

Lipid rich rhabdomyosarcoma

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Abstract

A lipid rich rhabdomyosarcoma of the paratesticular region was studied by light microscopy, histochemistry, immunohistochemistry and electron microscopy. The tumour was composed of primitive looking, vacuolated, and pleomorphic cells. Lipid was present in varying amounts in all cells but was especially abundant in the vacuolated and pleomorphic cells. Some cells showed eosinophilic fibrillary cytoplasm but cross-striations were not seen. Tumour cells were positive for desmin, muscle specific actin, and vimentin. A few cells were myoglobin positive. At electron microscopy, the presence of lipid was confirmed, while thick and thin filaments, Z disks, lamina and glycogen were observed, thereby confirming striated muscle differentiation.

Although moderate amounts of lipid can be expected in almost any tumour, lipid rich rhabdomyosarcomas have received little attention. The present report provides a comprehensively examined case of such a tumour initially presenting diagnostic difficulty because of its possible confusion with liposarcoma.

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Rhabdomyosarcomas are usually divided into three main types: embryonal, pleomorphic, and alveolar. Mixed,¹ solid,² spindle cell,³ clear cell⁴ and lipid rich⁵ types have been described. We describe a case of lipid rich mixed rhabdomyosarcoma occurring in the paratesticular region, which initially presented diagnostic confusion with liposarcoma.

Case report

A 19 year old man presented with a right scrotal swelling of three months' duration. It had been gradually increasing in size and was recently associated with a dull ache. An ultrasound scan showed the presence of a mass of mixed echogenicity adjacent to, but not arising from, the testis. A computed tomogram of intra-abdominal lymph nodes was normal at this time. Despite subsequent chemotherapy with doxorubicin and ifosfamide, the patient developed a right inguinal node metastasis containing similar tumour. Fourteen months after initial presentation the patient had multiple bilateral pulmonary metastases and possible metastases in the right femur and left acetabulum.

Methods

The tumour was fixed in 10% buffered formalin and sections were stained with haematoxylin and eosin, periodic acid Schiff (PAS) with diastase digestion, and Oil red O. For electron microscopy, tissue was retrieved from formalin, treated with osmium tetroxide and en bloc aqueous uranyl acetate, dehydrated in ethanol and embedded in epoxy resin. Some tissue was examined following retrieval from the wax block. Immunohistochemistry was performed using a streptavidin-biotin complex method with the following antibodies: CAM 5.2 (Becton Dickenson UK; 1 in 20 dilution); anti- α smooth muscle actin (Sigma UK; 1 in 1500); anti-vimentin (Sigma UK; 1 in 5000); anti-muscle specific actin (HHF 35) (Biogenex USA; undiluted); anti-desmin (D33) (Dako USA; 1 in 100); anti-myoglobin (Dako UK; 1 in 1000).

Pathological findings

The tumour mass measured 12 × 6.5 × 5 cm and was composed of pink-white tissue with yellow areas. It was closely opposed to, but not arising from, the testis and epididymis. The tumour was surrounded by a thin capsule, which looked intact. The testis and vas deferens looked normal. Histologically, the tumour cells were of three main types. Some were rather primitive and spindle-shaped with poorly defined cytoplasm; others were large, bizarre cells with pleomorphic, hyperchromatic nuclei (fig 1A), some being multinucleated, with eosinophilic, clear, or bubbly cytoplasm (figs 1A, B). A third population of cells was of clear cell type, with either a large, single cytoplasmic vacuole, or with fine septa dividing the cytoplasm into numerous locules (figs 1B, C). Often the nucleus was pushed to the side of the cell and some cells showed nuclear indentations rather like lipoblasts (fig 1C). There were also occasional cells with very eosinophilic, fibrillary cytoplasm, although no cross-striations were seen. The stroma contained myxoid and hyaline areas.

The different cell types were mixed together in some areas, but in others they formed discreet collections of one cell type. The mitotic rate was very high at 80 per 10 high power fields (× 40 objective magnification, × 10 eyepiece, Leitz Diaplan).

The testis, epididymis, and vas deferens were normal and although the tumour cells were seen adjacent to these tissues, there was no apparent tumour origin from them.

The stain for glycogen was positive, particularly in the clear cell areas, and Oil red O stain for lipid revealed extensive positivity

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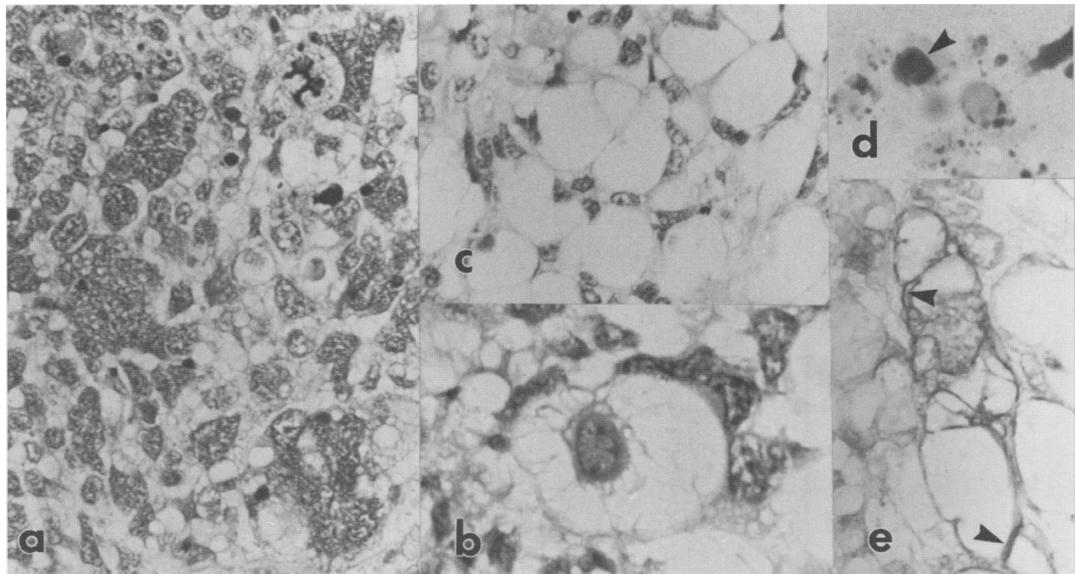


