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Hyperintense Signal Abnormality in Subarachnoid Spaces and Basal Cisterns on MR Images of Children Anesthetized with Propofol: New Fluid-attenuated Inversion Recovery Finding

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BACKGROUND AND PURPOSE: **MR imaging is the method of choice for pediatric neuroimaging. Sedation is often needed to suppress patient motion and ensure diagnostic image quality, and propofol is rapidly becoming the preferred anesthetic. The purpose of this study was to document a new finding on fast fluid-attenuated inversion recovery (fast-FLAIR) MR images of children anesthetized with propofol that can be mistaken for subarachnoid space pathologic abnormality.**

METHODS: **A retrospective analysis was conducted of 55 MR images of the brain for children who ranged in age from 1 week to 12 years. Forty-two patients received chloral hydrate, and 13 received propofol anesthetic. Multiplanar MR images were studied to detect the presence or absence of hyperintense signal (artifact) in the subarachnoid spaces and basal cisterns. The T1 values and null times of chloral hydrate, propofol, and CSF were determined in vitro at room temperature by using an inversion recovery pulse sequence at 1.5 T.**

RESULTS: **The fast-FLAIR images of all 13 patients who received propofol had hyperintense signal abnormality. For 10 (77%) of 13 patients, this artifact was in the basal cisterns and subarachnoid spaces overlying the brain convexity. For three (23%) of 13 patients, this artifact was in the convexity region only. Two patients underwent follow-up MR imaging with a nonpropofol anesthetic agent, and the artifact resolved. None of the images of the children who received chloral hydrate had this artifact. The Tl value of chloral hydrate was 0.2 s, of propofol was 1.86 s, and of CSF was 2.32 s at room temperature.**

CONCLUSION: **The fast-FLAIR images of children anesthetized with propofol have artifactual hyperintense signal in the basal cisterns and subarachnoid spaces, and this artifact mimics disease of the subarachnoid space. The T1 value of propofol approaches that of CSF. Depending on the chosen null time, there may be incomplete nulling of signal coming from propofol. To account for this observation, other possible causes include increased CSF pulsation in children creating motion artifact, changes in arterial oxygen concentration intrinsic to propofol or related to the supplemental oxygen normally administered, or changes in CSF protein levels related to propofol binding to proteins for uptake into CSF.**

The fluid-attenuated inversion recovery (FLAIR) pulse sequence has become a routine part of MR examinations of the brain. In many institutions, the fast-FLAIR sequence has replaced the balanced or proton-density sequence. Improved detection of lesions within or adjacent to the CSF and improved lesion conspicuity in the brain parenchyma are just two reasons for the widespread use of fast-FLAIR imaging (1–11).

In pediatric neuroimaging, MR examinations of the brain, which include this fast-FLAIR sequence, play a critical role in the diagnosis of many neurologic diseases. Because MR imaging uses no ionizing radiation, is noninvasive, and has multiplanar capability, it is the diagnostic tool of choice. However, considering that examination times can last up to 1 hour, motion degradation of image quality becomes an issue in young patients, and sedation is often needed to ensure that high-quality images are

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obtained without motion artifact. Chloral hydrate remains the first line of anesthetic agent used, particularly for children younger than 2 years. However, chloral hydrate is often unpredictable and can be slow to take effect (12–16). Propofol (2,6-diisopropyl phenol) is formulated in a lipid emulsion, Diprivan, for IV use as an anesthetic agent (17–20). Propofol has desirable qualities as an anesthetic agent, including rapid onset of action, low incidence of side effects such as emesis and nausea, quick onset of recovery after sedation, and ability to be IV administered (12–16). Thus, propofol is quickly becoming one of the preferred anesthetics for pediatric MR imaging of the brain.

We report our observations of hyperintense signal abnormality in the basal cisterns and subarachnoid spaces in the convexity region that we have typically seen on the images of children who have received propofol as an anesthetic. We have not observed this finding in children anesthetized with chloral hydrate. It is important to recognize this signal as an effect of propofol because other disease processes, such as hemorrhage or infection within the subarachnoid spaces, are known to generate hyperintense signal on fast-FLAIR images (1–7).

