Rhabdomyosarcoma of the brain

Case report

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The authors report a case of rhabdomyosarcoma originating in the fourth ventricle and review the eight comparable previous reports of true rhabdomyosarcoma, composed solely of mesenchymal elements. Tumors in most adults arose in the cerebral hemisphere, while those in children arose exclusively in the midline structures of the posterior fossa. The tumor in the authors' case was initially benign and well circumscribed, but within 2 years had changed into a malignant rhabdomyosarcoma. The histological documentation during the interval is presented and discussed.

KEY WORDS: brain tumor, rhabdomyosarcoma, medulomyoblastoma, posterior fossa, myoblastoma

Rhabdomyosarcomatous tumor originating in the brain is rare and its histopathological definition controversial. Tumors containing rhabdomyoblasts have generally been classified in three groups: teratoma, medulomyoblastoma, and rhabdomyosarcoma. Although clinical and histological differentiation of rhabdomyosarcoma is still difficult, use of the term should be reserved for tumors composed of pure mesenchymal derivatives with both embryonal and mature striated muscle cells and, as Russell and Rubinstein have postulated, should be devoid of neuroblastic elements.

According to these criteria only seven previous cases of the pure rhabdomyosarcoma have been described; this report presents the eighth such case, in this instance in the fourth ventricle of a 3-year-old child.

Case Report

First Admission

A 3½-year-old girl was first admitted to the Kumamoto University Hospital in November, 1966, with a 1-month history of headache and progressively severe staggering gait. There was early bilateral papilledema, truncal ataxia, and an ataxic gait. The clinical impression of a fourth ventricle tumor was strengthened by ventriculography, which demonstrated remarkable ventricular dilatation above the aqueduct of Sylvius and a central filling defect in the dilated fourth ventricle. After admission ataxia progressed and was complicated by urinary retention; however, no other neurological findings such as nystagmus, cranial nerve palsy, or stiff neck were observed.
FIG. 1. Photomicrographs of the original tumor (surgical specimen, 1966). **Upper Left:** Well differentiated striated muscle cells arranged in wavy or interlacing bundles. H & E, ×100. **Upper Right:** Cross striations in the cytoplasm of the neoplastic cells giving impression of benign rhabdomyoma. Masson trichrome staining, ×1000. **Lower Left:** Silver impregnation showed abundant fine network of reticular fibers. Silver stain for reticulin, ×240.
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Operation. Suboccipital craniectomy revealed a sharply demarcated encapsulated nodular mass in the fourth ventricle; it arose from the left side of the wall and occupied the dilated ventricle. There was no evidence of subarachnoid spread. The ependymal lining of the ventricle appeared normal, and the vermis and cerebellar hemispheres were not affected. The mass was totally excised and weighed 36 gm.

Pathology. The tumor was nodular, with solid and soft elastic portions; its total dimensions were $6 \times 3.5 \times 3.5$ cm. The grayish surface was covered with a fine fibrous membrane. The homogeneous cut surface was also gray and no cystic formation was seen. Most of the tumor was composed of densely packed, elongated, strap- or spindle-shaped cells with eosinophilic cytoplasm. The majority of cells were arranged in wavy or interlacing bundles, and contained faint longitudinal and distinct cross striations in the cytoplasm. The striations were seen even in hematoxylin and eosin preparations but were best demonstrated by Masson's trichrome (Fig. 1). The moderately hyperchromic nuclei were ovoid or rod-shaped with rather conspicuous nucleoli in most of them. Mitotic figures were not present. There were a few less mature cells of myoblastic type intermingled with well differentiated muscle fibers. The myoblastic cells were often large and ovoid with a markedly eosinophilic cytoplasm. A few cells showed short spindle-shaped tapering of the cytoplasm and no cross striations; these less mature cells were moderately pleomorphic, but no obvious mitotic figures were seen. The tumor was not highly vascular and silver impregnation showed a fine network of reticular fibers (Fig. 1). Although the free surface of the tumor was covered with a membrane of dense connective tissue, in the region of the basal attachment to the ventricular wall, subependymal glial cells could be seen infiltrating the stroma and forming small foci. Multiple sections of the surgical specimen were prepared and were carefully examined to determine whether the tumor was teratoid. Special attention was paid to the glial cells in the tumor base; these were sharply localized in the narrow zone of the ventricular attachment and were identified as reactive forms. There were no other neuroectodermal cells in any section of the tumor and the possibility of teratoma or teratoid tumor was excluded. The tentative diagnosis was benign rhabdomyoma.

