Primary Malignant Rhabdoid Tumor of the Brain: CT and MR Findings

Choon-Sik Yoon\textsuperscript{1}, Sylvester Chuang\textsuperscript{2}, and Venita Jay\textsuperscript{3}

--- Abstract ---

Purpose: To describe the CT and MR findings of primary malignant rhabdoid tumor (MRT) of the brain, which is a rare but very aggressive neoplasm in childhood. Materials and Methods: Retrospectively, we evaluated the CT and MR findings of 5 patients of primary MRT of the brain with a review of clinical records. Results: The primary MRTs of the brain were large (n=4) with a tendency to be associated with necrosis, hemorrhage (n=2) and calcification (n=2). Solid components of the tumor showed increased attenuation on precontrast CT scan and iso- or slightly hyper-signal intensity on T2-weighted images probably due to hypercellularity. Solid components of the tumor were also well enhanced on contrast-enhanced CT scan (n=5) and MRI (n=2). In 1 case with intratumoral bleeding, MR findings were variable on T1-weighted and T2-weighted images. Intracranial and intraspinal metastasis were found in 2 cases on preoperative MR studies. Follow-up CT and MR studies showed recurrence of the tumor and/or leptomeningeal metastasis in 3 cases. Conclusions: Although CT and MR findings of primary MRT of the brain are nonspecific, a tendency toward large size, calcification and intratumoral bleeding may be attributed to CT and MR findings. The solid components of tumors could present hyperdense on precontrast CT scan and iso- or slightly hyper-signal intensity on T2-weighted MR image. Preoperative and follow-up MR studies are important to detect metastatic foci.

Key Words: Brain, neoplasms, CT brain neoplasms, MR

INTRODUCTION

First described in 1978,\textsuperscript{1} malignant rhabdoid tumor (MRT) is recognized as one of the most malignant tumors of the kidney. Although MRTs were originally and most frequently reported as arising in the kidney,\textsuperscript{2, 4-6} similar neoplasms have been reported in the thymus,\textsuperscript{7} liver\textsuperscript{8} and various soft-tissue sites.\textsuperscript{9-10} To our knowledge, primary MRT in the brain is extremely rare, with fewer than 100 reported cases to date.\textsuperscript{11-20} Only some of these reports have included a description of the imaging findings.\textsuperscript{13-20} In this report, we describe CT and MR findings in 5 cases of intracranial MRT and review radiological findings of previously reported cases.

MATERIALS AND METHODS

We retrospectively evaluated 5 patients with primary MRT of the brain including 1 previously reported (case 1). All 5 patients underwent preoperative brain CT scans before and after intravenous injection of 2 ml/kg of non-ionic contrast agents with slice thickness of 5–10 mm. Two patients underwent MR studies with a Magnetom 1.5 T (Siemens medical System, Enlangen, Germany) with head coil. The unenhanced T1-weighted images (TR/TE, 520–608/ 10 msec) and T2-weighted images (TR/TE, 2800–3000/90–120 msec) were obtained, and then contrast-enhanced T1-weighted images (TR/TE, 680/22 msec) after intravenous injection of 0.1 mmol/kg of gadopentetate dimeglumine (Magnevist; Schering, Berlin, Germany) were acquired. The matrix size was 144–180×256, and various fields of view were applied according to the patients size, ranging from 20 to 25 cm. The slice thickness was 5 mm with 2.5 mm interslice gap. Our 5 patients were comprised of 2 girls aged 49 and 71 months and 3 boys aged 9

