Monophasic Synovial Sarcoma of the Left Ventricle of the Heart: An Extremely Rare Case and Literature Review

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Abstract

BACKGROUND: Cardiac sarcomas account for <25% of all cardiac tumors. Of these, angiosarcomas are the most frequent. Synovial sarcomas (SS) are exceedingly rare. We present a case of primary left ventricle (LV) SS, a form of sarcoma particularly rare in the heart.

CASE DESCRIPTION: A 19-year-old male was referred for further investigation of a LV tumor, presented with a 3-month history of exertional dyspnea and palpitations. He also experienced several syncopal episodes. The radiologic examination confirmed a mass in the LV, suspected for myxoma of the LV. Histopathologic examination revealed a malignant tumor with spindle cell components, suggesting leiomyosarcoma with differential diagnosis of monophasic SS. Immunohistochemistry demonstrated reactivity of the spindle cell component with the mesenchymal marker vimentin and BCL2 protein, while the smooth muscle marker, desmin, was negative, confirming the diagnosis of monophasic SS.

CONCLUSIONS: Monophasic SS in the heart is diagnostically challenging since it shares the broad list of differential diagnoses of spindle cell tumors. Immunostaining is helpful to differentiate those entities to obtain a definitive diagnosis and proper treatment.

Introduction

Primary cardiac tumors are very rare, and most of them are benign. Malignant primary cardiac tumor only represents 25% of all primary cardiac tumors, and most of them are sarcomas [1]. Undifferentiated sarcoma is the most common type of sarcoma in the heart, followed by angiosarcoma (25%), leiomyosarcoma (25%), and synovial sarcoma (SS) [2]. In another study, angiosarcoma was found as the most frequent sarcoma, followed by malignant fibrous histiocytoma, leiomyosarcoma, and SS. Cases with SS only account for 2% of the sarcomas in the heart [2], [3]. Primary cardiac sarcomas are predominantly located in the heart’s right side, with the right to left side ratio of 2:1 [4]. In this case, we report the left ventricle’s (LVs) primary cardiac SS, with a chief complaint of syncope. The diagnosis was confirmed by histopathological analysis and immunostaining.

Case Description

A 19-year-old male patient was suddenly unconscious when he was working 3 weeks prior to hospital admission. Palpitation or chest pain was not reported prior to unconsciousness event. Initially, the patient did not seek for medical help, however, a week later the symptom was repeated. He went to a private hospital, and congenital heart disease was suspected. An echocardiographic examination was performed and revealed a mass at the LV. He was referred to Dr. Sardjito General Hospital with the diagnosis of suspected LV Myxoma. Physical examination showed a 2/6 pan systolic murmur in the apex. Transthoracic and transoesophageal echocardiography examinations were performed, and showed two LV masses: one sized 2.6 cm × 1.5 cm attached to the posterior mitral left, and another, sized 1.2 cm × 2.1 cm with peduncle attached to the anterior mitral leaflet that obstructed the LV outflow tract (LVOT) (Figures 1 and 2). A Cardiac
Multi-Slice Computed Tomography was performed and showed a pedunculated mass in the LV, size 2.3 cm × 2.3 cm × 4.7 cm (Figure 3).

Enlarged lymph nodes or intrathoracic mass were not detected, and then open-heart surgery was performed. The procedure was started with cannulation of the aorta, inferior and superior cava veins. The cardiopulmonary bypass machine was started and cardioplegia administrated. The surgeons opened the right atrium and the interatrial septum to visualize the mitral valve and the tumor. A single encapsulated cardiac tumor with a size of 5 cm × 2.5 cm × 1.3 cm was found. The tumor was removed, and the mitral valve was replaced with a St. Jude mechanical valve size 29 mm. The atria were closed and the patient was rewarmed. The procedure was completed without any complications.

The tumor mass was sent to the Anatomical Pathology department for a morphologic examination. The histopathology analysis revealed a mesenchymal tumor arranged in hypercellular fascicular architecture with a small intervening stroma, infiltrative to surrounding stroma. Hyalinization and myxoid changes were observed. Tumor cells were polymorphic with scant amphophilic cytoplasm, ovoid-to-spindled vesicular nuclei with evenly dispersed chromatin, and inconspicuous nucleoli. Glandular differentiation was not observed in the morphological features. A suspicion of leiomyosarcoma, with differential diagnosis of monophasic SS of the heart, was established. Immunostaining analysis using specific antibodies was performed to differentiate those entities. The results showed positive expression of BCL2 and negative expression of desmin, suggesting SS with a monophasic variant. Tumor proliferation was observed with Ki67 immunostaining and exhibited a 25% proliferation index (Figure 4). The diagnosis was then confirmed as monophasic SS.
patient was discharged 10 days later with good postoperative condition. The patient was screened for any other similar malignancy in various body parts by performing a bone survey and abdominal ultrasound. However, none were detected. As a treatment plan, he was scheduled for chemotherapy with Doxorubicin-Ifosfamide-Mesna regimen for six times at 28 days intervals. The post-chemo evaluation was performed and showed no residuals nor relapse. The patient gave his consent to submit his case for publication.

