Focal rhabdomyosarcomatous differentiation in primary liposarcoma

J H Shanks, S S Banerjee, B P Eyden

Abstract
A unique case of primary myxoid liposarcoma of the thigh, in which focal pleomorphic areas were present containing rhabdomyoblasts, is described. Focal rhabdomyosarcoma in liposarcoma has only rarely been reported previously and only in dedifferentiated liposarcomas of the retroperitoneum. All but one have been recurrences with rhabdomyoblasts being absent in the primary liposarcoma. As rhabdomyoblasts were only focally present, the present case is regarded as liposarcoma with focal divergent rhabdomyoblastic differentiation rather than malignant mesenchymoma.

Keywords: liposarcoma, rhabdomyosarcoma, malignant mesenchymoma.

Liposarcoma may contain benign or malignant heterologous mesenchymal elements. Benign cartilage, smooth muscle, or rarely bone have been described in well differentiated liposarcoma/atypical lipomatous tumours or in myxoid liposarcoma. Until now, malignant heterologous elements have been found only in dedifferentiated liposarcoma.

Malignant myogenic elements found in liposarcoma have included leiomyosarcoma, rhabdomyosarcoma, or both. Other heterologous elements including angiosarcoma or osteoid have also been described rarely. Divergent rhabdomyosarcomatous differentiation has been reported previously in only seven cases of liposarcoma. All were dedifferentiated liposarcomas arising in the retroperitoneum and in all but one case rhabdomyosarcoma was found only in tumour recurrences. There is only a single previous case of rhabdomyosarcomatous differentiation in de novo liposarcoma, a retroperitoneal dedifferentiated tumour.

Here, we describe a unique case of divergent rhabdomyosarcomatous differentiation in a de novo liposarcoma, which was of combined myxoid and pleomorphic subtypes arising in the thigh. Immunohistochemical and ultrastructural evidence is provided to support our diagnosis.

Case report
A 75 year old man presented with a six week history of a swelling in the right thigh. This was associated with oedema of the right leg, but there were no systemic symptoms. There was no evidence of any abdominal mass. On exploration, a mass was found to be displacing, but not invading, the femoral vessels and nerves. The tumour was easily mobilised except on the posterior surface where it was adherent to the pectineus muscle.

Macroscopically, the tumour consisted of a partly encapsulated fatty mass measuring 12 cm at its maximum dimension with a small amount of surrounding soft tissue. It was partly necrotic. Histologically, the tumour was a liposarcoma which was predominantly of myxoid type with a typical delicate branching capillary network and myxoid stroma (fig 1). In places, the tumour had more cellular pleomorphic areas. The latter were composed of spindle cells with notable nuclear pleomorphism and bizarre lipoblasts containing typical scalloped nuclei and cytoplasmic lipid vacuoles (fig 1, left upper inset). Mitotic activity was frequent (21/10 high power fields) within the pleomorphic areas and large foci of necrosis were seen. The tumour grade was 3 based on the method by Trojani et al.

Cells within the pleomorphic areas had abundant eosinophilic cytoplasm and noticeably hyperchromatic nuclei (fig 1, right lower inset), many showing notable nuclear enlargement and irregular nuclear contours. Pleomorphic multinucleate tumour giant cells were also seen. No cross striations were visible by light microscopy. Immunohistochemistry was performed using the streptavidin-peroxidase complex technique with diaminobenzidine chromogen substrate. The pleomorphic cells showed intense cytoplasmic positivity using immunostains for desmin (diluted 1 in 25; Dako, High Wycombe, UK), Myoglobin (diluted 1 in 1000; Dako) and muscle specific actin (HHF 35) (diluted 1 in 40; Biomen, Finchampstead, UK) were also positive in these cells. A proportion of them were positive for fast myosin (diluted 1 in 600; Sigma, Poole, Dorset, UK) and sarcomeric actin (diluted 1 in 100; Sigma). No tumour cells stained for

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smooth muscle actin (SMA) (diluted 1 in 1500; Sigma). Smooth muscle and other heterologous elements were absent.

Paraffin wax embedded tissue from relevant areas was reprocessed for electron microscopy. Ultrathin sections of epoxy resin blocks were stained with uranyl acetate and lead citrate, and examined in an AEl electron microscope. Some tumour cells contained sarcomeric myofilaments (fig 2). These comprised thick myosin filaments with dense bodies compatible with Z-disks. Thin filaments were also present but were not well preserved.

Follow up revealed multiple bony metastases detected within three months of presentation. The patient has subsequently received radiotherapy to the groin.

Discussion

Until now the presence of heterologous rhabdomyoblastic elements has been described only in seven cases of liposarcoma. 3, 4, 7 In one of these cases divergent rhabdomyosarcoma and leiomyosarcoma were present concurrently. 4 Malignant heterologous elements were found only in recurrent dedifferentiated retroperitoneal liposarcomas except for one previous case in which rhabdomyosarcoma was present in a de novo dedifferentiated retroperitoneal liposarcoma. 3

Our case is the first account of liposarcoma with divergent rhabdomyosarcomatous differentiation at a site other than the retroperitoneum. Our case is only the second reported example of rhabdomyosarcomatous differentiation in the initial excision specimen of a liposarcoma rather than in a recurrence. Furthermore, until now rhabdomyoblastic differentiation had not been described in either pleomorphic or in combined myxoid and pleomorphic liposarcoma, having only been found in dedifferentiated liposarcoma.

