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Allen D. Elster and Geoffrey D. Rieser

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Gd-DTPA–Enhanced Cranial MR Imaging in Children: Initial Clinical Experience and Recommendations for Its Use

Allen D. Elster[1]
Geoffrey D. Rieser

Gd-DTPA was administered prospectively to 65 consecutive children (ages 1 day to 18 years, mean 9.6 years) to document its utility and safety for routine cranial MR imaging. Precontrast T1- and T2-weighted scans and postcontrast T1-weighted scans were obtained. No complications or significant adverse reactions were encountered. Contrast enhancement was seen in 14 lesions from seven patients, but each of these patients had some abnormality also present on precontrast images. Contrast enhancement was thought to be extremely helpful in characterizing four primary tumors and moderately helpful in characterizing four other lesions. Absence of contrast enhancement was helpful in clarifying the nature of abnormalities seen in an additional four patients.

Gd-DTPA may be used safely in children, but this study does not support its routine administration. The highest incremental diagnostic yield from its use will likely be among patients with suspected neoplasms or inflammatory diseases and among those requiring further characterization of lesions seen on precontrast scans.

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Gd-DTPA has enjoyed wide clinical success as an adjunct to cranial MR imaging in adults, but its use in children remains largely uninvestigated. We elected to administer Gd-DTPA prospectively to all pediatric patients referred for cranial MR imaging over a 4-month period. The goals of this study were to validate the safety and effectiveness of Gd-DTPA in an otherwise unselected pediatric population. The scans were reviewed to determine: (1) whether Gd enhancement revealed abnormalities not apparent on precontrast images, and (2) how Gd enhancement affected the radiologic diagnosis or surgical management of these children.

Subjects and Methods

The subjects comprised 65 consecutive pediatric patients referred for cranial MR scans over a 4-month period. The mean age of the patients was 9.6 years, with a range of 1 day to 18 years (Table 1). Informed consent of a parent or guardian was obtained in each case.

The protocol for administration of Gd-DTPA to minors was sanctioned by our Institutional Review Board after consultation with officials of the United States Food and Drug Administration (FDA). At the time our study began, the FDA had already declared Gd-DTPA to be an approved drug for human IV administration with specific indication for adult cranial MR imaging. While the safety and effectiveness of this agent had not yet been established in children, the FDA did not consider its administration to children at the discretion of licensed physicians to constitute "investigational use." Accordingly, the FDA did not require routine monitoring of blood counts, blood chemistries, urinalyses, EEG, or EKG for the pediatric patients involved in our study. Furthermore, Berlex Imaging had already amassed Gd-DTPA toxicity data for children from a prior multicenter trial, and had observed no significant differences from the minor effects noted in adults.

We obtained laboratory tests on the patients involved in our study only if there was clinical suspicion of preexisting renal insufficiency, hemolytic anemia, or hepatic disease. As a result

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[1] Both authors: Department of Radiology, Bowman Gray School of Medicine, 300 S. Hawthorne Rd., Winston-Salem, NC 27103. Address reprint requests to A. D. Elster.

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TABLE 1: Distribution of Patients by Age

Age Range (years)	No. of Patients
0–1	8
1–6	14
6–12	23
12–18	20

of these tests, two potential subjects were excluded from the study (one with SGPT values elevated beyond two times normal and another with sickle cell anemia). Five patients who could not complete the full examination because of illness or inadequate sedation were also excluded.

All our patients underwent physical and neurologic examinations before scanning and at least 3 hr after Gd-DTPA administration. Sedated patients were monitored during and after scanning by EKG or respiratory monitor. Each patient was observed clinically in the MR scanning suite by a resident physician for approximately 1½ hr after contrast administration. Any unusual complaints or untoward reactions were recorded by the resident physician.

