Variable Appearances of Subacute Intracranial Hematomas on High-Field Spin-Echo MR


AJNR Am J Neuroradiol 1987, 8 (6) 1019-1026
http://www.ajnr.org/content/8/6/1019

This information is current as of July 17, 2023.
Variable Appearances of Subacute Intracranial Hematomas on High-Field Spin-Echo MR

Subacute intracranial hematomas have variable appearances on high-field MR images. They are hyperintense on T1-weighted images owing to methemoglobin, but have variable intensities on T2-weighted images. Observation of the different high-field spin-echo MR intensity patterns of five subacute hematomas suggests that further subcategorization into different methemoglobin states may be possible. In particular, undiluted intracellular methemoglobin is hyperintense on T1-weighted images and markedly hypointense on T2-weighted images, undiluted free methemoglobin should be hyperintense on T1-weighted images and isointense or slightly hypointense on T2-weighted images, and dilute free methemoglobin is hypointense on both T1- and T2-weighted images. However, it appears that certain regions of subacute hematomas may be difficult to differentiate, by intensity patterns alone, from melanotic melanomas or fat.

We believe that, despite some limitations, MR is useful in dividing subacute intracranial hematomas into their respective methemoglobin states, and also that further subcategorization is possible.

Early experience with MR imaging of intracranial hematomas at 1.5 T has revealed three characteristic signal-intensity patterns [1]:

1. Acute hematomas (<1 week old) are isointense to gray matter on T1-weighted images and markedly hypointense on T2-weighted images. This is ascribed to a selective T2 proton relaxation enhancement (relaxation time shortening) by intracellular deoxyhemoglobin.

2. Subacute hematomas (about 1 week to <1 month old) are initially hyperintense at the hematoma periphery on T1-weighted images. The hyperintensity on T1-weighted images proceeds to fill the whole hematoma and eventually (by 2 weeks) becomes observable on T2-weighted images as well. This is attributed to the formation of intracellular methemoglobin, which is paramagnetic, and to subsequent cell lysis and watery dilution by resorption of the resultant free methemoglobin.

3. In subacute and chronic hematomas, the adjacent brain parenchyma is slightly hypointense on T1-weighted images and markedly hypointense on T2-weighted images. This is because hemosiderin deposits produce a selective T2 relaxation enhancement.

We report our observations on the previously unappreciated variability of the high-field MR intensities of subacute hematomas and discuss the underlying relaxation mechanisms and relevant differential diagnoses.

Subjects and Methods

Over a period of 1 year, we observed five patients with subacute intracranial hematomas from various causes. All hematomas were diagnosed and staged by clinical and CT findings. Two were confirmed surgically and pathologically. MR imaging was performed on a GE 1.5-T superconducting unit. Spin-echo pulse sequences were obtained with 5-mm-thick slices, two excitations, and 256 x 128 acquisition matrices. T1-weighted images were obtained with
TABLE 1: MR Intensities of Subacute Hematomas

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Type of Subacute Hematoma</th>
<th>Age of Hematoma</th>
<th>CT Density</th>
<th>Image Intensity Relative to Gray Matter</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>T1-Weighted</td>
</tr>
<tr>
<td>1</td>
<td>Spontaneous (normal angiography)</td>
<td>5 days</td>
<td>Increased</td>
<td>Increased</td>
</tr>
<tr>
<td>2</td>
<td>Small AVM (surgically confirmed)</td>
<td>12 days</td>
<td>Unchanged</td>
<td>Increased</td>
</tr>
<tr>
<td>3</td>
<td>Traumatic</td>
<td>6 days</td>
<td>Increased</td>
<td>Increased</td>
</tr>
<tr>
<td>4</td>
<td>Hypertensive</td>
<td>6 days</td>
<td>Decreased</td>
<td>Increased</td>
</tr>
<tr>
<td>5</td>
<td>Traumatic, subdural (surgically confirmed)</td>
<td>9 days</td>
<td>Increased</td>
<td>Increased</td>
</tr>
</tbody>
</table>

Note.—AVM = arteriovenous malformation.

Results

All subacute hematomas had regions of hyperintensity on T1-weighted images (Table 1 and Figs. 1–5). On proton-density-weighted images these regions were either isointense...
Fig. 2.—Case 2: concentric 12-day-old and 2-day-old hematomas caused by small vascular malformation (surgically confirmed).

A, Enhanced coronal CT scan shows acute hyperdense right temporal hematoma surrounded by isodense subacute hematoma. Subtle thin ring of enhancement surrounds hematoma (arrow) and hypodensity of edema is seen superomedially (arrowhead).

B, T1-weighted image, TR = 800 msec, TE = 20 msec. Central acute hematoma (white arrow) consisting of intracellular deoxyhemoglobin is slightly hypointense to gray matter. Surrounding subacute hematoma is markedly hyperintense (black arrow).

C, Proton-density-weighted image, TR = 1500 msec, TE = 20 msec. Central acute hematoma (large white arrowhead) has remained mildly hypointense to cortex. Surrounding subacute hematoma now shows mildly hyperintense inner region (curved arrow) representing dilute intracellular methemoglobin and markedly hyperintense outer region (black arrowhead) representing free methemoglobin. Thin peripheral ring of parenchymal hypointensity (straight arrow) corresponds to hemosiderin deposition. Surrounding edema (small white arrowhead) has become hyperintense.

