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Cardiac Metastases: Secondary Tumours of the Heart

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Abstract: Cardiac metastases are secondary tumours of the heart that originate from primary malignancy in other parts of the body. Secondary tumours are mostly diagnosed during post-mortem examination. However, the incidence rate of secondary cardiac tumours is much greater that of primary cardiac tumours. Secondary tumours are often diagnosed using imaging techniques such as TEE, TTE, CT scans and MRI. In most cases, a combination of these imaging methods is necessary to accurately diagnose the presence of a secondary cardiac tumour. In addition, surgical excision is the primary treatment option of secondary tumours due to the often delayed diagnosis of the disease.

Keywords: secondary tumour, cardiac metastases, metastasis, primary malignancy

Introduction

Cardiac metastases are the most frequent type of cardiac tumours identified at post mortem examination (Bussani et al, 2007). Over 10 % of patients with known primary malignancies demonstrate secondary cardiac involvement at autopsy (Bussani et al, 2007). Furthermore, cardiac metastases are 30 times more common than primary cardiac tumours (Leja et al, 2011). Most cardiac metastases are classified based on tumour location and this classification includes; pericardial, epicardial, myocardial, endocardial and intracavitary metastases (Leja et al, 2011). Metastasis to the heart occurs as a result of the systemic spread of non-cardiac primary malignancies such as melanomas, carcinomas, lymphomas, leukemia and sarcomas (Netter et al, 2014). These primary malignancies can spread to the heart via four pathways; retrograde lymphatic extension, haematogenous spread, direct invasion and transvenous extension (Netter et al, 2014; Goldberg et al, 2013). The lymphatic extension of carcinomas from the lungs, breast and esophagus often deposit metastatic tumours in the pericardium and epicardium (Goldberg et al, 2013). In addition, the haematogenous (embolic) spread of systemic melanomas, sarcomas, lymphomas and leukemia through the coronary arteries may result in myocardial metastases. (Chiles et al, 2001). Direct extension of bronchogenic carcinomas into surrounding tissue can form secondary tumours in the pulmonary vein of the heart (Goldberg et al, 2013). Also, the transvenous extension of hepatocellular carcinomas and renal cell carcinomas occurs through the inferior vena cava to the right atrium (Alghamdi et al, 2006).

Clinical Manifestations

Cardiac metastases appear as a result of widespread metastatic disease, however, solitary metastases to the heart are rare (Reynen et al, 2004). Patients presenting cardiac metastases are usually asymptomatic depending on the location of the tumour and the effect of the intrusion of malignant cells into neighbouring tissues (Netter et al, 2014). It is difficult to detect cardiac metastases because they possess signs and symptoms similar to common cardiovascular diseases such as palpitations, atrial fibrillation, angina, dyspnea and peripheral edema (Hoffmeier et al, 2014). Therefore, upon diagnosis of noncardiac malignant disease, cardiac metastases may be present if the patient presents certain cardiac manifestations such as pericardial effusion, arrhythmias, heart failure or valve disease (Reynen et al, 2004).

The most common sign of pericardial metastatic disease is pericardial effusion (Misra et al, 2014). Symptoms of pericardial effusion include shortness of breath, anterior and pleuritic chest pain and peripheral edema (Goldberg et al, 2013; Misra et al, 2014). In a patient with a known primary malignancy, the presence of pericardial effusion is highly suggestive of metastatic pericardial disease. Moreover, depending on the size of the pericardial

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effusion some patients may be symptomatic or asymptomatic (Goldberg, 2013).

On the hand, arrhythmias are the most common sign of metastatic myocardial disease. Tumour deposits are often found on the autonomic fibers of the myocardium which disrupt the conduction system of the heart (Misra et al, 2014). The type of arrhythmia depends on the size and location of the tumour in relation to the conduction system of the heart (Misra et al, 2014). Patients with a diagnosed arrhythmia and known history of malignant disease should undergo the imaging tests to detect any form of metastatic cardiac involvement (Misra et al, 2014).