Second Admission

The patient recovered well from the first operation. Cerebellar signs and symptoms due to increased intracranial pressure improved; a postoperative left abducens paresis remained. The patient was discharged without postoperative irradiation. She was readmitted 10 months after the operation complaining of headache and ataxic gait and showing left abducens paresis, spontaneous horizontal nystagmus to the right, and cerebellar ataxia more prominent on the left.

Operation. Recurrence of the tumor was obvious and suboccipital revision was performed in September, 1967. The dura of the posterior fossa was bulging markedly and was tightly adherent over the cerebellar cortex. When the left cerebellar hemisphere was split, an encapsulated solid tumor was encountered; this extended backward from the left lateral wall of the fourth ventricle. Once again the tumor was excised subtotally, since there was some obscure demarcation of the neoplasm in the basal attachment. The size of the excised mass was almost identical to that of the previous surgical specimen and it weighed 35 gm. This time a total radiation dose of 4000 rads with telecobalt 60 was given. When the patient was discharged in December, 1967, neurological evaluation was satisfactory and she showed only the preoperative left abducens palsy; cerebellar signs had subsided and there were no lateralizing findings in sensorimotor function.

Pathology. The tumor showed essentially the same microscopic features as those of the original tumor. There were more densely packed, well differentiated muscle cells with distinct cross striations. Intermingled with bundles of muscle fibers there were again large, round, eosinophilic myoblastic cells, some with spindle- and tadpole-shaped cells, all of which often showed clear striations. The nuclei were relatively large and occasionally multiple, but mitotic figures were not demonstrated.

Third Admission

The patient had done well for about 1 year after the second operation but then developed ataxia, this time in association with dysarthria and dysphagia. She was read-
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**Fig. 2. Photomicrograph of the postmortem tumor specimen (1969).** Majority of the tumor is now composed of undifferentiated mesenchymal cells and rhabdomyoblasts. H & E, × 500.

mitted in January, 1969, with evidence of increased intracranial pressure.

**Operation.** The third suboccipital exploration demonstrated a tumor which now occupied the fourth ventricle as an enormous mass compressing the brain stem ventrally. Suboccipital decompression was accomplished by partial removal of the re-current tumor plus extensive suboccipital craniectomy. This time the patient showed no post-operative response to surgery and died 1 month later with respiratory difficulty and brain-stem dysfunction.

**Postmortem Examination.** In the posterior fossa, the dura and arachnoid adhered tightly to the cerebellar hemispheres, especially in the field of the previous operations. A sagittal section through the brain stem and the cerebellum showed a sharply demarcated, round, solid yellowish tumor 6 × 4.5 cm in the dilated fourth ventricle with encroachment on the lower brain stem. A nodular extension of the tumor projected into the left cerebellar hemisphere from the left lateral wall of the fourth ventricle near the midline. The base of the tumor was surrounded by partly necrotic, gliotic tissue of the cerebellar hemisphere and the vermis. The expanding mass, part of which protruded from the right foramen of Luschka, compressed the pons and medulla oblongata dorsolaterally to the left. Part of the left cerebellar hemisphere had been removed at surgery and the remainder on both sides had undergone diffuse softening. There was no evidence of subarachnoid or ventricular spread of the tumor but the ventricular obstruction had produced advanced internal hydrocephalus. The cerebrum did not appear to be invaded by any tumor process. The spinal cord was not examined. A careful general autopsy revealed no neoplastic lesions in the heart, liver, spleen, kidneys, ovaries, or lymph nodes. Examination of the lung showed only pulmonary congestion and diffuse pneumonitis.

In marked contrast to previous specimens, the tumor now presented a malignant, sarcomatous appearance characterized by undifferentiated mesenchymal cells adjoining the striated muscle cells and bundles of muscle fibers (Fig. 2). Small round cells with scanty cytoplasm were mixed with relatively large bizarre-shaped cells scattered in the loose matrix. Large round multinucleated cells, short spindle cells, and tadpole cells were still seen in undifferentiated mesenchymal areas; cross striation was often observed in the short spindle cells. Transitional cells between the mesenchymal and myoblastic cells were clearly suggested; mitoses and vascular proliferation were commonly observed. Cerebellar tissue along the tumor margin contained small infiltrating foci of mesenchymal cells, which formed small foci in the adjacent brain tissue. No neuroblastic elements were seen.

