An uncommon case of primary cardiac sarcoma with an acute presentation: the role of multimodality imaging.

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Abstract

Background: Primary cardiac sarcomas are the most commonly encountered primary cardiac malignancies with a marked tendency of recurrence. In the complex and heterogeneous field of cardiac masses a proper differential diagnosis based on multimodality imaging approach is extremely useful in order to plan the most appropriate treatment. Case Summary: We report the case of a 69-year-old woman presenting with worsening dyspnoea and syncope due to cardiac pleomorphic sarcoma, emphasizing the critical aspects of differential diagnosis and management. Discussion: A stepwise diagnostic strategy through multimodality imaging evaluation is the cornerstone for an appropriate prompt intervention, even if histopathological characterization remains the diagnostic gold standard for histotype definition, to guide the treatment and define the prognosis.

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Case Summary : *We report the case of a 69-year-old woman presenting with worsening dyspnoea and syncope due to cardiac pleomorphic sarcoma, emphasizing the critical aspects of differential diagnosis and management .*

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Key words: cardiac masses; cardiac tumors; cardiac sarcoma;

*Learning Points***:**

- *The case highlights the value of contrast echocardiography in in raising clinical suspicion of malignancy, allowing a rapid diagnostic work-up and the subsequent treatment of the primitive heart tumour.*
- *Sarcoma is the most common primary cardiac tumour and is well known for its aggressive behaviour. When affecting the right ventricular outflow tract a rapid complete obstruction may occur causing an acute presentation.*
- *Given the poor response to medical treatment, a prompt surgical excision is essential to avoid cardiovascular collapse due to low RV cardiac output.*

Introduction

Primary cardiac tumors are rare and can cause a broad spectrum of unexpected symptoms and clinical manifestations. Primary cardiac sarcomas constitute approximately 1% of all soft tissue sarcomas and are the most common malignant primary cardiac tumor.[1,2] They occur most commonly in the left atrium, but can develop in any cardiac chamber.[3]

We report the case of 69-year-old woman presenting at the emergency department (ED) for worsening dyspnea, syncope and acute right heart failure due to a mass in the right ventricular outflow tract (RVOT) causing pulmonary obstruction.

Case Presentation

A 69-year-old obese woman with no previous cardiac history, was admitted to Emergency Department for syncope and recent onset of worsening dyspnea. Physical examination showed signs of peripheral congestion and revealed a new systolic heart murmur. The patient was normotensive and the ECG was nonspecific. Blood test showed a slight increase of cardiac troponin I and D-dimer.

The patient underwent transthoracic echocardiography (TTE) that showed right ventricular dilatation and dysfunction with McConnell's sign and a mobile mass was observed in the RVOT, which engaged the origin of the pulmonary artery. A subvalvular pulmonary stenosis with moderate to severe systolic RVOT gradient (peak/mean gradient: 54/22 mmHg) and high velocity jet of tricuspid regurgitation (peak vel. 4,4 m/s) were also documented.

In the suspicion of acute pulmonary embolism a chest CT angiography was performed, which confirmed the finding and documented another filling defect of the right branch of the pulmonary artery. Thus, heparin therapy was started. However, despite effective anticoagulant therapy, the mass persisted.

To improve diagnostic characterisation of the mass, contrast echocardiography was performed, showing a complete opacification of cardiac chambers with late inhomogeneous enhancement of the mass, raising the hypothesis of cardiac tumor (Fig.1). Since cardiac magnetic resonance was contraindicated due to the presence of cochlear implant, a cardiac-CT was performed in order to better characterize the mass. The CT scan showed a hypodense formation with origin from the wall of RVOT and confirmed the presence of a second mass in the right branch of pulmonary artery (Fig.2). Both the formations showed significant contrast enhancement, highly suggestive of neoplastic nature. 18-fluorodeoxyglucose positron emission tomography/computed tomography (18-FDG PET/CT) confirmed the high metabolic activity of the masses and excluded other extracardiac pathologic captations (Fig.3).

After Heart Team discussion, surgical mass debulking was planned. The intraoperative transoesophageal echocardiogram confirmed all the findings, showing also vacuolated and inhomogeneous aspects of the mass (Fig.4). The exeresis was macroscopically radical, despite the dimensions, friability and local invasivity of the masses. Since the pulmonary valve and the right pulmonary artery were infiltrated by the tumor, both of them were resected and replaced with a bioprostethic valve and a vascular prosthesis respectively. The histologic specimen examination revealed an undifferentiated primary mesenchymal neoplasm consistent with pleomorphic sarcoma with an elevated mitotic index (Ki-67>80%) with coexisting immunophenotypic traits guiding for dedifferentiated leiomyosarcoma (Fig.5). At post-operative echocardiography there was no evidence of intraventricular mass. Subsequently the patient started an adjuvant chemotherapy with epidoxorubicin and had close oncological follow-up.

Discussion

Undifferentiated pleomorphic sarcomas are the most commonly encountered primary cardiac malignancy, accounting for approximately 10% of all primary cardiac tumors[3]. The mean age at presentation is 45 years, with no sexual predilection. They occur most commonly in the left atrium, but can develop in any cardiac chamber[3]. Cardiac masses can be effectively identified and characterized by multimodality imaging. TTE remains the first diagnostic approach and permits to evaluate site of origin, size, mobility and hemodynamic impact of the mass[4]. Contrast-TTE is useful to assess the perfusion of the mass in order to differentiate vascular tumor from thrombi. Malignant tumors are frequently highly vascularized and show significant contrast enhancement, whereas, myxomas demonstrate mild enhancement by contrast on visual inspection and quantitatively less perfusion than the surrounding myocardium; thrombi, being avascular, show complete absence of contrast opacification[5]. CT can provide additional useful information, such as better definition of site of origin, anatomical relationships, extension to surrounding structures and evaluation of extracardiac localizations[6]

CMR is the best available non-invasive diagnostic tool to provide information about morphology, dimensions, location, extension, perfusion and tissue characterization of the mass, orienting towards the histopathological diagnosis[6].