Types of Cardiac Metastases

Pericardial Metastases

The pericardium is the most common site of metastases in the heart with about two-thirds (64-69%) of all cases involving the pericardium (Bussani et al, 2007; Misra et al, 2014). Pathologically, pericardial metastases may appear as a fibrionohemorrhagic pericarditis or pericardial infiltrate (Kalra, 2008). Most commonly, pericardial metastases result in the production of a serosanguineous malignant pericardial fluid (Bland et al, 2009). If this fluid cannot be reabsorbed as rapidly it collects in the pericardial space, there will be an accumulation of pericardial effusion (Bland et al, 2009). Consequently, cardiac tamponade may occur if ventricular filling reduces cardiac output (Bland et al, 2009). As such, patients may be asymptomatic or present some symptoms depending on the size of pericardial effusion or presence of cardiac tamponade.

The precise sensitivity and specificity of two-dimensional echocardiography in the diagnosis of pericardial metastases is unclear (Kotler, 2012). The restricted resolution properties of echocardiography prevents the recognition of small metastatic nodules less than 2-3mm (Kotler, 2012). However, pericardial metastases that protrude through the epicardium and pericardium have been identified on a two dimensional as having irregularly shaped cauliflower like structures (Kotler, 2012). These pericardial metastases are often found in the homogenous space of a pericardial effusion (Kotler, 2012). Furthermore, metastases found on the parietal pericardial surface are often immobile while visceral pericardial metastases are usually mobile isolated nodules (Kotler, 2012). CT is often better at detecting pericardial masses than echocardiography because soft tissue nodules or malignant masses can be clearly visualized and characterized (Buzaid et al, 1989).

The methods used in the treatment of malignant pericardial effusion, include pericardiocentesis, pericardial sclerosis, systemic chemotherapy, radiotherapy, and surgical treatment (Buzaid et al, 1989). The use of pericardiocentesis helps to diagnose pericardial metastases with cytological evaluation of the fluid or pericardial biopsy (Buzaid et al, 1989). Ultimately, the best treatment of pericardial effusion depends on the effectiveness of tumour chemotherapy, irradiation, life expectancy and the whether or not cardiac tamponade is present at diagnosis (Buzaid et al, 1989).

Epicardial and Myocardial Metastases

Metastatic epicardial and myocardial involvement of heart have an incidence rates of 25%-34% and 29-32% respectively. In other words, they both constitute about one third of cardiac metastatic cases (Bussani et al, 2007; Misra et al, 2014). These types of metastases often disrupt the heart's conduction system and ultimately cause lethal atrial fibrillation, ventricular fibrillation or complete atrioventricular node block (Casella et al, 2011). In addition, myocardial metastases may cause right heart failure if the right atrium or right ventricle is involved, therefore compromising cardiac output (Goldberg, 2013). Furthermore, myocardial metastases can present symptomatic coronary artery disease even in the absence of coronary artery involvement (Perazzolo et al, 2012). Metastatic tumour deposits on the myocardium can sometimes mimic acute coronary syndromes, presenting with chest pain, elevated cardiac biomarkers, and ST- and T-wave abnormalities (Perazzolo, 2012) .Valvular dysfunction caused by the distortion of adjacent valve apparatus is also a manifestation of myocardial metastases (Kotler, 2012).

Endocardial and Intracavity metastases

Endocardial and Intracavitary metastases (3-5%) are rare forms of cardiac metastases (Goldberg et al, 2013; Butany et al, 2005). Intracavitary tumours often obstruct inflow or outflow into the ventricular cavity (Goldberg et al, 2013). As such, right ventricular outflow obstruction may cause cardiogenic shock (Garg et al, 2011). Cardiac metastasis can also cause symptomatic left ventricular outflow tract obstruction, a phenomenon usually observed in hypertrophic obstructive cardiomyopathy (Goldberg et al, 2013). The embolization of the intracavitary tumour can cause a stroke from left-sided cardiac metastasis or pulmonary emboli from right-sided cardiac metastasis (Goldberg et al, 2013).

