Unenhanced and gadolinium-DTPA-enhanced MR imaging in postoperative evaluation in pediatric brain tumors

CURTIS A. DICKMAN, M.D., HAROLD L. REKATE, M.D., C. ROGER BIRD, M.D., BURTON P. DRAYER, M.D., AND MARJORIE MEDINA, R.N.

Divisions of Neurological Surgery and Neuroradiology, Barrow Neurological Institute, Phoenix, Arizona

Gadolinium-diethylenetriaminepenta-acetic acid (Gd-DTPA) is a chelated paramagnetic contrast agent under clinical trial for use in magnetic resonance (MR) imaging. The increased signal intensity following the intravenous infusion of contrast medium may improve the ability of MR imaging to delineate tumors. The use of this method in 15 pediatric patients with suspected brain-tumor recurrence was analyzed. All 15 patients underwent postoperative Gd-DTPA-enhanced MR imaging, and residual tumor was demonstrated in nine of them. Based on the findings of the enhanced MR studies, four patients had additional surgery, two underwent radiation therapy, and one was given immunotherapy. Continued surveillance was recommended for the remaining eight patients. In all cases the enhanced MR imaging studies were superior to the unenhanced studies in regard to the qualitative and quantitative assessment of the residual tumor. Gadolinium-DTPA-enhanced MR imaging appears to be a safe and effective means of providing an accurate postoperative assessment of residual disease in pediatric brain-tumor patients. It is as effective as contrast-enhanced computerized tomography and has the sensitivity and anatomic resolution provided by MR imaging. The most useful role of this agent was in the postoperative period, in assessing the adequacy of surgical resection. This technique is recommended as the procedure of choice in the postoperative assessment and long-term surveillance of patients with brain tumors.

KEY WORDS • brain neoplasm • magnetic resonance imaging • gadolinium-DTPA contrast medium • children

The chelated paramagnetic compound gadolinium-diethylenetriaminepenta-acetic acid (Gd-DTPA) is available as a contrast agent for use in magnetic resonance (MR) imaging. This agent defines areas of loss of blood-brain barrier integrity by causing increased signal intensity on T₁-weighted images. To assess the utility of Gd-DTPA-enhanced MR imaging in delineating tumor recurrence, a group of pediatric patients were evaluated following brain-tumor resection.

Clinical Material and Methods

An experimental protocol was established in which MR imaging studies were performed using a General Electric 1.5-tesla Signa Unit.† Informed consent as approved by the Institutional Review Board of St. Joseph's Hospital and Medical Center was obtained. Precontrast T₁-, intermediate-, and T₂-weighted imaging was performed. Gadolinium-DTPA was then injected intravenously at a dose of 0.1 mmol/kg body weight as part of a multicenter pediatric protocol.† Spin-echo T₁-weighted images (TR 600 msec, TE 20 msec) were obtained within 5 minutes, spin-echo T₂-weighted images (TR 2500 msec, TE 40, and 80 msec) within 15 minutes, and a second series of T₁-weighted images within 20 minutes following injection of contrast material. Laboratory studies (including electrolyte studies, complete blood count, urinalysis, renal and liver function, and serum iron determination) as well as physical examinations were performed prior to MR imaging and at regular intervals thereafter.

The patients' radiographic studies and case histories

† Gd-DPTA obtained from Berlex Laboratories, Cedar Knolls, New Jersey.
TABLE 1
Clinical summary in 15 children with enhanced MRI for postoperative evaluation of brain tumors*

