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Primary Rhabdomyosarcoma of the Cerebrum

An Ultrastructural Study

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Summary. A case of primary cerebral rhabdomyosarcoma in a 51-year-old female is reported. The histogenesis of this tumor is discussed. The clinicopathological features of 10 previously reported similar tumors of the CNS are briefly reviewed. Histologically the tumor was polymorphic, but composed of poorly differentiated cells interpreted as rhabdomyoblasts without definite cross-striation. Electron microscopy established that the poorly differentiated cells were of rhabdomyosarcomatous nature, compatible with presumptive myoblasts and analogous to developing fetal muscle.

Key words: Brain tumor – Rhabdomyosarcoma – Mesenchymal cell – Myotube – Ultrastructure

Rhabdomyosarcomas originating in the brain are rare and their histopathological definition is controversial. Tumors containing myoblasts have generally been of three kinds; teratomas, medullomyoblastomas and rhabdomyosarcomas. In teratomas, the myocytic component is merely an expression of divergent multipotential neoplastic differentiation. Medulloblastomas containing either smooth or striated muscle have been regarded as malignant teratomas (Russel and Rubinstein, 1977). The term rhabdomyosarcoma should be reserved only for malignant tumors composed of pure mesenchymal derivatives that include myoblasts. According to these criteria, only ten previous cases of pure rhabdomyosarcoma have been described. An additional example is reported here with comments on the histogenesis of this rare tumor.

Case Report

This 51-year-old female was presented to the neurological service of Kanagawa Rehabilitation Center in June 1978 with a recurrent tumor in the cerebrum. She developed muscle weakness of the left leg in September 1977 and underwent craniotomy for a brain tumor in Tokyo Metropolitan Ohkubo Hospital. At operation the greater part of the tumor was located in the right cerebral hemisphere, being attached to the falx. It was largely removed and weighed 120 g.

Shortly after operation, she developed a left-sided hemiplegia and was referred to our hospital. A second operation was performed on 6 June 1978, revealing obvious recurrence. A well defined gray and soft tumor was found in the previously operated site, being attached to the midportion of the falx. It was subtotally removed. The patient is now undergoing chemotherapy and radiation.

Light Microscopy

The specimen consisted of many fragments of tumor tissue with a gray to myxoid cut surface, with occasional hemorrhages and necroses. Multiple blocks of the formalin-fixed tissue were embedded in paraffin wax, and sections were stained with hematoxylin and eosin (HE), Masson's trichrome, phosphotungstic acid hematoxylin (PTAH), periodic acid Schiff, and Watanabe's method for reticulin fibers.

The histology of both the first and the second surgical specimens were essentially identical and will be described together, although the recurrent tumor was more dedifferentiated than the original one.

Numerous pleomorphic cells were arranged in trabeculae, sheets (Fig. 1), and formed incomplete alveoli (Fig. 3). The following types of neoplastic cells were noted; large polygonal cells with two or more nuclei and a abundant eosinophilic cytoplasm (Figs. 2 and 6), large ovoid cells with either homogeneous or granular brightly acidophilic cytoplasm (Figs. 2 and 5), small lymphoid cells and satellite or spindle-shaped cells reminiscent of fetal mesenchymal cells (Fig. 4). Both large polygonal and ovoid cells had spherical or rod-shaped hyperchromatic nuclei with rather conspicuous nucleoli. Most of these cells had a purple to red cytoplasm in Masson's trichrome and stained blue with PTAH. They were interpreted as myoblasts, but

