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Rhabdomyosarcoma of the Orbit

A Clinicopathologic Study of 55 Cases

By

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With 8 Figures in the Text

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Rhabdomyosarcoma of the orbit, once considered a rare tumor, has been recognized with increasing frequency during the past few years. As a matter of fact, recent experience at the Armed Forces Institute of Pathology (ZIMMERMAN) and elsewhere (FRAYER and ENTERLINE) suggests that this is the most common malignant orbital tumor occurring in childhood.

In a review of the literature to 1942, CALHOUN and REESE could find only 14 reported cases of orbital rhabdomyosarcoma, to which they added 5 of their own. STOUT (2), who by September 1948 had studied 35 cases, reported only 1 from the orbit. In 1950 STOBBE and DARGEON reported 15 cases of embryonal rhabdomyosarcoma of the head and neck; 3 of the tumors were primary in the orbit. Nine years later, MOORE and GROSSI added 37 more rhabdomyosarcomas of the head and neck regions, 8 of which arose in the eyelid or orbit.

HORN and ENTERLINE, in 1958, reported 39 cases of rhabdomyosarcomas from all anatomic locations. Five of their tumors were primary in the orbit. BLAXTER and SMITH found only 33 cases of orbital rhabdomyosarcoma reported in the literature to 1958, to which they added 2 of their own. FRAYER and ENTERLINE reported 12 embryonal rhabdomyosarcomas of the orbit in 1959. The present series of 55 cases of orbital rhabdomyosarcoma not only is the largest yet reported, but it doubles the number of published cases.

Materials and Methods

The present report is an outgrowth of a clinicopathologic study of over 1,000 orbital tumors on file in the Registry of Ophthalmic Pathology at the Armed Forces Institute of Pathology (PORTERFIELD). Among these we have found 55 examples of orbital rhabdomyosarcoma with sufficient data to include in this study.

Based on their histopathologic characteristics, each rhabdomyosarcoma was classified into one of three histologic types: embryonal, differentiated, or alveolar. The histologic features of the embryonal and alveolar types have been described in detail by other investigators [ENTERLINE and HORN; ENZINGER; HORN and ENTERLINE; RIOPELLE and THERIAULT; SHUMAN; STOBBE and DARGEON; STOUT (2)], whose criteria for classification have been utilized in the present study. We have added a "differentiated type" to our classification, anticipating that the more highly differentiated neoplasms might have a better prognosis.

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In some instances there was a mixture of histologic types; such cases were classified according to the predominant pattern. A "pleomorphic type" of rhabdomyosarcoma, which is usually located in the peripheral musculature of adults, has been described (HORN and ENTERLINE). A purely pleomorphic tumor comparable to theirs was not recognized in our cases, but there was a certain pleomorphism in many of our tumors.

In each case, sections were stained with hematoxylin-eosin. When adequate material was available, the following additional stains were prepared: MASSON's trichrome, periodic acid-Schiff reaction (with and without diastase), MALLORY's phosphotungstic acid hematoxylin, and WILDER's reticulum *(Manual of histologic and special staining technics)*.

Clinical and follow-up data were correlated with each of the three histologic types. These data will be discussed separately with each histologic type.

Results

A. Embryonal Type (40 Cases)

Clinical Features. All patients with the embryonal type of rhabdomyosarcoma were Caucasian. The youngest was a newborn baby; the oldest 19 years. Their average age was 8 years (Table 1). Twenty-five were male, and 15 were female. The most common presenting sign was rapidly developing proptosis (Fig. 1). Proptosis was present in 31 and absent in 3; no information concerning it was available in 6 of the 40 cases. With one exception, the displacement of the eye was in a downward and temporal direction in the 19 cases in which the direction of proptosis was described. The direction of proptosis corresponds well with the most frequently stated location of these tumors — the upper inner quadrant of the orbit.

Table 1. *Age distribution of 55 patients with orbital rhabdomyosarcoma (91% under 15 years old)*

Age (years)	Embryonal	Differentiated	Alveolar	Total
0—5	13	3	6	22
6—10	16	0	1	17
11—15	10	1	0	11
16—20	1	0	2	3
21—25	0	2	0	2
Total	40	6	9	55

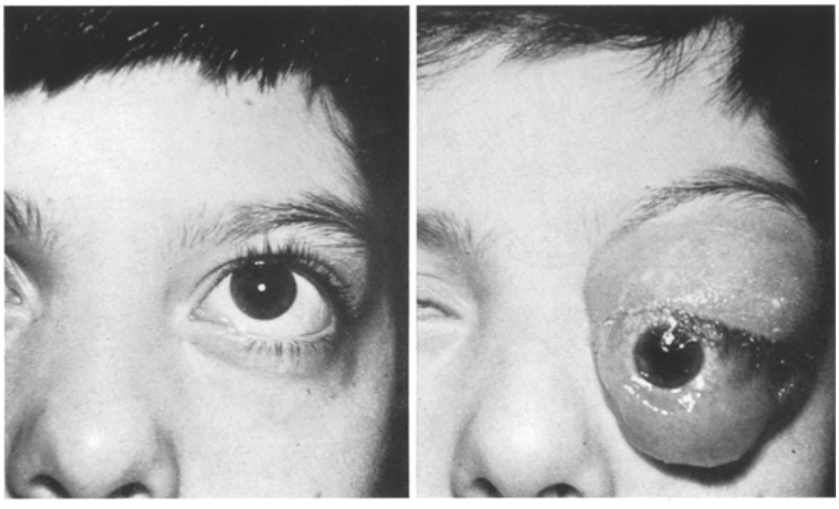
Less constant clinical signs and symptoms were palpable subconjunctival mass, redness of the eye, edema of the lids and conjunctiva, and ptosis of the lids. Pain was rarely an early symptom. Except for an orbital soft tissue density, results of roentgenographic studies were negative.

The tumors were described variously as soft, myxoid, grayish-white to yellowish, poorly defined masses in the upper inner quadrant of the orbit. In many instances the lesion extended into one of the eyelids, usually the upper lid. In no instance did the surgeon describe a tumor arising from one of the extraocular muscles. Except in a few cases in which no description was provided, the tumor was said to arise in the connective tissues, not in the extraocular muscles. At least two cases presented a multinodular subconjunctival mass similar to the sarcoma botryoides of the genitourinary tract. Since the term "botryoid" describes a gross characteristic, however, and since our two examples did not differ histologically from others classified as "embryonal", these cases were placed in the latter category.

Histologic Features. Although the histologic picture of embryonal rhabdomyosarcoma is fairly characteristic, there are many variations. Typically, stellate and spindle cells are arranged in a loose syncytium (Fig. 2a). In other areas, the syncytial pattern is less obvious, and the cells are more closely packed. Fre-

quently, there are alternating bands of loosely arranged and closely packed cells (Figs. 3a and b). The round to oval nuclei are rich in chromatin, and there are many mitotic figures. Although many of the cells are spindle shaped, most are stellate, round, or oval (Fig. 2b). The most important cell type is one with a long ribbon of brightly eosinophilic cytoplasm (Fig. 2c), for it is in such cells that longitudinal and cross striations are found.

