

Tumors of Striated Muscle

H. T. ENTERLINE, M.D.

*Department of Pathology,
Hospital of the University of Pennsylvania,
Philadelphia, PA 19104*

ABSTRACT

Three benign forms of muscle tumors and three variants of rhabdomyosarcoma are discussed from the point of view of their histology and behavior. Recent combined modality therapy has significantly improved the prognosis in at least the embryonal form of rhabdomyosarcoma.

Introduction

Tumors of striated muscle are important both from the standpoint of relative frequency and because of recent encouraging advances in their therapy. From 10 to 20 percent of all sarcomas belong in this series.⁹ Accuracy in diagnosis is essential. This brief review outlines the various guises in which neoplasms containing neoplastic striated muscle may present themselves.

Though the vast majority of tumors are malignant, some are benign. The term rhabdomyoma has been applied to at least three distinctive and rare neoplasms or pseudoneoplasms.

Cardiac Rhabdomyoma

This is the most familiar benign lesion and the least likely to be a true neoplasm. The majority of cases occur before the age of three, but they have been reported in adults. They present as gray-white nodules on the ventricular or, rarely, auricular septum or endocardium. The histology (figure 1) is that of a spongy-looking tissue owing to excessive glycogen accumulation within the cells. Many believe that these are best considered hamartomas, pointing out that over 50 percent of the cases are in patients with

tuberous sclerosis.^{1,13} Some consider them as a localized form of Von Gierke's disease.

Adult Type Rhabdomyoma

Twenty of these very rare tumors were reviewed by Olofsson;¹¹ the author has seen five such cases. Despite their name, these tumors may occur at any age and usually present in the oral, pharyngeal or laryngeal area. They are yellowish-brown lobulated tumors of striking histologic appearance. Cells are round, often quite large and polygonal or ovoid with eosinophilic cytoplasm, often coarsely vacuolated (figure 2). Myofibrils are present, but "out of register", producing a crystalline appearance at times with the phosphotungstic acid hematoxylin stain (PTAH). Occasional cells with cross striations may be found. All cases reported to date have been benign. The author has, however, recently seen one case in a 31 year old man which recurred six years after initial excision from its primary in the tongue. In the recurrence, there are areas that are freely infiltrating adjacent striated muscle and that cytologically look exceedingly ominous. There has not been sufficient time to determine whether or not this will metastasize. The usual diagnostic error, from the pathologist's point of view, is to mistake it for

