Clinical findings and therapeutic options in cardiac tumours

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Summary

Background

Primary cardiac malignancies are uncommon, with an estimated autopsy incidence of 0.001–0.05%, and the vast majority of malignancies involving the heart and pericardium are metastatic. Three quarters of these tumours are benign, and approximately half of adult cardiac tumours are myxomas. Rhabdomyomas, papillary fibroelastomas, lipomas, fibromas, and haemangiomas are the other benign tumours. Rhabdomyomas are also the most common paediatric primary cardiac tumours. Primary malignant cardiac malignancies make up one fourth of all cardiac tumours, and angiosarcoma, rhabdomyosarcoma, fibrosarcoma, leiomyosarcoma, malignant fibrous histiocytoma, pericardial mesothelioma and lymphoma are the major neoplasms. The diagnosis is often made by transthoracic echocardiography (TTE) but magnetic resonance imaging (MRI) and computed tomography (CT) are needed to determine the characterization, location and extent of cardiac and paracardiac masses. These imaging modalities are also used for both treatment planning and post-treatment follow-up.

Aim

In this report, we evaluate primary cardiac benign and malignant tumours and metastatic lesions with the treatment strategies by reviewing the recent literature.

Key words cardiac tumours • myxoma • heart • sarcoma


Word count: 2229
Tables: –
Figures: –
References: 33

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The vast majority of malignancies involving the heart and pericardium are metastatic, and primary tumours are rare, with an autopsy incidence of 0.001–0.05% [1,2]. Most primary cardiac tumours are benign, and nearly three quarters of these tumours are myxomas. Rhabdomyoma, lipoma, fibroma, teratoma, haemangiomata and fibroelastoma are the other benign neoplasms. Primary malignant cardiac malignancies make up one fourth of all cardiac tumours, and angiosarcoma, rhabdomyosarcoma, fibrosarcoma, leiomyosarcoma, malignant fibrous histiocytoma, pericardial mesothelioma and lymphoma are the major neoplasms. Most of both primary benign and malignant cardiac tumours originate from the atria [3–5].

**AIM**

Intracardiac obstruction and systemic embolisation findings and other systemic signs are generally present in most patients, and echocardiography, computed tomography (CT), magnetic resonance imaging (MRI) and whole body gallium scans are used for preoperative diagnosis [6].

**II. CLINICAL FEATURES**

Having a suspicion of a primary cardiac tumour is imperative in establishing the diagnosis since presenting symptoms can often mimic other non-neoplastic cardiac pathology. There are several clinical features but the classic triad includes signs resulting from intracardiac obstruction and systemic embolisation and other systemic symptoms [7,8]. Large atrial tumours may obstruct atrioventricular flow and mimic valvar stenosis. The main difference from classic valvar stenosis is that the symptoms caused by the tumour are paradoxical and may change with the patient’s body position.

Embolisation is also a frequent finding since either the tumour itself or adherent thrombus may migrate. These emboli may mimic endocarditis or vasculitis and cause cerebrovascular events. Pulmonary venous hypertension and pulmonary oedema can occur due to either embolisation or obstruction and cause right heart failure. In such cases dyspnoea and orthopnoea are the commonest symptoms. Cardiac tamponade due to right heart failure is also a frequent finding. The other findings are syncope, haemoptysis, claudication and angina. The symptoms such as weight loss, fever and fatigue that can also be present in infective endocarditis, vasculitis or other malignancies can raise difficulties in establishing the diagnosis. Arrhythmias such as atrioventricular block or ventricular tachycardia are frequent and may be the preceding symptoms of a cardiac tumour [7,8].

However, about 80% of primary malign cardiac malignancies present with systemic metastases so early diagnosis is hard to establish [9].

**III. BENIGN CARDIAC TUMOURS**

**A. Myxomas**

Cardiac myxoma is the most common cardiac tumour in adults. Comprising 50% of all cardiac malignancies, it is more common in women, and the median age at diagnosis is 50. 75% of myxomas are left atrial and are mainly located in the atrial fossa ovalis region. Complex cardiac myxomas are part of a familial autosomal dominant inherited disease and can be seen in younger ages. In such cases, myxomas are associated with at least two or more lesions such as cutaneous lentiginosis, at least one cutaneous myxoma, primary adrenocortical micronodular dysplasia with Cushing’s syndrome, testicular tumours (large-cell Sertoli-cell tumours), pituitary adenomas, and myxoid fibroadenomas of the breast [10].

They can also be part of syndromes like LAMB (atrial myxoma, lentigines, mucocutaneous myxoma, blue naevi) and NAME (atrial myxoma, naevi, myxoid neurofibromata, ephelides). Carney complex is the general name of these syndromes and the PRKAR1A germline mutation (gene deletion at the 17q2 locus) is associated with them [11].