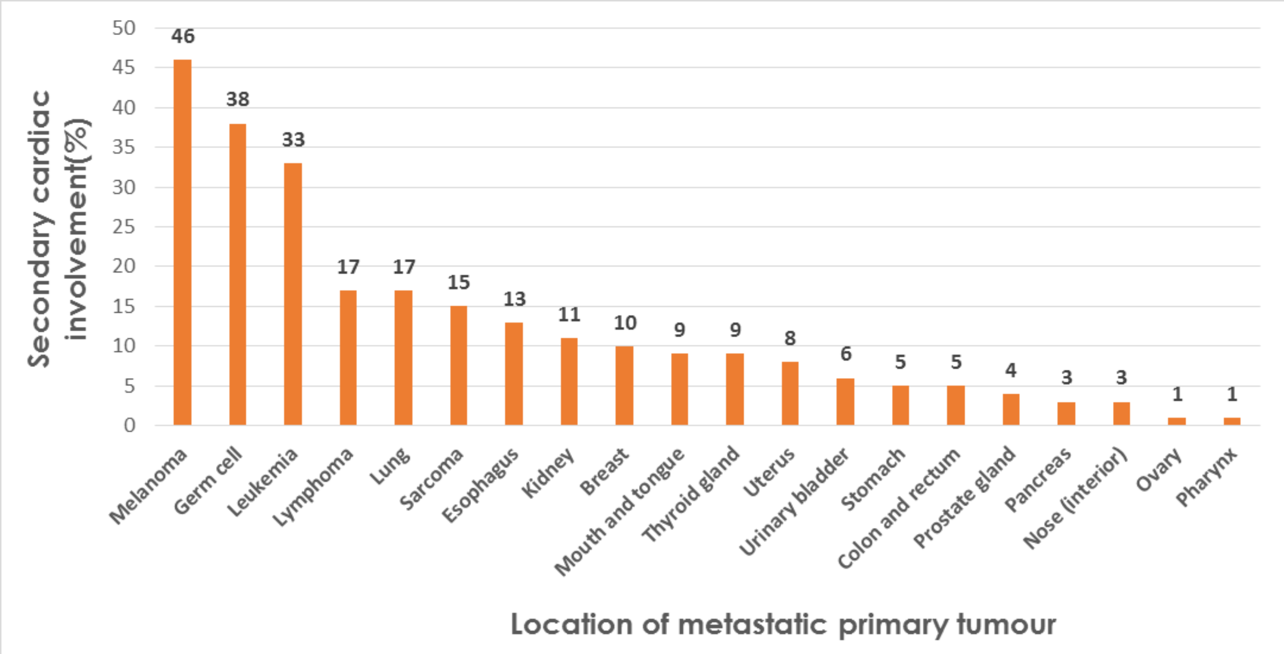

Figure 1. Percentage of primary malignancies that metastasize to the heart as cardiac metastases (Bussani et al, 2007)

Diagnosis: Imaging

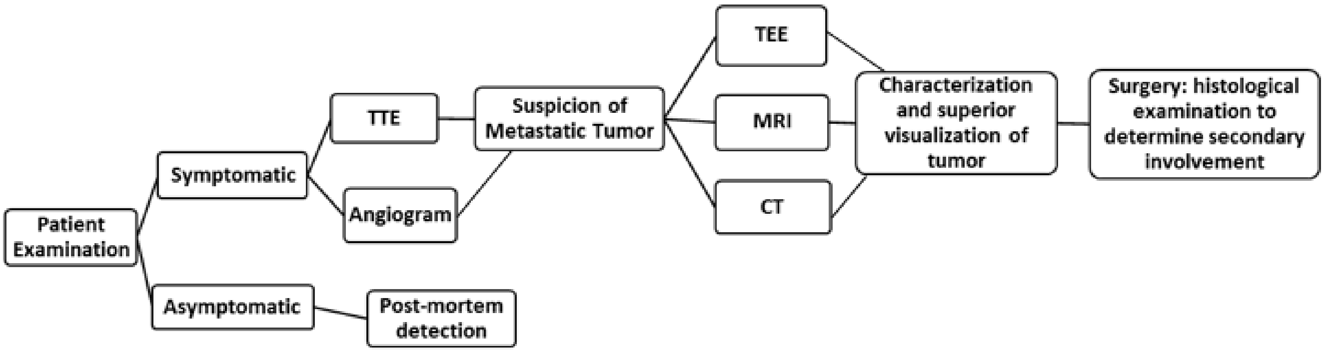

Fig 2. Flow chart illustrating the process of detecting and diagnosing of cardiac metastases.