We were able to demonstrate convincing cross striations in 24 (60 per cent) of our cases, usually after prolonged search. In most instances sections properly stained with hematoxylin-eosin were adequate for the demonstration of cross



a b

Fig. 1a and b. Embryonal rhabdomyosarcoma. a A 10-year-old girl with prominence of left eye of 3 weeks' duration. b Same patient 2 weeks later. This illustrates an exception to the observation that proptosis is characteristically in a downward and lateral direction. (Courtesy of Dr. J. A. C. Wadsworth, New York.) AFIP Neg. 61-2687-1 and 2

striations. Sometimes WILDER's stain for reticulum was helpful in demonstrating these structures (Fig. 2d). One of the most useful special stains was MASSON's trichrome. In addition to its value in demonstrating longitudinal and cross striations, this stain imparts a deep red color to the cytoplasm of muscle elements. Characteristically, reticular and collagenous fibers were very scanty or absent. In contrast to the experience of others, we had little success with the phosphotungstic acid-hematoxylin (PTAH) stain as a means of demonstrating striations. In most of the tumors there were diastase-sensitive cytoplasmic granules that stained deep purple with the periodic acid-Schiff reaction. We presume the granules contained glycogen.

Follow-Up Data. The follow-up data for embryonal rhabdomyosarcoma are summarized in Tables 2 and 3. Of the 33 patients for whom we have adequate follow-up information, 20 died of tumor. The average survival from the onset of symptoms was 12 months. One patient died 59 months after the first symptom. With this exception, all nonsurvivors died within 3 years. The brain and lungs were the most common sites of metastasis. Four patients were alive, but had recurrence or metastasis. Nine patients were alive 3 to 15 years after treatment

(Table 3). Insufficient follow-up information is available on seven patients, two of whom are "lost to follow-up". The other five have been followed for less than

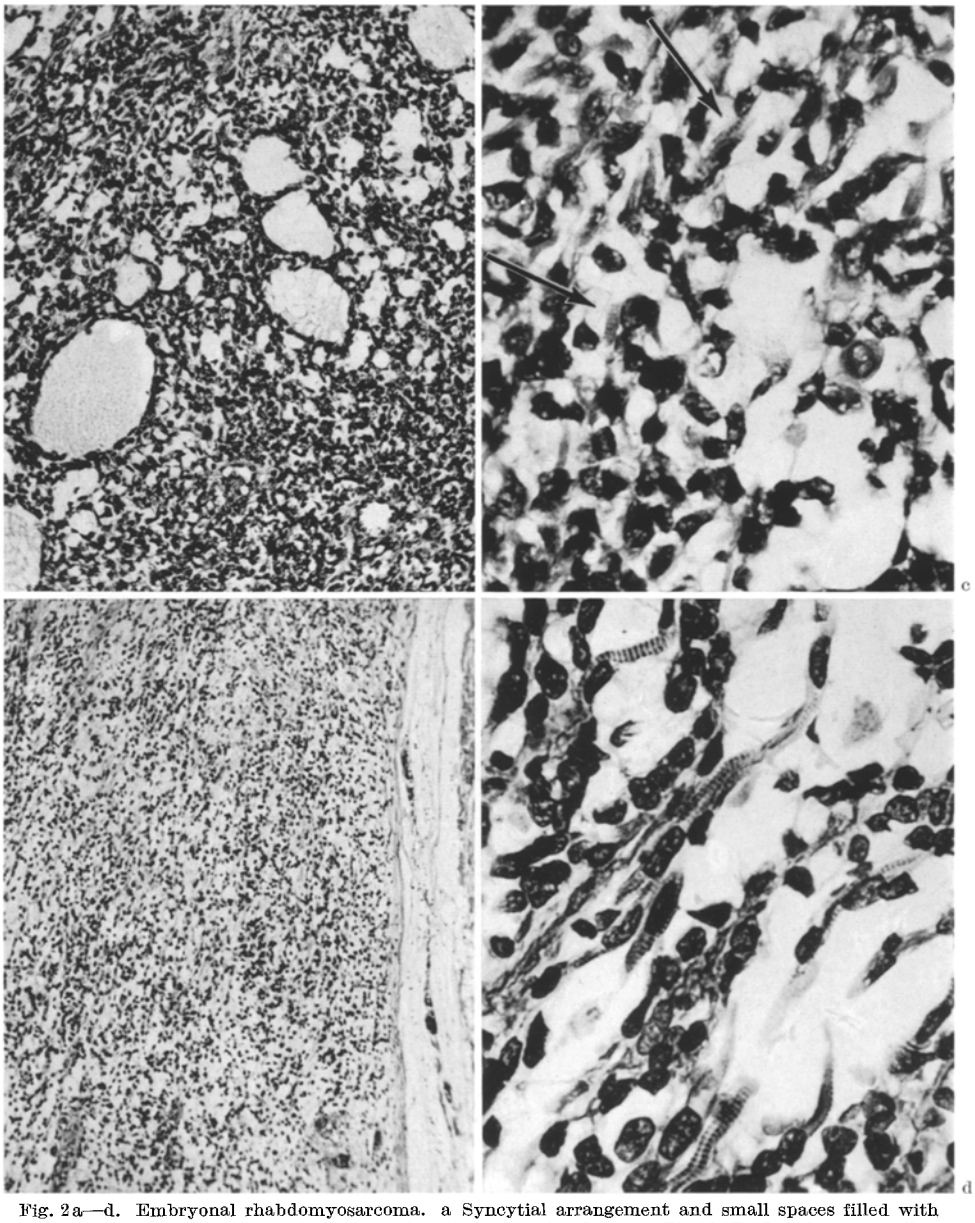


Fig. 2a—d. Embryonal rhabdomyosarcoma. a Syncytial arrangement and small spaces filled with faintly stained proteinaceous fluid. Hematoxylin and eosin. Mag. 104X. AFIP Neg. 61-1745. b Undifferentiated area resembling embryonic mesenchyme. Hematoxylin and eosin. Mag. 72X. AFIP Neg. 61-3786. c Hyperchromatic nuclei and ribbons of eosinophilic cytoplasm with faintly visible cross striations (arrows). Hematoxylin and eosin. Mag. 473X. AFIP Neg. 61-1747. d Cytoplasmic cross striations are present in many of the cells. WILDER's reticulum. Mag. 473X. AFIP Neg. 61-1746

1 year. As Tables 2 and 3 indicate, the primary mode of therapy in the nine surviving patients was by surgical procedure — usually exenteration of the orbit. None of the patients who received irradiation as the primary mode of therapy was

Table 2. *Follow-up data on 40 cases of embryonal rhabdomyosarcoma of the orbit*

Follow-up status	Number of cases*	Primary treatment	
		Surgical*	Irradiation*
Dead of tumor	20 (12)	11 (7)	9 (5)
Alive with recurrence	4 (3)	3 (2)	1 (1)
Alive and well 3 or more years	9 (5)	9 (5)	0
Insufficient follow-up information	7 (4)	0	0

* Numbers in parentheses indicate number of cases in which cross striations were demonstrated.

