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Clinical–patient studies

Diffusion-weighted MR imaging abnormalities in pediatric patients with surgically-treated intracranial mass lesions

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Summary

Introduction: Diffusion-weighted imaging (DWI) is a magnetic resonance imaging (MRI) technique that measures the degree of water diffusion *in vivo*. DWI abnormalities are frequently observed on immediate postoperative imaging following surgical resection of gliomas in adults. These abnormalities subsequently demonstrate contrast enhancement, which may be confused with lesion recurrence. The purpose of this study was to investigate the occurrence of these postoperative abnormalities in pediatric patients with intracranial mass lesions.

Methods: Thirty-three consecutive patients ≤18 years old with a newly diagnosed intracranial mass lesion underwent MRI, including DWI, before and immediately after surgical treatment.

Results: The median patient age was 9.9 years (range 0.2–18 years). Supratentorial and infratentorial lesions were identified in 22 and 11 patients, respectively. Infiltrative and noninfiltrative, as well as benign and malignant lesions, were included. Postoperative imaging demonstrated areas of reduced diffusion adjacent to the resection cavity in 20 (61%) cases. The median volume of these areas was 1.7 cm^3 (range 0.3 cm^3–12.0 cm^3). Subsequent imaging studies in 9 of the 18 cases showed contrast enhancement in the area corresponding to the DWI abnormality. There were no clinical deficits attributable to any of the diffusion abnormalities. There was no association between the occurrence of these abnormalities and whether the lesion was infiltrative, non-infiltrative, benign, or malignant.

Conclusions: DWI abnormality on immediate postoperative MRI is common following surgery for newly diagnosed intracranial mass lesions in pediatric patients. Focal contrast enhancement in the postoperative period may be confused with recurrence for some lesions. Our study suggests that immediate postoperative DWI is useful in interpreting new areas of focal contrast enhancement on subsequent imaging in children who have had surgery for brain tumors.

Introduction

Diffusion-weighted imaging (DWI) is a magnetic resonance (MR) imaging technique that measures the random translational mobility of water molecules, also known as Brownian motion. In DWI, traditional spin echo sequences are enhanced with strong gradient pulses which cause freely moving water molecules to lose significantly more signal intensity than more stationary water molecules. Water molecules with restricted movement or diffusion demonstrate increased signal intensity on DWI. The apparent diffusion coefficient (ADC) enables standardization of DWI quantification and is the slope of the plot of the diffusion gradient strength (B value) vs. the resulting signal intensity. The more the movement of water is restricted in a tissue, the higher the DWI signal intensity and the lower the ADC. DWI provides novel information about the microscopic behavior of tissues, and it has been applied to multiple disease processes [1–3]. Because areas of reduced diffusion can be seen in any type of acute brain injury that alters extracellular water motion, DWI is invaluable for the early diagnosis of acute stroke. It is also helpful to clarify other diagnoses such as abscess, multiple sclerosis, epidermoid tumor, diffuse axonal injury, and encephalitis [3–6].

Although the role of DWI in the management of brain tumor patients remains to be fully defined [7–13], a recent report by Smith and coworkers [14] described a series of adult patients with newly diagnosed infiltrative glioma who underwent serial MR imaging, including DWI, before and after craniotomy for tumor resection. Approximately two-thirds of these patients demonstrated areas of reduced diffusion adjacent to the tumor resection cavity immediately following surgery. These areas demonstrated a stereotypical temporal pattern: initial resolution of DWI abnormalities, replacement with corresponding areas of focal and nodular contrast

enhancement, and finally, replacement with areas of encephalomalacia. Conventional MR imaging of these areas during the period of gadolinium enhancement demonstrated a lesion that was indistinguishable from recurrent tumor. Without the benefit of postoperative DWI to aid in the interpretation of this enhancing area, the MR scan could be misinterpreted as recurrent tumor.

Postoperative DWI abnormalities have not been reported in the pediatric population. In the present study, we describe the presence of DWI abnormalities after surgical resection of newly diagnosed intracranial mass lesions in children. We show that postoperative DWI abnormalities are common in the pediatric population and that they occur regardless of tumor grade or location-supratentorial or infratentorial. These data provide further clues to the underlying etiology of postoperative DWI abnormalities and underscore the importance of early postoperative DWI in pediatric patients undergoing brain surgery for a malignant lesion.