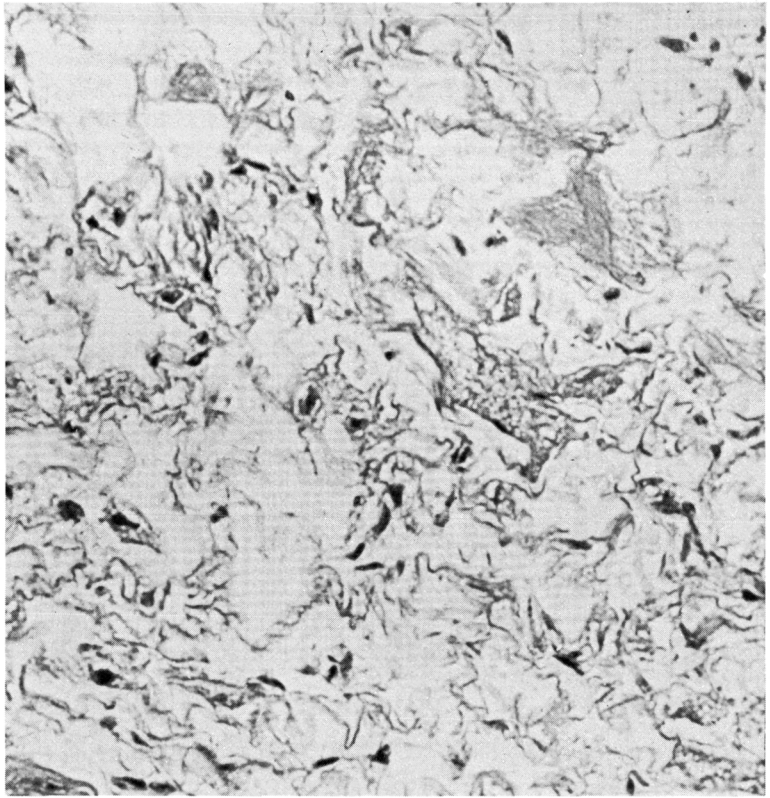


Figure 1. Cardiac "rhabdomyoma." Note enormously vacuolated cells with cytoplasm pushed to periphery producing a spongy appearance.

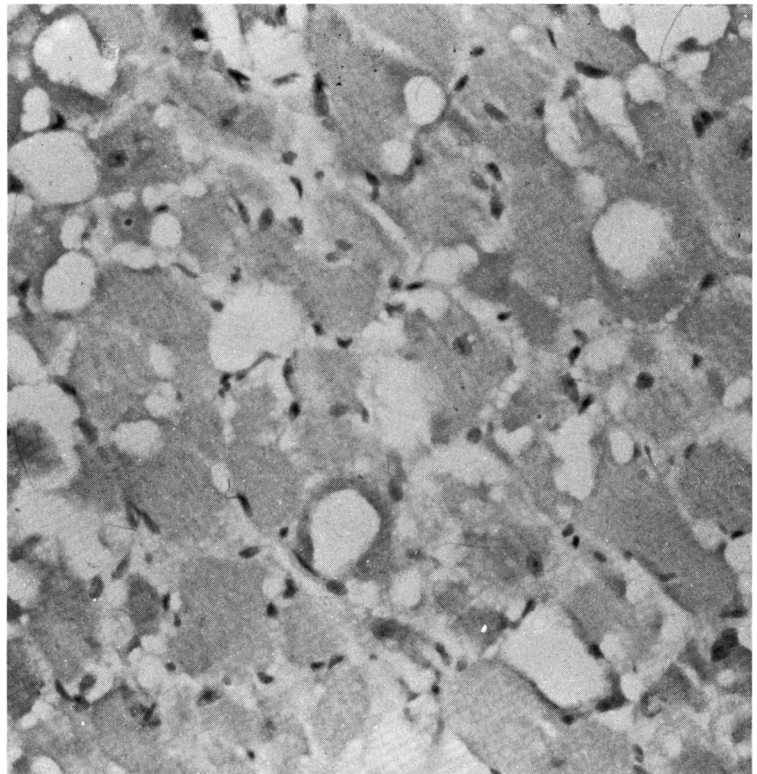


Figure 2. Adult type rhabdomyoma. Tumor of buccal region of middle-aged male. Note ovoid-to-polygonal cells and coarse (glycogen) vacuoles.

granular cell myoblastoma (which, despite its name, is not a tumor of muscle origin).¹⁰

Fetal Type Rhabdomyoma

This more recently recognized tumor has been seen also most frequently about the head and neck, especially in the postauricular region. Several cases have been reported from the vulva and vagina. These are composed of rather highly differentiated striated muscle cells in a haphazard pattern with admixed smaller cells of indeterminate nature (figure 3). There have, as yet, been no intermediary forms reported between this and the adult type. They require differentiation from highly differentiated rhabdomyosarcomas of the embryonal type, which very rarely may mimic them. The presence of mitoses, at present, is accepted as evidence of malignancy.²

Tumors with a Rhabdomyoblastic Component

Rhabdomyoblasts may be a component among other components of a variety of tumors. The most familiar is the malignant mixed mesodermal tumor of the uterus, where it is associated with carcinoma and with nonspecific sarcomatous elements. The rhabdomyoblastic component may or may not be prominent. These polypoid tumors chiefly occur in postmenopausal women and the prognosis is very poor. Occasional cases of pure rhabdomyosarcoma of the uterus have been reported without associated carcinomatous elements. Whether or not these are in the same series or should be considered differently is a moot point.

