Case Series
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Intracardiac Extension of Malignant Tumors: A Case Series with Seven Cases

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Abstract

Despite its scarcity, malignant tumor extending to the heart is a lethal condition. Cardiac metastases are considered to occur rarely. In the present paper, we represented a single-center experience in cardiac metastases diagnosis in addition to different treatment modalities for improving the patients' quality of life and survival. We could claim that this is the largest report of this kind to date. We retrospectively reviewed the patients' files in our hospital, from 2009 to 2022. These patients presented with radiological/ intraoperative evidence of intracardiac extension of malignant tumor. Seven patients with transvenous intracardiac tumor extension were referred to our center. There was primary tumor in the lung in four cases (57.14%), two with synovial sarcoma (14.3%), one with renal cell carcinoma with inferior vena cava extension to the right atrium, and one with osteosarcoma. Moreover, there was one case of thymic origin (14.3%). Four patients underwent urgent surgery upon diagnosis, in order to have higher quality of life, and R0 resection which was not possible in any of them (two patients had R1 and two had R2). Among them, one received palliative chemotherapy followed by chemoradiation after debulking surgery, one received concurrent chemoradiotherapy, one received palliative chemotherapy only, and one refused to get any treatment. Survival was better in the patients who received concurrent chemoradiotherapy. According to our results, urgent/unplanned surgery could not be a good candidate for intracardiac extension of malignant tumors and does not improve survival. Combined multidisciplinary approach, on the other hand, was found to be a better option for disease control.

Keywords: Heart atria, Lung, Quality of life, Cytoreductive surgical procedures

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Introduction

Malignant tumors extending to the heart are known as a challenging medical condition regarding presentation, diagnosis, and eventually treatment, with poor

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outcomes. This may be partially due to the discrete data regarding diagnosis and pool of patients across the globe. Malignant tumor extension to the heart may be hematogenous, lymphatic, by direct tumor extension, or by intracavitary diffusion through either the inferior vena cava or the pulmonary veins. A study showed the incidence of this condition to range between 2.3 and 18.3%.[1] Most malignant neoplasm can spread to the heart wherein the tumors with the highest rate of cardiac metastases are pleural mesothelioma (48.4%), melanoma (27.8%), lung adenocarcinoma (21%), undifferentiated carcinomas (19.5%), and lung squamous cell carcinoma (18.2%).

Regarding the treatment, there are no specific guidelines. The literature review mostly relies on case reports of sporadic cases with heterogenous treatment strategies due to its rare occurrence and the large spectrum of presentations and staging of these patients at the time of diagnosis. In our case series, we reviewed our 10-year experience of cases with direct extension.

In the present work, we retrospectively reviewed the patient files in our university hospital, from 2009 to 2022, who referred to the Clinical Oncology Department, Cardiothoracic Surgery Department, and Radiation Oncology Department, with radiological/intraoperative evidence of intracardiac extension of a malignant tumor. The patients' age, gender, performance status, primary tumor type and site, clinical presentation, and therapy data were documented and analyzed. Additionally, we recorded all the radiological imagings, laboratory tests, and histopathological analyses, and reviewed all the therapy data.

Case Presentation

Seven patients with transvenous intracardiac tumor extension referred to our center. Their age, gender, performance status, primary tumor type and site, clinical presentation, and any therapy data were reviewed, as displayed in table1. Our sample included five males and two females with a median age of 39 years (32-72). The primary tumor site was the lung in four cases (57.14%), while two cases represented synovial sarcoma, one renal cell carcinoma with inferior vena cava extension to the right atrium, one osteosarcoma, and one case showed thymic origin (14.3%).

Four patients received urgent surgery upon diagnosis, to have higher quality of life, and R0 resection, which was not possible in any of them (two patients had R1, while two had R2.); one received palliative chemotherapy, followed by chemoradiation after debulking surgery, one had concurrent chemoradiotherapy, one received palliative chemotherapy only, and one refused to get any treatment.

Four patients had upfront surgery through cardiopulmonary bypass (two patients had R1, whereas two had R2) for different reasons; one of them had acute ischemic mitral regurgitation, a concomitant open-heart surgery, and mitral valve replacement together with tumor excision, which were discovered on routine preoperative work-up; two of them presented with acute lower limb ischemia due to tumor showering, which the surgery aimed to control; one patient was diagnosed with complex septated effusion and was intraoperatively discovered that this effusion was a mass with central necrosis extending to the left atrium through the superior pulmonary vein, whose computed tomography (CT) scan is illustrated in figure 1. Extrapleural