Patients and methods

Patient population and surgical techniques

We retrospectively studied a case series of 33 consecutive pediatric patients (≤18 years old) with newly diagnosed intracranial mass lesions who had preoperative and immediate postoperative MR imaging, including DWI. Medical records were reviewed for each case, and clinical and operative data were collected. Preoperative systolic blood pressure, the range of documented intraoperative systolic blood pressure, and the minimum intraoperative oxygen saturation were obtained from the anesthesia record. This review was conducted in accordance with the UCSF Committee on Human Research (H40232-23679-01).

For the majority of cases, lesion resection was performed using a Cavitron Ultrasonic Aspiration System (Valleylab, Boulder, CO). Hemostatic agents, including Surgicel (Ethicon Inc., Somerville, NJ) and Gelfoam (Upjohn Co., Kalamazoo, MI) were routinely used. The former was typically used to line the surgical cavity at the end of the procedure, while the latter was removed from the resection cavity prior to closure.

MR acquisition

All imaging was performed using a 1.5 Tesla Sigma Echospeed Scanner (GE Medical Systems, Milwaukee, WI). Immediate postoperative imaging was performed within 72 hours of surgery in most cases. All patients underwent two different MR imaging protocols depending on whether the imaging was performed at the preoperative, immediate postoperative, or follow-up period. Both protocols included the following sequences: (1) three plane localizer (24.9/1.6/1 [TR/TE/excitations]), (2) sagittal T1-weighted (500/14/1, 4 mm section thickness with a gap of 1 mm and field of view (FOV) 22×22 cm), (3) axial fluid-attenuated inversion recovery (FLAIR) imaging (10,000/33/2200/1 [TR/TE/inversion time/excitation], FOV 22×22 cm, matrix 256×192 pixels, 5 mm section thickness with no gap), and (4) DWI (single-shot echo-planar, 10,000/101, FOV 36×36 cm, acquisition matrix 128×128 pixels, 5 mm section thickness with no gap, diffusion gradient 0 and 1000 mm^2/s, acquired in three orthogonal directions). The preoperative protocol also included three-dimensional fast spin-echo T2-weighted imaging and contrast-enhanced spoiled gradient-echo recalled imaging, both of which were used for surgical navigation in the operating room. Intravenous contrast material for T1-weighted and DCS perfusion MR imaging consisted of gadopentetate dimeglumine (Omniscan; Amersham Laboratories) given at a dose of 0.1 mmole/kg of body weight. The immediate postoperative and follow-up MR imaging protocol also included pre-contrast axial T1-weighted imaging (600/9, FOV 22×22 cm, 5 mm section thickness with a gap of 1 mm).

Image analysis

Clinical interpretation of MR imaging was performed by various neuroradiologists. One neuroradiologist (SC) reviewed all of the studies, and there were no significant discrepancies in reporting of DWI abnormalities. A DWI abnormality was objectively defined as an area of reduced diffusion with ADC values less than 500×10^{-6} mm^2/sec around or remote from the resection cavity. A thin linear rim of reduced diffusion around the resection cavity without focal areas of nodularity was not considered abnormal. All of the images necessary for the measurement of each volume of interest were loaded onto a Unix workstation. On a slice-by-slice basis, the abnormality was manually traced. The areas defined by each tracing were then calculated and summated using software written in C and Matlab (Mathworks, Inc., Natick, MA) to provide a total volume in cm^3. For all patients, the volumes of FLAIR abnormality (defined as the entire lesion, including both enhancing and non-enhancing components), edema (defined as non-enhancing FLAIR abnormality), tumor enhancement and necrosis were measured based on preoperative imaging. Postoperative diffusion territory and subsequent area of encephalomalacia were qualitatively assessed on a workstation where serial imaging could be viewed on one screen. Follow-up imaging was also assessed for patients who underwent studies beyond the immediate postoperative scan.