Imaging is the most common diagnostic tool used for detecting secondary tumours, however, experience and technique is needed to distinguish cardiac metastases from normal cardiac structures. Structures like the Crista terminalis in the right atrium are often misinterpreted as secondary masses found in the right atrium from poor modalities such as echocardiography (Kassop et al, 2014)

Transthoracic Echocardiography (TTE) and Transesophageal echocardiography (TEE)

Both TEE and TTE are equally effective in visualizing tumours originating from the heart. TTE is the first line diagnostic tool for visualizing and confirming the structure of a suspected cardiac mass (Otto et al, 2007). TEE is a more advantageous modality for mass visualization and characterization because it provides improved resolution of the tumour location and is able to detect some masses not visualized by TTE (Ragland et al, 2006). As such, cardiac metastases are often identified in 40% of patients using TEE and only 8% of patients using TTE (Ragland et al, 2006). In addition, TEE gives more information to the TTE approach regarding intra- and extra cardiac expansion and the morphological characterization of the tumour surface (Braunwald et al, 2001). Although. TEE provides greater resolution and advantages for detecting cardiac metastases, it should be considered only when TTE studies are not sufficient or where TTE cannot be used (surgery) (Ragland et al, 2006, Braunwald et al, 2001). Furthermore, the limited acoustic window of TTE and TEE can hinder the proper characterization of a detected mass, hence a CT and MRI should be used (Otto et al, 2007).

Computerized Tomography (CT) and Magnetic Resonance Imaging (MRI)

CT provides a distinct evaluation of cardiac metastases from distant tumours (Kassop et al, 2014). It uses spatial resolution and three dimensional reconstruction to depict direct tumour extension and extra cardiac involvement (Otto et al, 2007). CT is the only modality that can evaluate calcified masses and the invasion of neighbouring vessels and pulmonary metastases (Gross et al, 1983). However, a disadvantage with routine CT includes exposure to radiation and the risk of contrast induced nephropathy (Gross et al, 1983). Furthermore, CT provides lower soft tissue and temporal resolutions of the cardiac masses than MRI (Gross et al, 1983).

Cardiac CT is also useful to detect cardiac metastases in suspected malignancies especially when coupled with ^{18}F-fluorodeoxyglucose (FDG) positron emission tomography (PET) (Rahbar, 2012). F-FDG PET/CT help differentiate malignancies from benign tumours as it can detect high metabolic rate of glucose (Rahbar et al, 2012). For example, primary malignant cardiac tumours and metastatic tumours show significantly higher glucose uptake as quantified by ^{18}F-FDG PET/CT standardized uptake value (SUV) than benign cardiac tumours (Rahbar et al, 2012).

In comparison to CT, MRI provides superior visualization of the degree of involvement of a heart chambers, tissue heterogeneity of T1 and T2 weighted images, large size > 5cm and hemorrhagic pericardial effusion (Motwani et al, 2013). Malignant tumours are often have a low signal intensity on the T1 weighted images and high signal intensity on the T2 weighted images (Sparrow et al, 2005). In addition, the gadolinium contrast injections characterizes tumours based on highly and poorly vascularized, developing a strong enhancement for the former (Hoey, 2014)

Management of Cardiac Metastases

According to the literature, the prognosis of secondary tumours of the heart is very poor (Blackmon et al, 2008). Patients usually survive at most 7 months to 2 years from the time of diagnosis poor if left untreated (Brandt et al, 2005). Surgical resection in combination with post-operative chemotherapy is the most effective procedure adopted to manage isolated cardiac metastases. Complete tumour resection is carried out provided the cardiac metastases is confined to a certain region of the heart without infiltrating surrounding tissue (Scheld et al, 1988). In addition, ex-situ resection can also be done provided that the cardiac metastases involves the posterior wall of the left atrium or dorsal great vessels (Hoffmeier et al, 2014: Blackmon et al, 2008). Due to lack of circumferential view of the tumour, the heart is lifted from the body for better characterization and visualization of the tumour (Scheld et al, 1988). Thereafter, the heart is placed back into its cavity using artificial prostheses and valves (Hoffmeier et al, 2014, Scheld et al, 1988). Although complete and ex-situ resection are beneficial for long-term survival of patients, secondary complications of left/and or right heart failure may occur (Hoffmeier et al, 2014, Scheld et al, 1988).

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