REVIEW

CARDIAC TUMORS

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Abstract: *Cardiac tumors represent a rare and challenging clinical situation. They can be primary (benign or malignant) or secondary (metastatic). Secondary tumors are more frequent than the primary tumors. Most of the primary cardiac tumors are benign and originate from the endocardium or myocardium, while the metastatic tumors develop from lung, breast, kidney carcinoma, melanoma and lymphoma. The diagnosis of cardiac tumors is often difficult because of their rarity, variety and nonspecific symptoms. The clinical manifestations depend on tumor's size, location, infiltration and consist of four categories: systemic manifestations, cardiac manifestations, embolic events, and metastatic manifestations. Echocardiography represents the main imaging technique used to detect cardiac masses. Computed tomography (CT) and magnetic resonance imaging (MRI) are used to achieve more information about tumor's composition, extension, vascularization, and possibility of surgical treatment. The histological evaluation is necessary for a positive diagnosis and staging of the cardiac tumor. The treatment of cardiac tumors depends on the type of tumor and symptomatology.*

Keywords: cardiac tumors, echocardiography, metastases.

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INTRODUCTION

Cardiac tumors are extremely rare and represent a challenging clinical situation. They are classified in primary and secondary (metastatic). The prevalence of primary cardiac tumors is approx. 0.05% in autopsy series, while the secondary ones are 20-40 times more frequent than primary tumors [1]. 75% of primary tumors are benign (atrial myxoma being the most common) and 25% are malignant (mostly rhabdomyosarcoma) [1]. Usually, primary cardiac tumors originate from the myocardium or endocardium, while the metastatic cardiac tumors originate from lung, breast, kidney carcinoma, melanoma and lymphoma. 15% of patients suffering from a form of cancer develop heart metastases [2].

CLASSIFICATION

I. Primary cardiac tumors

I.1. Benign cardiac tumors

I.1.1 Myxoma

Myxoma represents the most common benign tumor, comprising 25% of all cardiac tumors and 50% of benign cardiac tumors [4]. It affects mostly women aged 30-65 years old. Myxomas have different locations: 75% in the

left atrium (originating from the fossa ovalis), 20% in the right atrium and 5% in the ventricles.

Myxomas may have a familial predisposition and be encountered in younger patients, consequently it is necessary to accomplish the screening of first-degree relatives. The most frequent syndrome is the Carney complex, an autosomal dominant inherited disease in which recurrent cardiac myxomas, extracardiac myxomas (skin, breast), pigmented skin lesions, schwannomas, and endocrine tumors (determining endocrine overactivity-pituitary adenoma, testicular tumors, thyroid adenoma, ovarian cysts) may coexist [5].

Myxomas originate from mesenchymal stem cells and can have a size up to 15cm. Most of them are pediculated and may obstruct the mitral valve, causing valvular dysfunction, while the rest are sessile and broad-based. They have a heterogeneous composition, with hemorrhage, fibrosis, calcification, and necrosis areas.

I.1.2 Papillary fibroelastoma

Papillary fibroelastoma represents the most common valvular tumor, accounting for 75-80% of cases. The papillomas appear frequently on the left heart and are small in diameter. They resemble 'sea anemonas' as they have a short pedicle arising from a central core [6]. They don't cause valvular dysfunction but have a high risk of cerebral and coronary arteries embolization, surgical resection being considered mandatory [7].

I.1.3 Rhabdomyoma

Rhabdomyoma represents the most frequent cardiac tumor in children, especially in those with tuberous sclerosis [1]. Rhabdomyomas are usually multiple, and they affect both ventricles, causing obstructive complications and arrhythmias. Sometimes, they regress spontaneously with age and treatment is usually conservative [8].

I.1.4 Fibroma

Fibroma represents the second most frequent cardiac tumor in children, even though it can also affect adults. Fibromas originate on the left side of the heart, mainly in the ventricular septum. They can constrain the conduction system, resulting in arrhythmias and sudden death. Sometimes, fibroma can be a part of a syndrome which associates generalized body overgrowth, skeletal abnormalities, and different benign and malignant tumors [1].

I.1.5 Lipomas and Lipomateous Hypertrophy of the Interatrial Septum

Lipomas represent the second most common primary tumor. They are located in the left ventricle, right atrium and interatrial septum. Many are asymptomatic, but some of them can determine conduction system disturbances, arrhythmias, and heart failure [9]. Lipomatous hypertrophy of the interatrial septum represents the accumulation of adipose tissue in the interatrial septum and affects the elderly and obese male patients [10].