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Sex, Age (yrs)</th>
<th>Pathological Diagnosis</th>
<th>Postop Time to Enhanced MRI</th>
<th>Pre-MRI Treatment</th>
<th>MRI Findings†</th>
<th>Treatment Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M, 12</td>
<td>pilocytic astrocytoma</td>
<td>10 days</td>
<td>resection × 2, XRT, shunt</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>2</td>
<td>M, 14</td>
<td>cerebellar astrocytoma</td>
<td>6 mos</td>
<td>resection, XRT, shunt</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>3</td>
<td>M, 10</td>
<td>choroid plexus carcinoma</td>
<td>4 days</td>
<td>resection</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>4</td>
<td>F, 14</td>
<td>astrocytoma</td>
<td>2 mos</td>
<td>open biopsy</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>5</td>
<td>M, 2</td>
<td>leptomeningeal melanoma</td>
<td>1 wk</td>
<td>open biopsy, shunt</td>
<td>−</td>
<td>+</td>
</tr>
<tr>
<td>6</td>
<td>M, 10</td>
<td>medulloblastoma</td>
<td>4 mos</td>
<td>resection, XRT, shunt</td>
<td>+</td>
<td>−</td>
</tr>
<tr>
<td>7</td>
<td>M, 13</td>
<td>pineocytoma</td>
<td>1 mo</td>
<td>stereotactic biopsy, resection, XRT, shunt</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>8</td>
<td>F, 13</td>
<td>craniopharyngioma</td>
<td>14 mos</td>
<td>resection</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>9</td>
<td>M, 13</td>
<td>pineal teratoma</td>
<td>2 yrs</td>
<td>2-stage resection, shunt</td>
<td>−</td>
<td>+</td>
</tr>
<tr>
<td>10</td>
<td>M, 13</td>
<td>cerebellar astrocytoma</td>
<td>4 yrs</td>
<td>resection, XRT, shunt</td>
<td>+</td>
<td>−</td>
</tr>
<tr>
<td>11</td>
<td>M, 6</td>
<td>primitive neuroectodermal tumor</td>
<td>9 mos</td>
<td>resection, XRT</td>
<td>−</td>
<td>+</td>
</tr>
<tr>
<td>12</td>
<td>M, 5</td>
<td>4th ventricular ependymoma</td>
<td>1 yr</td>
<td>2-stage resection, XRT, shunt</td>
<td>+</td>
<td>−</td>
</tr>
<tr>
<td>13</td>
<td>M, 11</td>
<td>astrocytoma</td>
<td>6 mos</td>
<td>resection, shunt</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>14</td>
<td>F, 2</td>
<td>medulloblastoma</td>
<td>22 mos</td>
<td>resection, shunt</td>
<td>−</td>
<td>+</td>
</tr>
<tr>
<td>15</td>
<td>F, 10</td>
<td>craniopharyngioma</td>
<td>2 yrs</td>
<td>resection × 2</td>
<td>−</td>
<td>+</td>
</tr>
</tbody>
</table>

* MRI = magnetic resonance imaging; XRT = external beam radiation therapy.
† + = Abnormal signal, indicating the possibility of recurrent or residual tumor; − = no evidence of tumor.

were evaluated by the Pediatric Brain Tumor Board of our institution, which is a multidisciplinary team composed of pediatric and radiation oncologists, pediatric neurologists, neuroradiologists, and neurosurgeons. The treatments recommended by this group were based on studies obtained before and after infusion of contrast material in conjunction with the clinical profile. Additionally, the precontrast and postcontrast studies were compared qualitatively and quantitatively to determine the presence of residual tumor or tumor recurrence. Follow-up studies consisted of interviews, physical examinations, and MR imaging as indicated. All surgical procedures were performed at our institution and all pathological diagnoses were verified by examination of gross and microscopic specimens.

Results

Fifteen pediatric patients received injections of Gd-DTPA in the postoperative evaluation of their brain neoplasms. The patients characteristics are displayed in Table 1. There were 11 boys (mean age 9.2 years, range 2 to 14 years) and four girls (mean age 9.8 years, range 2 to 14 years). The median interval from the most recent neurosurgical procedure for treatment of tumor

![Fig. 1. Case 2. Magnetic resonance (MR) images of a recurrent cerebellar astrocytoma. Left: Precontrast T2-weighted MR image displaying a homogeneous increased signal intensity. Right: Postcontrast T2-weighted MR sequence clearly demonstrating the extent and location of tumor recurrence.](image-url)
Gd-DTPA-enhanced MR imaging in pediatric brain tumors

to the enhanced MR study was 6 months (range 4 days to 2 years). Follow-up examination was obtained in all patients at a median interval of 8 months. None of the patients experienced any allergic or other adverse reactions following the administration of Gd-DTPA.

