case report

Primary leiomyosarcoma of the atrium with heterologous differentiation

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We report a case of a 47-year-old female who presented with breathlessness and palpitations for two weeks. On clinical evaluation, bilateral pedal edema was noticed. A CT pulmonary angiogram showed a mass in the left atrium causing significant obstruction to cardiovascular outflow. After extensive work-up, the mass was surgically resected. Histopathological findings from the acquired specimen revealed a high-grade leiomyosarcoma with extensive necrosis and heterologous (cartilaginous) differentiation. The early postoperative period was complicated by cardiac tamponade and the patient died on the second postoperative day due to ventricular arrhythmia, shock and multiorgan failure.

SIMILAR CASES PUBLISHED: No similar cases published.

Primary cardiac tumors are uncommon with an incidence of 0.02%.[1] Among all cardiac tumors, only 20.6% are malignant.[2] Malignant neoplasms are usually highly aggressive, locally invasive sarcomas with an invariably fatal outcome. The most common site is the left atrium in approximately 75% of all cases. Neoplasms occur least frequently in the right atrium (16%) and the ventricles (7%).[3] Primary leiomyosarcomas are exceedingly rare with an incidence of approximately 0.025% of all cardiac sarcomas. Tumor resection remains the treatment of choice in any cardiac tumor.[4]

Cardiac leiomyosarcomas are associated with a poor prognosis as they are highly aggressive, and due to extensive local invasion, it is often difficult to achieve complete surgical clearance.[5] The mean survival rate is 6 months after diagnosis.[6]

CASE

A 47-year-old woman known to have hypertension, type 2 diabetes mellitus and subclinical hypothyroidism presented with a two-week history of progressive shortness of breath at rest (New York Heart Association Class 4), which was associated with cough, palpitations and mild lower limb edema. CT pulmonary angiogram (CT-PA) excluded possible pulmonary embolus, but revealed a large heterogeneous mass in the left atrium infiltrating to the left hilum **(Figure 1)**. The mass lacked the typical features of a myxoma. The patient then underwent a transesophageal echocardiogram (TEE) which revealed a 2×4 cm heterogeneous mass attached to the roof of the left atrial wall with proximity to the left upper pulmonary vein, fungating into the left atrial cavity, and hence, causing significant obstruction to the cardiovascular outflow. An immediate surgical procedure was

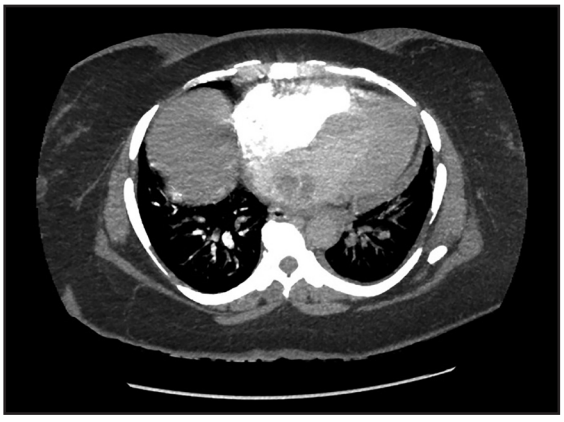

Figure 1. Spiral enhanced CT pulmonary angiogram showing large heterogeneous ill-defined low attenuation mass with central hyperdensity in the left atrium infiltrating to the left hilum.

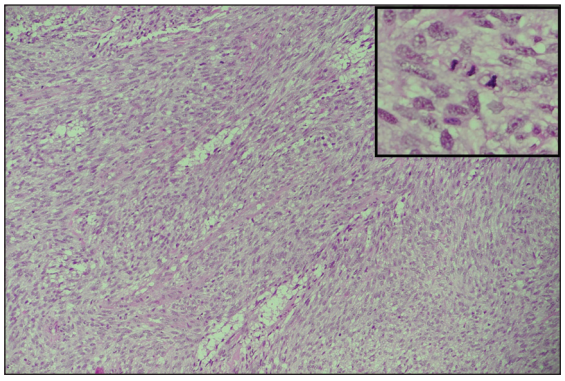

Figure 2. Photomicrograph of the neoplasm on low and high (inset) power showing hypercellularity with spindle cells arranged in interlacing bundles. These spindle cells have cigar-shaped and blunt-ended nuclei. Mitotic figures are seen. (Hematoxylin and Eosin, Magnification: 100× and 400×).

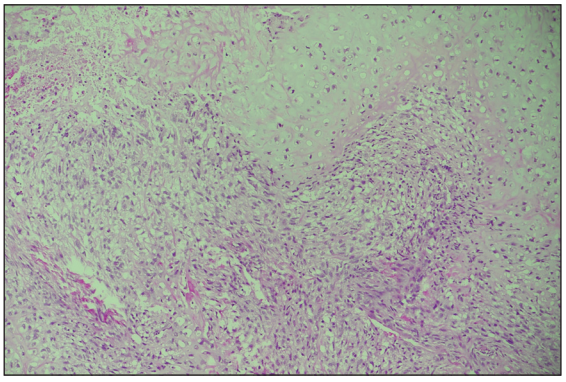

Figure 3. Photomicrograph showing areas of necrosis and heterologous (cartilaginous) differentiation within the neoplasm (Hematoxylin and Eosin, Magnification: 100×).

