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Diagnostic role of gadolinium-DTPA in pediatric neuroradiology

A retrospective review of 655 cases

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Summary. We retrospectively reviewed the findings in 655 consecutive young patients who underwent contrast-enhanced MR examinations (1.5T) of the head or spine. Their ages ranged from 4 months to 20 years (mean 10 years). There was a 1.7% incidence of minor adverse reactions to gadolinium (Gd)-DTPA, none of which required treatment; no serious adverse reactions were encountered. Based on the radiologic diagnosis the patients were divided into three groups: (1) normal, (2) CNS neoplasm, (3) abnormal but not neoplasm. There were 178 patients thought to have CNS neoplasms and of these 156 (88%) enhanced. Of 124 histologically confirmed noeplasms 115 (93%) showed enhancement after Gd-DTPA. Eight children had histologically confirmed spinal neoplasms; 5 of 6 neurofibromas and 2 ependymomas enhanced. In the 216 patients with abnormalities thought not to be neoplastic, the enhancement rate was 11%; most of the enhancing lesions were vascular malformations. There were very few examples of inflammatory disease, acute trauma or stroke among our patients.

Key words: Gadolinium-DTPA – Magnetic resonance imaging – Neoplasm

Magnetic resonance imaging (MRI) has been rapidly accepted for neurological diagnosis because of its sensitivity to pathology. The lack of artifact from bone and the availability of direct sagittal and coronal planes further advocate the use of MRI instead of computed tomography (CT) for imaging the brain, particularly the brain stem and cerebellum.

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Although MRI is highly sensitive to pathologic changes in brain tissue, the need for an MR contrast agent has become widely recognized. Experience with CT shows that demonstration of blood-brain barrier (BBB) abnormalities through the use of iodinated contrast material increased sensitivity to pathology, enhanced lesion conspicuity, and improved definition of the margins of lesions. This is true for intra- and extra-axial neoplasms, intracranial infection and vascular abnormalities.

Gadolinium-DTPA (Gd-DTPA) has gained wide acceptance because it allows evaluation of the BBB with MRI [1–4]. Its efficacy is established in the adult population but only a few studies have specifically addressed its use in pediatric CNS disorders [5–7].

Gd-DTPA is a stable paramagnetic metal ion chelate that crosses the disrupted BBB in a manner analogous to iodinated contrast. It provides enhancement by causing a change in proton relaxation. Tiny amounts of Gd-DTPA crossing a disrupted BBB can greatly shorten T1 relaxation times of the abnormal tissue, producing areas of contrast enhancement [8–11]. This report reviews our experience with the first 655 young patients who underwent CNS studies (brain, skull base, or spine) with Gd-DTPA. Its emphasis is on the enhancement rate of a cross-section of histologically proven pediatric CNS neoplasms.

Materials and methods

MR scans were performed on 655 consecutive patients (325 females, 330 males), aged 4 months to 20 years (mean age, 10.28 years) before and after intravenous injection of Gd-DTPA. Written informed consent was obtained from the parent or guardian. Children under 5 years of age were routinely sedated to ensure cooperation during the scan.

Gd-DTPA was available as an aqueous solution in a concentration of 0.5 mml/l Gd-DTPA. A dose of 0.1 mmol/kg body weight was injected intravenously at a rate of 10 ml/min after unenhanced MR images had been obtained. Depending on body weight, this dosage of

Table 1. Adverse reaction of use of Gd-DTPA with and without sedation

No adverse reaction	Sedated 200	Non-sedated 444
Adverse reactions		
Headache	2	4
Nausea	2	2
Vomiting	1	0
Total	205	450

Table 2. Enhancement rate of histologically proven CNS masses

Histological diagnosis	Cases	Enhancement	No enhancement	Enhancement rate
A. Intracranial neoplasms				
Craniopharyngioma	10	10	0	100%
Meningioma	2	2	0	100%
Medulloblastoma (primary)	3	3	0	100%
Medulloblastoma (recurrent)[a]	15	15	0	100%
Choroid plexus papilloma	3	3	0	100%
Pituitary tumor	3	3	0	100%
Pinealocytoma	1	1	0	100%
Recurrent/residual tumor	21	19	2	90%
Ependymoma	4	4	0	100%
Astrocytoma	30	25	5	83%
Anaplastic astrocytoma	3	3	0	100%
Mixed glioma	7	7	0	100%
Glioblastoma multiforme	2	2	0	100%
B. Skull base neoplasms				
Lymphangioma/hemangioma	5	4	1	80%
Rhabdomyosarcoma	7	7	0	100%
C. Spinal neoplasms				
Ependymoma	2	2	0	100%
Neurofibroma	6	5	1	83%
Total	124	115	9	93%