Table 3. *Data on nine patients surviving embryonal rhabdomyosarcoma*

Case	Age (years)	Sex	Race	Years survived	Cross striations found	Primary treatment*	X-ray treatment
1	4	♂	W	15	Yes	Excision (1) Radical exenteration (1)	Shortly after exenteration
2	15	♂	W	15	No	Exenteration (3)	None
3	13	♂	W	9	Yes	Excision (2) Exenteration (4)	None
4	2 1/4	♀	W	6	No	Excision (2) Exenteration (6)	None
5	7	♀	W	5	No	Excision (9) Exenteration (13)	None
6	9	♂	W	5	Yes	Exenteration (10) Actinomycin D (1 yr)	None
7	3 1/2	♂	W	4	Yes	Wide excision (6) Exenteration (27)	1 year after exenteration, reason unknown
8	6	♂	W	3	No	Biopsy (4) Exenteration (8)	None
9	10	♀	W	10	Yes	Excision (4) Exenteration (7)	After exenteration

* Numbers in parentheses indicate weeks after onset of symptoms.

alive 3 years later[1]. There was no apparent correlation between survival and our ability to demonstrate cross striations in tumor cells.

Differential Diagnosis. In addition to the diagnosis of rhabdomyosarcoma, the most frequent diagnoses made by contributing and consulting pathologists were neurogenic sarcoma, metastatic neuroblastoma, lymphosarcoma, and retinoblastoma. Many other diagnostic possibilities were considered. The basic embryonal pattern and the presence of cells with ribbons of brightly eosinophilic cytoplasm should stimulate a thorough search for the other features of embryonal rhabdomyosarcoma. Cross striations are a diagnostic feature.

"Neurogenic sarcoma" was the diagnosis made most often by contributing and consulting pathologists, but it is not clear to us what criteria were used in arriving at this diagnosis. STOUT (1) lists the term "neurogenic sarcoma" as a synonym for malignant schwannoma, a tumor that tends to occur in older individuals and in about half the cases is associated with von RECKLINGHAUSEN'S disease. Embryonal rhabdomyosarcoma is a tumor of childhood that in our experience is not associated with neurofibromatosis. Embryonal rhabdomyosarcomas often contain areas resembling both the Antoni A and B type tissues of neurilemomas, but they differ in being highly malignant, diffusely invasive, and unencapsulated

[1] Since the completion of this study we have received sections from an embryonal rhabdomyosarcoma of the orbit that was controlled by radiation therapy for 4 1/2 years. Recurrence was treated surgically, and the child is still alive.

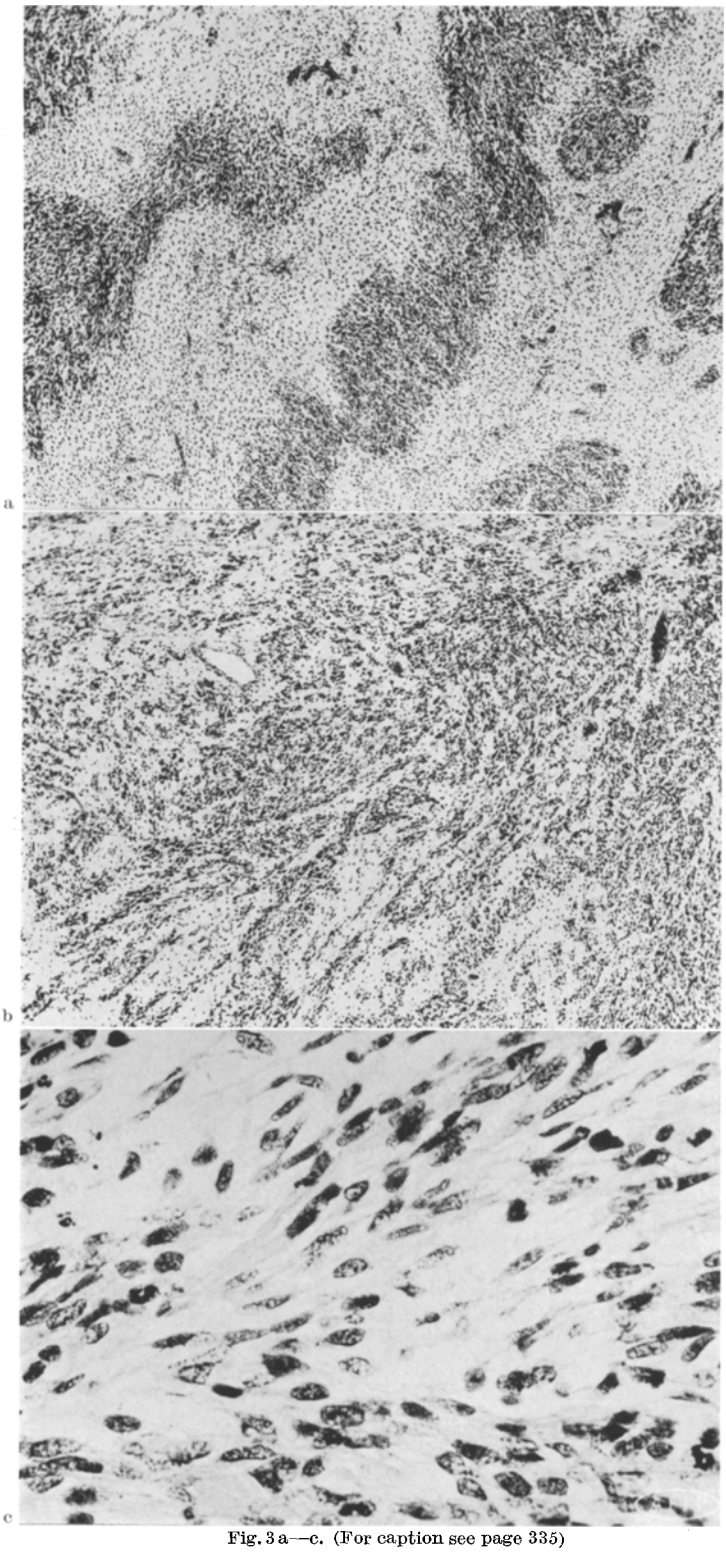


Fig. 3 a—c. (For caption see page 335)

neoplasms that rarely show the reticulin pattern and collagen content of nerve sheath tumors. Some pathologists use the term "neurogenic sarcoma" to denote a fibrosarcoma arising from peripheral nerves, but the paucity of reticulin and the absence of collagen in embryonal rhabdomyosarcoma should exclude fibrosarcoma. Most important in establishing the correct diagnosis of embryonal rhabdomyosarcoma is first to consider its possibility in the case of any orbital neoplasm of childhood; then to make a careful search for cells with long ribbons of eosinophilic cytoplasm, in which longitudinal or cross striations might be found (Figs. 2c and d).