Both cardiac and systemic symptoms such as dyspnoea, orthopnoea, syncope, fever, weight loss and haemoptysis can be present. Embolisation is also a major problem and multiple emboli can mimic infective endocarditis or vasculitis with major complications of cerebrovascular events and sudden death [10]. Right-side located tumours can embolise to the lungs, resulting in pulmonary hypertension. In such cases, murmurs are frequently present.

Diagnosis depends on a high index of suspicion, since signs and symptoms such as cachexia, fever, arthralgias, transient ischaemic attacks, stroke, murmurs, anaemia, raised acute phase
reactants, and erythrocyte sedimentation rate are also frequently found in other cardiac or infectious diseases, vasculitis or other malignancies [10]. Echocardiography is the main diagnostic tool and in most cases it is sufficient to verify the diagnosis. Cardiac embolisation or in situ thrombus is the main disease that must be considered in differential diagnosis especially in right atrial myxomas and in such cases the use of oral anticoagulants for a short period and observing if there is shrinkage in the lesion may be useful. If the confusion persists, MRI can be performed for further evaluation [12].

Early surgical resection is the main treatment strategy for especially large atrial myxomas since although these tumours are histologically benign, embolisation, obstruction or cardiac arrhythmias can be fatal. The goal of surgery is resecting the tumoural lesion with sufficient margins and this goal is achievable in most cases. Following successful surgery the prognosis is excellent, but there is always a small risk of local recurrence so close follow-up with echocardiography is of great importance [13].

B. Rhabdomyoma

Rhabdomyoma is the most common benign cardiac tumour in childhood and is associated with tuberous sclerosis in most cases. These tumours are also characteristically multiple and ventricular. Since spontaneous tumour resolution is common, surgical resection is performed only in patients with life-threatening complications and treatment is usually conservative. In patients who need surgery for a rhabdomyoma, subtotal excision to preserve surrounding structures may be reasonable, with the expectation of further stability or resolution [14,15].

C. Papillary fibroelastoma

The real incidence of papillary fibroelastomas is unknown since in most cases these tumours are silent and they are incidentally found in autopsies. Furthermore, most of the excised valves are not sectioned and many of the small tumours are possibly missed. Also these tumours can be mistaken for valvar vegetations. Most of the lesions are located on the valvular endocardium of the aortic and mitral valves, and the “sea anemone” appearance, with a short attaching pedicle, is typical [16]. Recent studies have shown that there is a high incidence of embolisation of cerebral and coronary arteries, and parallel to these findings clinically cerebrovascular and cardiac ischaemic events and sudden death are not infrequent. Regarding these facts, surgical resection is now considered more appropriate for these lesions but wider resections may require valvar replacement. The need for surgery should be weighed against the morbidity in such cases [17].

D. Haemangioma

Haemangiomas are benign vascular tumours that generally occur in the interventricular septum. Representing approximately 1–2% of heart tumours, they also arise from the epicardium and myocardium. They are mostly diagnosed in the fourth to fifth decades and are more frequent in males. “Tumour blush” is characteristic in coronary angiography. Since these lesions have a highly vascular nature, surgical excision is not generally possible and close follow-up is indicated [18].

E. Fibroma

Cardiac fibromas are low-grade tumours that are generally interventricular and typically they are seen in childhood. The median age at presentation is 13 years; however, one third of these tumours are seen in children younger than 1 year old. The major complications are arrhythmias, syncope, heart failure and sudden death [18]. The diagnosis can be made with fluoroscopy since there are multiple foci of calcification in the tumour. In small tumours total surgical excision can be performed but tumours with large dimensions may even require cardiac transplantation [19].

F. Lipoma and lipomatous hypertrophy

Lipomas are generally asymptomatic tumours that are usually subpericardially located and they constitute about 7–10% of primary cardiac neoplasms. These tumours are generally small but occasionally they become large and extend into the left atrial cavity, resulting in arrhythmias. The diagnosis can be made by MRI [20]. Lipomatous hypertrophy of the interatrial septum is the accumulation of fat in the interatrial septum. It is common in obese patients and can occasionally cause atrial arrhythmias. Diagnosis depends on establishing the presence of thickening in the atrial septum by ultrasonography or MRI. Weight loss may be beneficial in some cases [18].
G. Cystic tumour of the atrioventricular node

The cystic tumour of the atrioventricular node is a small lesion located at the base of the atrial septum in the region of the atrioventricular node. It is a very rare benign tumour and in most cases asymptomatic, but it has great importance since these tumours are the smallest tumours that can lead to sudden and unexpected death. The majority of these cysts are diagnosed during the autopsies of people who have died suddenly [18].