I.1.6 Other primary benign tumors - angiomas, teratomas, mesotheliomas, paragangliomas are rare and affect children. Teratomas appear in the anterior mediastinum and determine constrictive pericarditis [2].

I.2. Malignant tumors

I.2.1 Sarcomas

Sarcoma represents the most frequent malignant cardiac tumor. It affects adults aged between 40-50 years old. 40% of them are angiosarcomas and originate in the right atrium and 60% are represented by rhabdomyosarcoma, leiomyosarcoma, fibrosarcoma, liposarcoma, which originate in the left atrium [11]. Angiosarcomas appears especially in men. Clinically, patients have signs of cardiac failure, pericardial effusion, and chest pain. They frequently extend to epicardium, endocardium and intracavitary, pleura or mediastinum. Pulmonary metastases are common, and the prognosis is unfavorable [12].

Rhabdomyosarcomas are more common in men. They are characterized by the occurrence of non-specific signs and symptoms and, in comparison with

angiosarcoma, rhabdomyosarcomas rarely invade across the parietal pericardium. The prognosis is poor [13].

I.2.2 Pericardial mesothelioma is extremely rare. It affects especially men of all ages. It can determine cardiac tamponade and spinal and brain metastasis [2].

I.2.3 Primary lymphoma occurs in patients with immunodeficiency or HIV/AIDS. They cause heart failure, cardiac tamponade, arrhythmias, and superior vena cava syndrome [2].

II. Secondary (metastatic) cardiac tumors

Metastatic cardiac tumors are 30-40% more frequent than primary cardiac tumors. They originate from melanomas, lymphomas, lung, breast, and renal cancer [14]. Metastases develop via blood dissemination, direct extension, or propagation via superior or inferior vena cava to the right atrium.

The most affected structure is the pericardium, resulting in pericardial effusion which sometimes consists of cancer cells, blood clots or fibrin. The occurrence of heart failure, arrhythmias, and cardiomegaly in a patient with malignant disease should raise the suspicion of cardiac metastases. However, cardiac metastases are clinically silent in 90% of cases [15].

Some studies showed that melanoma has a propensity for heart metastases, affecting all four chambers. Leukaemias and lymphomas regularly invade the heart, creating intramyocardial masses [16].

POSITIVE DIAGNOSIS

The diagnosis of cardiac tumors often represents a challenge because of their rarity, variety and nonspecific symptoms. Patient's history and clinical examination rarely lead to direct diagnosis. Paraclinical criterias (electrocardiography, laboratory, echocardiography, angiography, cardiac MRI, scintigraphy) are necessary, but histological evaluation via biopsy is essential for the final diagnosis [1].

CLINICAL DIAGNOSIS

Systemic manifestations and cardiac manifestations, embolic events and metastatic manifestations are part of the clinical diagnosis.

1.Systemic manifestations are represented by fever, fatigue, rush and Raynaud syndrome, resembling vasculitis or other connective tissue disease. These symptoms are determined by the secretion of interleukin 6 and endothelin from tumor cells [1].

2. Cardiac manifestations depend on the location of the tumor, its size and the extension on adjacent tissues. Cardiac manifestations are frequently caused by obstructive mechanism of heart chambers or valves (with valvular dysfunction), compression of coronary arteries, compression of conduction system and pericardial effusion.

On one hand, intramural tumors cause insignificant cardiac manifestations. If these tumors are small in diameter, they can be clinically silent, while if they are large in size, they can determine obstruction of the coronary flow or compression of cardiac chambers.

On the other hand, intracardiac tumors produce important signs and symptoms. Myxomas can determine the triad of heart failure, embolic events and systemic symptoms. Myxomas located in the left atrium cause mitral valve obstruction (via mitral prolapse) and, consecutively, specific signs and symptoms as syncope, dyspnea and a diastolic murmur that resembles the mitral stenosis murmur.

Tumors located in the right atrium produce clinical manifestations of right-sided heart failure.

Fibroelastoma is asymptomatic, but it can be a source of systemic emboli. Rhabdomyomas are asymptomatic. Fibromas can cause arrhythmias. Sarcomas cause obstruction of coronary flow and tamponade. Teratomas cause respiratory disease and cyanosis because of aorta and pulmonary artery compression [2].