All scans were performed on a 1.5-T imager.* Precontrast T2-weighted axial images and T1-weighted sagittal images were obtained. Gd-DTPA (0.1 mmol/kg, Berlex Imaging) was administered intravenously. Postcontrast T1-weighted axial and coronal images were obtained beginning 5–10 min after injection. In cases of brainstem disease, sagittal T1-weighted images were also obtained.

Specific scan parameters varied somewhat with the age of the patient and plane of imaging. T1-weighted pre- and postcontrast sequences were exclusively spin echo, 500–700/20/2 (TR/TE/excitations). Slice thickness was 5 or 6 mm. T2-weighted sequences (2000–2500/60–80) were employed in most children, with other parameters similar to the T1-weighted scans. For infants less than 18 months old, very long spin-echo protocols were used (3500/120/1) following recommendations by Nowell et al. [1]. Motion artifact suppression software (MAST) was utilized with all T2-weighted sequences, since this has been shown by Elster [2] to be superior to cardiac gating for reducing phase-shift artifacts intracranially.

Upon completion of the study the scans were reviewed by a neuroradiologist who was experienced both with high-field pediatric MR imaging and in the use of Gd-DTPA in adults. MR diagnoses were grouped by major disease category to provide a profile of the patients studied (Table 2). The scans were then analyzed to determine the role Gd-DTPA enhancement played in the detectability and characterization of lesions.

Results

All 65 children tolerated the administration of Gd-DTPA well. There were no subjective complaints reported by the children or their parents, other than those relating to the local trauma of an IV injection. In no case did the physical or neurologic examination change appreciably after contrast administration. No allergic reactions or changes in cardiovascular status of the patients were noted by the supervising resident physician in the observation period following infusion.

Three patients experienced nausea or vomiting within the postinfusion observation period; however, this reaction could not be ascribed specifically to Gd-DTPA since each had also received sedative medications.

Contrast enhancement with Gd-DTPA was noted in 14 lesions in seven patients. In six of these lesions (mostly vascular malformations) the MR diagnosis was clear and unchanged despite contrast administration. In the remaining eight lesions (mostly neoplasms), contrast enhancement was considered to be either extremely helpful (four of eight) or moderately helpful (four of eight) in characterizing the lesion or planning therapy.

TABLE 2: Diseases Found Among 65 Children

Type of Disease	No. of Cases
No significant abnormality	37
Neoplasm	8
Congenital/developmental	6
Degenerative/atrophic	6
Vascular	3
Other	5

For example, Figure 1 demonstrates how the pattern of contrast enhancement significantly modified the differential diagnosis of a skull-base tumor in a 12-year-old boy. The patient had no history of nosebleeds, presenting only with nasal stuffiness and headaches. Because of its location and clinical presentation, a primary diagnosis of rhabdomyosarcoma was considered. Precontrast MR was useful in assessing the extent of tumor but not in further characterizing it. Postcontrast, intense enhancement of the neoplasm was demonstrated. The CT literature documents that skull-base rhabdomyosarcomas usually have only moderate contrast enhancement, less than or equal to that of skeletal muscle [3]. Conversely, juvenile angiofibromas are characterized by brilliant contrast enhancement [4]. While not totally excluding rhabdomyosarcoma in this case, the pattern of contrast enhancement after Gd-DTPA administration was believed to modify significantly the differential diagnosis so that the correct disease (juvenile angiofibroma) was considered as the primary diagnosis.

The presence of contrast enhancement with Gd-DTPA also modified the differential diagnosis in a patient with tuberous sclerosis (Fig. 2). On precontrast scans multiple parenchymal calcifications and hamartomas were noted. A subependymal mass was also seen near the left foramen of Monro. This mass had precontrast signal characteristics similar to the other parenchymal hamartomas, and clearly did not have exceptionally long T1 values like the proved giant-cell astrocytomas described by McMurdo et al. [5]. While malignant transformation could not be excluded, the provisional precontrast diagnosis remained benign subependymal hamartoma, since less than 15% of such lesions represent astrocytomas [6]. In the present case, however, intense enhancement of the lesion after Gd-DTPA administration documented unequivocally the hamartoma's neoplastic transformation.