Less familiar is the peculiar finding of rhabdomyoblasts in malignant (and in two cases, benign) peripheral nerve tumors. These have been reported in schwannomas

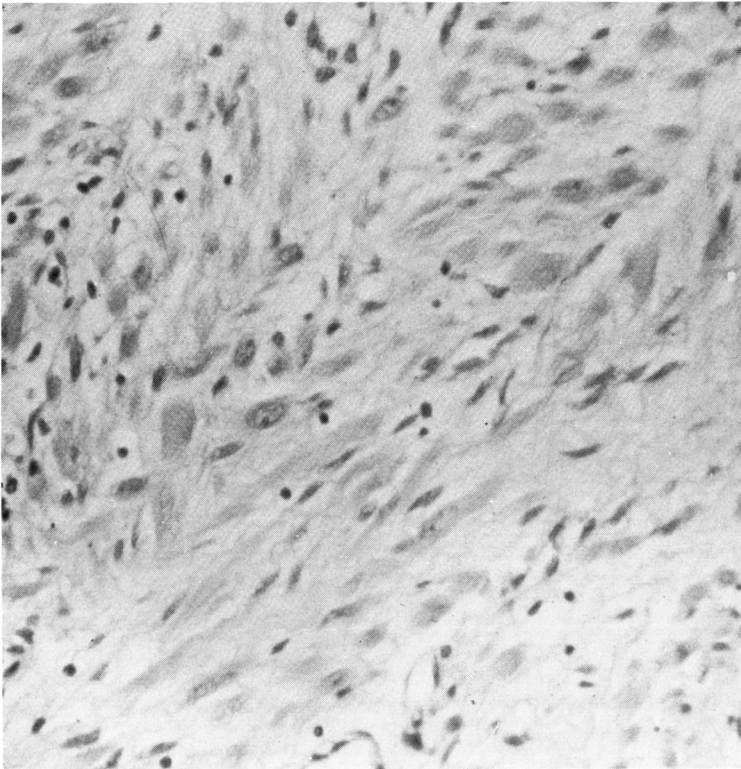


Figure 3. Fetal type rhabdomyoma—tumor of vagina. Elongated and highly differentiated striated muscle cells with admixed smaller cells of indeterminate nature. Courtesy Armed Forces Institute of Pathology.

TABLE I

Degrees of Differentiation of Rhabdomyosarcomas

<i>Horn and Enterline</i> ⁷	<i>Current Usage</i>
Pleomorphic	Pleomorphic
Alveolar	Alveolar
Embryonal	Embryonal
Botryoid	

in patients who usually have von Recklinghausen's disease. They illustrate the ability of the Schwann cell to differentiate in various directions. The term "triton tumor" has been applied to these because of the fancied similarity to the induction of limb buds in the triton salamander by motor nerve implants.¹⁶ Rhabdomyoblasts are also occasionally reported in medulloblastomas and medulloepitheliomas¹⁷ and, of course, may be a feature in certain teratomas.

Rhabdomyosarcomas

In these tumors, the rhabdomyoblast, in various degrees of differentiation, is the sole malignant element (table I). Although there is no doubt intergrading, there are several well defined variants which differ considerably in presentation and are best discussed separately.

The gross appearance of these variants is similar, usually presenting as soft, fleshy, pinkish tumors often considerably modified by hemorrhage and necrosis. Indeed some of these, where there has been a history of trauma, have been mistaken for hematomas. Certain of the embryonal forms differ in presenting as pale myxoid translucent tumors, this especially being true of the botryoid form.