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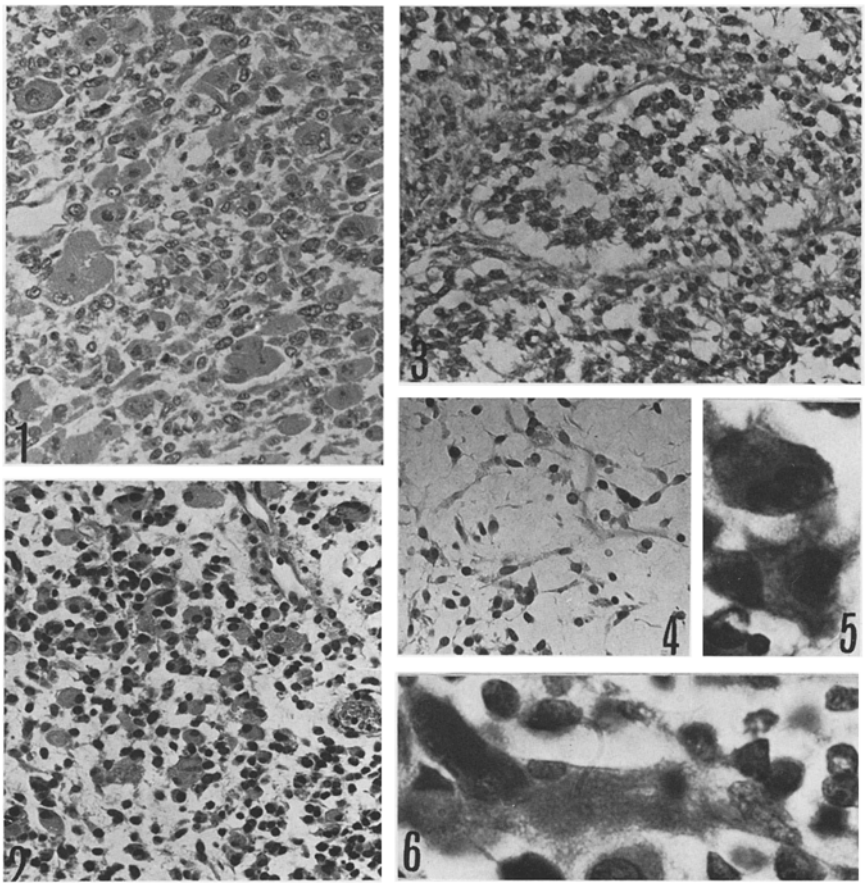


Fig.1. Highly cellular tumor consisting of pleomorphic cells. Many neoplastic cells have a abundant acidophilic cytoplasm. H.-E., ×156

Fig.2. Many large ovoid cells with acidophilic granular cytoplasm are seen. H.-E., ×156

Fig.3. Small cells are arranged in an abortive alveolar pattern. H.-E., ×156

Fig.4. Lymphoid cells and satellite cells are seen in a myxoid stroma. H.-E., ×156

Fig.5. Two large myoblast with acidophilic cytoplasm. H.-E., ×780

Fig.6. A strap-like cell in the center of the field. H.-E., ×780

Figs.1 and 3 are from the first surgical specimen. Figs. 2, 4, 5 and 6 from the second

definite cross-striations could not be demonstrated in any of the tumor cells.

Mitotic figures and necroses were frequent. The tumor was not highly vascular and silver impregnation showed a fine network of reticulin fibers. Some gemistocytic astrocytes were seen infiltrating the stroma.

Multiple sections of the surgical specimen were prepared and were carefully examined to determine whether the tumor was teratoid or not. Special attention was paid to the glial cells in the tumor; they were sharply localized in the narrow zone of parenchymal infiltration. There were no other neuroectodermal cells in any sections of the tumor and the possibility of a teratoma or of a teratoid tumor was therefore excluded. The satellite cells, presumably immature mesenchymal cells, showed no differentiation along other cell lines such as chondroblasts, osteoblasts, etc. The light microscopy diagnosis was that of primary rhabdomyosarcoma.

Electron Microscopy

For electron microscopy, small pieces of the tumor were fixed in phosphate-buffered 2.5% glutaraldehyde and postfixed in 1% osmium teroxide. After dehydration in graded alcohol followed by propylene oxide, they were embedded in Epon 812. Sections were stained with uranyl acetate and lead citrate and examined in a Hitachi HU-12 electron microscope operating at 75 Kv.