Neuroblastomas primary in the retroperitoneum are said to metastasize to the orbit with great frequency, but such metastasis usually occurs during the terminal phases of the disease. Rarely do we see an orbital metastasis as the initial manifestation when the child is still in good general condition. Microscopically the neuroblastoma tends to be more cellular and less pleomorphic. The cells contain less cytoplasm, which with the MASSON stain lacks the bright red color that is so characteristic of the cells in rhabdomyosarcoma. Formation of rosettes is so seldom demonstrated in metastatic tumors that it is not a helpful feature in differential diagnosis. The demonstration of cross striations in the cytoplasm of tumor cells clearly excludes neuroblastoma, however. In metastatic lesions of the extraocular muscles, there is always the danger of misinterpreting degenerating muscle cells as neoplastic cells. In our study, we have accepted as neoplastic cells with cross striations only those in which the tumor was quite readily separable from any preformed muscle tissue.

Formation of a tumor mass in the orbit may occasionally be the primary clinical manifestation of a malignant lymphoma or acute leukemia. In such cases complete hematologic, clinical, and radiologic study will reveal other evidence of the systemic disease. Microscopically these tumors are more cellular, more necrotic, and less pleomorphic than the rhabdomyosarcoma.

Retinoblastoma should not present any difficulty in differential diagnosis, except for the unusual occurrence of an orbital tumor following radiation therapy. In our experience retinoblastoma never produces an orbital tumor without first growing sufficiently large within the eye to be recognizable on clinical examination. We have observed, however, a number of pleomorphic sarcomas (mostly osteosarcomas) in the orbit several years after intensive radiation therapy for retinoblastoma. Clinically such "postirradiation" tumors are sometimes considered to be orbital recurrences of retinoblastoma, but microscopically they are easily distinguished. At least one case of rhabdomyosarcoma has been reported following treatment of retinoblastoma (REESE), but none of the cases we are reporting here have been complications of radiation therapy.

B. Differentiated Type (6 Cases)

Clinical Features. All six patients were Caucasian. The average age was 11 years (range: 1 month to 25 years). Five patients were male, and one was female. The presenting signs and symptoms were similar to those of the embryonal type. In contrast to the soft, poorly defined masses characteristic of the embryonal type, these tumors presented as firm, pinkish-brown, well-demarcated

Fig. 3a–c. Embryonal rhabdomyosarcoma. a and b Alternating bands of loosely arranged and closely packed cells. Pattern frequently confused with "neurogenic sarcoma". Hematoxylin and eosin. Mag. 45X. AFIP Negs. 61-330 and 61-329. c Cells with ribbons of eosinophilic cytoplasm. Hematoxylin and eosin. Mag. 396X. AFIP Neg. 61-3251

masses in the upper inner quadrant of the orbit. The data available regarding the relationship of these tumors to extraocular muscles are insufficient for analysis.

Histologic Features. The differentiated type differs from the embryonal in that virtually every cell has a ribbon of abundant brightly eosinophilic myoplasm (Fig. 4a). The nuclei are large, round, oval, or rectangular. Sometimes two or more nuclei are arranged in tandem in one cell. Frequently nucleoli are prominent. Mitotic figures are uncommon.

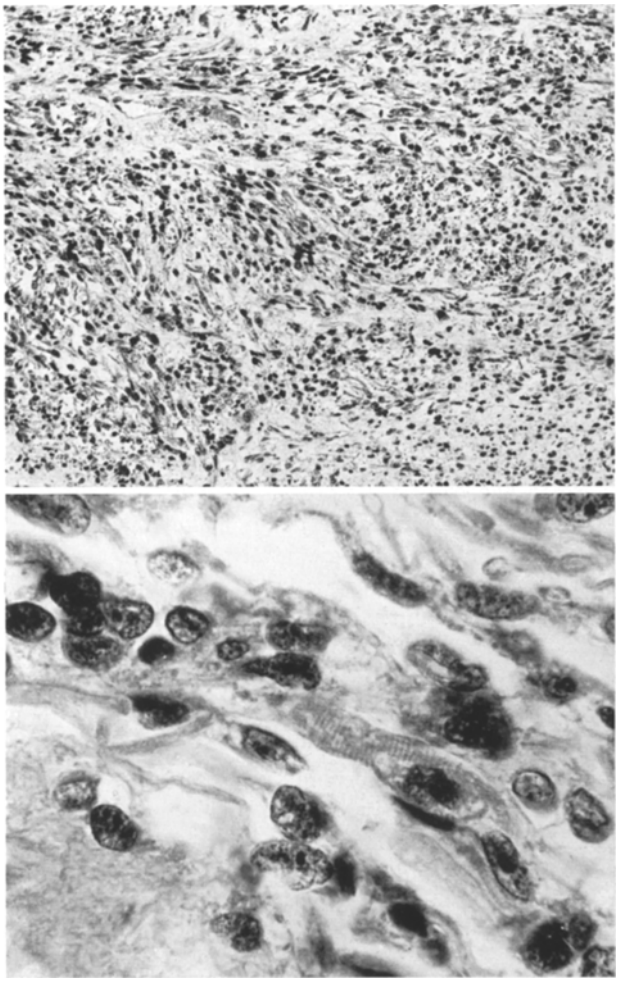


Fig. 4a and b. Differentiated rhabdomyosarcoma. a Most cells have a ribbon of eosinophilic cytoplasm. Hematoxylin and eosin. Mag. 105X. AFIP Neg. 61-3782. b Cytoplasmic striations and large, somewhat rectangular, centrally located nuclei. Hematoxylin and eosin. Mag. 660X. AFIP Neg. 56-20255

Longitudinal and cross striations were found with relative ease in every case, in sections prepared with hematoxylin-eosin, WILDER's reticulum, or MASSON's trichrome stains (Fig. 4b). The myoplasm appeared deep red with MASSON's trichrome stain. As with the embryonal type, histochemical tests for glycogen gave varied results from one tumor to another and in different areas of the same tumor.

Follow-Up Data. Two of the six patients died of tumor 23 and 25 months after the onset of symptoms. Both had metastasis to the brain and lungs. In one, the tumor was "shelled out of its capsule" as a primary treatment. When the tumor recurred, the orbit was exenterated and a suspected pulmonary metastatic lesion was irradiated. The primary treatment in the remaining cases was orbital exenteration. Three patients were alive 5 or more years after operation. The sixth patient has been followed for less than 1 year.

Differential Diagnosis. The diagnosis of rhabdomyosarcoma was made in each of these six cases by the contributing and consulting pathologists. Since the

histologic features are so characteristic, there should be no difficulty in correctly diagnosing rhabdomyosarcomas of the differentiated type.