**Discussion**

The heart’s primary SS is a rare tumor, accounting for only 2% of cardiac sarcomas, with the left atrium and pericardium as the predominant site [3]. Most SS of the heart is predominantly right-sided (ten cases), with seven tumors in the right atrium and three in the right ventricle. Predicted prognosis based on age is challenging to conclude because of the wide variation of age and few cases reported. Cardiac SS patients involving the left side of the heart are extremely rare; there are only three cases reported of primary SS of the LV [5], [6], [7].

A total of sixteen cases and the current case of cardiac SS are listed in Table 1. The average age was 38 years ranging from 17 to 66 years. At 19, the indexed case is much younger compared to the median age of previous cases. The clinical presentation is similar to the other tumors located in the heart. The symptoms are usually caused by a local obstruction or functional interference, which clinically can present as dyspnea, chest pain, congestive heart failure, and syncope [8]. The sarcoma may cause emboli to the cerebral vasculature and present as a cerebrovascular accident [6], [9].

**Table 1: Cases of synovial sarcoma of the heart, including the index case**

| Reference          | Case Age | Sex | Clinical feature                                                                 | Site | Size/Gross | Diagnosis | Treatment                                                                                     | Follow-up                          |
|--------------------|----------|-----|----------------------------------------------------------------------------------|------|------------|-----------|-----------------------------------------------------------------------------------------------|------------------------------------|
| Burke et al., 1992 | 38       | M   | Dyspnea, chest pain, syncope                                                      | RV   | 8 cm × 7 cm | MSS       | Resection and chemotherapy                                                                     | Doing well at her                  |
| Boulter et al., 2009 | 24      | F   | Dyspnea, palpitations                                                             | LA   | 5.1 cm × 2.9 cm | MSS       | Partial excision, Adjuvant chemotherapy with Adriamycin                                        | 4-month follow-up                  |
| Hussain et al., 2012 | 28     | M   | Facial oedema, distention of neck veins and systemic hypertension                 | RA   | 3.9 cm × 4.2 cm | MSS       | Surgical resection followed by radiation therapy                                               | 4 months following surgery         |
| Bittira et al., 2000 | 47     | M   | Transient right arm weakness, right-sided facial droop, and aphasia dyspnea        | RA   | 7 cm × 5 cm | BSS       | Complete resection and Adriamycin chemotherapy                                                  | After 1 month patient showed metastasis to D 8 and L 2 vertebral bodies |
| Sharma et al., 2015 | 26     | F   | Dyspnea and giddiness                                                             | LA   | 7 cm × 5 cm | BSS       | Complete resection and chemotherapy                                                             |                                   |
| Hazell et al., 2004 | 17     | M   | Anorexia, shortness of breath                                                      | RV   | 6.5 cm      | MSS       | Resection and chemotherapy                                                                     |                                   |
| Okoro et al., 2017 | 35     | M   | Cardiomegaly, pneumonia                                                            | RA   | 5 cm × 6 cm  | MSS       | Resection and chemotherapy                                                                     |                                   |
| Donsbeck et al., 1999 | 34    | M   | Dyspnea, orthopnea                                                                 | RA   | 7.0 cm × 5.0 cm | SS       | Local excision and patch reconstruction of the atrial wall                                    | Disease-free at 5 years            |
| Hamachi et al., 2001 | 45     | M   | Shortness of breath, dyspnea on exertion, paroxysmal nocturnal dyspnea, and intermittent hemoptysis of 1-month duration | RA, LA | 2.5 cm × 2.9 cm | MSS       | Biopsy and chemotherapy                                                                       | Overall condition and long-term outcome remain guarded. A recent follow-up echocardiogram revealed tumor regrowth in the RA |
| Maleki et al., 2017 | 21     | F   | Dyspnea and weakness                                                              | RA   | 7.5 cm × 5.5 cm | SS       | Excision                                                                                      |                                   |
| Okoro et al., 2017 | 41     | F   | Migraines with complaints of sudden onset of left-sided hemiplegia, facial paralysis, and dysarthria | LV   | 1.7 cm × 1.8 cm | BSS       | Excision and chemotherapy                                                                    |                                   |
| Brahm et al., 2018 | 63     | M   | Dyspnea, lipothymia and lower chest pain that had started 1 month earlier         | RV   | 1.7 cm × 1.8 cm | SS       | Surgical and adjuvant chemotherapy                                                             | 8-year survival time following surgical and adjuvant chemotherapy               |
| Vinod et al., 2018 | 66     | F   | Complaints of progressive exertional dyspnea, orthopnea, paroxysmal nocturnal dyspnea (PND) and exercise intolerance thrombocytopenia, bilateral lower extremity oedema | LA   | 4.1 cm × 3.4 cm | BSS       | Surgical and chemotherapy                                                                    |                                   |
| Zhang et al., 2019 | 52     | M   | 3-month history of exertional dyspnea and palpitations, several syncope episodes | MV   | 5 cm × 3.5 cm | BSS       | Surgical and chemotherapy                                                                    | Patient died suddenly 6 months later |
| Our case           | 19     | M   | Dyspnea, chest pain, syncope                                                      | LV   | 5 cm × 2.5 cm | MSS       | Surgical and chemotherapy                                                                    | Still receiving chemotherapy protocol |

