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Primary and Secondary Malignant Cardiac Tumors Overview

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Review Article

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Abstract: Cardiac tumors are massively uncommon disease, only seven instances of primary cardiac tumor found between more than 12,000 dissections. Cardiac tumors are proliferated in the heart or heart valves. Cardiac tumors may be primary (benign or malignant) or metastatic (secondary, malignant). Cardiac tumors may happen in any heart tissue. Primary tumorsstart growing in the heart, other side the secondary tumors begin in another part of the body and move to the heart (metastasize). Primary tumors influence just one out of 1,000 to 100,000 individuals. The most widely recognized sort of primary heart tumor is myxoma, the greater part of these are benign. In most cases, the tumor develops in the left upper chamber of the heart (left atrium) at the atrial septum, which isolates the two upper chambers of the heart. Successful treatment for benign cardiac tumors is typically proficient by surgery. Primary sarcomas of the heart are to a great degree uncommon, while secondary cardiac contribution inferable from malignancy is relatively common, particularly in the setting of across the board metastatic disease. Malignant primary tumors incorporate pericardial mesothelioma, primary lymphoma and sarcoma. Tumors that metastasize to the heart from different organs happen 100-to 1000-cases more commonly than primary cardiac tumors. Metastatic spread to the heart has been distinguished in approximately one-fifth of all patients who have metastatic disease with lung carcinoma being the most common primary tumor. Successful treatment for primary malignant tumors is normally accomplished by Surgery, notwithstanding, secondary tumors less effective as total resection is ordinarily not possible. Primary cardiac lymphoma might be effectively treated by chemotherapy.

Keywords: cardiac tumor, primary cardiac tumor, secondary cardiac tumor, and cardiac sarcoma.

INTRODUCTION

Being rare, primary cardiac tumors are about 0.02 % among population after revision of 22 large autopsy successions [1].

The primitive cardiac tumors to drop with age. It is 51.2% in age less than 64 years versus 26.7% in patients more than 85 years, in addition the cardiac metastases in patients less than 64 years are 16.8% and 4.9% in patients more than 85 years [2]. Young patient population mostly are attacked by malignant primary cardiac tumors that have bad prognosis specially without involving surgery, 10% only of the population has survival rate at 9 to 12 months 10% [3].

Benign primary cardiac tumors are about 75% and 50% of this are mostly myxomas [4]. Malignant cardiac tumors forms 25% of primary cardiac tumors and 75% of these malignant tumors are sarcomas.

Secondary cardiac tumor does not initiate in the heart but the tumor is transferred to the heart from any other part all over the body such as lungs, breasts, stomach, kidneys, liver or colon and settle in the heart. Secondary cardiac tumors are more common than primary cardiac tumors. Metastasis to the heart from other primary cancers is 30 times more common [5].

Primary cardiac tumor

Primary cardiac tumors have unreliable incidence [6, 7]. Malignant tumors account for approximately 25% of primary cardiac neoplasms, and these are predominantly various forms of sarcoma. Cardiac sarcomas are usually poorly differentiated and this often makes precise histologic classification extremely difficult. The most common sarcomas are tumors of vascular origin, in particular angiosarcoma, 33% some other types of sarcoma as rhabdomyosarcomas 20%, 10% fibrosarcomas,, leiomyosarcoma and liposarcoma [8, 9]. However, all varieties of bony, neurogenic, and soft tissue sarcomas have been reported to arise from cardiac tissue [10]. In addition, anecdotal reports of primary Iymphoma [11], plasmacytoma [12], pericardial mesothelioma, and malignant mesenchymoma [13] are available.

The inconsistent frequency of noticed serial deviations in the electrocardiograms of cancer patients may push physicians think about the medical and postmortum data of cancer deaths perceived in all cancer patient. The struggles in diagnosis of cardiac carcinoma may lead to change the percentage of discovering new cases of cardiac carcinoma.

Rarity of primary cardiac carcinoma

Presentation of primary cardiac tumor frequently is broad, patients may accompany appalling hemodynamic instability, and cannot have the accurate diagnosis of primary cardiac tumor, further clarification; it is misdiagnosed [14]. The right atrium is found to be the main site of malignant primary cardiac sarcomas and angiosarcomas is the most common type of cardiac sarcoma tumors ,nevertheless the left atrium, is the most common site for malignant tumors pleomorphic sarcoma that known as by malignant fibrous histiocytoma and leiomyosarcoma [15].

Another reason of cardiac carcinoma rarity is the difficulty of cardiac DNA mutation. To explain in more details, Principally, cancer has uncontrolled cell proliferation that can happen by mutations in genes that endorse the proliferation, named oncogenes, or another mutation in genes that hinder cell proliferation, named tumor suppressor genes, the cell proliferated for the error to be carried to its progeny, generally, pledges suicide by programmed cell death mechanism, if this is not happened, the defect will be carried to daughter cells and, over the time the number of diverse mutations will build up, finally the cancer will perform by these mutations [16]. This elucidation expresses, that the mutation will take a long time to be formed. The additional point that noticed is that cancers are more common in tissues that has a high rate of proliferation that will give a big chances for errors like bone marrow , skin, and the lining of the gut ,otherwise, the tissues that have a higher incidence that handle or sensitive to the toxins like kidneys, bladder, liver, etc) [17].

On the other hand, the cardiac muscle cells have insignificant ability for proliferation. That elucidated that why any defacement in the heart could not restore spontaneously. Consequently, fortunately, mutations in a cardiac DNA of the cell probably remain in that cell. For instance, the genetic imperfection does not habitually mobile to daughter cells, so the result is no cancer cells formed [18]. Dissimilar other damaged organs; the heart seems mostly unable of fixing injured tissue. Moreover, as stated by main cardiac researchers, for the reason that the cells that compose the muscle itself, cardiac myocytes, are terminally differentiated [7].

In other words, these cardiac cells have their specific end point that happens very early in a person's life at this end point the cardiac cell cycle stop dividing. After that, progress growth to form tumor occurs by enlargement in cell size, not over cell division, so the cardiac tumor mostly is not related to the number of cardiac cells but the size of the cardiac cell ,that may explain why no clear symptoms appear with primary cardiac carcinoma [3, 18-22].

Secondary cardiac carcinoma

Metastasis into the heart are rare and most of the cases are diagnosed postmortem during autopsy [23]. Less than 4% is the incidence of cardiac metastases in patients who died of cancer as per autopsy [5]. The affection of the heart by metastatis was found in 292 cases among 7767 cancer died patients [5]. Cardiac metastatis was found in 44% of patients who died of leukemia, in 33% of patients with breast cancer, in 44% of patients with malignant melanoma , in 31% of patients with carcinoma of the lung, and in 24% of patients with lymphoma [5].

Melanoma is a tumor with a high propensity for cardiac involvement. Lung and breast carcinoma, soft-tissue sarcoma, and renal cancer are also common sources of metastases to the heart [1, 2]. Leukemia and lymphoma often metastasize to the heart, but cardiac involvement is often clinically silent and detected incidentally. When Kaposi sarcoma spreads systemically in immunodeficient (usually AIDS) patients, it may spread to the heart, but clinical cardiac complications are uncommon [24].

Secondary cardiac metastases may be unnoticed in the assortment of clinical presentation that will be affiliated with widespread metastases. For all previous no real number of the actual primary cardiac tumors cases was reported [24].

Rarity of secondary cardiac carcinoma

The rarity of cardiac metastatic disease is affected much by running of the lymphatic system. The structure of the lymphatic system is differing from the heart and other organs like lung, brain and bone so the heart may elucidate the comparatively low incidence of secondary tumors than other organs [25]. There are two causes may inhibit formation of secondary cardiac tumors the first is intramural lymphatics, when the intramural lymphatics are obstructed by metastases from other organs , lymph will lie dormant in the myocardial regions upstream of the obstruction and endocardial to epicardial drainage by the lymphatics will be inhibited. This leads to tissue damage due to lymph stasis and oedema, and favors increased proliferation of neoplastic cells in the undrained regions and retrograde lymph flow, which might disseminate metastases to the more internal areas this, will inhibit formation of secondary cardiac tumor. Second cause

may be due to increasing the pressure, the lymphatic wall may also interrupt, causing at the end spreading of interstitial tumor [26].

Etiology and risk factors

Many internal and external factors can cause the cardiac tumors. The abnormal regulations of DNA as an example of internal factor lead to cardiac abnormality. Genetic Inherited reason may be one of the internal reasons like myxomas (benign primary tumor) about ten percent of all primary heart tumors are genetically inherited [27]. The cardiac tumors (myxomas) sometimes associate another disease such as in NAME Syndrome, LAMB Syndrome or Carney Syndrome [7].

External factors like radiation, tobacco, poisonous mushrooms, certain viruses, extreme exposure to the sun, and benzene can be a reason for cardiac tumors [7].

Cardiac metastases is another cause of cardiac tumor from another organ to any part of the heart as myocardium, endocardium, pericardium, epicardium, great vessels or coronary arteries are cardiac metastatic tumor, and also tumors in the heart cavities or producing intracavitary neoplastic thrombi [2]. Tumors can extend to the heart itself or heart components through four paths by direct invasion of the other tumor like lung or liver, through the transference of tumor cells through bloodstream, through lymphatic system and even by intracavitary extent through either the inferior vena cava or the pulmonary veins [2].

Signs and symptoms

Generally patients with cardiac tumors present with nonspecific symptoms depending on the site of the tumor and the extent of spread into the adjacent tissue [28].

The symptom presentation of primary cardiac tumor is somewhat diverse; the symptoms are depending on the tumor location and its size, more than the histologic characteristics of the tumors. The symptoms mostly are systemic embolization, congestive heart failure from obstructed heart, arrhythmias and constitutional symptoms. Left atrial sarcomas tends to be more solid and little invasive than right-sided ones; subsequently, the metastases stage will be later. The patient generally comes with symptoms of blood stream obstruction and fatal congestive heart failure. Right-sided cardiac tumors are mainly big malignant tumor and the infiltrative masses tend to grow outwards. Right-sided cardiac tumors are generally fast-growing tumors and its metastatic stage start early and unusually present with congestive heart failure until late stage of the disease [29].

The common symptoms of patient with lung or breast cancer are presenting in clinic with increasing dyspnoea, tachycardia and shock and mostly it will be cardiac tamponade [30]. The most feared complication is neoplastic pericardial effusions, that is often the main cause of death [2].

The first manifestation of a cardiac metastasis is haemorrhagic [31]. In secondary tumors located in the myocardium, the most common symptoms are dysrrhythmias, for example premature beats or ventricular arrhythmias, atrial flutter or fibrillation, conduction abnormalities and complete heart block, particularly if the conduction system of the heart has been involved [32]. In case of ventricular invasion, the presentation may include diastolic or systolic heart failure. Electrocardiographic abnormalities are very frequent in cardiac metastasis [33].

Diagnosis of cardiac tumor

Primary cardiac tumors are rare, whereas metastases to the heart are more frequent. Clinical symptoms are varied, non-specific, and depends on the location, size, and spread of the tumor. Radiology is essential in their evaluation, and studying characteristic features is primary to generate a differential diagnosis. Radiology imaging is a fundamental step in the diagnosis of alleged cardiac tumor. Echocardiography is best technique for initial diagnosis of cardiac malignancy, but for assessment of the tumor and its spread using CT and MRI is essential when curative management is anticipated.

Cardiac magnetic resonance imaging (MRI) has become the diagnostic tool for evaluation of a suspected cardiac tumor. Computed tomography (CT) provides additional information and, with electrocardiographic gating, has become a useful tool for cardiac morphological assessment [34]. The reference techniques for evaluating the lesion extent and morphology is the cardiac magnetic resonance (CMR) together with multidetector computed tomography (CT), which has an developing role for cardiac tumor assessment specially for detecting calcification [14].

In primary tumor**,** the key for early diagnosis is using multiple imaging techniques as cardiac magnetic resonance (CMR), echocardiography, three-dimensional (3-D) transthoracic echocardiography (TTE), PET, and cardiac computed tomography (CT) [34]. Three-dimensional (3-D) TTE has more advantages than 2-D TTE in imaging cardiac tumors by assissing complete volumes, live 3-D images, and 3-D zoom images. Three-dimensional TTE is the tool of choice in evaluating cardiac tumor volume [35, 36]. Three-dimensional TTE reveals clear data about the type of tumor and site, surface morphology, and the tumor's spatial relation to surrounding tissues For

prognosis we need to assess the size of the intracardiac tumor, the tumor mobility (an indicator of prognosis and embolic probability), cardiac chamber location and myocardial invasion [34].

