (LV) and right ventricular (RV) function were normal. For better tumour characterization, cardiac magnetic resonance imaging (cMRI) and transoesophageal echocardiography were carried out within the following 5 days (Figure 2).

Though a large pericardial effusion was present, there were no signs of cardiac tamponade. The patient was haemodynamically stable with mild diastolic hypertension (138/97 mmHg) and normal heart rate (82 b.p.m.). Pericardiocentesis showed a haemorrhagic effusion without any higher atypical cells.

The main pathological finding of the cMRI was observed on the LV inferolateral wall, growing exophytically into the ventricular lumen and pericardial space. Two further foci missed by the previous computed tomography (CT) were located in the RV wall and on the right coronary cusp of the aortic valve (Figure 3) with exophytic growth. The masses were slightly hyperintense with respect to myocardium in T1- and T2-weighted sequences, with an improved contrast in late gadolinium enhancement imaging. Due to these characteristics, the initially suspected diagnosis was lymphoma or metastases of unknown origin. However, in CT no other suspect organ lesions or lymph nodes were found. Biopsies were taken of the LV tumour mass via transaortal access. Histopathology demonstrated a poorly differentiated small cell tumour of the neuroendocrine type (G3) (Figure 4). Immunohistological analysis revealed diffuse strong positivity for keratin components as CK7, neuroendocrine markers as synaptophysin, and CD56. Additionally, weak focal detection of chromogranin and a clear response for p53 oncoprotein were found. Laboratory results showed that the tumour was not actively secreting proteins.

Despite further investigations (CT-neck/chest/abdomen/pelvis, dermatological examination, and somatostatin receptor scintigraphy), which were carried out within 2 weeks after the diagnosis, no primary was found.

After an interdisciplinary board decision (cardiology, cardiac surgery, and haemato-oncology), in the absence of resection options, chemotherapy was initiated with Carboplatin and Etoposid. Due to the extent of the tumour’s infiltration of the LV and RV walls, there was concern about a ‘tumour meltdown’ with perforation.

After six cycles of chemotherapy a size progression of the tumour was detected. After initial pericardial drainage, a recurrence of pericardial effusion did not occur (Figure 5). The patient was clinically stable. Detailed staging, including CT-chest/abdomen, scintigraphy, and PET-CT, revealed no metastases. Since no other suspect lesions were detected, the NEC in the heart was assumed to be a possible primary tumour.

For this patient heart transplantation was a possible treatment option. It was performed quickly after high urgency listing 6 months after...
Figure 1 Electrocardiogram at the first patient presentation showing sinus rhythm, 82 b.p.m., normal electrical axis and unspecific T-Inversion in the posterolateral leads.

Figure 2 Steady state free precession (SSFP) magnetic resonance images (MRI) in long- (A, B, D) and short-axis (C) view. Tumour marked with an asterisk, and pericardial effusion with an arrow. Ao, aorta; LV, left ventricle; RV, right ventricle.
diagnosis, followed by immunosuppression with Tacrolimus, Everolimus, and Prednisolon. Regular follow-ups were planned every 1–3 months, depending on the clinical situation. Unfortunately, the patient didn’t comply. He only went to the emergency room of another hospital when he suffered with fatigue 5 months after heart transplantation. CT and magnetic resonance imaging revealed pericardial, cerebral, pulmonal, pancreatic, and osseous masses.

**Discussion**

Cardiac neuroendocrine tumours are exceedingly rare and if present are usually metastatic. To our knowledge, there is only one publication of an apparently primary NEC of the heart published by Guajardo-Salinas et al. In this case, a solitary massive tumour in the right atrium, with involvement of interatrial septum and aortic root and moderate pericardial effusion, was described. Similar to our case, there were no other malignant lesions apart from those in the heart. The therapy in that case was resection with adjuvant chemotherapy. Local recurrence in the tumour bed occurred 18 months post-operatively.

Generally, resection of the tumour is the treatment of choice. If there is no resection possibility, alternative therapies (chemotherapy and symptomatic medical treatment) must be considered. The overall prognosis is poor, the median survival of high grade NEC as described for the colon carcinoma is 13 months. Most patients die in the course of remote metastasis.
As there are no randomized studies for NEC patients with solitary cardiac involvement, individual decisions have to be made. This case shows that undetected micrometastases exacerbate under the necessary immunosuppression, and therefore, cardiac transplantation may not be a suitable choice of treatment in a case like this.

**Supplementary material**

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

**Consent:** The author/s confirm that written consent for submission and publication of this case report including image(s) and associated text has been obtained from the patient in line with COPE guidance.

**Conflict of interest:** none declared.

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**Figure 5** Transthoracic echocardiography in apical four-chamber (A), two-chamber (B), and three-chamber (C) view. Tumour marked with an asterisk. Ao, aorta; LA, left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle.