CASE REPORT

Primary cardiac leiomyosarcoma presenting as haemoptysis in a 22-year-old patient: an unusual presentation of a rare condition

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SUMMARY

Primary cardiac sarcomas are rare malignant tumours and among them, leiomyosarcoma is extremely rare. They are especially rare in a young age group. We present a case of a 22-year-old male patient with primary leiomyosarcoma of the left atrium involving the pulmonary veins who presented with haemoptysis and shortness of breath. He underwent surgical excision of the tumour along with mitral valve replacement followed by adjuvant chemotherapy. No recurrence was reported on his second 6 monthly follow-ups.

BACKGROUND

Leiomyosarcoma is a rare and highly aggressive cardiac malignancy constituting only 8%–9% of all cardiac sarcomas. The left atrium is the most commonly involved site. Transthoracic echocardiogram (TTE) is the method of choice for evaluating such tumours. On immunohistochemistry, they are virtually always immunoreactive for alpha smooth muscle actin (ASMA). Chemotherapy and radiotherapy are not used as independent treatment modalities, instead, multimodality approach comprises surgical excision and chemotherapy is recommended. The purpose of this report is to highlight this unusual cause of haemoptysis in a young male and to provide a literature update on cardiac leiomyosarcomas.

CASE PRESENTATION AND INVESTIGATIONS

A 22-year-old male, non-smoker, presented to the outpatient department with three episodes of haemoptysis in the last 1 week. The haemoptysis was bright red but small in quantity. On further inquiry, the patient also reported a 3 months' history of mild non-productive cough, occasional shortness of breath, easy fatigability and weight loss. The patient had no significant medical or surgical history and there was no history of any hospitalisations. There was no history of anyone else in the family having similar complaints or features of any infectious disease. The patient worked as a labourer and belonged to a far flung city in an underdeveloped neighbouring country. On physical examination, the patient was not in apparent distress. His blood pressure was 110/80 mm Hg, pulse was 88 bpm, respiratory rate was 20 breaths per minute

and he was afebrile with a temp of 98°F. Chest examination revealed slightly muffled but otherwise normal heart sounds and examination of the respiratory system revealed crackles in the lower lung fields. At this point, the main differentials were a chronic pulmonary infection like tuberculosis, an occult malignant process like a lymphoma or some cardiac pathology that may have caused left-sided heart failure.

The patient was thoroughly investigated. ECG showed sinus tachycardia with no evidence of conduction abnormalities. Chest X-ray revealed mild pleural effusion. A large 5.8×5.5 cm well-defined lobulated mass was noted in the left atrial cavity on TTE, which was protruding through the mitral valve during diastole and was hence obstructing left ventricular inflow. CT scan revealed an enhancing mass in the left atrial cavity (figure 1) and thickening in the pericardial cavity. Moderate pericardial effusion, large mediastinal lymph nodes (figure 2) and partial thrombosis of right pulmonary veins were also noted. Other investigations including renal function tests, liver function tests, complete blood count, erythrocyte sedimentation rate, serum electrolytes and urinalysis were normal. Ultrasound of abdomen and pelvis were also normal. Based on the history and radiological testing, the patient was at this moment thought to be suffering from a left atrial tumour. A malignant cardiac neoplasm of the left atrium was at the top of the differentials list at this moment given the CT findings and enlarged mediastinal lymph nodes. Atrial myxoma was another possibility as it is the most common atrial tumour.

As the mass was causing left-sided outlet obstruction and the patient was symptomatic too, it was decided to operate on the patient to remove the tumour and perform biopsy to make a definitive diagnosis, too. Operative findings included a left atrial tumour adherent to the mitral valve and extending into pulmonary veins and left atrial appendage. Tumour excision and mitral valve replacement were done, and the specimen was sent for histopathological examination. Intraoperative section pathological diagnosis was performed to make sure no residual tumour was left behind.

Microscopic examination revealed a high-grade malignant neoplasm having hypocellular and hypercellular areas. The cellular areas comprised

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Figure 1 CT chest showing a left atrial tumour.

bundles of pleomorphic spindled and epithelioid cells arranged in sheets with focal whorled pattern (figure 3). These cells had vesicular to hyperchromatic nuclei, coarse chromatin, inconspicuous nucleoli and eosinophilic cytoplasm (figure 4). Scattered multinucleated tumour giant cells were also seen. Frequent atypical mitotic figures were noted along with foci of necrosis. The hypocellular areas showed scattered bizarre cells and thin-walled blood vessels embedded in a myxoid stroma. The margin of resection was free of tumour.