Left ventricular ejection fraction, and the affected chamber anatomy give the surgeon important data about the relationship of the tumor with adjacent structures [37].

Cardiac magnetic resonance (CMR) can detect in height specificity, cardiac masses which do not need surgical insertion elimination like thrombi, lipomatous hypertrophy, lipomas, pseudotumors, and fibroelastomas. Moreover, the establishment of cardiac tumors treatment needs tissue diagnosis [34, 38].

The recommended technique for imaging of cardiac tumors is multiple-technique approach, cardiac CT, 3-D TTE, CMR, and positron emission tomography (PET). If there is a mass inside the heart, baseline CMR for tissue characterization and 3-D TTE, with serial CMR every 2 - 3 months for staging and following up the tumor growth are recommended. The lung is the most common area of metastases to the heart so CT of the thorax with contrast must also be done every 3 months for monitoring lung metastasis. Work up should be done for diagnosis of primary cardiac tumor, exclusion of benign cardiac tumors and diagnosis of other malignant tumors, like lymphoma, which is best, treated mostly with chemotherapy. A definitive biopsy is best obtained if CMR and TTE fail to assess the cardiac mass [3].

Prognosis

The prognosis after surgery of benign tumors is usually excellent but is still limited in localized malignant tumors. Sarcoma Patients live up to 3 months to 1 year, and patients with lymphomas live for a mean of 5 years if treated, but will die usually within 1 month if untreated. Clinical presentation may range from sudden death, cardiac arrhythmias and congestive heart failure to valve obstruction or embolization [24]. The histopathologic cell type affects the treatment options or prognosis significantly [39].

Treatment

There is no clear evidence base to decide regarding the optimal treatment, particularly for malignant tumors [28]. As cardiac tumors can affect blood flow, surgical excision of the tumor is usually the treatment of choice. Decision of surgery depends on size of the tumor, symptoms, and general condition of the patient.

The best treatment of malignant cardiac tumor is the surgical intervention in combination with systemic chemotherapy. Because of the tumor's extensive involvement of cardiac structures mostly has been found, this become challenge for surgeon and make the cardiac surgical intervention is more difficult. The resection of left atrial sarcomas and pulmonary artery sarcomas has some benefit in survival however resection of right atrial sarcomas has not shown any benefit in overall survival. Improved survival rates were experimental in patients when negative surgical margins were achieved in right-sided surgery [39-42]. In a retrospective review by Reardon *et el*., [3] 54 sarcoma patients who had extensive resection of the right atrium with bovine pericardial reconstruction, they reported a 30-day mortality rate of 9%, with a survival advantage for patients with negative surgical margins. The overall 5-year survival rate was 17% and the median overall survival duration was 9 months. Cardio metastatic disease remains the challenge in malignant disease specially surgical techniques [3]. After surgery, serial echocardiography every year is needed to rule out recurrence of the disease [21].

SUMMARY

Primary cardiac tumors are rare and lack medical experience in dealing with. Diagnosis of cardiac tumors becomes more easier due to the progress in imaging techniques and early detection of the tumors [43]. Advanced imaging has an important role in describing the site of a tumor and its overall characteristics. Imaging can determine also the type of tumor whether it is benign or malignant, and the content tumors of fat tissue, fibrous elemnts and vascularity. Thus, the surgeon will have a good image about the tumor that will be resected. Malignant tumors have a poorer prognosis but can be early. The symptoms of cardiac tumors include sudden death, cardiac arrhythmias, and congestive heart failure to valve obstruction or embolization [17].

Secondary cardiac tumors are common in patients with metastatic tumor disease, making up to one-quarter of them. Usually, secondary cardiac tumors remain silent. However, echocardiography should be performed with symptoms of angina pectoris, heart failure, embolism or dysrhythia, or a new heart murmur becomes audible, or with cardiomegaly [24]. The treatment of primary cardiac tumor will be early surgical intervention and systemic chemotherapy [3]. Treatment of metastatic cancer depends on tumor character and origin but prognosis is generally poor [24].

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