Clinical, radiologic and operative parameters as predictors of postoperative reduced diffusion

Clinical, radiologic and operative data were collected for each patient and compared with the occurrence of postoperative reduced diffusion. Clinical parameters included: patient age, patient gender, and whether the lesion was infiltrative or noninfiltrative. Radiologic data included predominant anatomic location of the lesion (supratentorial vs. posterior fossa) and the occurrence and volume of: lesion edema, lesion enhancement, and lesion necrosis. Operative parameters included: surgeon,

total operating room time, surgical time, extent of resection (subtotal vs. gross total), estimated blood loss, whether intraoperative motor mapping was performed, intraoperative use of mannitol, net intraoperative fluid balance, and intraoperative use of brain cotton with hydrogen peroxide (0.05%).

Statistical analysis

Statistical analyses, including Pearson chi-square test, Fisher's exact test, and two-tailed *t*-test were performed using SPSS 11.5 (SSPS Inc, Chicago, IL). $P < 0.05$ was considered statistically significant. Data is presented as mean ± standard deviation.

Results

Patient demographics and tumor characteristics

Data were obtained from 33 cases (Table 1). The median age was 9.9 years (range 0.2–18 years). Lesions were located in the supratentorial compartment in 22 (66%) patients and in the infratentorial compartment in 11 (33%) patients. Gross total resection was achieved in 27 (82%) patients. The most common lesions grouped by histology were infiltrative glioma (24%), pilocytic astrocytoma (18%), germinoma (9%), ganglioglioma/gangliocytoma (9%), medulloblastoma (6%), meningioma (6%), and hamartoma (6%). Seven other lesions were each represented by a single case, including craniopharyngioma, desmoplastic neuroepithelial tumor (DNET), primitive neuroepithelial tumor (PNET), subependymal giant cell astrocytoma (SEGA), central neurocytoma, choroid plexus papilloma, and glioneuronal proliferation.

Preoperative imaging characteristics

Evidence of edema, defined as non-enhancing FLAIR abnormality, was evident in 31 (94%) cases on preoperative MR imaging. The median volume of edema was 7.2 cm^3 (range 0.1–193.1 cm^3). Gadolinium enhancement on pre-operative MR imaging was present in 26 (79%) cases, with a median volume of 5.5 cm^3 (range 0.9 –80.1 cm^3). Twelve (36%) cases showed evidence of necrosis on preoperative imaging, with a median volume of 2.1 cm^3 (range 0.2–30.5 cm^3). None of the lesions demonstrated reduced diffusion on preoperative imaging.

Table 1. Patient demographics and lesion characteristics

Parameter	Result
Patient age (years), median (range)	9.9 (0.2–18)
Gender, *n* (%)	
Male	20 (61)
Female	13 (39)
Lesion location, *n* (%)	
Supratentorial	22 (66)
Posterior fossa	11 (34)
Extent of resection, *n* (%)	
Subtotal	6 (18)
Gross total	27 (82)

Postoperative diffusion-weighted MR imaging

Postoperative DWI abnormalities were observed in 20 (61%) patients, with a median volume of 1.7 cm^3 (range: 0.3–12.0 cm^3). Areas of reduced diffusion were typically nodular or finger-like and contiguous with the resection cavity. Each of the areas demonstrated ADC values less than 500×10^{-6} mm^2/sec. Preoperative and postoperative MR images for a representative case that demonstrated postoperative reduced diffusion is shown in Figure 1.

Of 20 patients with a postoperative DWI abnormality, 18 had follow-up imaging available for analysis. The median length of follow-up imaging for these 18 patients was 13.1 months (range: 1.5–35.2 months). The course of each of these DWI abnormalities on follow-up imaging is shown in Figure 2. Postoperative MR imaging, including DWI, was obtained within four days of surgery for each patient, except for one who was imaged on postoperative day nine. The first follow-up MR imaging study for these 18 patients was performed at a median of 96.5 days (range: 8–769 days) following surgery. These follow-up studies demonstrated that the DWI abnormality had resolved in all patients (Figure 2). The area corresponding to the postoperative DWI abnormality was ultimately replaced with an area of encephalomalacia in all 18 patients. Imaging studies obtained at subsequent time points in 9 of the 18 cases showed contrast enhancement in the area corresponding to the DWI abnormality (Figure 2). This contrast enhancement resolved completely in 7 of the 9 cases by the time of the last imaging study and was replaced with an area of encephalomalacia. Notably, at the time of last imaging, two of the cases (numbers 2 and 6) showed partial replacement with encephalomalacia at the site of the previous reduced diffusion with the remainder of this site demonstrating persistent trace contrast enhancement. The first documentation of contrast enhancement at a site corresponding to previous reduced diffusion was in case 1 on postoperative day (POD) 8, and enhancement was documented as late as POD 214 in case 6 (Figure 2). Since these contrast enhancing areas were nodular or finger-like and contiguous with the resection cavity, they were indistinguishable from recurrent tumor.