Dedifferentiated liposarcoma as originally described by Evans 5 contains well differentiated liposarcoma in addition to a cellular mitotically active spindle cell component in which lipogenesis (presence of lipoblasts) is lacking. Our case contrasts with dedifferentiated liposarcoma in two respects. Firstly, it was composed predominantly of myxoid liposarcoma rather than well differentiated liposarcoma. Secondly, lipogenesis was clearly identified in the pleomorphic areas of our tumour. This component therefore fulfilled the criteria for pleomorphic liposarcoma. 6 A combination of myxoid and pleomorphic liposarcoma as noted in our case is unusual although all combined types represent approximately 5 to 10% of cases of liposarcoma. 8 None of the previous cases with divergent rhabdomyosarcomatous differentiation were of pure myxoid type, although Salzano et al. 9 reported that some myxoid areas were present concurrently.

It could be argued that our case is an example of malignant mesenchymoma, a term originally proposed in 1948 by Stout.1 Malignant mesenchymoma was defined as a sarcoma composed of two unrelated differentiated mesenchymal elements other than fibrosarcoma. In 1991 Neuman and Fletcher 10 described nine cases which they classified as malignant mesenchymoma. Four of these were liposarcoma combined with rhabdomyosarcoma arising in retroperitoneum or spermatic cord. Two further cases contained liposarcoma, rhabdomyosarcoma and osteochondrosarcoma (abdominal wall and retroperitoneum). More recently, the concept of malignant mesenchymoma as an entity has aroused some controversy and Evans et al. 11 suggested that most neoplasms for which this diagnosis might be considered should be more meaningfully and specifically classified according to the predominant component. They urged that the term malignant mesenchymoma be avoided where possible. Conversely, Enzinger and Weiss 12 seem to accept that tumours with myosarcomatous and liposarcomatous elements as true

![Figure 1](https://example.com/image1.png)

**Figure 1** Myxoid liposarcomatous area (L) merging with a rhabdomyosarcomatous area (R). Inset upper left: typical lipoblast; inset lower right: typical rhabdomyoblast (haematoxylin and eosin).

![Figure 2](https://example.com/image2.png)

**Figure 2** Electron micrograph showing sarcomeric myofilaments (arrow, A), Z-disks (arrowsheads, A) and an individual myofilament with thick straight myosin filaments (arrow, B). A, ×13 000; B, ×52 000.
malignant mesenchymomas but urge caution and application of strict diagnostic criteria in order to avoid a "diagnostic wastebasket". This area is therefore obviously controversial and our tumour could equally be regarded as a malignant mesenchymoma as it would appear to meet the strict definition of that entity. Enzinger and Weiss suggest classifying such a tumour as malignant mesenchymoma, stating the predominant tissue elements which in our case would be "malignant mesenchymoma (combined myoid and pleomorphic liposarcoma with focal rhabdomyosarcomatous differentiation)". In this paper we have preferred to classify the tumour according to the predominant component present as the rhabdomyosarcomatous elements were only present focally. This approach has also been taken by others.1

The clinical significance of heterologous elements is unknown but myoid or pleomorphic liposarcoma alone or in combination each have potential for metastasis (as occurred in our case) as well as local recurrence. It has been tentatively suggested that the presence of heterologous elements in liposarcoma in itself probably does not alter the prognosis.1

Immunohistochemical confirmation of rhabdomyosarcomatous differentiation in previously described examples of liposarcoma has been limited and electron microscopy has only been performed in one previous case.1 Myoglobin reactivity was found in the three cases tested and myosin in one case tested. No other skeletal muscle markers had been reported previously. Myoglobin was demonstrated immuno histochemically in all cases showing rhabdomyosarcomatous differentiation and classified as malignant mesenchymoma.11 The immunohistochemical and ultrastructural evidence which we have presented confirms the presence of rhabdomyoblasts in our case beyond all doubt. This phenomenon might be more frequent in liposarcoma than is generally realised.

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Pseudopyropoikilocytosis: a striking artefact

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Abstract
The blood films both of patients with hereditary pyropoikilocytosis and of those with severe thermal burns are characterised by budding erythrocytes and the presence of microspherocytes. Recently, a fourth example of similar morphological features, caused by overheating of a blood specimen in a motor vehicle during transport to the laboratory, has been observed. It is important to be aware of this artefact as failure to recognise it is likely to lead to diagnostic confusion and unnecessary further testing, causing inconvenience to the patient.


Keywords: pseudopyropoikilocytosis, artefactual results of laboratory tests, automated blood counters, erythrocyte morphology.

The blood films of patients with hereditary pyropoikilocytosis show some resemblance to the films of patients with severe burns.1 This observation led to the recognition of the thermal instability of the red cell membrane which characterises this condition. We have recently seen our fourth case of an artefactual change which simulates hereditary pyropoikilocytosis and thus can cause diagnostic confusion.

A routine antenatal screening specimen from an African woman who was 26 weeks pregnant was received in our laboratory on an April afternoon. An automated full blood count on a Technicon H.2 counter gave the following results: white blood cell count 11.8 x 10⁹/l; red blood cell count 3.85 x 10¹²/l; haemoglobin 10.6 g/dl; haematocrit 0.32; mean corpuscular volume 83 fl; mean corpuscular haemoglobin 27.4 pg; mean corpuscular haemoglobin con-
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