CASE REPORT

Squamous cell carcinoma of unknown origin metastasising to the right atrium causing acute heart failure

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SUMMARY

We describe a case of metastasis to the heart, which was initially suspected to be a myxoma, causing acute right heart failure. Emergency surgery was carried out by opening the right atrium and superior vena cava, and debulking the tumour in a piecemeal fashion, providing temporary relief of symptoms. The histology showed this to be metastatic squamous cell carcinoma possibly of head and neck origin. This is extremely rare, with few published cases. Full endoscopic and CT, including positron emission tomography CT, investigation of the head and neck was performed with no primary findings. Only two such cases of squamous cell carcinoma of unknown origin metastasising to the heart have been described, and, in both cases, the patients died within several weeks of diagnosis. This patient remains alive 2 months postoperatively and is receiving radiotherapy to the chest, but his prognosis remains poor.

BACKGROUND

Cardiac tumours can be classified as primary or secondary. Primary tumours are rarer with an incidence of 0.15% and can be benign or malignant. Thirty per cent of primary tumours are malignant and are mostly sarcomas. Metastasis to the heart is a rare occurrence but still constitutes the commonest malignancy of that region. The commonest malignancies that metastasise to the heart are leukaemias (54%), melanoma (34%) and bronchogenic carcinoma (10%); other types include breast, renal, oesophageal and ovarian carcinoma.¹

The first case of cardiac tumour was an anatomic finding by Realdo Columbus in Padua, Italy, in 1559.² Yater,³ in 1931, described nine cardiac tumours found at autopsy. Barnes *et al*⁴ made the first antemortem diagnosis of a cardiac sarcoma in 1934. Beck,⁵ in 1936, successfully removed a teratoma on the right ventricle surface.

We describe a case of this rare occurrence, which presented in a confounding way. The acute presentation and severity of symptoms are impressive, and a high index of suspicion for cardiac tumours must be maintained, as they could easily be clinically misinterpreted.

CASE PRESENTATION

A 66-year-old man with a history of hypertension, hyperlipidaemia and insulin-dependent diabetes mellitus, presented with sudden onset of shortness of breath, which had awakened him at night.

He mentioned recent bouts of orthopnoea and fainting episodes occurring almost daily when standing up or bending over. Several months previously, he was referred to ear, nose and throat (ENT) clinic by his general practitioner for bilateral facial swelling extending down the neck. ENT examinations, including flexible endoscopic assessment of the postnasal space, larynx and vocal cords, were normal, as was a CT scan of the head and neck at the time.

On examination, the patient was tachypnoeic and tachycardic with clear breath sounds bilaterally. Oxygen saturation was 92% on air. A CT pulmonary angiogram (CTPA) was carried out to exclude pulmonary embolism. The result was surprising. It revealed a mass in the right atrium, suspected to be thrombus (figure 1). This thrombus extended up the superior vena cava (SVC) and into the azygos vein. It was also prolapsing through the tricuspid valve partially and into the right ventricle of the heart.

The patient was transferred under cardiologist care where right upper limb and facial congestion were noted. Distended neck and chest wall veins confirmed the SVC obstruction. The patient was treated with enoxaparin.

Transthoracic echocardiography was performed the following day, revealing a large right atrial mass occupying all of the right atrium, prolapsing across the tricuspid valve and compromising right

Figure 1 A section of the CT pulmonary angiogram showing the lesion in the right atrium (arrow) suspected to be thrombus.

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Figure 2 Image from transthoracic echocardiogram four-chamber view showing the lesion in the right atrium.

ventricular filling. The mass was measured at 5.5×5.0 cm and the sonographer was not convinced that this was thrombus, due to a more inhomogeneous consistency (figure 2).

A transoesophageal echocardiogram (TOE) was performed by a consultant in cardiological imaging and the mass was diagnosed as a large right atrial myxoma attached to the interatrial septum, infiltrating the SVC (figure 3). This impression was supported by the patient's history of no known malignancy and the appearance of the mass, which seemed to originate from the interatrial septum on transthoracic echocardiography. The possibility of another type of cardiac tumour could not be excluded, especially since there was involvement of the SVC, which is unlikely in a myxoma.

Since the patient's severe symptoms of SVC obstruction and shortness of breath at rest were not improving, he was offered emergency surgery. The indication for surgery was obstructive right heart failure with secondary loss of left-sided preload. The diagnosis at this point was that of a myxoma and therefore resection was being planned on cardiopulmonary bypass with bicaval venous cannulation. Preoperatively, the anaesthetic team was unable to advance a central line through either jugular or subclavian veins, and ultimately resorted to a femoral venous line.

Immediately on performing the skin incision, there was massive bleeding due to large distended veins in the anterior

Figure 3 Image from transoesophageal echocardiogram where the lesion was suspected to be a myxoma, note the suspected attachment of the lesion to the interatrial septum, typical of myxomas.