[a] The diagnosis of recurrent medulloblastoma was based on multiple nodular enhancing lesions or the development of an enhancing mass on sequential scans in a patient previously diagnosed as having medulloblastoma (or posterior fossa primative neuroectodermal tumor). These were treated as recurrence without repeat biopsy

contrast agent corresponded to an injected volume of 1–20 ml. To ensure complete administration of Gd-DTPA, the catheter was flushed with 2 ml saline immediately after injection. Imaging began 5 min after administration of Gd-DTPA [3, 4].

MRI consisted of short TR (500/25-30/2 [TR/TE/excitations]) pre- and postinjection and long TR (2000/25,50,100/1) pulse sequences performed on two 1.5 T systems. The coil used for head imaging (diameter, 30 cm) had a normal spatial resolution of 1 mm in the section imaged. Sagittal, coronal, and axial sections of the brain were obtained by multiple-slice technique. Section thickness was usually 5 mm with 1–2 mm space between adjacent sections. All images were produced using spin-echo (SE) pulse sequences and a two-dimensional Fourier transform image reconstruction technique. Occasionally thinner section or inversion recovery techniques were also used. Image matrix was 256 × 256 or 256 × 128 in all cases. The imaging time varied from 3.5 to 13.8 m according to the pulse sequence used. In any given case, three to six sequences were used to examine the region of interest.

Radiologic diagnosis was based on the consensus opinion of two or more radiologists. The pathology reports available in the patients' medical records were reviewed. Pathologic correlation was available in 132 cases of neoplasm. The enhancement rates of the neoplastic lesions are based on these pathologically confirmed cases.

Results

All 655 patients tolerated the administration of Gd-DTPA well. Seven patients complained of mild headache, 4 of nausea and 1 patient vomited after the examination. The adverse reactions are summarized in Table 1. No allergic reaction or cardiovascular changes were noted during the observation period (at least 30 min) following infusion. In 1 patient, postinjection images were not obtained because of inadequate sedation. Six of the 12 patients who experienced headache, nausea, or vomiting had received sedation for the study. We compared the incidence of side effects in those patients who were sedated with those who were not and found no significant difference ($\chi = 1.043$, $P = 0.307$) (Table 1).

A radiologic diagnosis of CNS neoplasm (brain, skull base or spine) was made in 178 patients; and 124 were confirmed histologically (Fig. 1), of which 115 (93%) showed enhancement. Table 2 shows an analysis by histologic type. In 54 patients MRI was highly suggestive of neoplasm but no histologic confirmation was obtained: 29 children were thought to have low-grade or inoperable gliomas and were managed non-surgically; 9 were thought to have residual or recurrent brain neoplasms, but had no further surgery. The enhancement rate in the unconfirmed but suspected neoplasm group was 76%. These results are summarized in Table 3.

Twelve children had histologically confirmed tumors in the neck, adjacent to or involving the skull base. All except one, a lymphangioma, enhanced following contrast medium.

Table 3. Enhancement rate of unproven CNS neoplasms

MR diagnosis	Cases	Enhancement	No enhancement	Enhancement rate
A. Intracranial neoplasms				
Craniopharyngioma	3	3	0	100%
Meningioma	3	3	0	100%
Other non-specific tumor	7	6	1	86%
8th nerve sheath tumor	1	1	0	100%
Recurrent/residual tumor	9	8	1	88%
Glioma				
– Optic pathway glioma	10	7	3	70%
– Brain-stem glioma	3	2	1	67%
– Low grade glioma	16	7	9	44%
B. Spinal neurofibromas	2	2	0	100%
Total	54	41	15	76%