The tumor types were diverse. Five patients had astrocytomas, two had medulloblastomas, and two had craniopharyngiomas; one patient had each of the following tumors: pineocytoma, pineal teratoma, leptomeningeal melanoma, choroid plexus carcinoma, ependymoma, and primitive neuroectodermal tumor. Thirteen patients underwent craniotomy with gross total tumor resection prior to their enhanced MR studies. Two patients had a tumor biopsy performed. The initial postoperative treatment and MR imaging results are detailed in Table 1.

In 14 of the 15 patients, the unenhanced T₂-weighted images were without evidence of tumor. In all 15 patients, the enhanced T₂-weighted images were not useful because of their display of increased tissue water content, which masked the appearance of contrast-enhancing regions. The unenhanced T₂- and enhanced T₁-weighted images provided useful information and are therefore the focus of our analysis.

Residual or recurrent tumors were identified in nine of the 15 patients on the basis of the Gd-DTPA-enhanced MR studies. Tables 1 and 2 outline the MR imaging findings. In 13 patients (87%), the unenhanced T₂-weighted studies were abnormal, which raised the suspicion of residual or recurrent tumor. This issue was resolved in all cases after the administration of contrast material. Seven of these patients had enhancing lesions, indicating the presence of tumor. Of these seven patients, four underwent surgery with histological confirmation of residual tumor. Therefore, contrast enhance-ment appears to be useful in distinguishing the presence or absence of tumor in cases with suspicious unenhanced T₂-weighted studies.

When tumor was present, the contrast-enhanced studies demonstrated the location and extent of neoplastic tissue more clearly than the unenhanced studies (Figs. 1 and 2). Six patients with abnormal T₂-weighted unenhanced studies had no evidence of residual neoplasm after the administration of Gd-DTPA. Tumors not suspected on unenhanced studies were identified in two patients after the administration of contrast medium. In all cases with residual or recurrent tumor, the administration of contrast material improved delineation of the tumor boundaries. Contrast-enhanced imaging also improved differentiation of the tumor core.

Gadolinium-DTPA-enhanced MR images played an important role in determining the treatment and surveillance regimens of the patients in our study. The Gd-DTPA-enhanced studies confirmed the suspicion of residual tumor in seven patients and excluded it in six patients with abnormal unenhanced studies. Gadolinium-DTPA also provided evidence of tumor not apparent on the unenhanced studies in two cases. Therapy was altered as the assumptions regarding the presence or absence of tumor were changed by contrast-enhanced studies.

The findings of the enhanced MR studies were used to guide further therapy in patients with residual tumor. Four patients underwent additional surgery; three displayed a discrete tumor nidus and had further resection (Table 1). A patient with negative results from an open biopsy underwent stereotactic biopsy that yielded the diagnosis of low-grade astrocytoma. All of these patients had pathological confirmation of the presence of residual tumor. Chemotherapy and immunotherapy

![Fig. 2. Case 3. Radiographs of a residual choroid plexus carcinoma. Left: The precontrast T₂-weighted image is diffusely abnormal in the region of the operative site (arrows). Center: The postcontrast T₂-weighted MR image distinctly defines discrete residual subependymal nodules. Right: A contrast-enhanced computerized tomography scan of this region less clearly defines the extent and location of residual tumor (arrow).](image-url)
were initiated in a 2-year-old boy (Case 5) with a biopsy-proven primary leptomeningeal melanoma after the contrast-enhanced study demonstrated diffuse infiltration of the subarachnoid space with tumor (Fig. 3). This patient's tumor was not appreciated on the unenhanced T₁- and T₂-weighted studies, and he would not have received these treatments based on these studies. External beam radiation therapy was recommended for the treatment of a residual astrocytoma involving the basal ganglia in Case 13 and a pineocytoma with intraxial nodules involving the tectum in Case 7 (Fig. 4). Increased surveillance was initiated for a patient with benign pineal teratoma (Case 9) and for another with craniopharyngioma (Case 8) in whom the enhanced studies displayed an additional tumor nodule. Patients without evidence of residual or recurrent disease are followed annually or biannually with examinations and radiographic studies.