On immunohistochemistry, the tumour cells were positive for ASMA (figure 5). Epithelial membrane antigen (EMA) showed focal positivity (figure 6), while S-100, CD99, BCL2 and desmin were negative. Endothelial markers CD31 and CD34 were also negative. Based on morphology and immunohistochemistry, the tumour was diagnosed as primary cardiac leiomyosarcoma.

Figure 2 CT chest showing enlarged mediastinal lymph nodes.

Figure 3 H&E section at 10x magnification showing atypical mitosis and spindle cells forming fascicles.

DIFFERENTIAL DIAGNOSIS

Before the CT chest was performed the main differentials in our mind were:

- An acute or chronic pulmonary infection. Acute viral bronchitis and viral/bacterial pneumonia and the locally endemic pulmonary tuberculosis may cause haemoptysis, especially if there is severe coughing. However, what inclined us to think otherwise was that the patient was not febrile or septic, the lung fields were clear and most importantly, they could not explain the mass in the left atrium.
- Heart failure due to various aetiologies was another possibility we considered as the patient had fatigue and shortness of breath with a mild pleural effusion. Severe pulmonary congestion is known to cause haemoptysis. However, the probability of this differential was low as the patient had no other symptoms of acute left heart failure, for example, orthopnoea, severe dyspnoea with slight exertion or neck vein dilatation. An otherwise normal echocardiogram (besides the tumour) also ruled out other aetiologies of heart failure.

Figure 4 H&E section at 40x magnification showing pleomorphic spindled cells with hyperchromatic nuclei, inconspicuous nucleoli and eosinophilic cytoplasm.

Figure 5 Immunostaining with alpha smooth muscle actin at 10× magnification.

- Other rarer causes of haemoptysis that could have caused the patient's symptoms were a bronchial polyp, bleeding diathesis/anticoagulation use or autoimmune condition like Goodpasture's syndrome. All these can cause haemoptysis in a young patient. However, we excluded these possibilities as there were no supporting clinical/laboratory findings and the patient responded to the treatment.

OUTCOME AND FOLLOW-UP

Our patient was treated with surgical resection and combination chemotherapy with doxorubicin and ifosfamide. The patient was treated with 25 mg doxorubicin every 3 weeks for a total of 6 doses. The patient was also treated with ifosfamide, a single dose of 2000 mg intravenously. Our patient was followed up and was still in remission on his second 6 monthly follow-up visit.

DISCUSSION

Primary cardiac malignant tumours are rare and sarcomas are the most common among them. Leiomyosarcoma is a rare and highly aggressive cardiac sarcoma with no more than 200 cases reported in the literature.¹ It constitutes only 8%–9% of all cardiac sarcomas.² Owing to its extreme rarity, no large study

Figure 6 Immunostaining with epithelial membrane antigen at 40× magnification.

has been done so far.¹ The left atrium is the most commonly involved site but right atrial and ventricular involvement is also described in the literature.³ Besides these, mediastinal leiomyosarcomas have also been described and are also rare entities with very few cases reported so far.⁴

The clinical presentation depends on the location and size of the tumour.⁵ The tumours that are located in the cavity cause symptoms of cardiac failure while those infiltrating through the myocardium are associated with arrhythmias.⁵ However besides these typical presentations, leiomyosarcomas may have other presentations too. Venous thrombosis is also common as was present in our case. However intra-aortic thrombosis in a setting of an otherwise normal aorta, also dubbed non-aneurysmatic, non-atherosclerotic descending thoracic aorta has also been reported with leiomyosarcomas.⁴ In a review of 79 cases of cardiac leiomyosarcomas, none of the case presented with haemoptysis.¹ In our case, the patient had three episodes of haemoptysis at the time of presentation. The exact mechanism behind this was not known but we theorised two possibilities responsible for this. It may have been due pulmonary congestion from the cardiac inlet obstruction as severe pulmonary congestion is known to cause haemoptysis. The second possibility was it may be due pulmonary infiltration of the tumour. But in hindsight, this was less likely as the patient reported no symptoms on the following second 6 monthly visits.