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and 14 months and 15 years. The diagnosis of MRT was established by pathology following surgical resection. Abdominal CT scans also were obtained postoperatively in 4 patients to rule out renal neoplasm except for 1 case which was associated with rapid deterioration of clinical course after surgery. Pathologic investigations included light microscopic examination, immunohistochemistry and electron microscopy. Immunohistochemical studies were performed by the immunoperoxidase technique using a variety of markers including glial fibrillary acidic protein (GFAP, polyclonal, 1:200. Dako, Glostrup, Denmark), synaptophysin (monoclonal, 1:5, Sternberger-Meyer Immunocytochemicals Inc., Baltimore, MD, USA), neuron specific enolase (NSE, polyclonal, 1:250, Dako, Glostrup, Denmark), epithelial membrane antigen (EMA, monoclonal, 1:10, Dako, Glostrup, Denmark), low molecular weight cytokeratin (CEA, polyclonal, 1:200, Dako, Glostrup, Denmark), S-100 protein (polyclonal, 1:200, Dako, Glostrup, Denmark), vimentin (monoclonal, 1:300, Sigma, St. Louis, MO, USA), and desmin (monoclonal, 1:20, Dako, Glostrup, Denmark). For electron microscopy, tissue was fixed in the universal fixative (equal parts of 4% formaldehyde and 1% glutaraldehyde) and post-fixed in 1% Osmium tetroxide, dehydrated in graded alcohols and propylene oxide and embedded in epon. One micrometer-thick sections were stained

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age</th>
<th>Sex</th>
<th>Symptoms</th>
<th>Treatment</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>9 m</td>
<td>M</td>
<td>vomiting, irritability</td>
<td>partial resection, chemotherapy</td>
<td>died 4 months after op.</td>
</tr>
<tr>
<td>2.</td>
<td>15 y</td>
<td>M</td>
<td>headache, vomiting</td>
<td>total resection, chemotherapy, RT</td>
<td>alive 4 months after op.</td>
</tr>
<tr>
<td>3.</td>
<td>14 m</td>
<td>M</td>
<td>macrocephaly</td>
<td>biopsy</td>
<td>discharge 6 months after op. with 'DNR' state</td>
</tr>
<tr>
<td>4.</td>
<td>4 y</td>
<td>F</td>
<td>headache, vomiting, seizure</td>
<td>total resection, chemotherapy, RT</td>
<td>alive after 3 months after op.</td>
</tr>
<tr>
<td>5.</td>
<td>6 y</td>
<td>F</td>
<td>headache, left 7th nerve palsy</td>
<td>debulking excision, chemotherapy, RT</td>
<td>alive 13 months after op.</td>
</tr>
</tbody>
</table>

op., operation; RT, radiation therapy; 'DNR', 'do not resuscitate'.

Table 2. Summary of CT and MR Findings in 5 Cases of Primary Malignant Rhabdoid Tumor of the Brain

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Size (cm)</th>
<th>Location</th>
<th>Pre-contrast</th>
<th>CT post-contrast</th>
<th>MR T1WI pre/Gd</th>
<th>MR T2WI</th>
<th>Calc.</th>
<th>Edema</th>
<th>Necrosis</th>
<th>Hemo-</th>
<th>Intraspinal metastasis</th>
<th>F/U CT/MR</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>2.7×2.8×4</td>
<td>pineal</td>
<td>high diffuse</td>
<td>N/A</td>
<td>N/A</td>
<td>none</td>
<td>none</td>
<td>none</td>
<td>+</td>
<td>-</td>
<td>recurrence</td>
<td>no recurrence</td>
</tr>
<tr>
<td>2.</td>
<td>6×7×3.5</td>
<td>Rt.F</td>
<td>mixed patchy</td>
<td>N/A</td>
<td>N/A</td>
<td>fleck</td>
<td>mild</td>
<td>multiple</td>
<td>-</td>
<td>-</td>
<td>recurrence progression of metastatic lesion</td>
<td>recurrence</td>
</tr>
<tr>
<td>3.</td>
<td>9×7.8×9</td>
<td>L.t.FTP</td>
<td>mixed patchy</td>
<td>mixed</td>
<td>peripheral</td>
<td>none</td>
<td>mod.</td>
<td>multiple</td>
<td>+</td>
<td>preop.</td>
<td>Recurrence leptomeningeal spread</td>
<td>Recurrence</td>
</tr>
<tr>
<td>4.</td>
<td>5.5×4.9×6</td>
<td>L.t.T</td>
<td>high diffuse</td>
<td>N/A</td>
<td>N/A</td>
<td>Dense</td>
<td>mod.</td>
<td>multiple</td>
<td>-</td>
<td>postop.</td>
<td>Initial improvement</td>
<td>Initial improvement</td>
</tr>
<tr>
<td>5.</td>
<td>1×1.7×1.3</td>
<td>vermis</td>
<td>high diffuse</td>
<td>low iso diffuse</td>
<td>none</td>
<td>none</td>
<td>none</td>
<td>-</td>
<td>preop.*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>multifocal</td>
<td>inhomogeneous</td>
<td>leptomeningeal spread</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Calc., calcification; T1WI, T1-weighted image; T2WI, T2-weighted image; preop., preoperative; postop., postoperative; F/U, follow up; N/A, not available; F, frontal lobe; FTP, frontotemporalparietal lobe; T, temporal lobe; cbl, cerebellum; Ref., Reference; Rt., right; L.t, left; mod., moderate.
* also include left cerebellopontine metastatic nodule.
with toluidine blue. Ultrathin sections were examined under a Phillips 400 transmission electron microscope.