Clinical, radiographic and operative parameters

There were no statistically significant associations between the development of postoperative reduced diffusion and patient age, patient gender, tumor location (supratentorial vs. infratentorial), infiltrative character, noninfiltrative character, volume of FLAIR abnormality, edema, lesion enhancement, and lesion necrosis on pre-operative imaging (Table 2). The simple presence or absence of each of these imaging features was not significantly associated with the presence of postoperative diffusion abnormality (data not shown). In addition, there was no obvious correlation between postoperative DWI abnormalities and lesion type (data not shown).

The occurrence of postoperative reduced diffusion was not predicted by the surgical parameters evaluated,

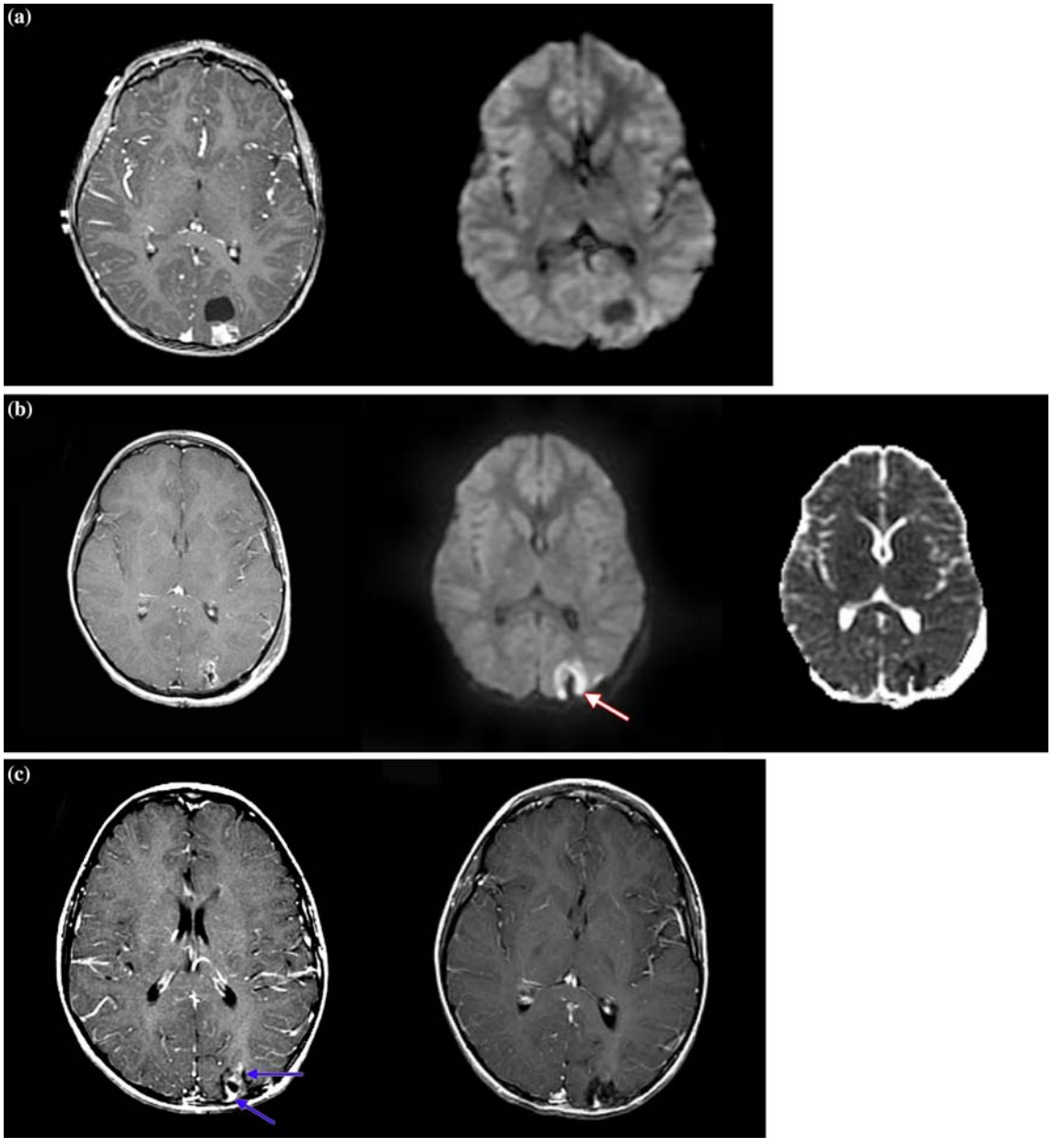

Figure 1. 7-year-old boy with left occipital ganglioglioma. (a) Axial post-contrast enhanced T1-weighted image (left) and diffusion-weighted trace image (right) demonstrate a right occipital enhancing mass with no evidence of reduced diffusion. (b) Immediate postoperative post-contrast enhanced T1-weighted image (left) shows gross total resection of the mass. Diffusion-weighted trace image (center) and ADC map (right) demonstrate a new area of reduced diffusion (arrow) in the surgical bed. (c) One-month follow-up examination shows emergence of new enhancement (arrows) corresponding to the area of reduced diffusion seen on the immediate postoperative scan (left). Ten-month follow-up imaging demonstrates almost complete resolution of the new enhancement seen on the one-month follow-up scan (right).

including surgeon, total operating room time, surgical time, extent of resection (gross total vs. subtotal), estimated blood loss, whether motor mapping was performed, intraoperative use of mannitol, net intra-operative fluid balance, and intraoperative use of brain cotton with hydrogen peroxide (Table 3). Brain cotton was used in only one case, a pilocytic astrocytoma, and no restricted diffusion was identified on postoperative imaging. There were no intra-operative complications or documented periods of significant intra-operative hypotension or hypoxia for any of the cases in this series. No clinical deficits could be attributed to any of the postoperative DWI abnormalities.

Discussion

MR imaging has revolutionized the diagnosis and treatment of intracranial mass lesions. For some benign lesions, surgical resection may be curative, but for other lesions follow-up imaging studies are critical to assess for evidence of lesion recurrence. For many neoplastic lesions, evidence of recurrence is based on the development of new contrast enhancement on follow-up imaging studies. Depending on the lesion, new enhancement may signify recurrence and result in significant changes in patient management, including further surgical procedures and addition of radiation therapies and chemotherapies. Thus, accurate interpretation of follow-up