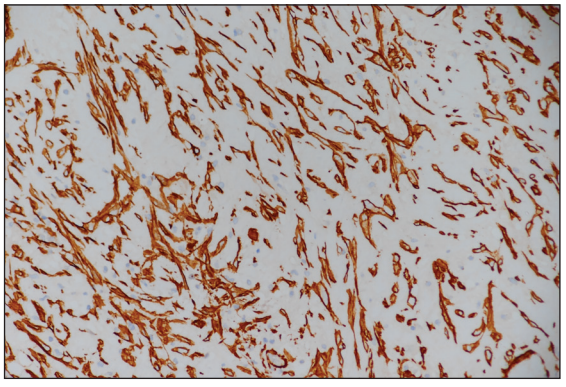

Figure 4. Photomicrograph of immunostaining with H-caldesmon (Magnification: 200×).

indicated to relieve the obstruction.

Median sternotomy, aortic-bicaval cannulation, and standard cardiopulmonary bypass were performed for excision of the left atrial mass. Only partial resection of the prominent tumor mass was possible as the tumor was unresectable, and thus, the surgical procedure was not radical. The left atrial wall was then repaired with a pericardial patch. Gross examination of the acquired sample showed multiple, grey white and hemorrhagic firm masses measuring in aggregate 7×6×1.5 cm. The surface was slightly irregular and hard to cut with the knife.

Microscopic examination of the histological sections showed both vital and necrotic areas. Vital areas revealed focal high cellularity, composed of round, irregular to pleomorphic spindle-shaped cells with considerable mitotic activity and atypical mitotic figures. Only minor portions of the tumor exhibited a more fascicular arrangement of tumor cells, with spindle cells and elongated nuclei). 'Cigar-shaped' nuclei were observed **(Figure 2)**. Moreover, pleomorphic, bizarre cells with marked anaplasia were also noted. The mitotic figures were found with a frequency of 8-9 per 10 high power fields. Additionally, multiple foci of necrosis (<50% tumor necrosis) and areas with calcification and cartilaginous differentiation were further observed **(Figure 3)**. According to French Federation of Cancer Centers Sarcoma Group (FNCLCC) grading, tumor score was 6 and it was under Grade III.

Immunohistochemically, the tumor cells were positive for smooth muscle actin, vimentin, H caldesmon **(Figure 4)**, INI-1, and focally positive for calponin. The following stains were negative: desmin, CD99, epithelial membrane antigen, S-100, CD34, nonspecific enolase, CD68 and myogenin. The proliferative index (Ki-67 index) was approximately 40%. Based on the histopathology and immunohistochemical findings, the diagnosis of grade III leiomyosarcoma with heterologous differentiation was rendered. The patient developed cardiac tamponade on the second post-operative day and later died in the hospital following ventricular arrhythmia, shock and multiorgan failure.

DISCUSSION

Primary cardiac tumors are rare as metastatic tumors to the heart are encountered with more frequency. Sarcomas constitute the dominant group of primary cardiac malignant tumors, with angiosarcoma being the most common.[7,8]

In our case, CT scan raised the suspicion of an intracardiac tumor by depicting a low attenuation-filling defect, and the TEE confirmed the diagnosis of an infiltrative, most-likely malignant tumor. Histopathologically,

this case is extremely rare, as in addition to classical leiomyosarcoma, there was extensive cartilaginous differentiation, calcification and large areas of necrosis. Heterologous differentiation of a leiomyosarcoma has been described occurring in soft tissue tumors including the uterus, gastrointestinal tract and to a lesser extent the retroperitoneum, abdominal cavity, or the extremities. Heterologous differentiation has not yet been reported in any primary cardiac leiomyosarcoma.

The criteria of malignancy in smooth muscle cell leiomyosarcoma includes significant nuclear atypia and coagulative necrosis. Mitotic activity varies considerably. However, even low levels of mitotic activity (<1/10 hpf) in the face of significant atypia, is sufficient evidence of malignancy. The identification of areas of smooth muscle differentiation on immunohistochemistry reveals the true nature of the tumor as in our present case. Smooth muscle actin is detected in almost all leiomyosarcomas.[9]

Treatment requires rapid action and a comprehensive approach. Surgery for cardiac sarcoma carries high mortality[10] and is rarely curative due to the typically progressive extent of disease on diagnosis. However, it offers the best option for prolongation of survival, improvement of hemodynamics, and amelioration of symptoms in such patients.

Cardiac leiomyosarcoma with cartilaginous differentiation should be kept in mind whenever a sarcoma of the heart is encountered. As the foci of classical leiomyosarcoma may be minimal in these variants, extensive sampling would increase the chance of demonstrating areas of histologically classical leiomyosarcoma. Its clinical features, treatment and significance of gains/amplifications in the development of these tumors are still inadequately understood; further research and reporting of such cases should be encouraged.

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