RESULTS

Details of symptoms and clinical course are summarized in Table 1. Clinical symptoms were variable in each case. The tumors were large, except for case 5. MRT occurred mostly in early childhood, less than 6 years of age in 4 cases but 1 patient (case 5) was 15 years old. CT and MR findings are summarized in Table 2. We also summarized previously reported cases in Table 3 and 4. Solid components of MRT except the necrotic area showed increased attenuation compared to normal gray matter in precontrast CT scan in all cases (Fig. 1A, 2A, and 3A), which were well enhanced after contrast administration (Fig. 1B, 2B, and 3B). Calcifications were seen in 2 cases (case 2 and case 4) (Fig. 3A). In case 3, marked tumor necrosis and severe hemorrhage were observed on MR images with iso- to high signal intensity on T1-weighted image and decreased to iso-signal intensity on T2-weighted images (Fig. 2, C and D). In case 5, CT scan showed a small lobulated enhancing mass located in the midline posterior fossa (Fig. 4A), but
<table>
<thead>
<tr>
<th>Case No.</th>
<th>Size (cm)</th>
<th>Location</th>
<th>CT</th>
<th>MR</th>
<th>Calc.</th>
<th>Edema</th>
<th>Necrosis</th>
<th>Hemorrhage</th>
<th>Intraspinal metastasis</th>
<th>F/U CT/MR spread</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ref. 15</td>
<td>large</td>
<td>Lt. cbll multifocal</td>
<td>mixed precontrast enhanced pattern</td>
<td>intense postcontrast enhanced pattern</td>
<td>N/A</td>
<td>linear, punctate</td>
<td>none</td>
<td>several</td>
<td>N/A</td>
<td>multiple recurrence, frontal recurrence, cerebellomedulline</td>
</tr>
<tr>
<td>Ref. 16</td>
<td>N/A</td>
<td>6x5x5.5</td>
<td>high precontrast enhanced pattern</td>
<td>intense postcontrast enhanced pattern</td>
<td>N/A</td>
<td>none</td>
<td>few flecks</td>
<td>none</td>
<td>multiple recurrence, cerebellar and intraventricular dissemination</td>
<td></td>
</tr>
<tr>
<td>Ref. 17</td>
<td>6x5 x 6</td>
<td>Lt. P</td>
<td>mixed precontrast enhanced pattern</td>
<td>patchy postcontrast enhanced pattern</td>
<td>N/A</td>
<td>severe</td>
<td>multiple</td>
<td>multiple</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td>5.5 x 5.5</td>
<td>Lt. trigone</td>
<td>N/A</td>
<td>N/A</td>
<td>iso</td>
<td>iso</td>
<td>patchy</td>
<td>N/A</td>
<td>mod.</td>
<td>multiple</td>
</tr>
<tr>
<td>Ref. 19</td>
<td>large</td>
<td>Lt. F</td>
<td>inhomogeneous</td>
<td>N/A</td>
<td>N/A</td>
<td>calcification</td>
<td>N/A</td>
<td>multiple</td>
<td>N/A</td>
<td>multiple</td>
</tr>
<tr>
<td>Ref. 20</td>
<td>N/A</td>
<td>vermis</td>
<td>high precontrast enhanced pattern</td>
<td>diffuse postcontrast enhanced pattern</td>
<td>N/A</td>
<td>low</td>
<td>iso</td>
<td>diffuse</td>
<td>N/A</td>
<td>multiple</td>
</tr>
<tr>
<td>Ref. 27</td>
<td>N/A</td>
<td>vermis</td>
<td>high precontrast enhanced pattern</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>multiple</td>
</tr>
</tbody>
</table>

Calc., calcification; T1WI, T1-weighted image; T2WI, T2-weighted image; preop., preoperative; F/U, follow up; N/A, not available; F, frontal lobe; P, parietal lobe; cbll, cerebellum; Ref., Reference; Rt., right; Lt., left; mod., moderate.