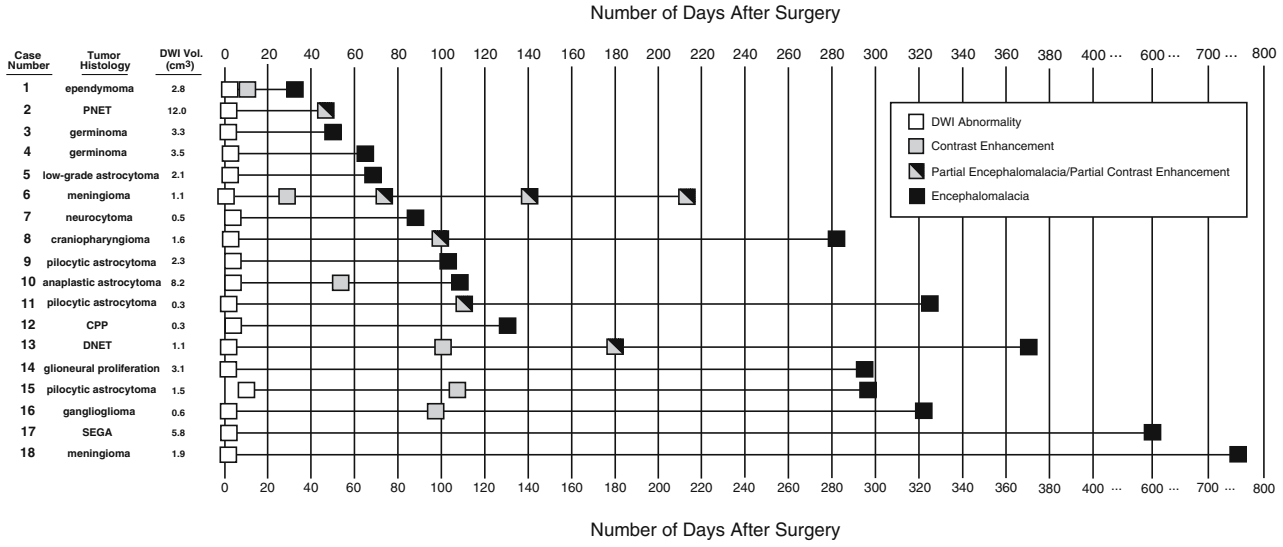

Figure 2. Summary of diffusion-weighed imaging (DWI) abnormalities in 18 pediatric intracranial lesions ordered based on the earliest documented partial or complete replacement of a previous DWI abnormality with a corresponding region of encephalomalacia. Each horizontal line represents a different patient, and the center of each square indicates an imaging time point relative to the day of surgery. White squares represent presence of DWI abnormality (reduced diffusion). Grey squares represent contrast enhancement of the specific area of DWI abnormality. Black squares indicate replacement of the area initially showing DWI abnormality with encephalomalaica. The lesion histology and volume of reduced diffusion in cubic centimeters are shown to the left for each patient. Squares split diagonally indicate the replacement of a previous DWI abnormality with a corresponding region that demonstrates partial contrast enhancement and partial encephalomalacia. PNET = primative neuroectodermal tumor, CPP = choroid plexus papilloma, DNET = desmoplastic neuroepithelial tumor, and SEGA = subependymal giant cell astrocytoma. Two of the total 20 patients who had post-operative DWI abnormality did not receive further follow-up imaging at our institution and are not included in this figure.

Table 2. Statistical associations between non-surgical parameters and occurrence of postoperative diffusion-weighted imaging abnormality

Parameter	*P*-value
Patient age	0.42
Patient gender	0.16
Location of lesion[a]	0.27
Infiltrative lesions	0.14
Preoperative volume of lesion edema[b]	0.73
Preoperative volume of lesion enhancement	0.94
Preoperative volume of lesion necrosis	0.51

[a] Supratentorial vs. posterior fossa location.
[b] Edema was defined as non-enhancing fluid attenuated inversion recovery (FLAIR) abnormality on MR imaging.

Table 3. Statistical associations between surgical parameters and occurrence of postoperative diffusion-weighted imaging abnormality

Parameter	*P*-value
Surgeon	0.60
Total operating room time	0.41
Surgical time[a]	0.13
Extent of resection[b]	0.74
Estimated blood loss	0.11
Motor mapping	0.98
Use of intraoperative mannitol	0.42
Net intraoperative fluid balance[c]	0.79
Use of brain cotton with hydrogen peroxide	0.39

[a] Time from skin incision to skin closure
[b] Classified as either subtotal or gross total resection
[c] Total fluids administered minus total fluid output

imaging is requisite to providing appropriate management for these patients.

We previously investigated the occurrence, time-course, and outcome of these abnormalities in a series of 44 prospectively imaged adult infiltrative glioma patients presenting for initial surgical management [14]. We demonstrated that reduced diffusion abnormalities adjacent to the surgical resection cavity were present in approximately two-thirds of cases on immediate post-operative imaging and that the vast majority of these abnormalities underwent a predictable progression from contrast enhancement to ultimate demonstration of encephalomalacia. Although DWI is currently not a part of the standard reference imaging for most intracranial mass lesions, our prior study suggests that immediate postoperative DWI provides important information for interpretation of subsequent follow up MR imaging in patients with infiltrative gliomas.

This study extends the findings from our earlier report [14] by identifying the appearance and time course of these abnormalities among pediatric patients. Unlike our prior report, this case series was not limited to supratentorial infiltrative gliomas, but included a range of pathologic types in either a supratentorial or infratentorial location. The present series included patients with benign lesions, including meningioma, hamartoma, and choroid plexus papilloma, as well as malignant lesions, including infiltrative glioma, germinoma, and medulloblastoma. Despite the more heterogeneous composition of this series, the incidence of postoperative diffusion abnormalities, 61%, is comparable to the 64% incidence in the previously reported series consisting only of adult infiltrative glioma patients [14].