In the evaluation of cardiac tumours, imaging modalities have an important role in predicting primary from secondary and benign from malignant cardiac tumours.⁶ TTE is the method of choice for evaluating cardiac tumours and provides important morphological and functional information of the heart.⁷ A unique finding on live/real-time three-dimensional TTE of high-grade cardiac sarcomas described by Suwanjutha *et al* is the presence of the dense band like echo density which surrounds small echolucent areas imparting doughnut-like configuration.⁷ Moreover, this three-dimensional imaging modality is also helpful in evaluating the change in volume of cardiac tumours during the period of follow-up as the two-dimensional TTE may underestimate the volume by 20%–25%.⁷ Another study also concluded that three-dimensional echocardiography is ideal for determining the relationship of cardiac tumours with adjacent structures and the haemodynamic effects produced by them.⁸ Cardiovascular MRI is helpful in determining the extra cardiac extension of tumour and involvement of surrounding structures.⁹ On CT scan leiomyosarcoma appears as an irregular lobulated low-attenuated mass with pericardial effusion. They usually invade mitral valve and pulmonary veins which appear as filling defect. Dystrophic calcification may be seen.¹⁰ In our patient, the characteristic finding of doughnut-like configuration was not present on TTE but it gives an impression of a benign tumour but enlarged mediastinal lymph nodes, pulmonary vein thrombosis, pericardial thickening with pericardial effusion on CT scan pointed towards a malignant neoplasm which was then confirmed by immunohistochemistry.¹⁰ Both CT and MRI not only provides valuable information regarding the malignant nature of tumour by evaluating the infiltrative growth, broad base of the tumour and extra cardiac extension, but are also helpful in the guidance of surgical management.^{10 11}

Microscopically, the tumour is composed of fascicles of spindled tumour cells with cigar-shaped nuclei and eosinophilic cytoplasm. Pleomorphic cells along with multinucleated tumour giant cells are also present. Coagulative tumour necrosis is seen along with the variable atypical mitotic activity.¹² On immunohistochemistry, these tumours are virtually always positive for ASMA,^{13 14} while desmin and muscle-specific actin (HHF35)

may be positive.^{13–16} Cytokeratin and EMA show focal positivity.¹³ Other muscle markers that may be positive in leiomyosarcoma include smooth muscle myosin heavy chain, calponin and caldesmon.¹⁶ Our case showed strong positivity for ASMA and focal positivity for EMA. Desmin was negative in our case.

In a study of 353 cases of leiomyosarcoma of extremities, abdomen and trunk, the size of the tumour along with grade and positive surgical margins were found to have prognostic importance.¹⁷ Age of greater than 50 years is associated with decreased overall survival in primary cardiac leiomyosarcoma.¹ The 5-year overall survival rate is 25.4% which is far less than their soft tissue counterpart (50%–66%).¹ Median survival is reported to be 6 months with a mean survival of 11 months, however, two cases of 8 and 9-year survival are reported; the first one managed by surgery and adjuvant chemotherapy while the second one with surgery and adjuvant radiotherapy.^{3 18}

Surgical therapy is the best approach in cases of resectable tumours but should be followed by adjuvant chemotherapy to improve survival.¹⁹ In cases of unresectable tumours, surgical resection is still needed for relief of obstructive symptoms hence improving the quality of life.²⁰ A multimodality approach is recommended, comprising preoperative chemotherapy, followed by surgical resection and postoperative chemotherapy and radiotherapy.²¹ Some authors recommend adjuvant chemotherapy in all cardiac sarcomas and neoadjuvant therapy in sarcomas of the right heart.²²

Combination of doxorubicin and ifosfamide is the most common regimen used in the treatment of cardiac sarcomas.²³ These two drugs are also used in combination with other agents in mesna, doxorubicin, ifosfamide and dacarbazine, and doxorubicin, ifosfamide and mesna regimen.²⁴ Other treatment regimens include combination of docetaxel and gemcitabine, and cyclophosphamide, vincristine, doxorubicin and dacarbazine.²³ A very recent case of left atrial leiomyosarcoma in a 51-year-old patient was reported, who was also treated with surgery and six cycles of doxorubicin and ifosfamide and was found free of any recurrence after 2 years.²⁵ We also gave six cycles of doxorubicin and ifosfamide in adjuvant setting to our patient. Although the follow-up period in our case was short (1 year), it still gives some insight into the management of such cases.

Learning points

- Cardiac leiomyosarcoma is one of the rarest malignant cardiac tumours.
- It can have various presentations, though the most common presentation is symptoms due to cardiac outlet obstruction.
- It is diagnosed with histopathology and is usually treated with a combination of surgery and chemotherapy.
- It has a very low 5-year survival rate at 25%.

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Competing interests None declared.