Large polygonal and multinucleated giant cells often contained easily recognizable myofilamentous structures in their cytoplasm. Groups of filaments in parallel arrangement resembling poorly formed myofibrils occupied the greater part of the cytoplasm in the polygonal cells (Fig. 7). They were divided into abortive sarcomeres by linear or irregularly ovoid densities resembling Z-bands (Fig. 8). The sarcomeres were usually incomplete since other bands were rarely present. The filaments were chiefly composed of thick filaments. Thin filaments were absent in many myofibrils. In parts of the cytoplasm, groups of filaments were distributed in a random fashion, so that both transverse and longitudinal filaments were intermingled. Their hexagonal distribution was usually distorted in the transverse plane of section (Fig. 9). Some groups of thick filaments appeared to have interconnecting bridges resembling those of M-lines (Fig. 10). Some cells were occasionally arranged in a chain-like manner, and the cytoplasmic membrane of adjoining cells

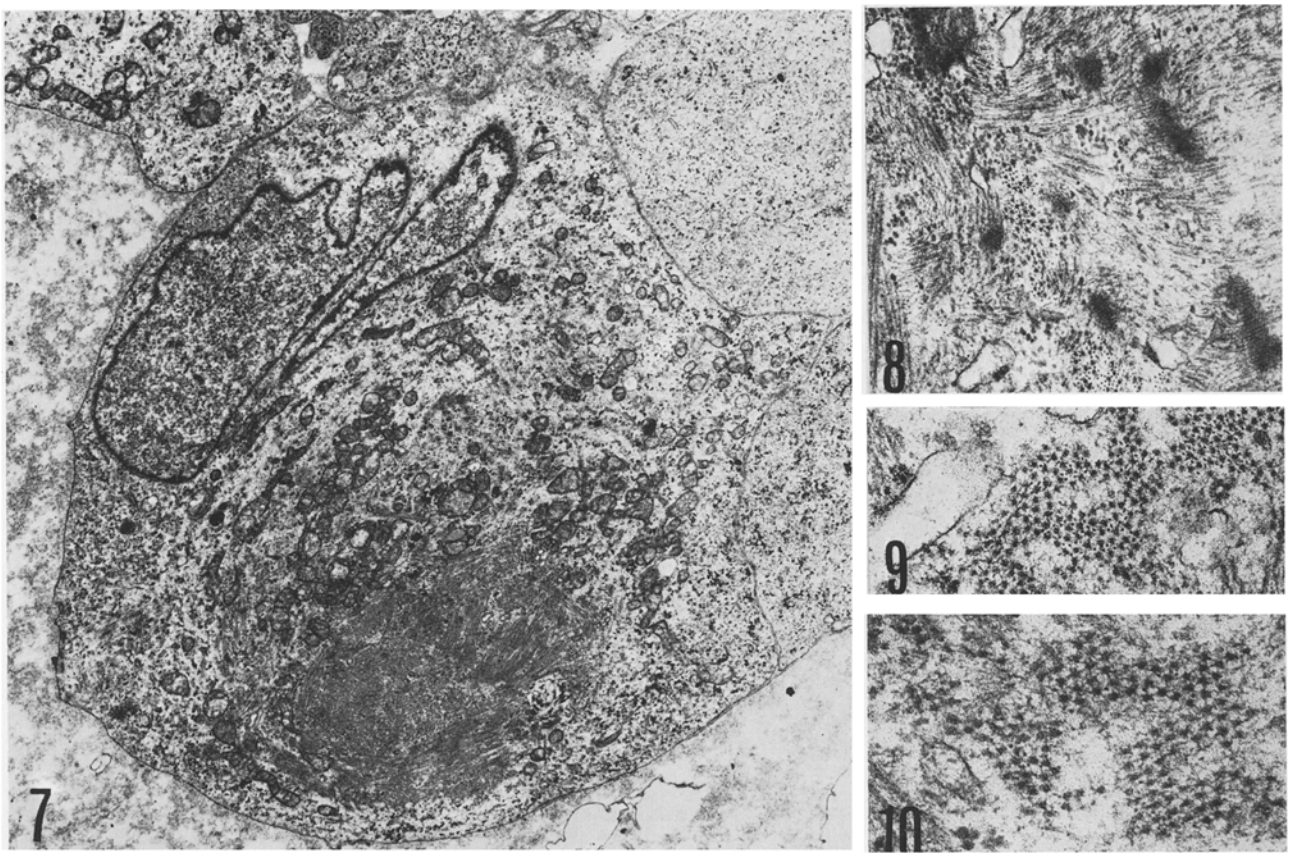


Fig. 7. A large polygonal cell containing a myofilamentous mass in its cytoplasm. × 7,650

Fig. 8. Groups of filaments are distributed in a random fashion. Several ovoid densities resembling abortive Z-bands are seen. × 21,420

Fig. 9. The hexagonal distribution of thick and thin filaments seen in normal muscle fibers is distorted. × 76,500

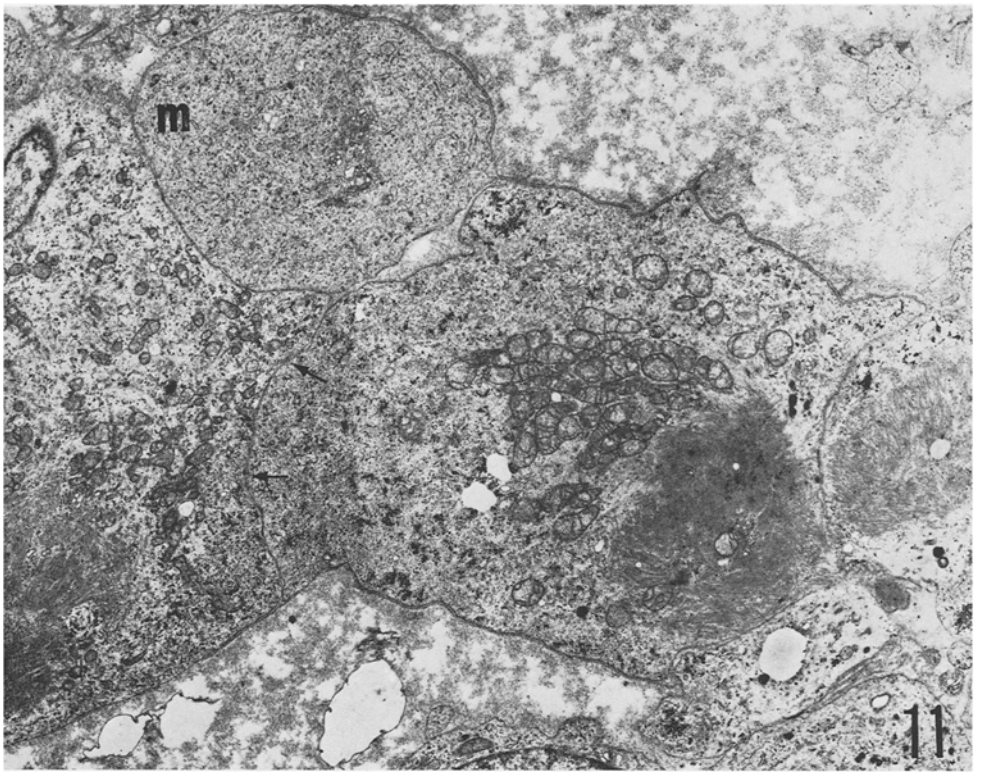
Fig. 10. Myosin filaments with interconnecting bridges reminiscent of M-lines. × 112,200

appeared to fuse or partly dissolve, which was reminiscent of a developing myotube (Figs. 11 and 12). Glycogen granules were dispersed between myofibrils or found in large aggregates. Mitochondria were moderate to few, but were occasionally grouped near the nucleus or the myofilamentous mass. Smooth-surfaced vesicles and cisterns were numerous, but they were usually less abundant in cells whose cytoplasm was filled with myofibrils. The nuclei were large and irregular, showing many indentations.