Methods

A retrospective analysis of 55 MR images of the brain was conducted during an 8-month period for children who ranged in age from 1 week to 12 years (average age, 4 years). All studies were conducted using a 1.5-T whole-body MR imager equipped with high-performance gradients (GE Echospeed; GE, Milwaukee, WI) using a manufacturer-supplied quadrature head coil. Sagittal T1-weighted (300/14/1 [TR/TE/excitations]), axial fast spin-echo T2-weighted (3000/91/1), and axial fast-FLAIR (10002/172/1) images with a null time of 2.2 s were obtained for all patients. Coronal fast-FLAIR (10002/172/1) and coronal spoiled gradient-recalled acquisition in a steady state T1-weighted volumetric (17/5/1; flip angle, 45 degrees) sequences were obtained for 38 patients. After the administration of 0.1 mmol/kg gadopentetate dimeglumine (Magnevist; Berlex Laboratories, Wayne, NJ), axial T1-weighted (500/14/1) and coronal T1-weighted (600/20/1) images were also obtained. In general, all axial sequences used a section thickness of 5 mm, an intersection gap of 2.5 mm, a 256 × 192 matrix, the same imaging angle along the orbitomeatal line, and a 22- or 24-cm field of view.

Forty-two children ranging in age from 1 week to 12 years (mean age, 3.6 years) received chloral hydrate as a sedative agent at a dose of 50 mg/kg, with an additional 35 to 50 mg/kg if needed. Thirteen children ranging in age from 6 months to 12 years (mean age, 5.3 years) were anesthetized with propofol using an induction dose of 2 mg/kg, with supplemental doses of 1 mg/kg as needed. All patients were monitored for heart rate, heart rhythm, and oxygen saturation. All except two of these patients received supplemental oxygen via nasal cannula, which is part of the routine protocol. The two patients who did not receive supplemental oxygen had recorded oxygen pulse saturations of 100% via pulse oximetry. Two of the patients underwent subsequent MR imaging for which a non-propofol anesthetic was used. Patients with suspected or known CSF pathologic abnormality were excluded to obviate the need for lumbar puncture. Reasons for MR imaging included developmental delay (18 patients), increased head circumference (eight patients), question of seizure (seven patients), the need to rule out stroke (five patients), hearing difficulty (five patients), headache/migraine (four patients), decreased vision (two patients), growth hormone deficiency (two patients), to rule out neurofibromatosis (two patients), precocious puberty (one patient), and chromosome abnormality (one patient). Two neuroradiologists reviewed the MR images without any knowledge of which anesthetic agent was used and without knowledge of the temporal dates of the images. Each MR image was reviewed to detect the presence or absence of hyperintense signal abnormality (artifact) in the subarachnoid spaces and basal cisterns. Any discrepancies in interpretation were resolved by consensus, and the reviewers were blinded, as noted, before consensus review.

The T1 values of chloral hydrate, propofol, and CSF were determined in vitro at room temperature by using an inversion recovery pulse sequence at 1.5 T. Data were fitted using a T1 relaxation curve in which the signal intensity was $(S) = S_0 - 2e^{(-x)}$, where x = TI (inversion time)/T1. Null times and T1 values were calculated from the curve.

Fast-FLAIR signal abnormality in children who received propofol anesthetic

	Signal in Subarachnoid Spaces in Convexity Region	Basal Cistern Signal Abnormality
Chloral hydrate patients	0/42	0/42
Propofol patients	13/13	10/13

Results

The fast-FLAIR images of all the children who received propofol anesthetic had hyperintense signal abnormality in the subarachnoid spaces in the convexity region and the basal cisterns (Table). In those areas, no signal abnormality was detected by any of the other routine MR pulse sequences, and there was no abnormal enhancement with the administration of contrast medium. The images of 10 (77%) of 13 patients had this artifactual hyperintense signal abnormality in both the basal cisterns and subarachnoid spaces overlying the brain convexity (Fig 1A and B), and the images of three (23%) of 13 patients had this artifact detected only in the subarachnoid spaces in the convexity region.

Two of these patients underwent follow-up MR imaging in which a non-propofol anesthetic was used for sedation, and the artifact was not observed (Fig 1C and D). None of the 42 patients who received chloral hydrate exhibited this finding of increased signal in the basal cisterns or subarachnoid spaces.

Using an inversion recovery sequence at 1.5 T, the T1 value of chloral hydrate at room temperature in vitro was determined to be 0.2 s. The null time was 0.14 s (Fig 2). The T1 value of propofol was 1.86 s, and the null time was 1.3 s (Fig 2). The T1 value of CSF was 2.32 s, and the null time was 1.6 s (Fig 2).