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REFERENCES

- 1 Wang JG, Cui L, Jiang T, *et al.* Primary cardiac leiomyosarcoma: an analysis of clinical characteristics and outcome patterns. *Asian Cardiovasc Thorac Ann* 2015;23:623–30.
- 2 Jellis C, Doyle J, Sutherland T, *et al.* Cardiac epithelioid leiomyosarcoma and the role of cardiac imaging in the differentiation of intracardiac masses. *Clin Cardiol* 2010;33:E6–E9.
- 3 Muthukumar L, Jan MF, Taylor R, *et al.* Biatrial High-Grade leiomyosarcoma with Nine-Year Post-Surgical survival. *Ann Thorac Surg* 2017;103:e43–e45.
- 4 Yoshida M, Ando S, Naito Y, *et al.* Mediastinal leiomyosarcoma concurrent with intra-aortic thrombosis. *BMJ Case Rep* 2013;2013:bcr2012007527.
- 5 Gierlak W, Syska-Sumińska J, Zieliński P, *et al.* Cardiac tumors: leiomyosarcoma—a case report. *Kardiochir Torakochirurgia Pol* 2015;12:251–4.
- 6 Yuan SM, Shinfeld A, Lavee J, *et al.* Imaging morphology of cardiac tumours. *Cardiol J* 2009;16:26–35.
- 7 Suwanjuthat T, Singh H, Plaisance BR, *et al.* Live/real time three-dimensional transthoracic echocardiographic findings in primary left atrial leiomyosarcoma. *Echocardiography* 2008;25:337–9.
- 8 Espinola-Zavaleta N, Morales GH, Vargas-Barrón J, *et al.* Three-dimensional transesophageal echocardiography in tumors of the heart. *J Am Soc Echocardiogr* 2002;15:972–9.
- 9 Clarke NR, Mohiaddin RH, Westaby S, *et al.* Multifocal cardiac leiomyosarcoma, diagnosis and surveillance by transoesophageal echocardiography and contrast enhanced cardiovascular magnetic resonance. *Postgrad Med J* 2002;78:492–3.
- 10 Araoz PA, Eklund HE, Welch TJ, *et al.* CT and MR imaging of primary cardiac malignancies. *Radiographics* 1999;19:1421–34.
- 11 Astarcioglu MA, Kalçık M, Gürsoy MO, *et al.* Multimodality imaging of a recurrent case of right-sided cardiac leiomyosarcoma with an unusual clinical course. *Türk Kardiyol Dern Ars* 2015;43:372–5.
- 12 Srividya VV, Sailendra V. An Extremely Rare Case of left atrium and right pulmonary vein leiomyosarcoma. *J Clin Diagn Res* 2015;9:ED18.
- 13 Donsbeck AV, Ranchere D, Coindre JM, *et al.* Primary cardiac sarcomas: an immunohistochemical and grading study with long-term follow-up of 24 cases. *Histopathology* 1999;34:295–304.
- 14 Kumar N, Agarwal S, Ahuja A, *et al.* Spectrum of cardiac tumors excluding myxoma: experience of a tertiary center with review of the literature. *Pathol Res Pract* 2011;207:769–74.
- 15 Rangdaeng S, Truong LD. Comparative immunohistochemical staining for desmin and muscle-specific actin. A study of 576 cases. *Am J Clin Pathol* 1991;96:32–45.
- 16 Nicolas MM, Tamboli P, Gomez JA, *et al.* Pleomorphic and dedifferentiated leiomyosarcoma: clinicopathologic and immunohistochemical study of 41 cases. *Hum Pathol* 2010;41:663–71.
- 17 Gladly RA, Qin LX, Moraco N, *et al.* Predictors of survival and recurrence in primary leiomyosarcoma. *Ann Surg Oncol* 2013;20:1851–7.
- 18 Glaoui M, Benbrahim Z, Belbaraka R, *et al.* An uncommon long-term survival case of primary cardiac leiomyosarcoma. *World J Surg Oncol* 2014;12:338.
- 19 Neragi-Miandoab S, Kim J, Vlahakes GJ. Malignant tumours of the heart: a review of tumour type, diagnosis and therapy. *Clin Oncol* 2007;19:748–56.
- 20 Centofanti P, Di Rosa E, Deorsola L, *et al.* Primary cardiac tumors: early and late results of surgical treatment in 91 patients. *Ann Thorac Surg* 1999;68:1236–41.
- 21 Shapira OM, Korach A, Izhar U, *et al.* Radical multidisciplinary approach to primary cardiac sarcomas. *Eur J Cardiothorac Surg* 2013;44:330–6.
- 22 Leja M, Reardon MJ. Cardiac sarcomas: therapeutic options? *Future Cardiol* 2011;7:595–7.
- 23 Yusuf SW, Bathina JD, Qureshi S, *et al.* Cardiac tumors in a tertiary care cancer hospital: clinical features, echocardiographic findings, treatment and outcomes. *Heart Int* 2012;7:e4.
- 24 Steen S, Stephenson G. Current treatment of soft tissue sarcoma. *Proc* 2008;21:392–6.
- 25 Behi K, Ayadi M, Mezni E, *et al.* Two years survival of primary cardiac leiomyosarcoma managed by surgical and adjuvant therapy. *Clin Sarcoma Res* 2017;7:5.

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