3. Embolic events occur due to the capacity of embolization of tumor cells or thrombi formed on the tumor area. The risk of

embolization depends on type of tumor, location, and consistency. The highest risk is presented by the small tumors with friable surface [2].

4. Metastatic manifestations. The metastases are usually localized in the pericardium, determining pericardial effusion, constrictive pericarditis, tamponade, arrhythmias and sudden cardiac death [17]. Cardiac manifestations in a patient suffering from neoplasia are usually correlated to cardiotoxicity induced by chemotherapy or occurrence of cardiac metastases.

PARACLINICAL DIAGNOSIS

- **Imaging techniques** are used to determine the presence of the tumor and for differential diagnosis with thrombi and vegetations. They are represented by echocardiography, computed tomography (CT) and magnetic resonance imaging (MRI).
  1. **Echocardiography** represents the most used technique for detecting cardiac function, chambers' dimensions and possible cardiac masses, as it can be easily performed at the patient's bedside [18]. Transthoracic echocardiography (TTE) can evaluate the location, size, shape, mobility and extent to other cardiac structures [19][20]. TEE can identify small tumors (<5mm) and tumors localized in the posterior cardiac segments [21]. Moreover, when the transthoracic image is difficult, TEE can be used to achieve clear information about the nature of the tumor and its consequences on cardiac function [22].

     Malignant tumors are extremely vascularized, and they appear with higher accumulation on echocardiography when contrast is administered, leading to a clearer diagnosis. In comparison, benign tumors are less vascularized, the administration of contrast does not give a clear image of the origin of the tumor and, consequently, it can be difficult to differentiate them from thrombi [23].
  2. **CT** is less efficient compared to MRI, but it can provide useful information about the nature of the tumor by measuring X-ray attenuation and tumor extension to other cardiac structures. Multidetector CT can evaluate the grade of calcification of the mass tumor, define small lesions and is needed for staging of malignant tumors [24].
  3. **MRI** represents the most useful tool in detecting and diagnosing cardiac tumors. MRI can evaluate the extension to cardiac structures, its hemodynamic consequences and the possibility of a surgical intervention. It can also describe the content of the tumor by studying the signal in T1, T2-weighted images and help in differential diagnosis with thrombi by administering contrast [25]. Hence, MRI is capable of rapid acquisition of heart images with very high spatial and temporal acquisition and superior cardiac tissue description [26].
- **Histology.** The histopathological evaluation is necessary for a positive diagnosis and staging the cardiac tumors. This can be determined by using the cytological exam of pericardial or pleural fluid, percutaneous/transvenous cardiac biopsy conducted by echocardiography or via thoracoscopy/thoracotomy.

TREATMENT

1. **Benign tumors.** The treatment of benign primary tumors is surgical resection, followed by echocardiographic monitorization over 5-7 years. Surgical excision is curative, with 95% survival in 3 years [2].

   Myxomas have a high indication of surgical resection because of the risk of embolic events. However, rhabdomyomas do not require surgical excision, as they regress spontaneously.

   In case of large (>1cm) or mobile tumors, papillary fibroelastomas are surgically removed, while conservative treatment is preferred in small, immobile tumors, even though these

masses have a high risk of embolization [1].

Lipomas and lipomatous hypertrophy of interatrial septum are surgically removed in case of hemodynamic instability [27][28].

2. **Malignant tumors.** Treatment of malignant primary tumors is usually palliative (radiotherapy, chemotherapy, management of complications), as the prognosis is poor.
3. **Metastatic cardiac tumors.** The treatment of metastatic cardiac tumors depends on tumor's origin. It requires management of the primary tumor and control of the cardiovascular complications (chemotherapy, palliation, pericardiocentesis) [2][28].

CONCLUSIONS

In conclusion, a proper diagnosis of cardiac tumors is essential in order to initiate an appropriate treatment. Imaging techniques such as echocardiography, CT, MRI may increase the sensitivity and specificity for characterizing the lesions. However, a gold standard positive diagnosis requires histopathological examination for establishing the most appropriate treatment and prognosis.

Author Contributions:

L.B.G. conceived the original draft preparation. L.B.G. and C.D. were responsible for conception and design of the review. L.B.G. and C.D. were responsible for the data acquisition. L.B.G, was responsible for the collection and assembly of the articles/published data, and their inclusion and interpretation in this review. L.B.G. and C.D. contributed equally to the present work. All authors contributed to the critical revision of the manuscript for valuable intellectual content. All authors have read and agreed with the final version of the manuscript.

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