PLEOMORPHIC TYPE

These, as described in the classic paper of Stout,¹⁵ are basically spindle cell tumors with a highly pleomorphic, eosinophilic cell component. Typical band forms with tandem nuclei or racket-shaped multinu-

cleated cells are classical (figure 4). Cross striations fulfill the diagnosis. The average age of presentation of these is about fifty; however, they may occur in children. Most are in the extremities or limb girdle and are deep-seated tumors within or between major muscle masses. The prognosis has been poor. Lymph node metastases in this and other variants of rhabdomyosarcoma are not uncommon, and must be considered in surgical therapeutic maneuvers. Venous invasion is frequently identifiable and pulmonary metastases are frequent. Better survivals are reported for more superficial tumors, but this may reflect some errors of diagnosis. Certain atypical fibrous histiocytomas may closely mimic pleomorphic rhabdomyosarcoma. Enzinger has emphasized this problem. The pleomorphis (adult) type of rhabdomyosarcoma was once considered the most common. It is distinctly less common than the embryonal in current experience. The Armed Forces Institute of Pathology now so classifies only 87 out of 773 cases of rhabdomyosarcoma as compared with 536 of the embryonal type. Every effort should be made to demonstrate myofibrils and cross striations in order to avoid misdiagnosis. Proliferative myositis has also been confused with rhabdomyosarcoma and other sarcomas.

ALVEOLAR TYPE

This peculiar variant became well recognized only in the late 1950's.^{4,12} It has been reported at all ages, but the median age is in the late teens. It is almost always intimately associated with mature muscle of the extremities. It currently carries the worst prognosis of any variant. In Enzinger's series,⁵ only eight of 108 cases were alive and only four were free of metastases.

The tumors vary in appearance, but all show a tendency for the tumor cells to line spaces with nuclei, often at the luminal termination of the cell, giving a hobnail appearance. In addition, there are invariably

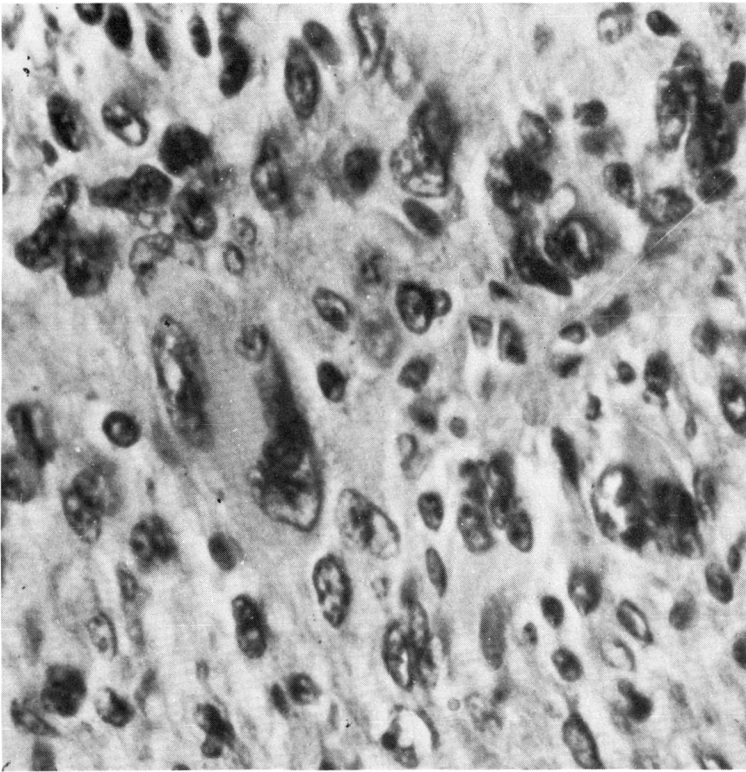


Figure 4. Adult type rhabdomyosarcoma. Note marked pleomorphism and hyperchromatism of eosinophilic cells with scattered multinucleated giant forms. Cross striations were identified (not shown) in other areas of this tumor of the thigh.