The ultrastructural characteristics of the large ovoid cells were basically similar to those of the polygonal cells; they contained large numbers of disoriented myofibrils and glycogen granules. The other cell organelles were scanty. These cells were usually invested by a thin basal lamina (Fig. 13). The fine structure of both satellite cells and small lymphoid cells showed similar features; however the majority of these cells were devoid of filamentous structures and their cytoplasm was scanty. They contained abundant free ribosomes and Golgi complexes (Fig. 14). Dense bodies, myelin figures and lipid bodies were inconstant features. The stroma consisted only of blood vessels and floccular amorphous material. Collagen fibers were virtually absent, indicating fetal mesenchymal tissue.

Discussion

The microscopic features of this tumor, particularly the presence of cells with strongly acidophilic perikarya and of myofibrillary structures in their cytoplasm as demonstrated in the electron microscope, are diagnostic of rhabdomyosarcoma. This tumor was subdural and attached to the adjacent meninges (falx), indicating its intracranial localization, and failure to find any tumor outside the neuraxis on examination and investigation of the patient nine months after the onset of his initial symptoms supports its primary nature. However, it should be distinguished from other primary intracranial muscle-containing neoplasma such



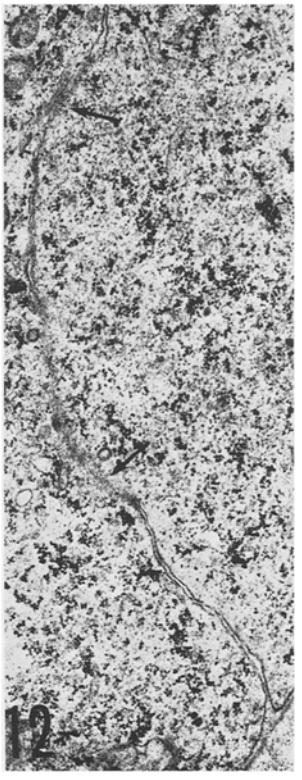
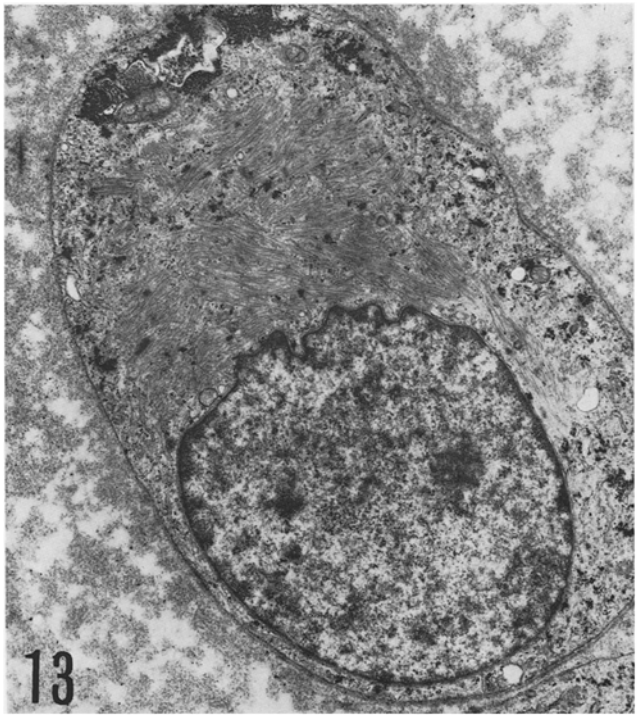


Fig. 11. Three myoblasts are arranged in a chain-like manner suggesting a possible myotube. Note undifferentiated mononuclear cell (m), presumably a myoblast, adjoining the surface of the myotube. Arrows show fusion of cytoplasmic membrane. × 48,880

Fig. 12. Higher magnification of Fig. 11. Arrows indicate dissolution of adjoining membranes. × 12,480