Figure 1A Pleomorphic nuclei (arrowheads) and an abnormal mitotic figure (small arrow) (haematoxylin and eosin). **(B)** Spider web type of rhabdomyoblast (haematoxylin and eosin). **(C)** Lipid rich rhabdomyoblasts mimicking primitive adipocytes (haematoxylin and eosin). **(D)** Abundant lipid droplets in tumour cells (oil red O). **(E)** Lipid rich rhabdomyoblasts showing slender strands of desmin-immunoreactive cytoplasm (arrowheads) (streptavidin-biotin complex).

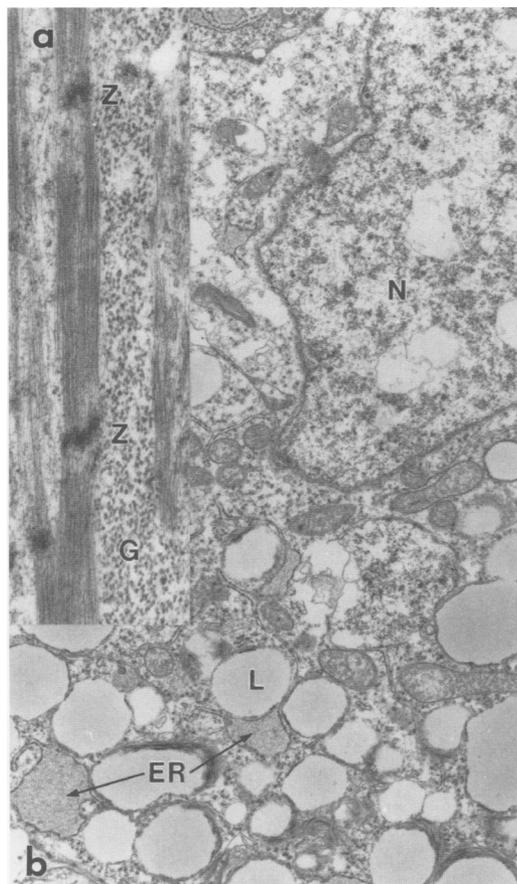
throughout the tumour in all cell types, which was most pronounced in the clear cells (fig 1D): the primitive cell types showed fine granular cytoplasmic staining.

Tumour cells showed positive immunostaining for desmin (fig 1E), muscle specific actin, and vimentin, and negative staining for

cytokeratin (CAM 5-2) and smooth muscle actin. A few cells were myoglobin positive. The vacuolated clear cells were particularly strongly stained for desmin and muscle specific actin around the cell periphery and along the septa dividing the multi-vacuolated cells.

At electron microscopy, cells contained alternating thick and thin filaments, sometimes arranged in a hexagonal array, Z disks, external lamina and glycogen lakes (fig 2A). Lipid was also abundant in some of the large, pleomorphic cells (fig 2B).

Figure 2A Myofibrils of striated muscle type showing Z discs (Z). Note glycogen (G). **(B)** Pleomorphic lipid rich tumour cell with multiple nuclear profiles (N), rough endoplasmic reticulum (ER), and abundant lipid (L).



Discussion

Lipid is found in varying amounts in a wide variety of both epithelial and mesenchymal tumours.⁶ When the lipid content is high, the tumours are often described as “lipid rich” and in some of these cases diagnostic confusion with liposarcoma may arise. In this case the features on light microscopy were of a pleomorphic sarcoma, thought to be a mixed rhabdomyosarcoma (with pleomorphic and embryonal areas) but focally mimicking a liposarcoma. Although liposarcomas of the paratesticular region have been described, they are very rare,⁷ in contrast to rhabdomyosarcomas which are said to occur with greatest frequency in this area.⁸

The immunohistochemistry strongly suggested skeletal muscle differentiation and this has been confirmed by the ultrastructural demonstration of organelles characteristic of striated muscle: clearly defined thick and thin filaments with Z disks, as well as other features typical of but not specific for muscle cells, such as glycogen and lamina.

Lipid is reported as a “not infrequent” finding in rhabdomyosarcoma,⁹ and according to Bundtzen and Norback in their review,

lipid is described in a number of case reports.¹⁰ However, there are few well documented examples of pleomorphic rhabdomyosarcoma with abundant cytoplasmic lipid. Zuppan *et al* recently published a study of three lipid rich, poorly differentiated childhood rhabdomyosarcomas; desmin, muscle specific actin, and myoglobin were variably expressed, but ultrastructurally only one specimen contained rare cells with myosin-ribosome complexes, and no thick and thin filaments or Z disks were present in the tumours.⁵ By contrast, our case in a young adult showed a high level of immunohistochemical and ultrastructural differentiation. We believe it represents a rare example of a lipid rich rhabdomyosarcoma. It is important to recognise that tumours containing large amounts of lipid may lead to diagnostic confusion. Appropriate immunohistochemistry and especially electron microscopy should be performed and correlated with the clinical findings to reach the correct histological diagnosis.

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