**DISCUSSION**

MRT is a highly aggressive malignant neoplasm that has been described as a separate entity based on its unique histologic features. The term "rubeloid" originally described a papillary variant of retinoblastoma, but this term is now applied to tumors with similar histologic features. The tumors are characterized by the presence of rosettes, which are composed of bundles of intermediate filaments that are immunolabeled with antibodies against keratin and synaptophysin. Ultrastructural and immunohistochemical studies have shown that these filaments are composed of intermediate filaments, including vimentin, synaptophysin, and neuron-specific enolase. The tumors also demonstrate a nested pattern of growth, with rosettes forming a papillary configuration. These features are consistent with the diagnosis of retinoblastoma, but the tumors are distinct from other retinoblastomas due to their more aggressive behavior.

In every case, the pathologic diagnosis of retinoblastoma was made, and the patients were referred for further treatment. The treatment options include neoadjuvant chemotherapy followed by surgical resection, adjuvant chemotherapy, and radiotherapy. The response to treatment is variable, with some tumors responding well to chemotherapy and others being refractory. The outcome of treatment is also variable, with some patients achieving long-term survival and others succumbing to their disease.

The clinical course of the tumors is characterized by rapid growth, withvasion into the subarachnoid space and leptomeninges, and dissemination to the brain and other organs. The tumors are often large and invasive at the time of diagnosis, and the treatment is often complex and extensive. The prognosis is determined by the extent of disease at the time of diagnosis and the response to treatment. The survival rates are generally low, with a median survival of 2-3 years. The follow-up imaging studies are critical in monitoring the response to treatment and identifying recurrent disease.

**MR study showed a small low-to-isointense tumor on T1-weighted images and contrast administration (Fig. 4B). Follow-up T2-weighted images showed new areas of enhancement, and contrast administration confirmed the findings.**
The renal tumor usually occurs in early childhood with a peak incidence at 13–16 months. Bonin et al. reported the coexistence of renal MRT with cerebellar medulloblastoma, pineoblastoma, cerebral
primitive neuroectodermal tumor, and malignant subependymal giant cell astrocytoma. A case of concomitant renal and presumed primary brain MRT has also been described. The CNS MRT can occur in the fourth ventricle. Brain metastases from renal MRT may also occur and tend to favor the cerebrum and may be multiple. Due to similar pathologic features, it may be difficult to distinguish between primary CNS MRT and metastases from a renal primary MRT in cases of coexistent renal and brain MRT. Our 4 cases with postoperative abdominal CT scan had no renal tumor, but the abdominal CT scan was not available in case 3.

Previous reports of primary MRT of the brain have usually shown a large tumor at the time of diagnosis with variable symptoms such as headache, lethargy, irritability and vomiting. Our cases also showed large tumors and similar clinical symptoms except for case 5, which presented as a small tumor arising from cerebellar vermis with left facial weakness due to metastatic lesion to the left cerebellopontine angle area. Caldemeyer et al. described that 9 of 11 known cases of primary central nervous system MRT occurred in cerebellum alone or in combination with a
Fig. 5. (A) MRT with vimentin-positive globular inclusions in the cytoplasm of the tumor cell (arrows). The tumor shows large nuclei with prominent nucleoli and mitotic figures. Immunoperoxidase stain for vimentin, ×280. (B) Prominent cytokeratin immunoreactivity in the cytoplasm of tumor cells in the same case as illustrated in figure 5 (A). Immunoperoxidase stain for low molecular weight cytokeratin, ×280.

supratentorial tumor. But Hanna et al. described 3 cases arising from the left cerebral hemisphere with 2 cases of intraventricular origin. Our cases occurred in variable locations including the pineal region (case 1), supratentorial region (cases 2, 3, 4) and cerebellar vermis with intraventricular extension (case 5).