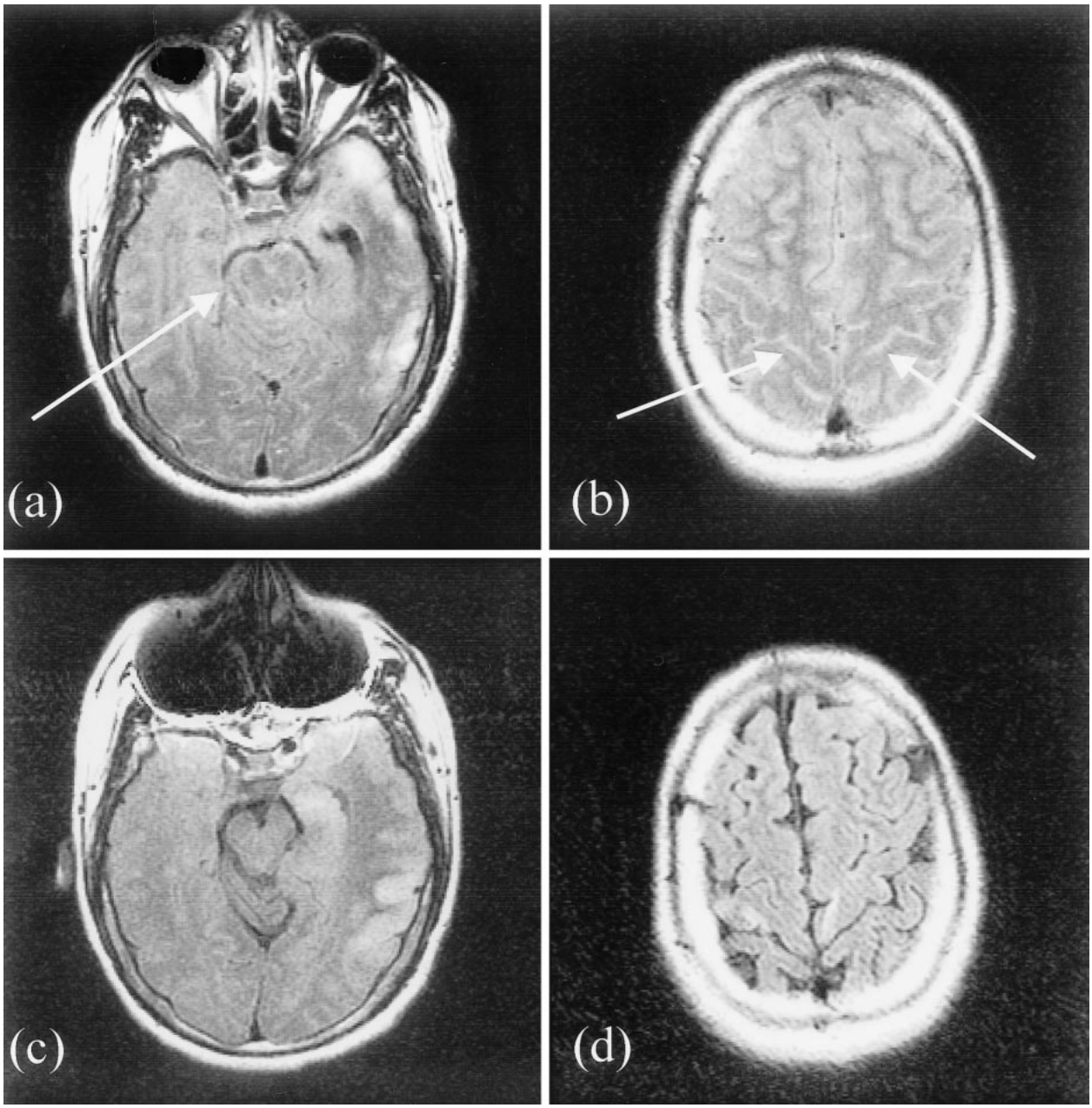

FIG 1. MR images of a child with left middle cerebral artery ischemia and sickle cell disease.

A, Transaxial FLAIR (10002/172/1) image obtained with the child under propofol anesthesia has hyperintense signal abnormality in the basal cisterns.

B, Similar abnormal hyperintense signal is seen in the subarachnoid spaces bilaterally in the convexity region of this same patient.

C, Follow-up transaxial FLAIR (10002/172/1) image shows resolution of the signal abnormality in the basal cisterns. Chloral hydrate was administered, and patient's retainer was not removed, creating the paranasal sinus artifact that was not present on the previous study.

D, Resolution of the abnormal signal intensity in the convexity subarachnoid spaces is also noted on the follow-up image obtained with the child under chloral hydrate sedation.