The location of contrast enhancement in brain tumors may have important neurosurgical implications, particularly when only a limited biopsy or subtotal resection is planned. Figure 3 shows a brainstem glioma in which only the lower part of its exophytic component demonstrated contrast enhancement. This pattern of enhancement was of potential neurosurgical importance for biopsy purposes, since a specimen from the upper part of the mass might have misleadingly revealed a lower-grade neoplasm than was present inferiorly.

* Picker International, Highland Heights, OH.

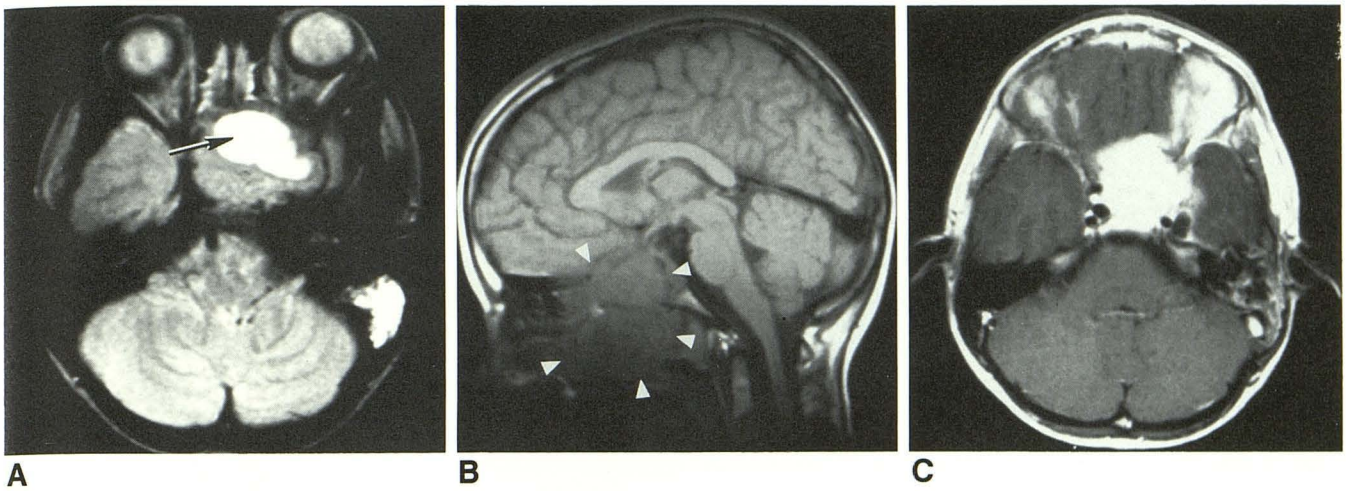


Fig. 1.—12-year-old boy with mass at nasopharynx and at base of skull.
A, T2-weighted axial image (2300/80) shows a complex mass at skull base with cystic component (*arrow*). No appreciable vascular flow voids are noted.
B, T1-weighted sagittal image (600/20) shows full extent of the lesion.
C, T1-weighted axial image (600/20), postinfusion, reveals exceedingly intense contrast enhancement. This degree of enhancement was thought atypical for sarcomas and other base of skull lesions, so the correct preoperative diagnosis of invasive juvenile angiofibroma was made.