Although new enhancement in a malignant or infiltrative lesion is more concerning than in a benign, non-infiltrative lesion, the incidence of postoperative DWI abnormalities in a heterogeneous series of lesions may provide clues to the etiologies of these imaging findings. None of the lesions in the present series and only three lesions (7%) in our previous series [14] demonstrated reduced diffusion on preoperative imaging. In addition, there was no apparent association between the occurrence of postoperative DWI abnormalities and whether the lesion was infiltrative or non-infiltrative, benign or malignant, or intra-axial or extra-axial. Furthermore, none of the pre-operative imaging features, including presence or volume of lesion-associated edema, enhancement, or necrosis were associated with the occurrence of postoperative DWI abnormalities. Together, these observations suggest that the development of postoperative DWI abnormalities is not specific to any particular lesion.

There were no statistically significant associations between the surgical parameters evaluated in this study and the occurrence of postoperative DWI abnormalities (Table 3). Notably, no significant associations were identified when the incidence of postoperative reduced diffusion was stratified based on operating surgeon. Gelfoam was routinely used for hemostasis but was not left in the surgical cavity at the completion of the surgical procedure. Although resection cavities were often lined with Surgicel, there were no resulting imaging findings that could be attributed to this material. The specific patterns of delayed contrast enhancement and encephalomalacia described in this report were always preceded by a corresponding area of restricted diffusion. The use of Surgicel in the resection cavity has not been reported to result in restricted diffusion, and, based on the inconsistent occurrence and typical pattern of post-operative restricted diffusion, the present study does not suggest such an association either.

Other potential explanations for the development of postoperative DWI abnormalities related to surgical technique include: (1) interruption of small *en passant* blood vessels that vascularize normal parenchyma, (2) interruption of small tumor vessels and subsequent devascularization of tumor tissue, and (3) microhemorrhagic injury from retraction or direct trauma to brain parenchyma. The present study is not designed to specifically assess the plausibility of these potential explanations, and it may be that one or more of these apply in any given patient with positive postoperative DWI.

The resolution of the time interval in which postoperative DWI abnormalities resolved and were ultimately replaced with an area of encephalomalacia was limited by the number and time intervals of follow-up imaging studies. By the time of the first follow-up MRI, all patients in this study with a postoperative DWI abnormality demonstrated complete resolution of the abnormality. Only 50% of the 18 patients with a postoperative DWI abnormality who had additional follow-up imaging demonstrated a corresponding area of contrast enhancement. This differs from our previous study in adult infiltrative glioma patients in which nearly all of the patients with a postoperative DWI abnormality subsequently demonstrated a corresponding area of contrast enhancement. This apparent discrepancy is likely related to the number and timing of follow-up imaging studies. Our prior study was performed prospectively with early and regular follow-up imaging, whereas the present study was performed retrospectively and lacked early and regular follow-up imaging for a subset of patients, particularly for those with benign lesions. The time interval in which contrast enhancement was demonstrated in the present study was between POD 8 and POD 214. We reported a similarly broad interval, POD 15 to POD 198, in our previous study [14]. Ultimately, all of the lesions in the present study demonstrated an area of encephalomalacia corresponding to the original area of DWI abnormality. Although two cases demonstrated partial contrast enhancement at the time of the last imaging study, this enhancement was trace. None of the lesions in this series demonstrated evidence of recurrence at the site of a previous DWI abnormality.

Conclusions

DWI abnormality on immediate postoperative MRI was not infrequent following surgical resection of newly diagnosed intracranial lesions among pediatric patients, occurring in 61% of cases studied. There were no apparent clinical deficits that could be attributed to any of the areas of postoperative reduced diffusion. These abnormalities resolved, were typically replaced with contrast enhancement on follow-up imaging and ultimately demonstrated encephalomalacia on long-term follow-up. Among the malignant and infiltrative lesions, imaging during the period of enhancement could be confused with recurrent tumor and interpreted as early treatment failure, prompting treatment with salvage and trial therapies. Our study strongly suggests that immediate postoperative MRI with DWI is essential for all intracranial neoplastic lesions for which there is any concern for possible recurrence. New enhancement following resection of an intracranial neoplastic lesion should be interpreted in the context of immediate postoperative DWI.

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