Discussion

Among the methods of pediatric neuroimaging, MR imaging is the diagnostic tool of choice because it is noninvasive, uses no ionizing radiation, and produces high-contrast, high-quality multiplanar images. However, motion degradation of image quality is a potential limitation, and sedation is needed to suppress motion and to ensure diagnostic image quality. Chloral hydrate is the usual first-line anesthetic, but it induces sedation slowly and often fails to provide adequate sedation to suppress motion (12–16). Propofol is a highly lipophilic IV administered anesthetic agent that is becoming more frequently used to suppress patient motion for MR imaging of the brain. It induces anesthesia quickly, has antiemetic qualities, and is rapidly cleared from the system, which makes propofol safe and effective to use (17–20).

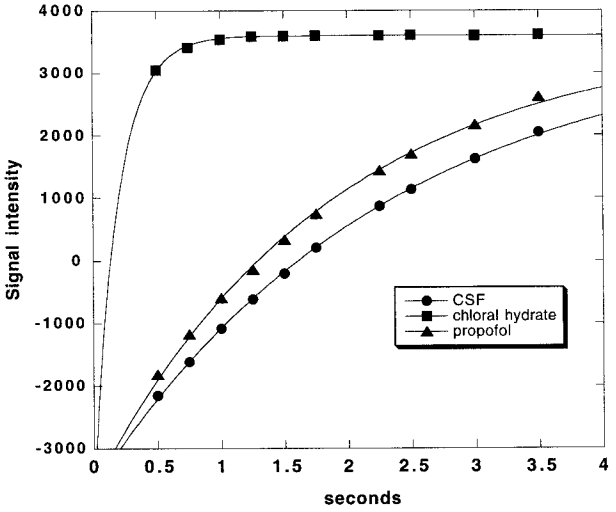

FIG 2. T1 value of chloral hydrate, propofol, and CSF determined in vitro at room temperature using an inversion recovery pulse sequence at 1.5 T. T1 value of CSF is 2.32 s, of propofol is 1.86 s, and of chloral hydrate is 0.2 s. The null time of CSF is 1.6 s, of propofol is 1.3 s, and of chloral hydrate is 0.14 s.

Fast-FLAIR imaging is one of the most heavily relied on pulse sequences with which to diagnose pathologic abnormality on MR images of the brain. It has replaced proton-density acquisition at many institutions. With fast-FLAIR imaging, signal from CSF is nulled by the use of an inversion recovery pulse sequence and then a heavily T2-weighted sequence. It is this loss of signal from CSF on FLAIR images that renders any abnormality markedly hyperintense in contrast to the relatively hypointense white matter and nulled CSF. This allows for easier detection of lesions within or adjacent to CSF-containing spaces, creating greater lesion conspicuity in the brain parenchyma. When lesions occur within the CSF spaces, the long relaxation time of CSF is shortened, which translates into inadequate nulling of CSF. This explains the observed hyperintensity within the CSF spaces in cases of subarachnoid hemorrhage (3). Elevations in CSF protein or cellularity likely account for the observed hyperintense signal within the CSF-containing subarachnoid spaces, which has been reported in carcinomatous or infectious meningitis (3, 21), because these elevations in protein and/or cellularity likely reduce the T1 relaxation time of CSF. For all these reasons, fast-FLAIR imaging has quickly become one of the cornerstone pulse sequences in any brain MR imaging protocol. In pediatric neuroimaging, it is especially useful in the assessment of white matter diseases (leukodystrophies, demyelinating diseases), metabolic disorders, congenital malformations, and developmental disorders (mesial temporal sclerosis).

Despite the usefulness of the fast-FLAIR sequence, there are a number of artifacts that have been reported that may obscure pathologic findings or mimic pathologic abnormality, leading to misdiagnosis. Susceptibility artifacts from the paranasal sinuses, metallic artifacts, CSF pulsation artifacts, and truncation artifacts may affect image interpretation (2, 11, 22–24).

In this study, the fast-FLAIR pulse images of all the children who received propofol anesthetic had some sort of hyperintense signal abnormality, either in the basal cisterns, the subarachnoid spaces near the brain convexity, or both areas. Interestingly, the follow-up MR images of two of the children who then received non-propofol anesthetic had resolution of the signal abnormality. The cause for this is unknown, but there are several possible explanations.

One explanation for this observed finding on fast-FLAIR images might relate to the intrinsic T1 value of the anesthetic agent. The T1 value of chloral hydrate is an order of magnitude lower than that of propofol, such that any signal from the chloral hydrate itself would be completely relaxed at any null time chosen for fast-FLAIR imaging. However, the T1 value of propofol approaches that of CSF. Therefore, depending on the inversion time chosen, there may be incomplete nulling of any signal coming from the propofol, which, in theory, could be part of the explanation for this finding encountered in children anesthetized with propofol. However, this finding has not been observed in adults, which one might expect if the T1 value of the anesthetic were the primary factor for this observation.