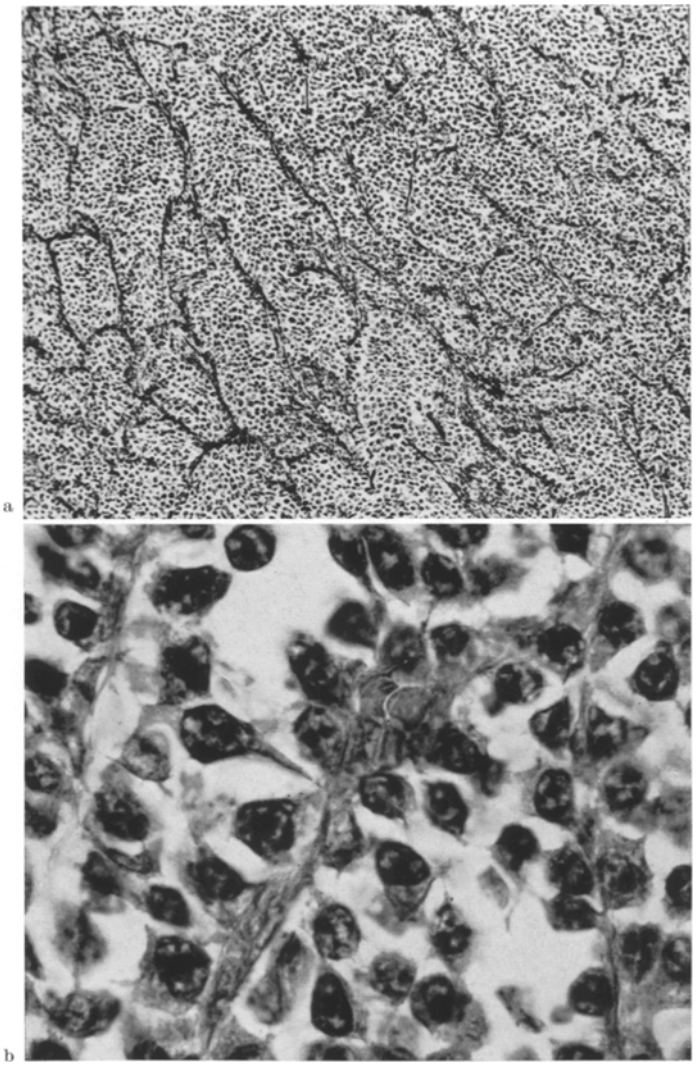


Fig. 5a and b. Alveolar rhabdomyosarcoma. a Alveolar pattern with closely packed uniform cells. WILDER's reticulum. Mag. 80X. AFIP Neg. 61-1741. b Hyperchromatic nuclei with eosinophilic cytoplasmic processes extending into "septa". Tadpole-shaped cell with indistinct cytoplasmic striations. Hematoxylin and eosin. Mag. 630X. AFIP Neg. 61-1742

C. Alveolar Type (9 Cases)

Clinical Features. Eight patients were Caucasian, and one was Negro. Six patients were male, and three were female. The average age was 6 years (range: birth to 17 years). The general clinical features of this group differed from those in the embryonal and differentiated types in one important respect. Whereas the eye usually was proptosed downward and temporally in the embryonal and

differentiated types, the proptosis in the alveolar type was more frequently in an upward direction. The direction of proptosis corresponds well with the most frequently stated location of the tumor in the lower orbit. The tumors were

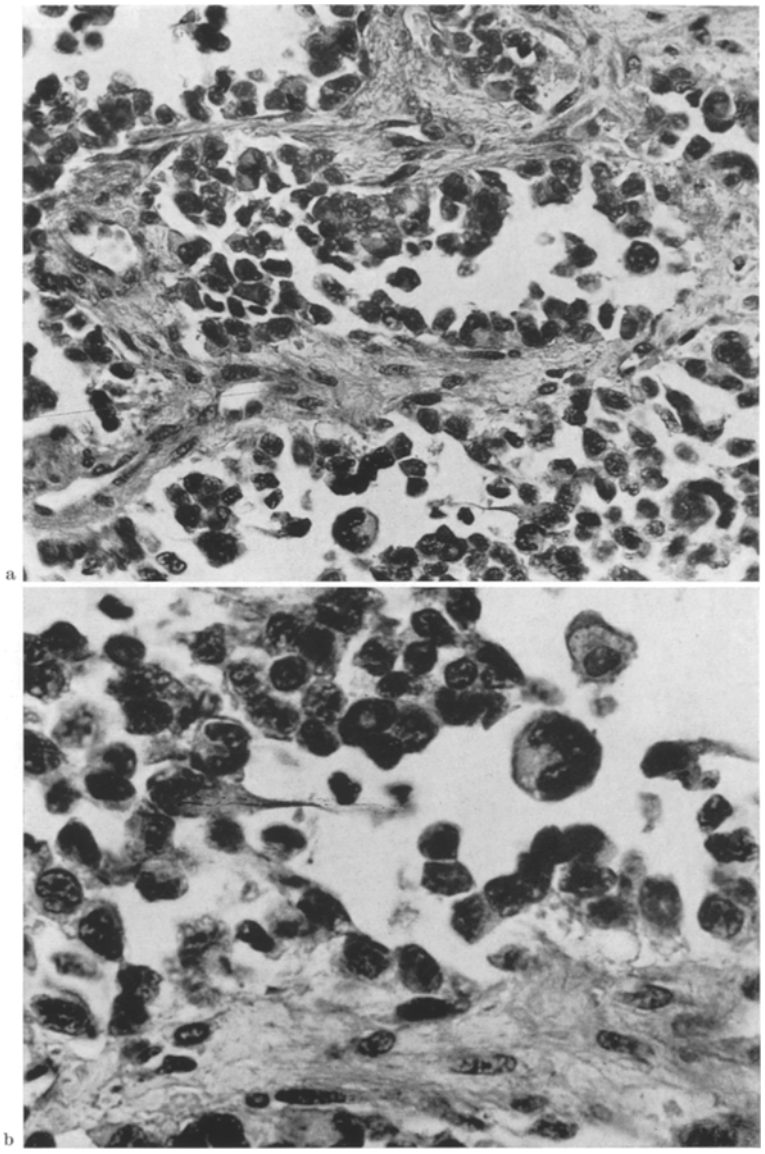


Fig. 6a and b. Alveolar rhabdomyosarcoma. a Alveolar arrangement with "floating" cells. Hematoxylin and eosin. Mag. 305X. AFIP Neg. 61-377. b Portion of same field, with tadpole-shaped and large, bizarre cells. Hematoxylin and eosin. Mag. 615X. AFIP Neg. 61-378

variously described as soft to firm, rubbery, grayish-pink, infiltrative masses in the lower orbit. In at least three instances the surgeon thought the tumor arose from an extraocular muscle. On sectioning, it was seen that the tumors frequently contained foci of necrosis and hemorrhage.