Primary MRTs of the brain have been reported from newborns up to 13 years of age, with the highest incidence of MRT in the first 2 years of life. Ages of 4 of our cases were less than 6 years, similar to that of previously reported cases, but one case was 15 years old.

Hanna et al. described that although the preoperative imaging findings described were nonspecific, there was some consistency among their cases such as large tumor size, multiple necrotic or cystic foci, a patchy pattern of enhancement on CT and MR studies and association with moderate to marked adjacent parenchymal edema. In our cases, preoperative enhanced CT scans showed hyperdense solid components of tumors with or without necrotic foci. Hyperdense tumors enhanced well after contrast administration. The hyperdense solid component represented the hypercellular portion of the tumor by microscopic study and pathologic correlation. Low density areas of tumor without enhancement were necrotic areas by histology. Intratumoral calcification has been described in 3 of 14 reported cases. In our cases, parenchymal edema due to tumor was variable, ranging from none to a moderate degree, similar to another report.

Because the most common site of MRT in the brain is the posterior fossa, differential diagnosis must include medulloblastoma and ependymoma. Age at onset of MRT is younger than in medulloblastoma, and size of MRT is larger than that of medulloblastoma. CT and MRI may show polymorphic zones in MRT and more homogeneous in medulloblastoma.

MR findings of primary MRT of the brain have been very limited. Tumors were hypo- or isointense on T1-weighted image and iso- or hyperintense on T2-weighted image relative to the gray matter. In our cases, case 5 showed relatively homogeneous signal characteristics on T1- and T2-weighted images, but case 3 showed mixed signal intensity on T1- and T2-weighted images due to extensive necrosis and intratumoral hemorrhage. Our 2 cases with intratumoral hemorrhage (cases 1, 3) had very poor clinical outcomes similar to the previously reported case with tumor hemorrhage. Tumors in case 1 and case 3 were very vascular as confirmed by surgery and pathology.

Postoperative follow-up CT and MR studies have invariably shown tumor recurrence at the primary site and tumor spread to the subarachnoid space or meninges suggesting an aggressive clinical course. Even preoperative CT or MR studies have demonstrated multiple metastatic foci as in our case 3 and case 5.

Prognosis for reported cases has been generally poor. Survival of all reported cases was less than 8 months except for one case, who died 15 months after initial diagnosis even though surgery, chemo-
therapy and radiation therapy were given. 17-20 In our cases, case 1 died 4 months after operation and postoperative chemotherapy with carboplatinum, ifosfamide and etoposide and case 3 had a poor clinical outcome after operation due to tumoral bleeding. The 3 remaining cases are still alive after surgery and postoperative chemotherapy with ifosfamide, Vp-16 and carboplatinum, and radiation therapy. Case 5 is alive more than 13 months after surgery.

The histogenesis of MRT is underdetermined. MRT is characterized by light microscopic features that include a diffuse growth pattern of predominantly polygonal cells, vesicular nuclei with prominent nucleoli, and scattered cells that contain a cytoplasmic hyaline globular inclusion adjacent to the nucleus. 14 MRTs show immunohistochemical positivity for vimentin and epithelial markers such as epithelial membrane antigen and cytokeratin 14,14,18,24,27 as demonstrated in all our cases. Unlike rhabdomyosarcoma, immunoreactions for myoglobin, desmin or myosin are negative. 4,10,14,20 Immunohistochemically, MRTs are also negative when stained with antisera to synaptophysin, S-100, neuron-specific enolase, and neurofilaments in contradistinction to primitive neuroectodermal tumors. 27 Electron microscopy demonstrates intracytoplasmic whorling filaments that represent vimentin. 17,22,27

In summary, although CT and MR findings of primary MRT of the brain are nonspecific, a tendency toward large size, calcification and intratumoral bleeding may be attributed to CT and MR findings. The solid components of MRT, presenting hyperdense on precontrast CT and iso- or slightly hyper-signal intensity on T2-weighted MR image due to hypercellularity, are well enhanced after contrast administration. Preoperative and follow-up MR studies of the brain and spine with contrast enhancement are necessary for evaluation of the primary site as well as metastatic foci.

REFERENCES