Propofol is highly lipophilic and rapidly crosses the blood-brain barrier where it redistributes quickly within the CNS. It may be that propofol induces a transient change in the protein level within the CSF. By an unknown mechanism, propofol has been shown to facilitate optimal disruption of the blood-brain barrier by hyperosmotic solutions in normal and diseased rat brains without causing neurotoxicity or neuropathologic abnormality (17). Propofol may induce leakage from intravascular spaces by changing membrane permeability, which would change the distribution of proteins in the CSF within the subarachnoid spaces. This change in protein level within the CSF could be detected as hyperintense signal on a fast-FLAIR pulse sequence.

Because elevations in protein concentration within the CSF could be detected, in theory, as areas of signal abnormality on fast-FLAIR images, differences in CSF protein concentration in children may be another mechanism by which this observed FLAIR finding may be explained. Normal CSF protein concentrations in adults range from 15 to 45 mg/dL. In children, there is a far wider range of normal values, from 20 to 120 mg/dL. Pathologic conditions in which the protein CSF concentration is elevated have been detected as areas of hyperintense signal abnormality on FLAIR images. Thresholds for detection of this protein elevation have been determined experimentally, with the FLAIR images routinely having signal abnormality in the subarachnoid spaces and protein concentra-

tions ranging from 110 to 125 mg/dL for effective TE between 150 and 200 (21). Thus, for an effective TE of 172, it is conceivable that younger patients with CSF protein concentrations in the upper limits of normal (range, 110–120 mg/dL) may have hyperintense signal abnormality on the fast-FLAIR images.

The partial pressures of oxygen and carbon dioxide are physiological parameters that are influenced by anesthetic agents. These have a modulatory effect on vascular tone (17). Propofol may induce changes in vascular tone on this basis, which could lead to hyperdynamic CSF pulsations during the cardiac cycle. Thus, alterations in vascular tone encountered during the cardiac cycle could create another kind of CSF pulsation artifact, and this may be another possible explanation for this finding in children.

Animal studies have shown that the administration of 100% oxygen before breath holding increases the T2* signal intensity on echo-planar images (25). In a similar study, signal changes on gradient-echo images were closely related to changes in arterial oxygen saturation during hypoxia when 10% FiO_2 was administered (26). Because patients receiving propofol are monitored with pulse oximetry and usually receive supplemental oxygen, the oxygen administered during the same time as the anesthetic agent could account for the hyperintense signal abnormality observed in the subarachnoid spaces and basal cisterns. At the 2000 Annual Meeting of the American Society of Neuroradiology, one poster exhibit presented data showing that the fast-FLAIR images of 12 of 14 patients who underwent imaging while under general anesthesia had abnormal signal intensity (27). At the 1999 Annual Meeting of the Radiological Society of North America, another group presented an exhibit showing changes in T1 relaxivity and T1 shortening of the CSF of patients who had undergone imaging while under general anesthesia (28). Although supplemental oxygen may create CSF T1 shortening, allowing for this observed artifact on fast-FLAIR imaging, this may be only a partial explanation. We observed this artifact in two cases in which patients were monitored with pulse oximetry but did not receive supplemental oxygen because their oxygen saturation was 100%. In the other 11 cases, all children received supplemental oxygen as part of the routine protocol.

In this study, the artifactual signal intensity was never seen within the ventricles. If the artifact is a consequence of the T1 properties of the anesthetic agent and/or an interaction between the anesthetic agent and the supplemental oxygen, the artifact could be dependent on the concentration of the anesthetic agent. Because propofol would be more highly concentrated within the blood vessels near the subarachnoid spaces of the basal cisterns and the convexity region, its ability to affect the T1 relaxation value of CSF, which is a dipolar property occurring over very short distances, would be expected to be greater in these CSF-containing spaces as opposed to the ventricles where this effect would be more negligible.

Conclusion

Although the exact mechanism for this FLAIR artifact is unclear, hyperintense signal abnormality is frequently observed in the convexity subarachnoid spaces and basal cisterns in children anesthetized with propofol. Careful examination of all the other pulse sequences, particularly the contrast-enhanced sequences, is necessary to ensure that the subarachnoid compartment is unremarkable because this hyperintense signal abnormality could be easily confused for subarachnoid space pathologic abnormality.

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