Figure 4 Photograph taken during surgery; note the large friable and irregularly shaped mass. Underlying cardiac structures are not visible.

chest wall under high venous pressure. After a troublesome opening, an anterior mediastinal mass was identified. It was a 4×4 cm round thymic tumour without infiltration into surrounding tissues, and this was resected completely.

The pericardium was opened and the right atrium and SVC were found to be completely solid and impossible to cannulate. The tumour was seen infiltrating through atrial wall at the junction of the SVC. Aortic and inferior vena caval cannulations were performed, the patient was put on cardiopulmonary bypass and cold blood cardioplegia was administered. The right atrial anterior wall was incised perpendicular to the insertion of the SVC. Suddenly, large amounts of friable irregular tissue prolapsed out of the atrium with a minor amount of bleeding despite not having cannulated or controlled the SVC. This was noted to be highly suspicious for malignancy and unlikely to be a myxoma (figure 4). A sample was sent for frozen section. Meanwhile, gentle removal of the tumour bulk was performed manually. By scooping a finger around the tumour, large parts of it would detach with no force required (figure 5). The SVC was opened distally using an incision at 90° to the previous one and joining it in its midpoint. It was cleaned out using forceps and the tumour was removed in pieces. This was noted to be successful, as a sudden large rush of blood escaped from the SVC and control with venous clamps was necessary. The frozen section confirmed malignancy, and the

Figure 5 Photograph taken during surgery; the mass could easily be scooped out in pieces as it was friable (IVC, inferior vena cava).

impossibility of complete resection meant that only a thorough debulking of the atrium and SVC would be performed. The vertical incision over the SVC and its insertion into right atrium, extended slightly over the right atrium, was closed using a diamond-shaped pericardial patch. The atrial incision was closed with continuous non-absorbable sutures in two parts on either side of the patch. Haemostasis was ensured and routine closure performed.

Postoperatively, in the intensive care unit (ICU), there were no complications and minimal bleeding, and the patient was extubated after 7 h. He was transferred out of the ICU the next day and discharged home after 6 days pending the formal histology result. During his stay in hospital, his facial and upper limb oedema had improved significantly.

The patient was seen again 2 weeks postoperatively with marked improvement in symptoms and feeling well. The histological analysis revealed soft brown tissue measuring 90×80×20 mm. The tissue was neoplastic with mostly solid and some focal papillary growth patterns with delicate fibrovascular cores. The neoplastic cells were epithelioid cells with high N/C ratio, enlarged irregular nuclei and brisk mitotic activity. Immunohistochemistry staining showed diffuse positivity for cytokeratin (CK) (AE1/AE3) and p63. Focal positivity for MNF-116, epithelial membrane antigen and CK5/6 was present. The conclusion was that of metastatic poorly differentiated squamous cell carcinoma of unknown origin, but most likely from the head and neck. The thymic tumour removed was an incidental type B2 thymoma.

The patient was referred to oncology and began receiving radiotherapy 1 month postoperatively. A positron emission tomography CT (PET-CT) scan of the whole body only showed the known cardiac tumour and repeat ENT examination identified no malignancies. A flexible cystoscopy and an oesophagogastroscopy were also performed, and yet the primary tumour was never discovered.

The patient was readmitted 2 months postoperatively with full recurrence of symptoms, and on echocardiography (echo) was found to have his right atrium obstructed with tumour again. Three months postoperatively, in January 2015, the patient was still alive, symptomatic and receiving palliative radiotherapy. The source of this squamous carcinoma was still unknown.

INVESTIGATIONS

Investigations included preoperative CTPA showing suspected thrombus in right atrium and SVC; echo and TOE showing large atrial tumour suspicious for myxoma; and postoperative PET-CT showing right atrium as the only positive tracer uptake.

DIFFERENTIAL DIAGNOSIS

- ▶ Right atrial and SVC thrombosis
- ▶ Atrial myxoma
- ▶ Primary cardiac tumour

OUTCOME AND FOLLOW-UP

The patient was referred to oncology and began receiving radiotherapy 1 month postoperatively. A PET-CT scan of the whole body showed only the known cardiac tumour, and repeat ENT examination identified no malignancies. A flexible cystoscopy and an oesophagogastroscopy were also performed, and yet the primary tumour was never discovered.

The patient was readmitted 2 months postoperatively with full recurrence of symptoms and on echo was found to have his right atrium obstructed with tumour again. At present, four months postoperatively, in February 2015, the patient is still

alive, symptomatic and receiving palliative radiotherapy. The source of this squamous carcinoma is still unknown.