18F-FDG offers an accurate evaluation of the metabolic activity of tumors. The extent of FDG uptake by tumors improve differentiation between benign and malignant tumors. 18F-FDG could also be useful for staging malignancies and in the evaluation of early responses to cancer therapy[7].

Nevertheless, histopathology remains the diagnostic gold standard in any resected cardiac mass, allowing

to establish the benign or malignant nature and the precise histotype[4]. Optimal treatment approach for these neoplasms is still unclear. Surgery when feasible is the best therapeutic strategy[8]. A complete surgical resection of the malignancy was found to be significantly associated with longer survival (17 vs 6 months when complete resection was not possible)[9]. The benefit of adjuvant chemotherapy and/or radiation is unknown, but is a treatment option, especially for patients with incomplete resections. Furthermore, the role of radiotherapy (RT) is limited, considering that high-dose radiation protocols used to treat sarcomas in other locations are poorly tolerated by the heart. In our case, surgical exeresis was the chosen treatment. However, it has to be noted that, despite radical exeresis of the mass, local recurrence and metastasis within 1 year are frequent and the median progression-free survival is 5.9 months[10], ranging from 6 to 18 months[9]. To date, since a clear evidence of adjuvant treatments effectiveness is lacking, surgery must be considered the pivotal therapy for a successful management. Future efforts should be directed to the improvement of surgical techniques to permit safe radical excision and, potentially, to the development of effective adjuvant therapy.

Conclusion

Neoplastic cardiac masses require an integrated diagnostic-therapeutic work-up to guarantee a tailored therapy. Optimal treatment for these neoplasms is unclear and surgery continues to be the best treatment option. In the complex field of cardiac masses a prompt and accurate diagnosis is crucial but challenging and often the definite diagnosis may requires histologic examination. Cardiac sarcomas are associated with poor prognosis, especially in case of metastatic disease.

From our experience, palliative and supportive therapies should always be offered to relieve symptoms and improve quality of life.

References

1. Basso C, Valente M, Poletti A, Casarotto D, Thiene G. Surgical pathology of primary cardiac and pericardial tumors. Eur J Cardiothorac Surg 1997;12:730–737; discussion 737–738
2. Oliveira GH, Al-Kindi SG, Hoimes C, Park SJ. Characteristics and survival of malignant cardiac tumors: a 40-year analysis of > 500 patients. Circulation. 2015;132: 2395– 2402.
3. Neuville A. et al. Intimal sarcoma is the most frequent primary cardiac sarcoma: clinicopathologic and molecular retrospective analysis of 100 primary cardiac sarcomas. Am. J. Surg. Pathol. 38, 461–469(2014).
4. Basso, Cristina & Rizzo, S. & Valente, M. & Thiene, G.. (2012). Prevalence and pathology of primary cardiac tumours. Cardiovascular Medicine. 15. 18-29.
5. Bhattacharyya S, Khattar R, Senior R. Characterisation of intra-cardiac masses by myocardial contrast echocardiography. Int J Cardiol 2013;163:e11–e13.
6. Maleszewski JJ, Anavekar NS, Moynihan TJ, Klarich KW. Pathology, imaging, and treatment of cardiac tumours. Nat Rev Cardiol. 2017;14(9):536-549. doi:10.1038/nrcardio.2017.47.
7. Sara Tyebally, Daniel Chen, Sanjeev Bhattacharyya, Abdallah Mughrabi, Zeeshan Hussain, Charlotte Manisty, Mark Westwood, Arjun K. Ghosh, Avirup Guha, Cardiac Tumors: JACC CardioOncology State-of-the-Art Review, JACC: CardioOncology, Volume 2, Issue 2, 2020,Pages 293-311,ISSN 2666-0873, https://doi.org/10.1016/j.jaccao.2020.05.009.
8. Murphy MC, Sweeney MS, Putnam JB Jr, et al. Surgical treatment of cardiac tumors: a 25-year experience. Ann Thorac Surg 1990;49:612–617; discussion 617-618.
9. Simpson L, Kumar SK, Okuno SH, et al. Malignant primary cardiac tumors: review of a single institution experience. Cancer. 2008;112: 2440– 2446.
10. Hamidi, M., Moody, J. S., Weigel, T. L., & Kozak, K. R. (2010). Primary cardiac sarcoma. The Annals of thoracic surgery, 90(1), 176–181

FIGURE LEGEND

Figure 1. Contrast transthoracic echocardiography, parasternal short axis view. A) early acquisition after contrast administration, hypoechoic aspect of the mass. B) late acquisition with significant enhancement of

the mass.

Figure 2. Cardiac computed tomography reconstructions showing the two masses involving the right ventricular outflow tract and the right branch of pulmonary artery.

Figure 3. 18-fluorodeoxyglucose positron emission tomography/computed tomography (18-FDG PET/CT). Hypercaptation of the two masses, consistent with elevated metabolic activity.

Figure 4. Intraoperative transoesophageal echocardiography. A and B) coarse and inhomogeneous mass of the right ventricular outflow tract. C) mass involving the right branch of the pulmonary artery.

Figure 5.

The lesion consists of highly pleomorphic, large tumor cells with marked atypia with a solid pattern and hemorrhagic areas [Fig. A, HEx10, Fig. B, HEx20]. Some cells showed no reactivity to any immunohistochemical marker, while others were positive for muscle markers showing focal skeletal muscle differentiation [Fig. C Desmin x20, Fig D SMA x20, Fig, E Myo D1 x20, Fig F HHF35 x20].