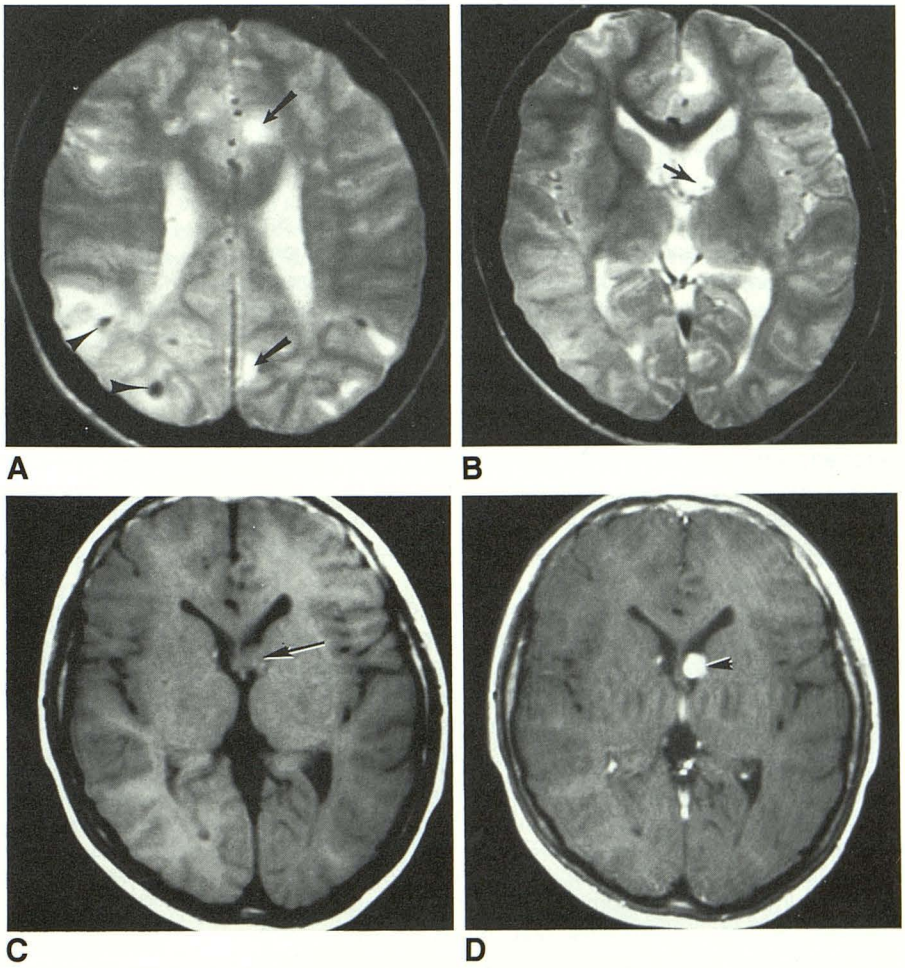
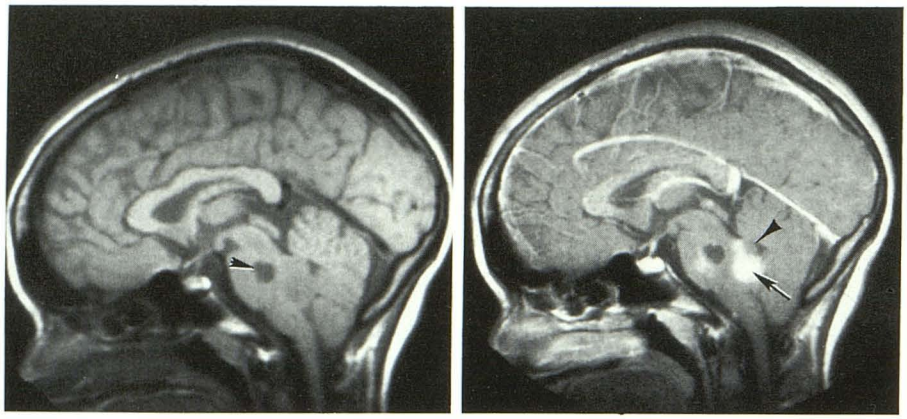


