CASE REPORT

Merkel cell carcinoma cardiac metastasis causing cardiac tamponade

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SUMMARY

We describe an unusual presentation of Merkel cell carcinoma (MCC), a rare neuroendocrine cutaneous tumour. A 59-year-old man presented with a 2-week history of dyspnoea on a background of MCC of the left elbow that was diagnosed after an axillary lymph node metastasis had appeared. He was clinically diagnosed with cardiac tamponade and received urgent pericardiocentesis. Thoracic CT imaging revealed a large infiltrating mass within the inferior aspect of the heart, confirmed to be MCC via immunohistochemistry of the pericardial fluid. On review of prior fluorine-18 fluorodeoxyglucose positron emission tomography (FDG-PET) imaging, avid uptake was evident at the corresponding site of disease. This case has several important illustrative aspects, including the clinical manifestations of cardiac metastases, the challenges of MCC histopathological diagnosis and the role of imaging (in particular FDG-PET) in this aggressive disease.

BACKGROUND

Merkel cell carcinoma (MCC) is a rare and aggressive cutaneous tumour.¹ It arises from neuroendocrine mechanoreceptor cells found in the epidermis, cells that are associated with light touch sensation.² It has a propensity to recur locally following surgical resection and has a high metastatic potential.¹ Its incidence is on the rise, and the disease has a higher mortality rate than metastatic melanoma.³ We report a patient who developed a MCC metastasis to the heart and presented with cardiac tamponade. To our knowledge, this is the 10th reported case of MCC metastasis to the heart, and the second case of it causing cardiac tamponade.⁴

CASE PRESENTATION

In August 2016, a 59-year-old man presented with a 2-week history of worsening shortness of breath and chest tightness. His medical history included metastatic MCC. This was diagnosed in May 2015 after presenting with a left axillary mass that was found to be a MCC lymph node metastasis on biopsy. The patient had previously had a left elbow lesion excised 2 years prior which was reported to be basal cell carcinoma. The left elbow lesion recurred in 2014 and was re-resected. In retrospect, this left elbow lesion was thought to be the primary site of MCC.

The patient underwent chemoradiotherapy for MCC, receiving three cycles of cisplatin/etoposide chemotherapy, 50Gy/25# radiation to his left

elbow and 60Gy/30# to the left axilla. Chemotherapy and radiotherapy were completed 9 months and 6 months prior to presentation, respectively. Fluorine-18 fluorodeoxyglucose positron emission tomography (FDG-PET)/CT monitoring during treatment showed post-therapy changes in the left elbow and mild residual activity in the larger lymph nodes of the left axilla. A post-treatment surveillance FDG-PET/CT showed no FDG-avid locoregional recurrence in the left elbow or axilla; however, high-grade uptake was noted in a left internal mammary node in the fourth intercostal space. The patient's history was also significant for non-Hodgkin's lymphoma diagnosed in 1999, for which he had early relapse following first-line therapy (cyclophosphamide, vincristine, prednisolone). He subsequently went into complete remission following cyclophosphamide, doxorubicin, vincristine, prednisolone chemotherapy.

At presentation, the patient was dyspnoeic and experienced dizziness and chest tightness. His blood pressure was 82/57 mm Hg, pulse rate 108 bpm, body temperature 35.6°C, respiratory rate 18, SPO₂ 90% on 1 L O₂ via nasal prongs and capillary refill time 3 s. He had muffled heart sounds and a raised jugular venous pressure at 5 cm. Lung auscultation revealed vesicular breath sounds. No pulsus paradoxus was detected. Chest radiography showed an enlarged heart and right-sided pleural effusion. Blood tests revealed acute kidney injury (Cr 259, previously 83) and acute hepatic injury (ALT 998, ALP 164, GGT 332) with synthetic dysfunction (International Normalised Ratio (INR) 2.0).

Bedside echocardiography showed a large pericardial effusion (2.5 cm at the apex). The patient was diagnosed with cardiac tamponade and received urgent pericardiocentesis, with 700 mL of dark blood-stained fluid aspirated. The patient clinically improved immediately, with his blood pressure and heart rate normalising and his dyspnoea resolving. A subsequent formal echocardiogram showed a large homogeneous mass in the pericardial space and right atrium. CT of the chest showed a large infiltrating mass centred at the inferior aspect of the heart, extending along the inferior left and right atrioventricular grooves and surrounding the distal right and circumflex coronary arteries, without obstruction of those vessels (figure 1). Bilateral small to moderate pleural effusions and a right lower lobe pulmonary artery thrombus were also noted. Immunohistochemistry of the pericardial fluid confirmed MCC, with the neoplastic cells positive for cytokeratin 20 (CK20) in a

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Figure 1 Contrast-enhanced transaxial CT chest demonstrating a large mass extending along the inferior surface of the heart.

characteristic paranuclear dot pattern (figure 2). Other positive markers included CAM 5.2 and CK 5/6, neurofilament, CD56, synaptophysin and chromogranin. The patient was started on cisplatin/etoposide chemotherapy and, after remaining well for 3 days, was discharged home.