Discussion

The N-methylglucamine salt of Gd-DTPA has been available experimentally for use as a contrast agent in MR imaging since 1983. The ionic form of Gd is toxic; however, chelation with DTPA neutralizes the toxicity by tightly binding the Gd molecule, preventing the release of free Gd. Extensive laboratory and clinical trials in humans have demonstrated that Gd-DTPA is a safe and effective agent for use in contrast-enhanced MR imaging.

Gadolinium-DTPA is distributed primarily in the extracellular space, and enhancement persists for approximately 1 hour following administration. It has a half-life of approximately 20 minutes and is excreted unchanged by glomerular filtration. The short half-life after intravenous administration and the high binding constant (10²² to 10²³) of Gd-DTPA account for its stability and favorable kinetic properties.

In a similar fashion to iodinated computerized tomography contrast agents, Gd-DTPA must leak into the extracellular space to produce a contrast effect. By delineating areas of disruption of the blood-brain barrier, Gd-DTPA has been particularly useful in defining the margins between tumor and edema within the central nervous system (CNS). The paramagnetic properties of Gd are due to the presence of unpaired electrons. Gadolinium-DTPA does not directly produce an increased signal; it produces local changes in the magnetic environment that alter the signal intensity obtained. Both T₁ and T₂ relaxation times are shortened. This effect is best visualized on T₁-weighted images by a marked increase in signal intensity.

Our study specifically addressed the value of enhanced MR imaging compared to unenhanced MR imaging in the postoperative evaluation of children with primary CNS neoplasms. Gadolinium-DTPA was most useful in the immediate postoperative period for assessing whether the extent of the surgical resection was adequate; however, a number of features displayed by the enhanced MR studies demonstrate the efficacy of this technique in the immediate and long-term surveillance of patients with brain tumors. Edema, ischemia, postoperative and radiation-induced tissue alterations, and tumor appear similar on unenhanced T₂-weighted MR images. These changes are more clearly distinguished from residual or recurrent tumor after the administration of contrast material because of the tumor enhancement. Neoplastic tissue was demonstrated most clearly on the postcontrast T₁-weighted images. A number of authors have recommended the precontrast T₂-weighted sequence (which is most sensitive in detecting focal lesions within the brain) as a screening test, and the postcontrast T₁-weighted sequence to help characterize the abnormality by the presence or absence of blood-brain barrier breakdown.

![Fig. 3. Case 5. Magnetic resonance (MR) images of a primary leptomeningeal melanoma in a 2-year-old boy. Left: Precontrast T₁-weighted MR image showing no evidence of tumor. Right: Postcontrast T₁-weighted MR image showing extensive infiltrating tumor in the subarachnoid spaces of the posterior fossa, sparing the fourth ventricle and involving the cervical spinal subarachnoid space.](image1)

![Fig. 4. Case 7. Magnetic resonance (MR) images of a residual pineocytoma. Left: Precontrast T₂-weighted MR image showing multiple foci of increased signal intensity (arrows), consisting of radiation-induced changes and tumor. Right: Residual tumor is clearly differentiated on the T₁-weighted postcontrast image.](image2)
Gd-DTPA-enhanced MR imaging in pediatric brain tumors

In two patients in this series, Gd-DTPA identified tumor not apparent on precontrast studies. We advocate the use of contrast-enhanced MR imaging in patients with a high risk of tumor recurrence, even with normal precontrast MR studies.

Gadolinium-DTPA-enhanced MR imaging has been a safe, effective means of detecting residual or recurrent tumor. Similar to CT contrast material, Gd-DTPA defines areas of disruption of the blood-brain barrier. Compared to CT, this technique has the additional advantages of the superior anatomical resolution, sensitivity, and multiplanar graphic depiction of disease processes visualized with MR imaging. This technique provides an improved method of differentiating edema and postoperative and postradiation changes from residual tumor tissue. Identification and delineation of the tumor core are also improved with enhanced MR imaging. Enhanced MR imaging is of most value when it is applied to the long-term surveillance and the postoperative assessment of patients with CNS neoplasms.

References

Address reprint requests to: Harold L. Rekate, M.D., c/o Editorial Office, Barrow Neurological Institute, 350 West Thomas Road, Phoenix, Arizona 85013.