Reminder of important clinical lesson

Primary liposarcoma of the heart

Christina Maria Steger

Department of Pathology, Innsbruck Medical University, Innsbruck, Austria

Correspondence to Dr Christina Maria Steger, christina.m.steger@i-med.ac.at**Summary**

The author reports a case of a 64-year-old man, who presented with a 4-week history of dyspnoea and dizziness suffering from a large mass in the pericardium. CT of the chest showed a lobulated mass in the pericardial sac located between the pulmonary veins and the ascending aorta reaching the superior vena cava. The tumour was completely resected and histopathological analysis revealed the tumour to be a well-differentiated lipoma-like and focal sclerosing liposarcoma, which was composed predominantly of adipocytes with hyperchromatic nuclei and eosinophilic-to-vacuolated cytoplasm disrupted by fibrous septa. Two years after initial tumour diagnosis the patient is still alive without signs of tumour recurrence.

BACKGROUND

Primary liposarcoma of the mediastinum is extremely rare, representing <1% of mediastinal tumours with <150 cases reported in the literature. Differentiation from lipomas can be difficult and is based on histological examination of excised specimens. Mediastinal liposarcoma develops more commonly in the posterior mediastinum and usually occurs in adults, with a peak incidence in individuals aged 40–60 years.¹ Men are affected twice as often as women.²

Liposarcoma, first described by Virchow in 1857,³ normally occurs in the deep soft tissue of extremities and in the retroperitoneum. Other unusual locations may include the peritoneal cavity, spermatic cord, axilla, vulva, breast and the heart. It is the most common soft tissue sarcoma and accounts for 20% of all mesenchymal tumours.

According to the experience of the Armed Forces Institute of Pathology, in collaboration with the Mayo Clinic, 75% of the cases of liposarcoma develop in deep muscle tissues

Figure 1 Chest x-ray with the enlarged heart silhouette.

of the extremities, 20% develop in the retroperitoneum and the remaining develop at other sites.⁴

The cell of origin of liposarcomas is presumed to be an undifferentiated, pluripotent mesenchymal cell.

A number of cytogenetic correlations have been made with liposarcomas. Well-differentiated liposarcomas have been found to be associated with abnormalities derived from the q13-15 region of chromosome 12.⁵ However, the molecular basis for wide range of differentiation of these tumours is unknown.^{6 7}

Diagnosis and classification of liposarcoma is based on histopathological criteria established by the WHO. Liposarcoma can be classified into four distinct histological types: well-differentiated (or atypical lipoma), dedifferentiated, myxoid/round cell and pleomorphic (table 1). Well-differentiated liposarcoma accounts for 40–45% of all liposarcomas and the lipoma-like form is by far the most common of its variants.

CASE PRESENTATION

In April 2009, a 64-year-old male presented with a 4-week history of exertional dyspnoea and dizziness.

Chest x-ray demonstrated a markedly enlarged heart silhouette (figure 1). Echocardiography revealed normal-sized ventricles and a normal global contractile function. Chest CT suspected a lipoma or liposarcoma with

a maximum diameter of 14 cm. The mass was located between the ascending aorta and the truncus pulmonalis, reached the superior vena cava and lead to compression of the right atrium and the superior vena cava (figures 2 and 3). Radiologically, no evidence of metastases or further tumour formations were apparent. Laboratory tests showed no signs of inflammation (erythrocyte sedimentation rate,

Table 1 Liposarcoma subtypes

Well-differentiated	Includes atypical lipoma Most common subtype (50% of liposarcomas) Low grade (does not metastasise, but may recur locally) Risk of dedifferentiation
Myxoid	Intermediate grade Includes round-cell variant as its high-grade counterpart Most common type in pediatric age group Metastatic risk especially in round-cell variant
Pleomorphic	Rarest type (5–10% of liposarcomas) High grade May mimic MFH or even carcinoma or melanoma High risk of local recurrence and metastasis
Dedifferentiated	High-grade sarcoma arising in association with well-differentiated liposarcoma (MFH, fibrosarcoma) Most common with retroperitoneal lesions Risk of metastasis

MFH, malignant fibrous histiocytoma.

Figure 2 Chest CT showing the lipomatous tumour mass.

Figure 3 3D reconstruction of the heart with the liposarcoma between truncus pulmonalis and ascending aorta.

fibrinogen, C reactive protein, lactate dehydrogenase were all within the range).

Respiratory function tests and arterial blood gas analyses were within normal limits. Two weeks later, tumorectomy was performed with the support of cardiopulmonary bypass under cardiac arrest. After median sternotomy and incision of the pericardium the lipomatous tumour mass was encountered. The tumour was pedunculated with origin from the right atrium and was radiologically suspected behind the ascending aorta and truncus pulmonalis reaching the left auricle of the heart. Mobilisation of the tumour mass was difficult due to adhesions between the tumour and the pericardium. Surgically, complete resection was obtained. The pericardium was not resected.

The early postoperative course was uneventful and the patient was discharged 6 days after open heart surgery.

INVESTIGATIONS

Grossly, the lobulated tumour mass measured $14 \times 10 \times 8$ cm in size, weighted 712 g, and showed haemorrhage on the surface. On sectioning, it was yellow, soft and smooth with a light-coloured glossy nodule (5×4 cm) inside. Histologically, the tumour was characterised by a variation in size of adipocytes, some of which showing round hyperchromatic nuclei, often prominent nucleoli, and variably eosinophilic-to-vacuolated cytoplasm. Within the

tumour formations fibrous septa and focal chronic inflammatory infiltrates, mainly consisting of lymphocytes, were found (figure 4). No lymph vessel or vessel infiltration, no significant necrosis or mitosis was present. The resection margins were free of tumour formation.