Fig. 2.—12-year-old boy with clinical stigmata of tuberous sclerosis.
A, T2-weighted axial image (2300/80) shows characteristic high-signal cortical hamartomas (*arrows*) as well as dense calcifications (*arrowheads*).
B, T2-weighted axial image (2300/80) inferiorly to *A* shows another high-signal mass at left foramen of Monro (*arrow*) consistent with a hamartoma.
C, T1-weighted axial image (650/20) through same level as *A* again shows the mass (*arrow*) with signal similar to normal brain.
D, Gd-DTPA–enhanced T1-weighted image (600/20) demonstrates marked enhancement of this lesion (*arrowhead*), which has undergone malignant transformation into a giant-cell astrocytoma.

While the presence or pattern of contrast enhancement was frequently helpful, lack of enhancement was thought to be an important finding in four cases. The presence of a high-signal mass and lack of enhancement on T2-weighted images allowed proper preoperative staging of low-grade glioma in two cases. Lack of enhancement was thought to exclude tumor recurrence in a third patient and to exclude an abscess in a fourth.

A finding of considerable interest from our study was that in no case was an enhancing abnormality noted when the



A B

Fig. 3.—Teenage girl with brainstem astrocytoma.

***A*, T1-weighted sagittal image (600/20) shows a mass in the pons with cystic (*arrowhead*) and exophytic components. Tonsillar herniation is also noted.**

***B*, Gd-DTPA–enhanced image (600/20) shows that most of the enhancement is confined to inferior portion of exophytic mass (*arrow*), corresponding to grade III tumor. Upper portion of mass (*arrowhead*) did not enhance and was pathologically lower-grade glioma. A single biopsy from the upper zone could have potentially misrepresented the tumor.**

precontrast scans were entirely normal. All studies diagnosed as normal before contrast administration remained normal after infusion. This result, if confirmed in larger series of patients, could have important implications for the cost-effectiveness of routine Gd-DTPA administration in children.

Discussion

The safety and efficacy of Gd-DTPA for adult cranial MR imaging are now convincingly demonstrated [7–13], but its usefulness in children remains largely uninvestigated. Two recent reports [14, 15] have documented the effectiveness of Gd-DTPA in children with known brain tumors; however, the number of patients in each study was relatively small (15 and 20, respectively), and by experimental design, all patients imaged had lesions with a high likelihood of contrast enhancement. Furthermore, most of the patients in these two series were teenagers, and none was less than 2 years old.

By comparison, our study was prospectively designed and included a consecutive series of pediatric patients of all ages who were preselected only to the extent that they were referred for routine cranial MR imaging. Over half our patients were under 10 years old; 15% were under age 2. A wide range of disorders was encountered, including tumors, vascular malformations, infections, and developmental anomalies.

In our study, enhancing lesions were not detected in any patient who had a perfectly normal precontrast scan. Within a limited clinical spectrum, therefore, a normal precontrast cranial MR scan in a child might well provide all the information necessary for proper diagnosis. In adults, however, many additional lesions demonstrated by Gd-DTPA and not seen on precontrast images have been reported. Most frequently, these lesions have included occult meningiomas [12, 16] or metastases [10, 13]. Since the occurrence of such lesions is low in the general pediatric population, the incremental diagnostic yield obtained by administering Gd-DTPA routinely to pediatric patients with normal precontrast scans is correspondingly low. On the basis of this data, it would seem that the use of Gd-DTPA in the pediatric population should continue to be based on clinical circumstance rather than be considered an absolute requirement.

Conversely, if a lesion (other than a structural congenital anomaly) is encountered before contrast administration, a postcontrast study may be of significant benefit. The diagnostic yield will likely be highest for characterizing and delineating neoplasms both pre- and postoperatively, as well as in cases of suspected infection. Although we did not encounter any strokes in our patients, contrast enhancement could conceivably be helpful to stage or time a vascular event. Future research in even larger groups of pediatric patients will be required to predict more accurately who will most benefit from contrast-enhanced MR imaging.

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