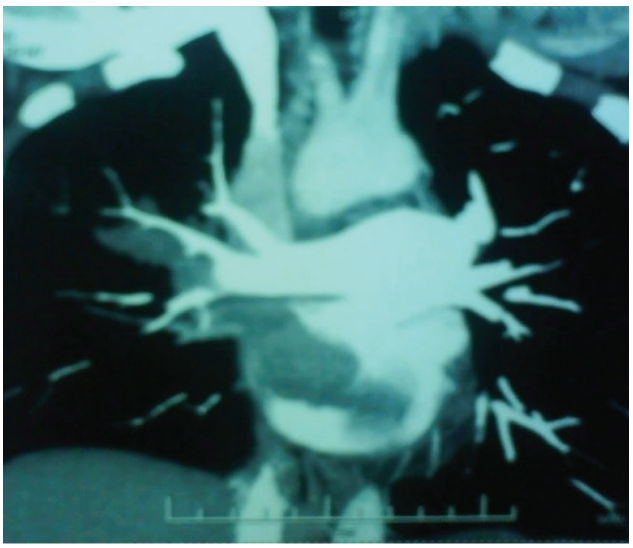

Figure 1. CT scan of a 40-year-old lady who presented with lower limb ischemia. CT scan shows the right upper lobe mass extending to the left atrium through the superior pulmonary vein proven histologically to be synovial sarcoma.
CT: Computed tomography

Table 1. Summary of the presentation, management plan, and outcome of the patients with intracardiac extension of malignant tumors

Age	Presentation	Tumor type	Origin	Route of entry	Surgery	Chemotherapy	Radiotherapy	Outcome
70	Lower limb ischemia	Squamous cell carcinoma	Lung	Superior pulmonary vein	Extra pleural pneumonectomy on CPB	No	No	Died on the 8th postoperative day of pulmonary embolism
42	Hemoptysis	Squamous cell carcinoma	Lung	Inferior pulmonary vein	-	-	-	The patient refused all interventions and was lost in the follow-up
39	Dyspnea, diagnosed as encysted effusion	Synovial sarcoma	Lung	Inferior Pulmonary vein	Debulking of the intrathoracic part	Palliative chemotherapy -	Concurrent chemoradiation -	4 months
40	Lower limb ischemia	Synovial sarcoma	Lung	Superior pulmonary vein	Open heart surgery removing only the intracardiac part			Died on the 14th days postoperative with ARDS
42	Hematuria	Renal cell carcinoma	Kidney	IVC	-	Palliative Chemotherapy		8 months
70	Discovered accidentally on routine preoperative workup	Osteosarcoma	Lung metastasis	Pulmonary vein	Open heart surgery with en-bloc removal of tumor + mitral valve replacement	-	-	Died intraoperative due to uncontrolled bleeding from the tumor site
57	Dyspnea and buffy face	Undifferentiated squamous cell carcinoma	Thymus	SVC	-	Palliative chemotherapy (Paclitaxel Carboplatin)	Concurrent chemoradiation	Alive 1 year post-chemotherapy developed brain metastasis, and died at 18 months due to COVID-19

CPB: Cardiopulmonary bypass; ARDS: Acute respiratory distress syndrome; IVC: Inferior vena cava; SVC: Superior vena cava

pneumonectomy surgery was done with intrapericardial control for the first case (R1), while for the other cases, resection of the intracardiac part that showers malignant emboli was performed. For the last case (R2), we carried out debulking for the intrathoracic part.

Among the patients who did not receive any surgical treatment, one had thymic undifferentiated squamous cell carcinoma that directly infiltrate superior vena cava (SVC) and extended to the right atrium; figure 2 depicts the CT scan for this patient. The patient received urgent chemotherapy dose-dense paclitaxel carboplatin. There was gradual improvement in the symptoms for two cycles, and once orthopnea disappeared, she was shifted to concurrent chemoradiotherapy 45 Gy in 25 fractions via 3D conformal technique concurrently with Taxol 50 mg/m^2. The gross target volume (GTV) includes the mass plus the thrombus with respect to the tolerability of the lung and heart. One month after the radiotherapy, a CT assessment revealed a partial response. One patient had lung cancer that extend intracardiac through the inferior pulmonary vein, who received palliative chemotherapy followed by concurrent chemoradiation after debulking surgery of the intrathoracic part. Another one had renal cell carcinoma extending to the right atrium through inferior vena cava (IVC) and received palliative chemotherapy. Furthermore, there was a case who refused to get any treatment. Survival was better in those receiving concurrent chemoradiation.

Ethics approval

The Ethical Committee of the Faculty of Medicine, Assiut University, approved the study protocol. The research was conducted in accordance with the provisions of the Declaration of Helsinki (IRB no.17300533).