IV. MALIGNANT CARDIAC TUMOURS

A. Angiosarcoma

Angiosarcomas are the most common malignant cardiac tumours, constituting about one third of all primary cardiac neoplasms. The vast majority are located in the right atrium and are mostly seen in men between the third and fifth decades. Cardiac signs such as pericardial effusion, chest pain, and arrhythmias can be seen as well as systemic findings such as weight loss, fatigue and fever. Systemic metastases develop in most patients and the lung is the most common metastatic organ, followed by bone and brain. Local invasion of the epicardium and endocardium, intracavitary extension and local spread to pleura and mediastium are also frequent. Diagnosis is made by echocardiography or MRI showing a right atrial mass. Prognosis is very poor (3–6 months following diagnosis) and there is no effective systemic treatment [18,21].

B. Rhabdomyosarcoma

Rhabdomyosarcomas are rare tumours with nonspecific cardiac symptoms and distal embolisation. These tumours can be bulky but unlike angiosarcomas they rarely infiltrate beyond the parietal pericardium. A good response to chemotherapy is reported in only some cases and survival is quite poor [22].

C. Osteosarcoma

Osteosarcoma constitutes 5–10% of cardiac sarcomas. They are generally located in the left atrium and can grow to large dimensions. These tumours are histologically heterogeneous and fibrosarcoma or malignant fibrous histiocytoma foci can accompany osteosarcoma cells. Cardiac symptoms are the major findings and distant metastases can occur in an important part/occur in a large proportion of the patients. Prognosis is poor [23].

D. Leimyosarcoma

These very rare tumours (<1%) are highly invasive and can cause arrhythmias, atrioventricular blocks, dyspnoea, chest pain, right heart failure and sudden death. They are also usually located in the left atrium and like other sarcomas there is no effective treatment and a poor survival rate [24].

E. Other sarcomas

Fibrosarcomas, liposarcomas, undifferentiated sarcomas and malignant fibrous histiocytomas are the other primary cardiac sarcomas. Fibrosarcomas and histiocytomas can be multiple and characteristically all of them can invade all cardiac chambers and pericardium. Prognoses are poor [24].

F. Treatment strategies for cardiac sarcomas

The outcome of cardiac sarcomas is very poor with a median survival of less than 1 year and long-term survival less than 15% [25]. Since patients who undergo complete excision have the possibility of a cure, the goal of surgery is excision of the tumoural lesion with clear margins. However, this can be achieved only in a small proportion of the tumours because of the anatomical and surgical limitations. In such cases repeated re-excisions in an attempt to control the symptoms of local progression can be made since the efficacy of chemotherapy and radiotherapy in delaying local progression of residual disease is unknown [25,26]. There is limited evidence showing that patients can benefit from cardiac transplantation since even low-grade sarcomas have the potential of early systemic metastasis, so this approach remains controversial.

Postoperative radiotherapy following complete resection has the potential to reduce local recurrence rate, but a radical dose cannot be given to the heart because of the high risk of radiation cardiomyopathy and pericarditis, which can be fatal. Therefore only low dose radiotherapy can be safely used in a pre- or postoperative setting [27].

The use of chemotherapy shows no significant beneficial effect on survival for cardiac sarcomas and can be used only for cyto reduction before surgery or for palliation of unresectable disease [28].
G. Primary cardiac lymphomas

The term primary cardiac lymphoma is used for lymphomas with the absence of disease outside the heart and/or pericardium and the presence of cardiac lymphatic infiltration at the time of initial diagnosis. These tumours have historically been very rare tumours but parallel to the growing incidence of AIDS (acquired immunodeficiency syndrome) and organ transplantations the incidence of cardiac lymphomas has also increased. B-cell lymphomas (follicle centre-cell lymphomas, immunoblastic lymphomas, diffuse large-cell lymphomas, and Burkitt’s lymphoma) are the major histological types and they generally present with arrhythmias, cardiac failure or tamponade. Surgery, chemotherapy and radiotherapy can be used for treatment but the response is limited and the prognosis is poor [29].

V. CARDIAC METASTASES

The incidence of cardiac metastases is about 10% and they are about 20 times more common than primary cardiac neoplasms [30]. However, a large proportion of the metastatic lesions are silent and they are generally found in autopsies. These lesions are usually epicardial but can also be myocardial or endocardial. Malign melanoma is the major tumour that metastasizes to the heart since 50% of melanoma patients are found to have cardiac metastases during the autopsies [31]. Germ cell tumours and malign melanoma also have a high rate of metastasis to the heart. Leukaemias and lymphomas are also commonly associated with cardiac metastasis.

There are four major paths for cardiac metastasis: local invasion (mediastinal tumours such as lung, breast cancer), haematogenous spread, lymphatic spread and extension from the inferior vena cava (renal cell carcinoma) [32].

Metastases to the heart or pericardium from the other common tumours such as lung, breast, colon-rectum, liver or cervix cancers are also rarely reported.

Although the great majority are silent, in some cases pericardial effusion or cardiac tamponade may be the first signs of cardiac metastases. Arrhythmias, tachycardia or heart failure can also develop and in some cases be fatal [33].

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