Table 4. Enhancement rate of non-neoplastic abnormalities

MR diagnosis	Cases	Enhancement	Noenhancement	Enhancement rate
Dermoid cyst	8	0	8	0%
Arachnoid cyst	12	0	12	0%
Choroid plexus cyst	1	0	1	0%
Pineal region cyst	3	0	3	0%
Old infarct	14	0	14	0%
Hematoma	7	0	7	0%
Venous angioma	6	5	1	83%
Abscess	1	1	0	100%
Cerebritis/meningitis	5	4	1	80%
Venous thrombosis	3	3	0	100%
Neurofibromatosis	7	1[a]	6	14%
Development abnormality	73	0	73	0%
Other	76	9	7	12%
Total	216	23	193	11%

[a] Typical NF lesion in globus pallidus with minimal enhancement. This lesion is being followed to be certain that it is not an early neoplasm

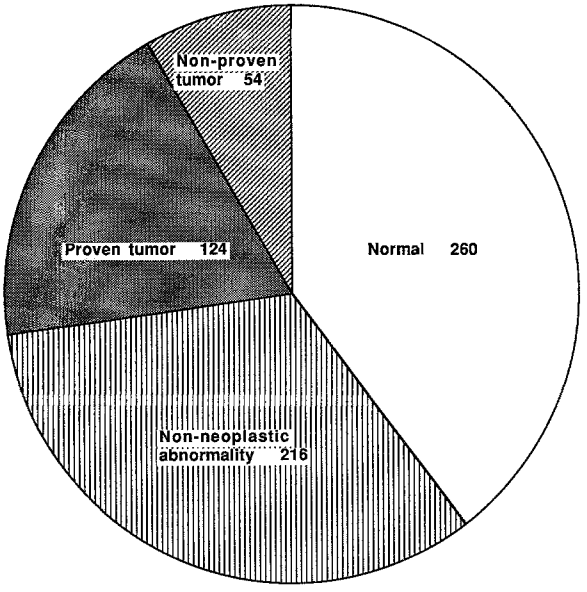

Fig. 1. Diagnosis in 654 enhanced MR scans

Eight children had histologically confirmed spinal neoplasms: 5 of 6 neurofibromas and both ependymomas enhanced following contrast medium.

A radiologic diagnosis of non-neoplastic CNS abnormality was made in 216 patients; 23 (11%) showed abnormal contrast enhancement with Gd-DTPA. The findings in the non-neoplastic group are summarized in Table 4.

The 11% enhancement rate of non-neoplastic CNS abnormalities was much lower than the 93% enhancement rate of proven neoplasms and the 76% enhancement rate of suspected but unproven CNS tumors. Six venous angiomas were suspected on the basis of MRI and in 5 (83%) the caput medusae enhanced. Three cases of suspected venous sinus thrombosis were encountered. These patients all had moderately intense signal in the straight or superior sagittal sinus on short and long TR spin echo sequences in multiple imaging planes. In all 3, the abnormal venous sinus enhanced, including the presumed intraluminal clot. Two cases were corroborated by CT but none was studied by angiography. There were very few cases of inflammatory disease in the study population. One patient had a surgially confirmed abscess which enhanced. There were 260 patients with normal contrast-enhanced CNS studies.

Discussion

Gd-DTPA enhancement occurred in 115 of 124 pathologically proven tumors involving the CNS: in 97 of 104 intracranial neoplasms (93%), 11 of 12 skull base neoplasms (91%), and 7 of 8 spinal neoplasms (87%) (Table 2). Tumors with a 100% enhancement rate in our series included 10 craniopharyngiomas (6 recurrent or residual), 2 meningiomas, 3 pituitary adenomas, a pineocytoma, 7 sarcomas involving the skull base, 3 medulloblastomas, and 3 choroid plexus papillomas.

Of the gliomas, we observed enhancement in all 7 mixed gliomas, 6 ependymomas (4 in the brain and 2 in the spinal cord), 3 anaplastic astrocytomas, and 2 glioblastoma multiformes. Low-grade astrocytomas were the only histologically proven glial tumors which did not have a 100% enhancement rate: 5 of 30 surgically proven low-grade astrocytomas did not enhance following Gd-DTPA. T2-weighted images were required to detect these unenhancing low-grade neoplasms. Low grade lesions may have a relatively intact BBB and demonstrate less enhancement than higher-grade tumors. Some investigators have successfully classified gliomas using unenhanced MR features [12]; it is possible that enhancement characteristics may further refine MR classification.