Discussion

The prevalence of heart involvement with neoplastic lesions during autopsy ranges between

2 and 20% of all the patients dying of malignancy.[2] Invasion of pulmonary veins by a primary lung tumor is not uncommon. In principle, every malignant tumor can metastasize to the heart. To date, only tumors of the central nervous system have not been proven to develop cardiac metastases. Secondary tumors of the heart and pericardium are much more common than primary ones, with at least 100 times higher rate of incidence than primary tumors of the heart.

Secondary intracardiac neoplasms frequently arise from renal cell carcinoma, bronchogenic carcinoma, Wilms' tumor, chondrosarcoma, and osteogenic sarcoma. Some intra-abdominal, retroperitoneal, or intrathoracic tumors extend into the vena cava from the drainage vein, which rarely grow into the right atrium or right ventricle through the bloodstream. Approximately 0.7%-1% of cases with abdominal tumors formed in IVC lumen and spread into the heart have been identified as renal carcinomas. These tumors are a serious risk factor for pulmonary embolism and sudden death when they reach the right atrium and tricuspid valve.[3]

Tumor infiltration of great vessels is not uncommon; that said, several instances of primary pulmonary malignancies with the intra-left atrial extension via the pulmonary vein have been reported. Primary pulmonary malignancies with the invasion of the pulmonary veins and left atrium (LA) frequently occur in non-small cell lung carcinoma, but have been also reported in primary pulmonary sarcoma. Metastases to the heart occur in approximately 15% of all sarcomas. Nonetheless, metastases to the heart and pericardium are generally associated with a poor prognosis. In our study, we had two cases of primary squamous cell carcinoma with direct extension to the left atrium through the pulmonary veins; one case had surgery, and unfortunately, the other patient refused to get any treatment modality and was lost in the follow-up. We keep this case in this series to highlight the significance of patients' wishes when dealing with such advanced-stage tumors. The other two patients had synovial sarcoma, one of whom was treated with concurrent chemoradiotherapy, and the other had surgery and died on the 14th day postoperative.

In this retrospective study, the decision to do upfront surgery or start with chemoradiotherapy was made by a multidiscrepancy team, considering the patient's condition, presentation, and choice. There is no standard treatment yet; the therapy generally consists of primary tumor treatment or palliative care. Surgical treatment, however, seems to be a better option when obstruction symptoms overcome the risk of surgical treatment or medical therapy alone. Other criteria for choosing a surgical treatment could be a preoperative Karnofsky performance status of 80% retrieved in the patients considered, minimal extracardiac disease, or a deteriorating clinical picture due to cardiac symptoms. Previous embolic events, syncopal attacks, and echocardiographic evidence of a multilobulated mass indicate the necessity of urgent surgery.

Surgery is indicated in patients with primary cardiac tumors, but there has been no standard treatment for cardiac metastases so far. Surgery is recommended for treatment in early pre-symptomatic cases; in this case, the treatment would not be just palliative, but curative, leading

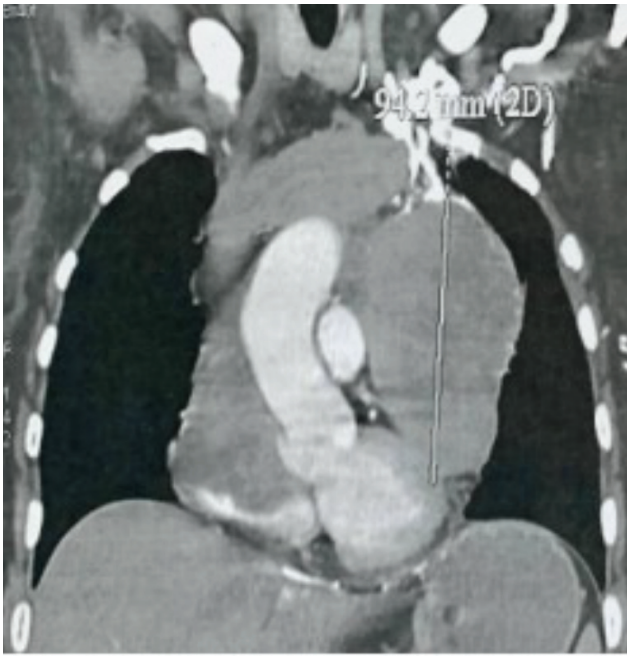

Figure 2. CT scan of a 57-year-old lady who presented with buffy face showing malignant thymoma invading the SVC with propagating thrombus to the right atrium.
CT: Computed tomography; SVC: Superior vena cava

to a complete recovery in most patients. Surgical treatment aims to prevent metastasis complications, such as SVC syndrome, dysrhythmia, cardiac tamponade, heart failure, ventricular obstruction, and embolism; these complications could lead to severe impairment of the general clinical condition. A better outcome is acquired, if there are no signs of valve obstruction, ventricular inflow, or outflow obstruction. Additionally, provided that ventricular function is preserved, a more desirable outcome would be achieved. Surgery is also recommended when important symptoms of obstruction outweigh the mortality risk of operating and the benefit of medical therapy alone, or when the clinical picture deteriorates due to cardiac symptoms. Previous embolic events, syncopal attacks, and echocardiographic evidence of a multilobulated mass are indications for urgent surgery. Unfortunately, it is just a palliative treatment with a poor outcome in case of emergency surgery. Recent case reports advocate a two-stage surgical approach to treat malignancies with intracardiac extension in a high-risk situation.[4]