**Discussion**

**Histology**

Brain tumors containing striated muscle fibers are quite rare and have been variously described as rhabdomyosarcoma, medullo-myoblastoma, teratoma or teratoid tumor. There is no definite histological pattern of so-called medulloblastoma or rhabdomyosarcoma in which various developmental stages of both neuroblastic and rhabdomyo-
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### TABLE 1
Summary of eight cases of primary rhabdomyosarcoma of the brain

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Age (yrs)</th>
<th>Sex</th>
<th>Location, Extension</th>
<th>Microscopic Findings</th>
<th>Treatment</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lopez, 1934</td>
<td>18</td>
<td>F</td>
<td>cerebellopontine angle, strictly localized</td>
<td>striated muscle, stellate cells</td>
<td>none</td>
<td>several weeks</td>
</tr>
<tr>
<td>Lopes de Faria, 1957</td>
<td>52</td>
<td>F</td>
<td>cerebellar hemisphere, well circumscribed</td>
<td>striated muscle, undifferentiated mesenchymal cells</td>
<td>none</td>
<td>5 mos</td>
</tr>
<tr>
<td>Koide &amp; Ishizone, 1958</td>
<td>15</td>
<td>M</td>
<td>cerebral hemisphere; sharply demarcated, nodular, later infiltrative</td>
<td>striated muscle, undifferentiated mesenchymal cells</td>
<td>decompressive surgery with irradiation</td>
<td>5 mos</td>
</tr>
<tr>
<td>Ozeki, 1960</td>
<td>29</td>
<td>M</td>
<td>cerebral hemisphere, encapsulated</td>
<td>pleomorphic spindle cells with cross striation</td>
<td>none</td>
<td>1½ mos</td>
</tr>
<tr>
<td>Legier &amp; Wells, 1967</td>
<td>3½</td>
<td>M</td>
<td>vermis, infiltrative and subarachnoid spread</td>
<td>rhabdomyoblasts, undifferentiated mesenchymal cells</td>
<td>excision with irradiation</td>
<td>2 yrs</td>
</tr>
<tr>
<td>Shuangshoti, et al., 1968</td>
<td>4</td>
<td>F</td>
<td>vermis, subarachnoid spread</td>
<td>striated muscle, undifferentiated mesenchymal cells</td>
<td>none</td>
<td>1 mo</td>
</tr>
<tr>
<td>Leedham, 1972</td>
<td>45</td>
<td>F</td>
<td>cerebral hemisphere, infiltrative</td>
<td>striated muscle, undifferentiated mesenchymal cells</td>
<td>excision</td>
<td>10 mos</td>
</tr>
<tr>
<td>Matsukado, et al., 1975</td>
<td>3½</td>
<td>F</td>
<td>4th ventricle; encapsulated nodular, later infiltrative</td>
<td>striated muscle, undifferentiated mesenchymal cells</td>
<td>excision with irradiation</td>
<td>2 yrs</td>
</tr>
</tbody>
</table>

Blastic elements have been observed. Several authors reporting primary intracranial rhabdomyosarcomas have included medulloblastomas,\(^\text{10,11}\) which Russell and Rubinstein\(^\text{20}\) regard as malignant teratoid tumors. In 1933, Marinesco and Goldstein\(^\text{14}\) reported a fourth ventricle tumor that originated from the vermis and was composed of nerve cells, other neuroectodermal cells, and cross-striated muscle cells with myoblasts; since that first report of a medulloblastoma, many debates have defined and histogenesis of that kind of tumor.\(^\text{17,22}\) Careful analyses of the reported cases under the name of either medulloblastoma or rhabdomyosarcoma of the brain have been made, and Marubayashi, et al.\(^\text{15}\) have reported 11 cases of medulloblastoma.