Contrast medium appears to be essential in postoperative examinations, particularly in posterior fossa primitive neuroectodermal tumors ($n = 15$) (medulloblastomas). In 4 cases nodular CSF-borne metastases invisible on unenhanced T1- and T2-weighted images were detected only on Gd-DTPA-enhanced images. Similarly, in 4 patients with a recurrence in the operative bed, a definite diagnosis could be made only on the enhanced images. However, it is difficult to evaluate patients in the immediate postoperative period, when enhancement in the operative bed may be attributable to disruption of the BBB due to the surgical trauma alone.

There is little controversy regarding the usefulness of contrast-enhanced CT when inflammatory disease is suspected, but our experience with MRI is much more limited. In 655 cases, we encountered only one proven cerebral abscess, which enhanced. There were 5 cases of suspected cerebritis, 4 of which enhanced. These patients were treated medically, so that there was no pathologic correlation. We had no cases of meningitis, but the ability of MRI to demonstrate meningeal inflammation has been established by others [13, 14].

Gd-DTPA was helpful in investigation of some vascular malformations, particularly venous angiomas, where the anomalous veins were more conspicuous after contrast medium. We found enhancement of the small veins of the venous angioma (the caput meduse) in 5 of 6 cases.

These lesions were, however, incidental findings and therefore our analysis was of surgically, and angiographically unproven cases.

Three patients had suspected venous sinus thrombosis but the enhancement pattern was confusing. These patients had absent flow and high T1 signal in the straight (2 cases) or superior sagittal sinus (1 case) in multiple imaging sequences and planes. Two were corroborated by CT, but none angiographically. In all cases, the presumed thrombus and the tissue surrounding the sinus enhanced following Gd-DTPA. The mechanism of enhancement is unknown. One possibility is that the sinus was not thrombosed, but simply that flow within it was slow. Gd-DTPA staining of intraluminal clot in a partially recanalized sinus or enhancement of "cavernous tissue" [15] around the thrombosed segment are other possible explanations.

Although Gd-DTPA-enhanced MRI surpasses the sensitivity of enhanced CT in detecting disturbances of the BBB, it still has significant limitations. As noted above, low-grade gliomas may not enhance. Two of 21 pathologically proven CNS tumor recurrences in our series (10%) did not enhance. The identification of tumor margins is imprecise even using T1- and T2-weighted images and Gd-DTPA-enhanced images. Neoplastic infiltration beyond the enhancing areas is characteristic of glial neoplasms. In this non-enhancing region the neoplastic infiltration may be too sparse to produce detectable disruption of the BBB. This suggests that contrast-enhanced images should be used to direct biopsy of brain lesions; the areas that show the most enhancement are more likely to represent the aggressive, highly cellular regions of the tumor [16].

Children with known neoplastic or inflammatory disease should usually receive contrast medium [17]; enhanced images show whether the lesion has damaged the BBB. From experience accumulated first with CT and now with MRI, we know that this information aids in lesion detection, localization, and characterization. The problem arises when trying to decide whether to give contrast medium routinely to children with neurologic complaints (e.g. headaches, seizures) but no previous diagnosis. Normal unenhanced T1- and T2-weighted images usually suffice to exclude CNS pathology in children, with the exception of meningeal disease [6]. Extra care must be taken in sedated children; the costs and risks of resedation, and delays in diagnosis must be weighed against the low risk and cost of over-use of Gd-DTPA on initial studies. In our study, the frequency of adverse reactions to Gd-DTPA in young people was 1.7%; all adverse reactions encountered were mild and required no treatment.

We conclude that Gd-DTPA is an effective contrast medium for use in children, providing information on the BBB not given by unenhanced images. Assessment of the BBB is particularly helpful in characterizing neoplasms, and its utility in inflammatory disease, particularly meningitis, is well established. While we do not advocate its use in all cases we feel that the difficulties inherent in scanning children, particularly those who are sedated, warrant the liberal use of Gd-DTPA in initial studies in order to minimize the need for repeat examinations.

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