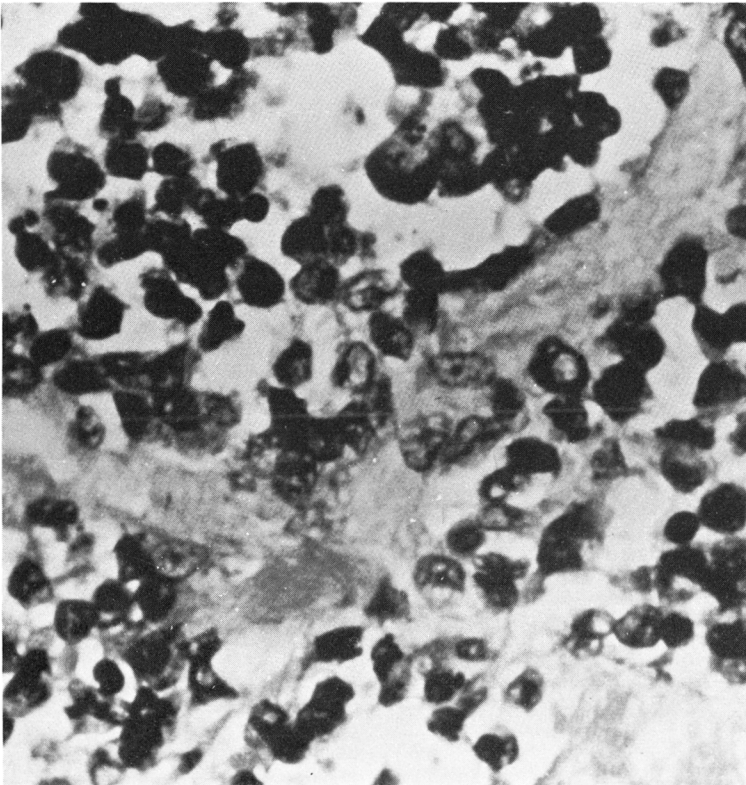


Figure 5. Alveolar type rhabdomyosarcoma. Note vaguely defined septae with cells both lining septae and free in "alveolar" spaces.

“cast-off” cells floating within the alveolar spaces (figure 5). The cells may be small, round and hyperchromatic and are, therefore, apt to be confused with malignant lymphomas. Usually, some will show eosinophilic cytoplasm or be large and multinucleated with abundant cytoplasm, assuming a round or strap shape. Cross striations may be identified in certain of these. Small foci with this histologic appearance may be seen in embryonal rhabdomyosarcomas. The definitely worse prognosis argues for keeping this form distinct. It requires differentiation from malignant lymphoma, adenocarcinoma and alveolar soft part sarcoma. The latter is confusing, but can be readily separated by the complete reticulin sheath about the pseudoacini and by the crystalloid material demonstrated with the periodic acid-schiff (PAS) technique. It is too early to tell whether or not newer methods of therapy will improve the prognostic picture.

EMBRYONAL AND BOTRYOID RHABDOMYOSARCOMA

These are by far the most common type of rhabdomyosarcoma. The botryoid form is now agreed to be identical to the embryonal, differing only in the gross appearance because of its position beneath the lining of a hollow viscus, such as the antrum, vagina or bile duct. They may occur at any age, but are most often found in infancy and the preschool child. Similarly, they may occur anywhere, but markedly cluster in the head and neck area as well as in the genitourinary area, such as vagina, cervix, bladder, prostate and the paratesticular region. It is the most common malignant neoplasm of the orbit in children.