Histologic Features. The histologic features of alveolar rhabdomyosarcoma have been described in detail by ENTERLINE and HORN, RIOPELLE and THERIAULT, and SHUMAN. These workers have described two features common to all alveolar rhabdomyosarcomas. One is the tendency of the neoplastic cells to form "alveolar" spaces (Fig. 6a). The other feature is the arrangement of varying numbers of neoplastic cells within the alveolar structure, some floating free in the spaces while others are attached to the "septa" by delicate cytoplasmic processes. The cytoplasmic processes seem to merge with, and participate in the formation of the "alveolar septa" (Fig. 5b). There are several variations on these general patterns. In some tumors the cells are closely packed and have little pleomorphism (Fig. 5a), and the cytoplasm is usually deeply eosinophilic. In others, the cells have great pleomorphism (Figs. 6a and 6b). Some cells are tadpole or racquet shaped; others are large and multinucleated. In still others the cells are closely packed and have small hyperchromatic nuclei and clear or vacuolated cytoplasm (Fig. 7a).

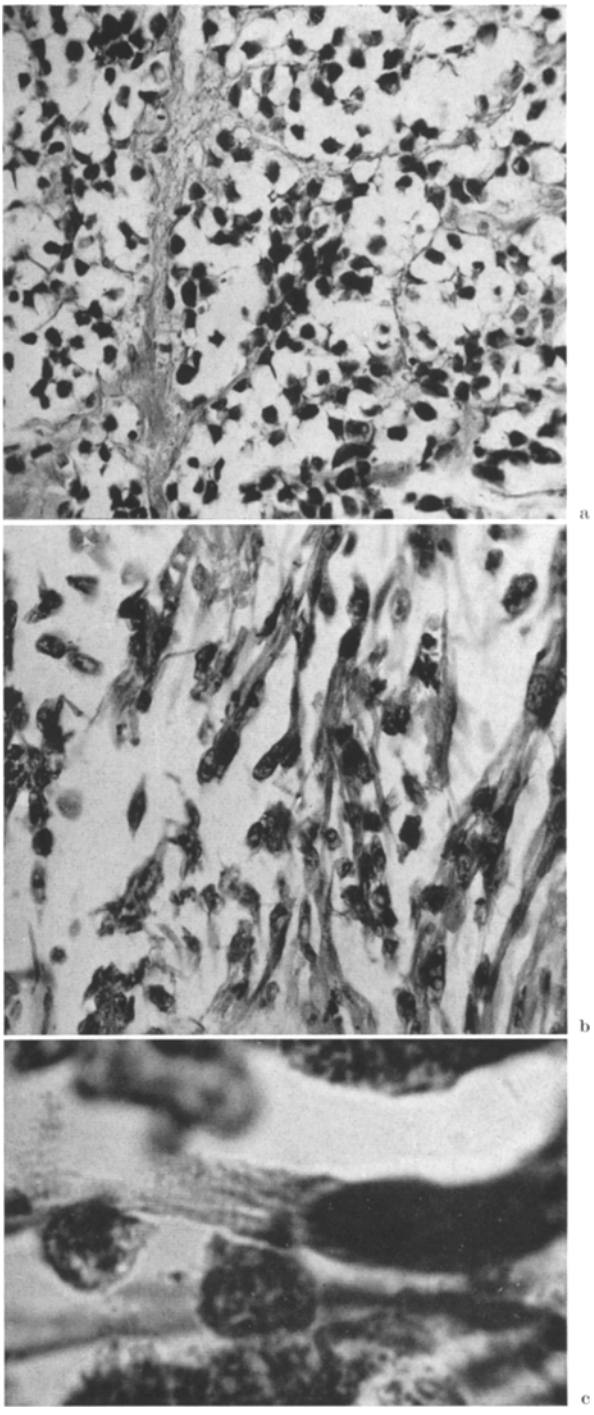


Fig. 7a—c. Alveolar rhabdomyosarcoma. a Small, hyperchromatic nuclei with clear or vacuolated cytoplasm and alveolar pattern. Hematoxylin and eosin. Mag. 300×. AFIP Neg. 61-322. b Metastatic lesion in brain; cells with ribbons of eosinophilic cytoplasm. Hematoxylin and eosin. Mag. 300×. AFIP Neg. 61-323. c Section of brain showing metastatic tumor with cross striations. Masson. Mag. 1,240×. AFIP Neg. 61-2478

Some tumors have varying mixtures of these patterns. Metastatic tumors may resemble the primary lesion very closely; some, however, more closely resemble mature muscle (Figs. 7b and c).

We were able to demonstrate convincing cross striations in the primary lesion in only three of our nine cases after prolonged search of sections prepared with hematoxylin-eosin, WILDER's reticulum, and MASSON's trichrome stains. In three other cases we found cross striations only in metastatic lesions. Most of the neoplastic cells contained granules that stained deep purple with the periodic acid-Schiff reaction. The granules, which disappeared after pretreatment with diastase, were most numerous in cells with vacuolated cytoplasm.

Follow-Up Data. Only one patient with alveolar rhabdomyosarcoma has survived more than 2 years. Six of the nine patients died of tumor. The most common sites of metastasis were the regional lymph nodes, lungs, and brain. The average survival from onset of symptoms was 14 months. The primary treatment was surgical in three, while irradiation was employed in two of the patients, who are now dead. One patient was alive 9 months after the onset of symptoms, but had evidence of local recurrence and pulmonary metastasis. The primary treatment for this patient was with irradiation and methotrexate. At last report, there was a marked decrease in size of the recurrent tumor and metastatic lesions after administration of Actinomycin D. The remaining patient has been followed for less than 2 years.

Differential Diagnosis. The diagnosis of rhabdomyosarcoma was seldom made by the contributing and consulting pathologists. Their most frequent diagnoses included angiosarcoma, reticulum cell sarcoma, undifferentiated carcinoma, neuroblastoma, retinoblastoma, and nonchromaffin paraganglioma. Demonstration of cross striations will, of course, exclude all of these possibilities. Although alveolar rhabdomyosarcoma does not have the vascular pattern seen in angiosarcomas, differential diagnosis from that lesion was, nevertheless, our most difficult problem in two cases. The diagnosis of reticulum cell sarcoma should be regarded with suspicion if the orbit is the only demonstrable site of disease. Carcinoma in a child is exceedingly rare, and a primary site should be demonstrated before this diagnosis is made. Neuroblastoma and retinoblastoma have been discussed under embryonal rhabdomyosarcoma. The characteristics of nonchromaffin paraganglioma have been described by SMETANA and SCOTT.

Discussion

The orbit is one of the most common sites for the development of rhabdomyosarcoma, particularly embryonal rhabdomyosarcoma (ENZINGER). Rhabdomyosarcoma of the orbit appears to be exclusively a disease of infants, children, and very young adults, since the oldest patient in our series was only 25 years old and 91 per cent of the patients were under 15 years of age.

ASHTON and others state that the term "embryonal rhabdomyosarcoma" should be reserved for embryonal sarcomatous tumors in which cross striations are demonstrated. If cross striations are not demonstrated, he prefers the term "embryonal sarcoma". Although we have no serious disagreement with this view, we believe the tumors without demonstrable cross striations that we have included are otherwise identical in their histologic features and behavior. Moreover, the success in demonstrating cross striations depends on such variables as adequate fixation and staining, the number of samples examined, and the time and effort in searching for them.