DISCUSSION

Metastasis to the heart may be present in up to 20% of patient with cancer at autopsy but rarely presents antemortemly. Up to 4% of neuroendocrine tumours will cause cardiac metastasis, especially if the primary is in the midgut.⁶

The commonest location of cardiac secondaries is the pericardium followed by the epicardium, myocardium and, lastly, the endocardium. Spread by direct inoculation such as in pulmonary, breast, thymic and oesophageal malignancies, is more common than haematological spread.⁷ Therefore, the case we present here carries two rare variations, in that it involved haematogenous spread to the endocardium. The reasons for this being so uncommon may be due to the rapid diastolic and systolic motion of the myocardium, the specific myocardial metabolism, the rapid blood flow through the heart and the lack of direct communication of the heart with order organs via lymph vessels.^{8 9} Endocardial metastases are more frequent in the right chambers, as in this case.^{10 11}

The histology made this case even more interesting as metastasis from squamous cell carcinomas of the head and neck are rarely described. Alhakeem *et al*,¹² in 2007, described the case of a 49-year-old patient with metastasis of a laryngeal squamous cell carcinoma; Nagata *et al*,¹³ in 2012, presented two cases of metastasis from tongue and soft palate cancers, both patients died within 3 weeks of diagnosis of metastasis.

The fact that despite the histology, no primary source was identified, is even rarer. Fouladi *et al*,¹⁴ in 2013, described a case of cardiac, pulmonary and paraspinal metastasis of squamous cell carcinoma from an unknown primary. Panduranga *et al*, in 2014, reported a case of a 65-year-old patient with a large right atrial tumour of unknown source, although lymph nodes were positive for squamous cell carcinoma. The cardiac tumour was never biopsied or debulked and the patient died of heart failure 2 weeks after admission.¹⁵

Symptoms are rare, as most are discovered at autopsy. When present, they include symptoms of heart failure due to obstruction of venous return to the filling chambers. Also, symptoms of heart failure (including orthopnoea, dyspnoea, oedema and hypotension) are exacerbated by the pericardial effusion that often accompanies this condition. Patients may rarely present with arrhythmias if the tumour is invading the conduction systems causing atrial fibrillation or flutter, atrioventricular block or any variety of bundle blocks.^{16–18} Echo is the gold standard diagnostic tool, with cardiac CT useful for further characterisation.¹⁹ A large, mobile mass attached to an interatrial septum with a narrow stalk can be diagnosed as an atrial myxoma confidently with echo. However, often it is difficult to differentiate cardiac masses from intracardiac thrombi. Moreover, it is very challenging to differentiate benign from malignant cardiac tumours preoperatively. Several authors have suggested the use of contrast echo, cardiac CT and cardiac MRI. Kirkpatrick *et al* have suggested that malignancy causes hyperenhancement in contrast echo due to its rich vascularisation. On the other hand, a complete lack of enhancement suggests the presence of thrombus.²⁰ Cardiac MRI has been also recently extensively studied for the use for differentiating cardiac masses. Size, first pass perfusion enhancement and heterogeneity have been identified as markers for malignancy.²¹

Treatment is mostly palliative with chemotherapy or radiotherapy, depending on the primary histology. Surgery may be indicated for palliation if the intracardiac mass is causing poor

venous return or valvular obstruction, and if the patient is fit for surgery with a reasonable prognosis. Surgery with curative intent may be possible if there is a solitary intracardiac mass with sufficient chamber or vessel wall for reconstruction.⁷ As seen in this case, the tumour was very friable and mobile in the right atrium, meaning if complete surgical excision is somehow achieved the possibility of metastatic emboli passing into the bloodstream is very high. Our patient has survived longer than most other cases encountered in the literature, and symptoms were temporarily improved, however, his prognosis remains poor, as with all cases of malignant metastasis to the heart.

Learning points

- Squamous cell carcinoma metastasising to the right atrial endocardium is a very rare antemortem diagnosis. The fact that the primary tumour is subclinical makes it an extremely rare case.
- Presentation may be varied, but most commonly it is acute heart failure. Our patient presented with superior vena cava obstruction from tumour invasion and right heart failure due to tumour prolapsing through the tricuspid valve orifice and effectively starving the right ventricle of any preload.
- Correct diagnosis is often difficult, as seen in this case. Radiologists thought the lesion to be thrombus on CT and cardiologists thought it to be myxoma on echocardiography. Obtaining a histological diagnosis would have been difficult, as no other extracardiac tumour source was present and access via the neck veins for line insertion was impossible and therefore a myocardial biopsy was not an option.
- Surgery is rarely successful due to the extent of resection that would need to be performed in order to achieve negative margins. The heart chambers would not be restored if such a resection were to be carried out. Prognosis is poor and most other published cases succumbed to the illness within several weeks. Our patient survived longer than most and experienced temporary symptom relief postoperatively.

Contributors Two of the authors are cardiologists and have provided care for the patient from admission until surgery. They were responsible for all the investigations and for referring the patient for urgent surgery. The other two authors are the surgeons who performed the procedure and cared for the patient postoperatively,

and made the diagnosis of the tumour. All the authors have given their specific input into the writing of this manuscript.

Competing interests None declared.

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