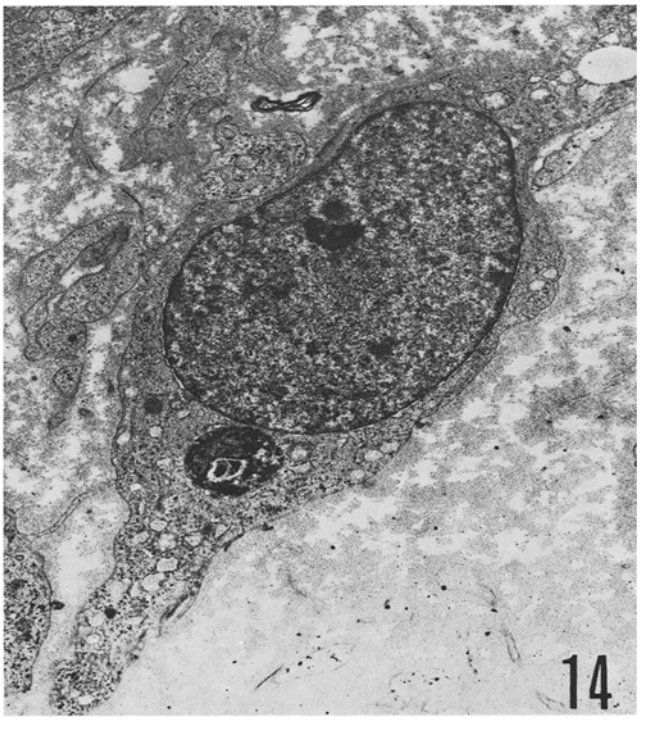


Fig. 13. A large ovoid cell invested by a basal lamina. Myofibrils occupy the greater part of the cytoplasm. Glycogen granules are present between myofibrils. × 6,360

Fig. 14. A small immature cell with a scanty cytoplasm, devoid of myofilamentous structure. Numerous free ribosomes and smooth-surfaced vesicles are seen. The intercellular spaces contain only amorphous material. × 6,360

as teratomas, medullomyoblastomas, and combined neoplasms of mesenchymal and neuroepithelial origin (Misugi et al., 1970); Banerjee and Kak, 1973; Zimmermann et al., 1972; Shuangshoti, 1971). Elements other than myoblastic cells were absent in this case; hence it was not teratomatous. Teratoid tumors with a myoblastic component arise preferentially in the infratentorial level, whereas pure rhabdomyosarcoma do so equally in both the infratentorial (6 cases) and the supratentorial levels (5 cases), as demonstrated in the 11 cases reported in the literature including the present one. The case of Shuangshoti and Phonprasert (1976) seems to have originated in a paranasal sinus and is therefore excluded from present considerations.

The clinical behavior of this tumor is that of a highly malignant neoplasm, as demonstrated in our case. Rapid recurrence after surgical resection is usual. There is no 5-year survival in reported cases so far.

The histogenesis of this rare tumor is not yet clarified. Shuangshoti (1971) reported a number of neoplasms of mixed mesenchymal and neuroepithelial type and proposed that these tumors might arise directly from mesenchymal cells. It is well known that rhabdomyosarcomas are more frequent in sites where no or scanty striated muscle is normally present such as in the urinary bladder (Sarkas et al., 1973) and the prostate (Clark and O'Connel, 1973), and it is widely accepted that this type of tumor is derived from multipotent mesenchymal tissue that can differentiate into aberrant muscle tissue (Woodruff et al., 1973, Karcioglu et al., 1977). Chondrosarcomas (Waga et al., 1972) and liposarcomas (Sima et al., 1976) may also originate as intracranial tumor from such aberrant differentiation.

Another histogenetic possibility is suggested by the presence of heterotopic muscle tissue in the meninges (Viragh et al., 1977; Hoffman and Rorke, 1971). However, rhabdomyosarcomas do not typically arise from mature striated muscle (Willis, 1967).

It is suggested that the rhabdomyosarcoma in this case arose from intracranial mesenchymal tissue present in the meninges.

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