It is frequently assumed that embryonal rhabdomyosarcoma arises within preformed muscle (REESE, WINTER). Our data do not support this view. In the orbit, at least, our data support the contention of WILLIS "that the usual source of rhabdomyomatous tumors is not adult muscular tissue but embryonic tissue, either immature prospective muscular tissue or indifferent mesenchymal tissue with the potency for aberrant differentiation of muscle fibres".

With regard to treatment, MOORE and GROSSI state that "embryonal rhabdomyosarcomas are radiosensitive in almost every instance, many of them highly so". LEDERMAN, reporting results of a series of seven cases of orbital rhabdomyosarcoma treated with irradiation, states that these tumors "occur mostly in children, remain localized to the orbit, and are highly radiosensitive. They are, however, only exceptionally radio-curable, since prompt recurrence is nearly always the rule". LEDERMAN, curiously, concludes that the primary treatment of orbital rhabdomyosarcoma always should be irradiation! In our series none of the patients whose primary treatment was irradiation remained alive for 3 years[1]. Furthermore, in at least six instances the primary or recurrent tumor was said to grow rapidly in spite of irradiation. On the other hand, nine patients treated initially by surgical procedures have survived 3 or more years. In view of the fact that with a single exception all of our deaths occurred within 3 years, we believe that a "cure" has probably been obtained if there are no signs of recurrence or metastasis after 3 years. Therefore, our data seem to support statements by REESE, DUKE-ELDER, and BLAXTER and SMITH that orbital exenteration should be the primary mode of therapy. Our data regarding the role of the cytotoxic agents are insufficient for analysis. PINKEL and PICKREN recently reported their results with Actinomycin D.

The differentiated rhabdomyosarcomas were segregated from the other types with the hope that they might show a better prognosis. Since three of the six patients are alive 5 or more years after onset, it is possible that this may prove to be the case. If so, it is unfortunate that the differentiated type comprises the smallest group of our rhabdomyosarcomas.

Alveolar rhabdomyosarcoma differs from the other types in that it appears to arise in preformed skeletal muscle. Initially, we were reluctant to accept this tumor as one of muscle origin. We felt the final proof must rest on the demonstration of convincing cross striations in a metastatic lesion in a site that normally does not contain striated muscle. We have found three such examples: two in the brain and one in the lungs (Figs. 7 and 8).

Our data regarding the prognosis of alveolar rhabdomyosarcoma agree with those of ENTERLINE and HORN. All of their nine patients were either dead or had metastatic lesions, but none of them had a primary orbital tumor. In one of the six patients with alveolar rhabdomyosarcoma reported by RIOPELLE and THERIAULT, the orbit and maxillary sinus was the primary site. All of their patients are dead.

In the ophthalmic literature the statement has often been made that rhabdomyosarcomas may have a better prognosis than other orbital sarcomas (CALHOUN and REESE; FRAYER and ENTERLINE; and WINTER). While this may be

[1] See footnote, page 333.

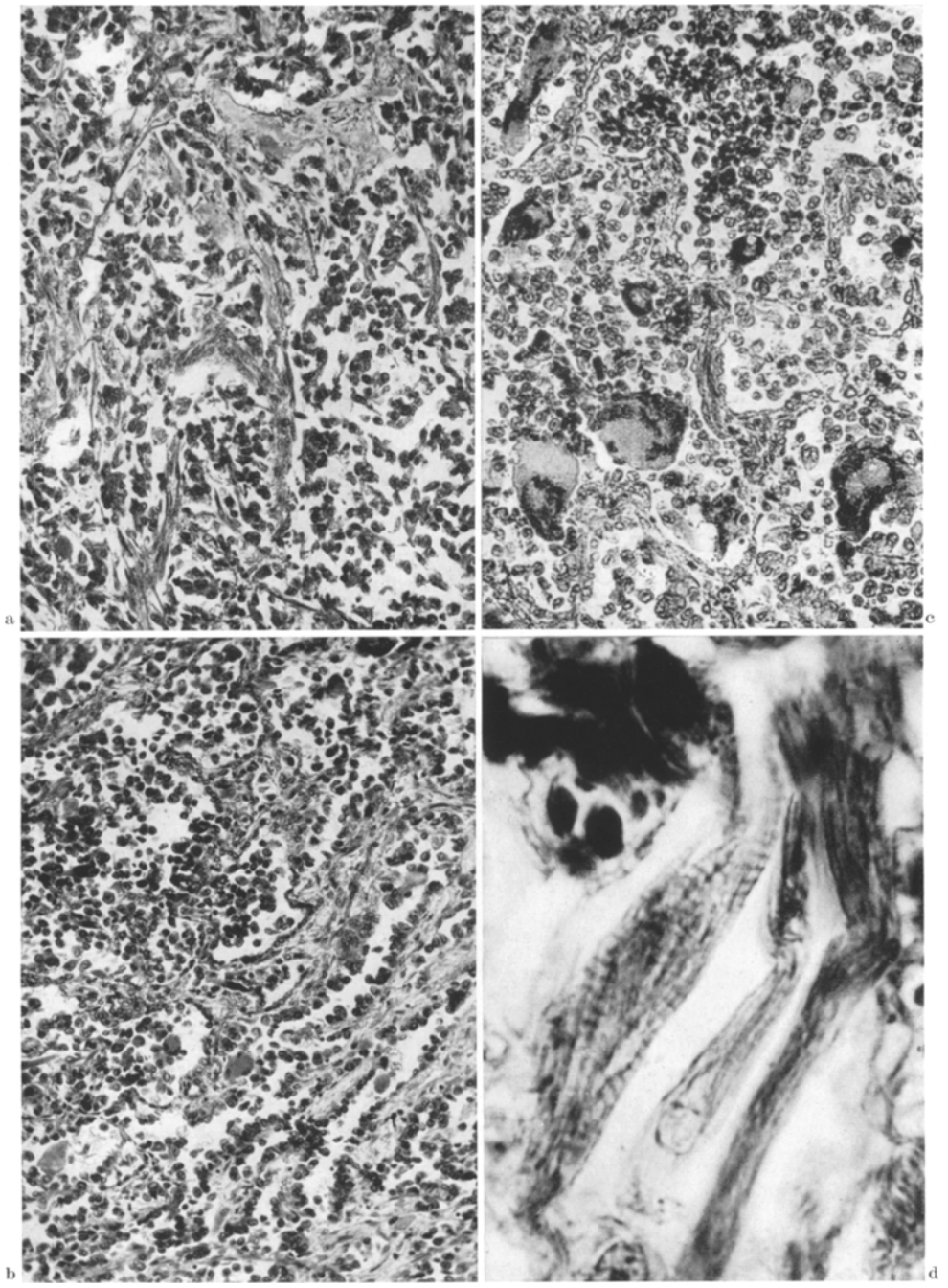


Fig. 8a—d. Alveolar rhabdomyosarcoma. a Primary orbital tumor. Hematoxylin and eosin. Mag. 150×. AFIP Neg. 61-3781. b Metastatic tumor in lung, with alveolar pattern. Hematoxylin and eosin. Mag. 135×. AFIP Neg. 61-3780. c Metastatic tumor in lung, showing giant cells. Masson. Mag. 175×. AFIP Neg. 61-2473. d Longitudinal and cross striations in metastatic tumor tissue in lung. Masson. Mag. 1575×. AFIP Neg. 61-2476