In our study, it is apparent that the cases who had upfront surgery were urgent surgery in three cases and unplanned/discovered intraoperatively in one case. The decision concerning the first three cases was made for trial to improve their quality of life as two of them had lower limb malignant emboli and one had concomitant mitral valve surgery. Despite this fact, those patient survival outcomes were not desirable. On the other hand, the patient who had unplanned resection showed favorable outcomes, but it seems that it might be less invasive for him to get a more accurate diagnosis preoperatively. Given these premises, it would be highly recommended to search for other non-surgical options due to the sub-optimal results obtained with emergency surgery.

Surgery is mostly recommended to improve patients' quality of life rather than improving their survival as most patients had frequent showering of emboli to the lung in case of right-sided lesions and the whole body in case of left-sided ones, leading to stroke and/or acute peripheral ischemia. Complete tumoral excision followed by adjuvant therapy may positively affect patients' survival time.[5]

Besides the surgical approach, concurrent chemoradiation could be used alone as a treatment in case of cardiac metastases. Herein, it showed good results and longer overall survival. Chemotherapy alone or combined with radiation could also follow the debulking for better control of the neoplasm. The efficiency of the treatment depends on the primary tumor.

Primary synovial sarcoma of the lung is a very rare entity and commonly presents as chest pain. While historically termed due to its similarity to synovium on histology, it is thought to arise from primitive pluripotent mesenchymal cells rather than the synovium.[6] On histopathological examination (HPE), it needs to be differentiated from fibrosarcoma. Moreover, immunohistochemistry (IHC) is needed to differentiate it from other sarcomas.[7] Of note, it is an aggressive tumor with a propensity to invade the adjacent tissue. Ipsilateral pleural effusion is common. Management of such tumors is difficult as these tumors are poorly sensitive to chemotherapy. Surgical resection, whenever feasible, is the treatment of choice.[6] In our study, there were two cases of primary synovial sarcoma; one presented with irritative cough and acute limb ischemia. Surgery via cardiopulmonary bypass (CPB) was suggested to control showering with the removal of intracardiac part only (R2 resection), but the patient developed ARDS and died on the 14th day postoperative. The other case was unplanned surgery as the patient was diagnosed with complex septated effusion and discovered intraoperatively to have a large lower lobe tumor extending to the left atrium. For this subject, we performed the surgery via thoracotomy without CPB with the removal of the intrathoracic part only (R2 resection). The patient survived the surgery, continued concurrent chemoradiotherapy, but died after four months.

Renal cell carcinoma is a malignant tumor with the propensity to invade the IVC and extend into the right heart.[8] The factors guiding prognosis

are local infiltration to perinephric tissue, lymph node involvement, distant metastasis, and involvement of IVC and right atrium. Regardless of the level of tumor extension, the best treatment is believed to be radical surgical resection of the entire tumor using CPB with or without deep hypothermia and total circulatory arrest.[3] The operation should be scheduled soon after diagnosis to prevent pulmonary embolization or heart failure caused by tricuspid valve obstruction. One case in our series had renal cell carcinoma, who received chemotherapy not followed by surgery as the tumor was infiltrating the hepatic veins, making surgery impossible.

The antemortem diagnosis of cardiac metastases in osteogenic sarcoma has been documented in only 26 cases over the past 60 years. However, the extension of metastatic lung tumors into the left atrium via pulmonary veins is very rare, with only three cases previous documented.[9] Unlike primary osteosarcomas of the heart, metastases from osteosarcoma to the heart are often right-sided, suggesting intravascular and intracardiac seeding and/or spread. There are very few reported cases of the tumor reaching the right heart via pulmonary venous extension. Osteogenic sarcoma involving the heart is unique in the metastases affecting bones. In patients with osteogenic sarcoma, the calcific areas of increased opacity may be visible on chest radiographs, but high-attenuation lesions are better demonstrated on CT scans.

Conclusion

Despite the small number of cases with the intracardiac extension of malignant tumors in this series, urgent/unplanned surgery was not found to be a good option for improving survival in these cases. Combined multidisciplinary approach could be highly recommended to provide better options for disease control.

Informed Consent

All patient involved in the study provided informed consent and consent for publication.

Conflict of Interest

None declared.

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