DISCUSSION

MCC is a rare neuroendocrine cutaneous tumour associated with a high risk of locoregional disease recurrence.¹ Its incidence is on the rise, with data from the Surveillance, Epidemiology and End Results registry in the USA demonstrating an almost 300% increase in incidence from 1986 to 2011.⁵ It is unclear whether this increased incidence is due to increased occurrence or heightened awareness and improved diagnostic techniques.⁵ Incidence studies in Western Australia and Queensland have shown some of the highest incidence rates of MCC in the world (0.82/100 000 and 1.6/100 000 population per year, respectively).^{6,7} MCC is associated with a mortality rate of 30%, which is higher than that of melanoma.³

Figure 2 Immunohistochemistry of pericardial fluid showing positive staining for cytokeratin 20 in a classic paranuclear dot pattern.

Figure 3 Transaxial fused fluorine-18 fluorodeoxyglucose positron emission tomography demonstrating avid tracer uptake in the heart corresponding to sites of malignancy identified in the contrast-enhanced CT.

MCC is more common in the elderly Caucasian population, with the average age of onset being 75.⁸ Risk factors for the development of MCC include increasing age, male gender, ultra-violet exposure, immunosuppression and infection with Merkel cell polyomavirus.⁹ Merkel cell polyomavirus is thought to be found in 80% of MCC (though this may be an underestimate) and is thought to be a causative agent in tumourigenesis.^{10,11} It is unclear what molecular pathways are responsible for the pathogenesis of the other 20% of MCC. The presence of Merkel cell polyomavirus in the patient's disease was not tested.

MCC usually manifests as a red to violaceous, painless smooth nodule.⁹ It has a predilection for the sun-exposed head, neck and extremities, with 70%–90% of MCC occurring on these areas. Biopsy is required for diagnosis, and immunohistochemical staining is necessary to differentiate it from other poorly differentiated small blue neoplasms such as small cell carcinoma of the lung, melanoma and lymphoma.⁹ MCC is also clinically and histologically reminiscent of basal cell carcinoma (both have a basophilic appearance), thus cases of MCC can be misdiagnosed as such. MCC is consistently positive for CK20 (figure 2) which differentiates it from basal cell carcinoma.⁹ It is thought that the patient's left elbow lesion, which was first excised in 2013 and diagnosed as basal cell carcinoma, was actually the primary site of his MCC. This case reinforces the importance of clinicians and pathologists being aware of MCC as a differential diagnosis in cutaneous lesions, as misdiagnosis can delay early aggressive surgical therapy which is the best treatment for local Merkel cell neoplastic disease.

The majority (73%) of patients with MCC present with localised disease, 23% have regional disease and 4% have distant metastases.¹² Common sites of metastatic spread include distant lymph nodes, distant skin, lung, central nervous system and bone.¹³ Metastases to bone marrow, pleura, pancreas, testes, bladder, small bowel and stomach have also been reported.¹³ MCC metastases to the heart are rare, with only nine reported cases in the literature. Comparatively, an autopsy series in patients with any malignancy showed 10%–20% had cardiac metastases.¹⁴ Cancers most likely to metastasise to the heart are lung, oesophageal, lymphoma, breast, melanoma and leukaemia.¹⁴ It is exponentially more likely for a cardiac tumour to be a metastasis than a primary cardiac tumour, and it is uncommon for the heart to be the only site of metastatic disease from a non-cardiac malignancy.¹⁵ Our patient presents a unique

Figure 4 Maximum intensity projection demonstrating diffuse fluorine-18 fluorodeoxyglucose uptake within the right inferior aspect of the heart (arrow).

case of MCC where, apart from an internal mammary lymph node, the heart was the only site of distant metastatic spread.