the case, there is no documentation of the statement. As a matter of fact, other primary orbital sarcomas are so rare that it is difficult to make comparative studies. Nevertheless, the number of previously published acceptable "cures" of histopathologically proved cases of rhabdomyosarcoma are very few. This is particularly true for the embryonal and alveolar types. We suspect that most of the recognized cases of rhabdomyosarcoma reported before 1959 were of the better differentiated type. Since these seem to have a much better prognosis than the more common embryonal and alveolar types, this might account for the impression that all rhabdomyosarcomas have a somewhat more favorable prognosis than our studies would indicate.

Summary

Rhabdomyosarcoma is the most common primary malignant orbital tumor of childhood, and the orbit is one of the most common sites for the occurrence of this neoplasm. This paper summarizes histopathologic and clinical data obtained in the course of a study of 55 cases of rhabdomyosarcoma of the orbit in the Registry of Ophthalmic Pathology. Based primarily on their microscopic characteristics, three main types are recognized. The "embryonal" accounts for almost three-quarters of the cases, and of these, only 9 of the 33 patients followed are living and free of tumor after 3 or more years. The next largest group, the "alveolar", accounts for about 15 per cent; only one patient has survived more than 2 years. The smallest group, the "differentiated", accounts for only 10 per cent of the cases. This type appears to have the best prognosis, since half of the patients are living and well 5 or more years after operation.

Because of its relative frequency and very poor prognosis, rhabdomyosarcoma is one of the most important orbital lesions to be considered in the differential diagnosis of unilateral proptosis in childhood. In the embryonal and differentiated types, the tumor usually arises in the superior nasal part of the orbit, and the resultant displacement of the eye is downward and outward. Alveolar rhabdomyosarcomas, on the other hand, tend to occur in the lower part of the orbit and to displace the eye upward.

While the prognosis for all types is poor, there is reason for the optimistic belief that early diagnosis and prompt exenteration will be curative in certain cases, especially in the differentiated and embryonal tumors. Our data, however, provide no reason for believing that radiation treatment is efficacious, and we have not had adequate experience to evaluate chemotherapeutic agents.

Zusammenfassung

Die Augenhöhle ist die häufigste Lokalisation der Rhabdomyosarkome und gleichzeitig ist das Rhabdomyosarkom die häufigste maligne Geschwulstform der Augenhöhle im Kindesalter. Auf Grund von 55 Rhabdomyosarkomen der Augenhöhle, die in der Ophthalmologischen Abteilung des Armed Forces Institute of Pathology, Washington, D. C., zur Untersuchung gelangten, können drei Typen unterschieden werden:

1. der embryonale Typus (40 Fälle);
2. der differenzierte Typus (6 Fälle);
3. der alveolare Typus (9 Fälle).

Unter diesen kommt dem differenzierten Typus die beste Prognose zu. Therapeutisch ist die Radikalexcision der Bestrahlung vorzuziehen. Gesamthaft haben die Rhabdomyosarkome der Augenhöhle eine eher schlechte Prognose.

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References

Ashton, N.: Discussion of paper by Blaxter and Smith. Trans. ophthal. Soc. U.K. **78**, 96—97 (1958).

Blaxter, P. L., and J. L. Smith: Rhabdomyosarcoma of the orbit: report of two cases. Trans. ophthal. Soc. U.K. **78**, 83—97 (1958).

Calhoun jr., E. P., and A. B. Reese: Rhabdomyosarcoma of the orbit. Arch. Ophthal. (Chicago) **27**, 558—578 (1942).

Duke-Elder, W. S.: A Text-Book of Ophthalmology, vol. 5, p. 5564. St. Louis: C. V. Mosby Comp. 1952.

Enterline, H. T., and R. C. Horn jr.: Alveolar rhabdomyosarcoma, a distinctive tumor type. Amer. J. clin. Path. **29**, 356—366 (1958).

Enzinger, F. M.: Personal communications.

Frayer, W. C., and H. T. Enterline: Embryonal rhabdomyosarcoma of the orbit in children and young adults. Arch. Ophthal. (Chicago) **62**, 203—210 (1959).

Horn jr., R. C., and H. T. Enterline: Rhabdomyosarcoma: A clinicopathological study and classification of 39 cases. Cancer (Philad.) **11**, 181—199 (1958).

Lederman, M.: Radiotherapy in the treatment of orbital tumours. Brit. J. Ophthal. **40**, 592—610 (1956).

Manual of Histologic and Special Staining Technics, edit 2 (U.S. Armed Forces Institute of Pathology). New York: Mc Graw-Hill Book Company, Inc., Blakiston Division 1960.

Moore, O., and Grossi, C.: Embryonal rhabdomyosarcoma of the head and neck. Cancer (Philad.) **12**, 69—73 (1959).

Pinkel, D., and J. Pickren: Rhabdomyosarcoma in children. J. Amer. med. Ass. **175**, 293—298 (1961).

Porterfield, J. F.: Orbital tumors in children. In: International Ophthalmology Clinics No. 2, Vol. 2. Boston: Little, Brown & Company 1962 (in preparation).

Reese, A. B.: Tumors of the Eye, p. 440. New York: Paul B. Hoeber, 1951.

Riopelle, J. L., and J. P. Theriault: Cited by Enterline and Horn.

Shuman, R.: Personal communications.

Smetana, H. F., and W. F. Scott jr.: Malignant tumors of non-chromaffin paraganglia. Milit. Surg. **109**, 330—349 (1951).

Stobbe, G. D., and H. W. Dargeon: Embryonal rhabdomyosarcoma of the head and neck in children and adolescents. Cancer (Philad.) **3**, 826—836 (1950).

Stout, A. P.: (1) Tumors of the peripheral nervous system. Atlas of Tumor Pathology, Section II, Fascicle 6. Washington, D. C.: Armed Forces Institute of Pathology, 1949.

— (2) Tumors of the soft tissues. Atlas of Tumor Pathology, Section II, Fascicle 5. Washington, D. C.: Armed Forces Institute of Pathology, 1953.

Willis, R. A.: Pathology of tumors, edit. 2, p. 757. St. Louis: C.V. Mosby Comp. 1953.

Winter, F. C.: The orbit: a review of the literature for 1959. Arch. Ophthal. (Chicago) **64**, 447—472 (1960).

Zimmerman, L. E.: In: Surgical Pathology, edit. 2, p. 1018. L.V. Ackerman, Editor. St. Louis: C.V. Mosby Comp. 1959.

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