From the developmental point of view, neuroectodermal and mesenchymal cells can be classified histologically into the following four patterns: 1) tumors composed of nerve cells, undifferentiated neuroectodermal cells, and mature or embryonal striated muscle cells;\(^\text{8,14,17}\) 2) medulloblastoma containing cross-striated muscle cells and rhabdomyoblasts, or smooth muscle cells and myoblasts;\(^\text{2,7,26}\) 3) tumors composed of neuroectodermal cells in various developmental stages plus cross-striated muscle cells;\(^\text{6,20}\) and 4) tumors composed of cells resembling those of a medulloblastoma and cross-striated muscle cells.\(^\text{5,15,24}\)

We are convinced that medulloblastomas are formed from either mature or undifferentiated neuroectodermal and mesenchymal cells, and that the primary intracranial rhabdomyosarcoma is quite distinct from medulloblastoma or teratoma. The marked argyrophilic reaction of the rhabdomyosarcoma has also been noted as a characteristic differentiation from medulloblastoma.\(^\text{10}\) Russell and Rubinstein\(^\text{20}\) have accepted several cases of pure rhabdomyosarcoma devoid of neuroblastic elements and interpreted them as embryonal sarcoma showing rhabdomyoblastic differentiation. We have collected seven such reported cases of pure rhabdomyosarcoma of the brain in Table 1, and added our present case, in which the tumor was composed of striated muscle cells, rhabdomyoblasts, and other mesenchymal tissues but without any neuroblastic or teratomatous elements.
Clinicopathological Correlation

Three cases of rhabdomyosarcoma of the brain were found in the first 5 years of life and two were in females. All tumors arose in the midline of the posterior fossa and two were encapsulated. Three cases occurred in adolescence and early adulthood, between the ages of 15 and 29; one was localized to the cerebellopontine angle and the other two were sharply demarcated, nodular masses in the cerebral hemispheres. El-Gothamy, et al., reported a case of rhabdomyosarcoma arising from the middle ear of a 4-year-old girl; the tumor extended from the internal auditory meatus through the cerebellopontine angle, compressing the fourth ventricle, and showed no distant metastases. Although this case is not listed in Table 1, it bears a marked resemblance to that of Lopez. Two cases were found in an older age group; one was in a 45-year-old woman who had an infiltrative mass of the cerebral hemisphere and the other in a 52-year-old woman who had a well-circumscribed mass of the cerebellar hemisphere. The term “rhabdomyoma” has been assigned to the non-neoplastic, congenital nodule which was, for instance, found in the heart muscle and showed no neoplastic proliferation, although there was one exception that was a truly neoplastic, benign rhabdomyoma of the tongue. However, a rhabdomyomatous tumor of the brain should be regarded as rhabdomyosarcoma. Our present case and others were initially sharply circumscribed or encapsulated tumors but they formed recurrent masses within 2 years after the radical excision or even radiation.

We found several interesting differences between rhabdomyosarcoma of the brain and medulloblastoma. Medulloblastoma was found exclusively in childhood; ages in the reported cases ranged between 2½ and 10½ years, with an average of 6 years. The incidence in boys was four times that in girls. All reported cases of medulloblastoma were found in the fourth ventricle arising from the vermis. Rhabdomyosarcoma, on the other hand, was found in a much wider age group that ranged from 3½ to 52 years. Five such cases of tumor located in the posterior fossa had the following sites of origin: two from the vermis, one from the fourth ventricle, one in the cerebellar hemisphere, and one in the cerebellopontine angle. All three cases under the age of 4 years were located in the midline structure of the cerebellum. On the other hand, three cases of rhabdomyosarcoma were found in the cerebral hemisphere of patients over 15 years old. Rhabdomyosarcoma showed a higher incidence in females, with a ratio of 5:3. Although the prognosis for both tumors was poor, the survival time was slightly longer for rhabdomyosarcoma.

The currently accepted concept of the histogenesis of rhabdomyosarcoma is that it is mesenchymal in origin and that the embryonic rhabdomyosarcomas most frequently affect children and adolescents. Willis postulated that rhabdomyosarcoma is derived from either immature muscle tissue or undifferentiated mesenchymal cells found along the vessels of the pia mater. Because of the original fourth ventricular site of the tumor in our case, we also suggest the possibility of hamartomatous development. Ohanian described striated muscle within the cerebellum of the albino rat, while Shimoda reported a 19-year-old patient in whom the only attachment of a rhabdomyoma was to the septum pellucidum. Those reports could constitute additional evidence of the hamartomatous origin of rhabdomyosarcoma of the brain.

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