Complete surgical excision is the primary treatment of localised MCC. Sentinel lymph node biopsy is recommended for those with clinically and radiographically node-negative disease.¹⁶ There are data to suggest that adjuvant radiotherapy reduces the local recurrence rate of MCC.¹⁷ There is no convincing data to suggest any survival benefit with adjuvant chemotherapy.¹⁷ MCC is a chemosensitive tumour, although the duration of response to treatment is limited.¹⁷ Chemotherapy is most commonly used in a palliative setting in patients with metastatic disease, as it was with our patient. Response rates to chemotherapy are approximately 60%–70%, with platinum and etoposide combinations most frequently used.¹⁸ Palliative radiotherapy can be valuable in treating symptoms arising from painful, bleeding or ulcerated disease.¹⁷ There is no standard treatment for MCC cardiac metastases. Two cases describe the use of palliative radiotherapy to cardiac MCC metastasis with significant reduction in tumour volume, suggesting this may be a good treatment to alleviate symptoms, particularly in patients with chemoresistant MCC.^{19 20}

While cardiac metastases are most often asymptomatic, they can also present with symptoms that mimic many types of cardiac disease including chest pain, palpitations, dyspnoea and peripheral oedema.²¹ Cardiac metastases are most commonly found in the pericardium (64%–69%), followed by the epicardium (25%–35%) and myocardium (29%–32%).²² Pericardial metastases can cause pericardial effusions which when rapidly accumulated can cause cardiac tamponade.²¹ Cardiac tamponade is characterised by hypotension, raised jugular venous pressure and

muffled or distant heart sounds.²¹ It is a medical emergency which requires urgent pericardiocentesis to avoid complete haemodynamic compromise. Our patient's renal and hepatic function were impaired at presentation secondary to hypotension. Epicardial and myocardial metastases can cause lethal arrhythmias (eg, atrial fibrillation, ventricular fibrillation, complete atrioventricular block), acute coronary syndrome, congestive cardiac failure and cardiac rupture.²¹ This case highlights the importance of having a high level of suspicion of cardiac metastasis in a patient with known malignancy presenting with a cardiovascular complaint.

To our knowledge, there are no guidelines or algorithms for the imaging of MCC. FDG-PET/CT is a useful modality for imaging MCC. In a study of 23 patients (66 scans), George *et al* found FDG-PET changed MCC staging in 39% of patients at initial presentation and changed patient management in 33% of patients at initial presentation, 32% during monitoring and 36% of patients during evaluation of response to chemotherapy.²³ The sensitivity, specificity and positive and negative predictive values for FDG-PET were 97%, 89%, 94% and 94%, respectively. A systematic review of the diagnostic performance of FDG-PET in MCC patients demonstrated both high sensitivity (90%) and specificity (98%), however concluded that more prospective and larger clinical trials are needed.²⁴ Maury *et al* and Liu *et al* have recommended that FDG-PET should not replace sentinel lymph node biopsy in staging as they describe failure of FDG-PET in identifying lymph node micrometastases.^{25 26}

Review of the patient's FDG-PET imaging shows a diffuse pattern of tracer activity in the inferior and basal aspect of the heart, including the right ventricle (figure 3 and figure 4). Interpretation of FDG uptake in the myocardium can be challenging as normal left ventricular myocardium has variable uptake of glucose.²⁷ Right-ventricular or atrial activity is less commonly seen and raises suspicion for underlying pathology.²⁸ Myocardium preferentially uses fatty acids for energy in the fasting state, so it is recommended patients fast overnight prior to their PET scan.²⁹ Unfractionated heparin releases free fatty acids into the blood and its use 15 min prior to FDG administration is suggested to be effective in reducing cardiac FDG uptake.³⁰ In the setting of malignancy, focal FDG activity in the heart on FDG-PET imaging should raise suspicion for cardiac metastasis. A diffuse pattern of activity is however more difficult to interpret, as this may be physiological. This case reinforces the importance of reviewing the heart as a potential site of metastatic disease in FDG-PET imaging.

This case describes a patient with a rare cutaneous neuroendocrine tumour that unusually metastasised to the heart without, excluding an internal mammary lymph node, evidence of other distant metastatic disease. This case highlights the importance of early and accurate diagnosis of MCC with aggressive surgical treatment for localised disease. A high level of suspicion for cardiac metastasis should be present in any patient with cardiac symptoms and a known malignancy. FDG-PET is a useful imaging modality for the staging, monitoring and response to treatment of MCC; the heart must be carefully reviewed for metastatic disease given its variable uptake of glucose.

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Contributors MDL reviewed case history, performed background literature review and is primary author of the manuscript. RF supervised and assisted planning and editing of manuscript and images.

Learning points

- ▶ Consider Merkel cell carcinoma (MCC) in the differential diagnosis of red to violaceous cutaneous nodules, particularly in the elderly, immunosuppressed and sun exposed.
- ▶ New cardiac symptoms in the setting of malignancy should raise suspicion of cardiac metastasis.
- ▶ Fluorine-18 fluorodeoxyglucose positron emission tomography (FDG-PET) is a useful imaging modality for MCC.
- ▶ The heart must be carefully reviewed for metastatic disease in FDG-PET imaging.

Competing interests None declared.

Patient consent Obtained.

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