M: Male, F: Female, LA: Left atrium, LV: Left ventricle, MV: Mitral valve, RA: Right atrium, RV: Right ventricle, SS: Synovial sarcoma, MSS: Monophasic synovial sarcoma, BSS: Biphasic synovial sarcoma.
In this case, the SS had originated from the LV and obstructed the LVOT; thus, it manifested as syncope in this patient.

The sarcoma can arise from any part of the heart, and when it originates from the valvular structure, it usually has pedunculated morphology [8]. In this case, at first, the pedunculated mass was suspected as myxoma, since it accounts for 50% of cardiac mass cases [10]. We concluded that the SS in the heart was a primary tumor since we did not find another tumor outside the heart. We also did not find any evidence of SS with metastasis, especially in the lungs, as the most common metastatic site. The average tumor size was 7 cm (range 0.5–7.5 cm) in seventeen SS cases of the heart, with the largest at 15 cm and the smallest was 1 cm. Histologically, SS may display biphasic patterns, with epithelial and spindle cell components, while spindle cell components characterize the monophasic variant [4], [8]. In our review, there were six cases with monophasic SS, six cases with biphasic SS, and five cases that did not elaborate in detail concerning their histologic variants. In monophasic SS cases, the diagnosis can be challenging since it is frequently confused with leiomyosarcoma, fibrosarcoma, hemangiopericytoma, or malignant nerve sheath tumor. To differentiate those entities, immunostaining is needed to confirm the diagnosis [4], [8]. The SS shows positive immunostaining of the spindle cells for BCL2 and epithelial cells for cytokeratin and epithelial membrane antigen. The SS in our case was of the monophasic variety positively stained with vimentin, BCL2 protein, and negatively stained desmin [2], [4]. In some cases, the difference can only be made using chromosomal translocation analysis, with the hallmark being the detection of t(X;18)(p11.2;q11.2), which presents in 90% of cases [5].

Surgery has been the primary treatment of the SS cases since wide excision is required for a better outcome, followed by chemotherapy. The prognosis of SS is poor, with the most common causes of death as tumor recurrence and metastasis [8], [11]. Favorable factors for better survival are the young age when the diagnosis was made, the absence of chromosomal abnormalities, and the pericardium origin tumor. In contrast, older age at diagnosis contributes to poor prognosis. However, since the incidence of SS is rare, the prognostic factors are hard to ascertain [4], [12].

The primary cardiac tumor has a poor prognosis. A recent study by Yin et al. in 2020 showed that patients with primary cardiac tumors had a median survival of 7 months, but the survival can be improved with surgery and chemotherapy [12]. The surgical procedure is aimed to remove the tumor completely, and the radical excision has the lowest recurrence [13]. In SS, chemotherapy after the surgical procedure will improve survival since SS is relatively more chemosensitive than any other soft-tissue sarcoma. The combination of ifosfamide and doxorubicin showed a better outcome than high-dose ifosfamide alone. There are several novel therapies for SS that are still under investigation, such as tyrosine kinase targeted therapy, epigenetic modifiers, and immunotherapy, that showed some promising preclinical and early results [14].

Conclusions

Primary cardiac SS is rare, and SS originating from the LV is extremely rare. Classic histopathology of the SS is a biphasic variant, showing glandular differentiation. Monophasic SS is diagnostically challenging since it shares the broad list of differential diagnoses of spindle cell tumors and needs immunostaining or molecular analysis for definitive diagnosis. SS is more chemosensitive than other soft-tissue sarcomas. Ifosfamide and doxorubicin combination had a better outcome; recently, some novel therapies were developed to improve patient survival. This new development substantiates the importance of definitive diagnosis to differentiate SS from other soft-tissue sarcomas.

Consent

Written informed consent for publication of his detail was obtained from the patient. Institutional approval was not required to publish this case report.

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