Finally, the diagnosis of a well-differentiated lipoma-like and focal sclerosing liposarcoma was made.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis includes

- ▶ Mediastinal lipoma
- ▶ Thymolipoma
- ▶ Angiolipoma
- ▶ Fibromyxolipoma
- ▶ Teratoma.

OUTCOME AND FOLLOW-UP

Two years after surgery the patient is alive without any signs of tumour recurrence or metastatic disease, although a subsequent irradiation or chemotherapy was not performed.

DISCUSSION

Although liposarcoma is the most common tumour of mesenchymal origin in adults, a mediastinal location is extremely rare.^{4 8–14} Primary mediastinal liposarcoma

Figure 4 Histological examination revealed adipocytes with eosinophilic-to-vacuolated cytoplasm, fibrous septa and lymphocytic infiltration (H&E staining, (A) – original magnification $\times 4$, (B) – original magnification $\times 10$, (C,D) – original magnification $\times 40$).

accounts for only 0.13–0.75% of all mediastinal tumours¹⁵ and constitutes about 13% of all cardiac sarcomas.^{6 7 16–17} By definition, pericardial liposarcomas must be confined to the pericardium, at the time of presentation or the bulk of the tumour must be within the pericardial cavity. In every case exclusion of an occult primary is essential as secondary tumours are 100–1000 times more common.^{6 7}

About 20–24% of the cardiac sarcomas remain unclassified either due to inadequate sampling of those tumours which demonstrate focal areas of differentiation or due to lack of adequate material for complete immunohistochemical and ultrastructural analysis.

Needle biopsies, either fine needle or core, are often inadequate for accurate diagnosis of lipomatous tumours. Low-grade liposarcomas are difficult to distinguish from benign lipomas on needle biopsy and larger tissue specimens, from incisional or excisional biopsies, are usually required.

Depending on their size and location within the heart, liposarcomas may present with chest pain, symptoms of right- or left-sided heart failure, pericarditis with or without cardiac tamponade, palpitation, rhythm disturbances, syncope, angina, cough and constitutional symptoms like fever and weight loss.^{18–20} Dyspnoea is the most common symptom. In cases where the tumour does not interfere with cardiac function, patients may be entirely asymptomatic.^{2 21}

Liposarcomas can invade adjacent organs, so they are more likely to be symptomatic than benign lipomas, which simply compress adjacent structures. Liposarcomas have a predilection for local recurrence but do not generally metastasise.

The role of adjuvant chemotherapy remains controversial,²² and is best addressed on a case-by-case basis.

In this case complete surgical resection was possible, so a subsequent chemotherapy was not performed.

In general, the treatment of choice is surgery, and complete resection of the tumour is recommended whenever possible.^{8 23 24} According to the literature, aggressive surgical intervention seems to favour the quality of life of patients and prolong survival, being considered the most effective treatment.¹⁴

The prognosis depends on the histological subtype and on surgical resection with wide margins of safety.^{24 25} Recurrence is seen in approximately 40% of the cases and has been reported at up to 14 years after the initial surgical procedure.²⁵

Behaviour of a specific tumour is ultimately dependent on its histological subtype. When treated with surgery and perioperative radiation therapy, well-differentiated liposarcomas exhibit a <10% local recurrence rate and a virtually 0% rate of metastasis.²⁶ In contrast, pleomorphic liposarcomas recur in about 1/3 of cases and spread in about 40%. Five and 10-year survival rates for patients with liposarcomas have been reported as 100% and 87% for well-differentiated, 88% and 76% for myxoid variants and 56% and 39% in the pleomorphic subtype.^{26 27} Features associated with longer survival include (1) left-sided tumour, (2) complete tumour resection, (3) postoperative adjuvant therapy and (4) tumours with less than 10 mitoses/HPF and absent necrosis.^{6 16 17}

Once the tumour has been excised and adjuvant therapy completed, continued surveillance is required to promptly detect any evidence of local recurrence or distant metastasis. This typically involves careful physical examination, chest x-rays and serial imaging of the chest and abdomen (usually CT).

In conclusion, surgical resection is the treatment of choice, and depending on the histological subtype an additional irradiation or chemotherapy may be necessary to avoid tumour recurrence. However, long-term follow-up evaluation is indicated in all cases of liposarcomas of the heart.

Learning points

- ▶ Primary mediastinal liposarcomas are extremely rare. They comprise less than 1% of all mediastinal tumours.
- ▶ Depending on the tumour size, liposarcomas can be asymptomatic or symptomatic. Symptoms include dyspnoea, chest pain, palpitation, rhythm disturbances, syncope, angina, cough and constitutional symptoms like fever and weight loss.
- ▶ Histological distinction between liposarcomas and lipomas can be very difficult and adequate sampling of tumour specimens is required to confirm the suspected diagnosis.
- ▶ Needle biopsies are often inadequate for accurate diagnosis of lipomatous tumours.
- ▶ For successful treatment complete surgical resection is required, sometimes supplemented by subsequent radiation or chemotherapy.

Competing interests None.

Patient consent Obtained.

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