The histology was well brought out in the classical paper by Stobbe and Dargeon.¹⁴ It is basically a tumor of bipolar spindle elements with eosinophilic cytoplasm (figure 6). These often have an admixture of small rounded cells. They frequently have an

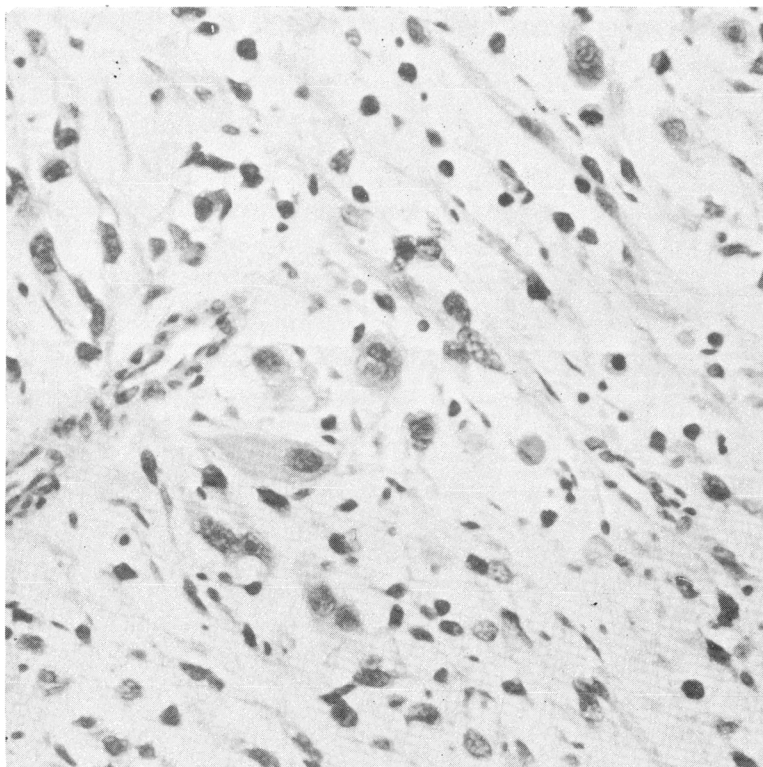


Figure 6. Embryonal rhabdomyosarcoma. Note eosinophilic slender band forms in a somewhat myxoid background. Some large plump ovoid cells with eosinophilic cytoplasm are also present.

overall myxoid appearance, but there is marked variation in cellularity. Cross striations may be difficult to find. Often the cells are somewhat better differentiated at the periphery. Thus, a so-called "cambium" zone is often seen in the subepithelial zone of a botryoid sarcoma, which may be helpful in making the diagnosis. Often one may find cross striations in this area. They require careful differentiation from certain benign myxoid processes including the rare myxoid polyp of the vagina. Thus, the PTAH stain will again be helpful.

Prognosis of this group in the past, as with all rhabdomyosarcomas, has been dismal. Even the most radical surgical approach was nearly always frustrated by prompt appearance of pulmonary metastases. Kilman and coauthors⁸ reported 64 cases with only five survivors (representing a compendium of three different series). Seventy-four percent developed metastases within six months and 85 percent within the first year. The contrast in their own experience prior to and after 1967 is striking. The salvage rate for Stage I was 30 percent in the earlier period contrasted with 86 percent for the later series, and for Stage II, 0 percent as compared with 58 percent.

Similarly encouraging results have recently been published by the Memorial Hospital group with an overall 62 percent survival of urogenital embryonal rhabdomyosarcomas. Twelve of 13 survived when diagnosed at the localized stage before obvious spread of tumor had occurred.⁶ Donaldson and coauthors report a 74 percent two to seven year survival.³ In all of these reports, the therapy has consisted of a combined modality approach consisting of removal of all gross tumor possible, radiation to 5000 to 6000 rads, and combination chemotherapy, usually consisting of actinomycin D, vincristine and cyclophosphamide. This represents a real breakthrough which has transformed a uniformly discouraging picture to one of considerable hope. Cautious approaches to less deforming surgery may now be more reasonably explored. The embryonal group appears to be

the most responsive to radiation and chemotherapy. Results in other variants are currently less well documented because of their small numbers. With such results, accurate diagnosis is all the more essential to our understanding of this group of sarcomas.

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