D, T2-weighted image, TR = 1500 msec, TE = 40 msec. Acute hematoma has become more hypointense. Inner region of subacute hematoma has become isointense to gray matter, while outer region remains markedly hyperintense. Hemosiderin ring appears more hypointense and wider. Surrounding edema remains hyperintense. Acute central hematoma is composed of intracellular deoxyhemoglobin. Outer region of subacute hematoma corresponds to free dilute methemoglobin. Inner region of subacute hematoma corresponds to dilute intracellular methemoglobin.

Discussion

The mechanism for the selective T2 relaxation enhancement of intracellular deoxyhemoglobin, intracellular methemoglobin, and of hemosiderin deposits is the dephasing of water molecules diffusing across field gradients owing to the heterogeneity in the distribution (intracellular or intralysosomal) of the paramagnetic substance (Fe²⁺ with four unpaired electrons for deoxyhemoglobin and Fe³⁺ with five unpaired electrons for methemoglobin, ferritin, and hemosiderin) [2]. In the absence of unpaired electrons, the protons of water molecules relax (realign with the magnetic field) via fluctuations in their local magnetic field caused by the motion of adjacent protons. The presence of unpaired electrons (for example, five unpaired electrons per methemoglobin molecule) creates fluctuations 1000 times larger owing to the electrons' larger magnetic moment. These larger fluctuations enhance the relaxation of protons. This is called the proton-electron dipolar-dipolar proton relaxation enhancement. The hyperintensity of T1-weighted images of subacute and chronic hematomas was ascribed to the proton-electron dipolar-dipolar proton relaxation enhancement of methemoglobin. This interaction drops off extremely rapidly with distance; the water proton must approach within 3Å of the unpaired electron for the interaction to occur. Unlike methemoglobin, the unpaired electrons of deoxyhemoglobin, ferritin, and hemosiderin are inaccessible to water protons for the dipolar-dipolar interaction. Intracellular methemoglobin, which has both relaxation mechanisms, causes significant T1- and T2-relaxation-time shortening. Cell lysis and the dilution of the liberated methemoglobin by resorption leads to a decrease in the T1 and T2 relaxation enhancement of the proton-electron dipolar-dipolar mechanism, and the cessation of the selective T2 relaxation enhancement caused by the intracellular (heterogeneously distributed) methemoglobin.

Heterogeneity in the distribution of any paramagnetic substance (for example, intracellular deoxyhemoglobin or methemoglobin) results in heterogeneity of magnetic susceptibility, which produces field gradients when an external magnetic field is applied. On spin-echo MR, diffusion of water protons
The study that the proton-electron magnetic susceptibility. The lengthening of the interecho interval, because the T2 relaxation enhancement is not caused by different degrees of cell lysis, resulting in a variable amount of selective T2 proton relaxation enhancement by the intracellular methemoglobin [2]. Cell lysis is more effective in decreasing the selective T2 relaxation enhancement of intracellular methemoglobin than is simple dilution because the methemoglobin released from the lysed cells increases the extracellular magnetic susceptibility. Thus, cell lysis decreases the differences in the magnetic susceptibility between the inside and the outside of the remaining intact RBCs containing methemoglobin. This decrease in the heterogeneity of magnetic susceptibility causes a marked decrease in the selective T2 relaxation enhancement, because the T2 relaxation enhancement is proportional to the square of the variation (heterogeneity) of the magnetic susceptibility [1, 2]. However, a change in the concentration of RBCs containing methemoglobin by dilution with a non-paramagnetic fluid such as plasma causes mild changes in the heterogeneity of magnetic susceptibility until the hematocrit exceeds 90% or is under 10% [1]. Therefore, dilution without lysis of intracellular methemoglobin does not greatly influence the selective T2 relaxation enhancement until it is under a hematocrit of 10%.

Recently, we studied the in vitro MR relaxation times of blood and their variations with field strength, oxidation state, and cell integrity [2]. That study confirmed the hypothesis of selective T2 relaxation enhancement for intracellular deoxyhemoglobin and methemoglobin and of proton-electron dipolar proton relaxation enhancement for methemoglobin. The study also confirmed that the selective T2 relaxation enhancement of intracellular deoxyhemoglobin and of intracellular methemoglobin increases as the square of the magnetic field strength and as the square of the heterogeneity of magnetic susceptibility. The selective T2 relaxation enhancement also increased with prolongation of the interecho interval and was not present after cell lysis. The study demonstrated that the proton-electron dipolar dipolar relaxation enhancement of methemoglobin was unaffected by field strength, the length of the interecho interval, or cell integrity.

The variable intensities of subacute hematomas on proton-density-weighted images are from differences in dilution. The variable intensities on the T2-weighted images are from both differences in dilution and variations in the selective T2 relaxation enhancement. The variability in the T2 relaxation enhancement is primarily caused by different degrees of cell lysis, resulting in a variable amount of selective T2 proton relaxation enhancement by the intracellular methemoglobin [2]. Cell lysis is more effective in decreasing the selective T2 relaxation enhancement of intracellular methemoglobin than is simple dilution because the methemoglobin released from the lysed cells increases the extracellular magnetic susceptibility. Thus, cell lysis decreases the differences in the magnetic susceptibility between the inside and the outside of the remaining intact RBCs containing methemoglobin. This decrease in the heterogeneity of magnetic susceptibility causes a marked decrease in the selective T2 relaxation enhancement, because the T2 relaxation enhancement is proportional to the square of the variation (heterogeneity) of the magnetic susceptibility [1, 2]. However, a change in the concentration of RBCs containing methemoglobin by dilution with a non-paramagnetic fluid such as plasma causes mild changes in the heterogeneity of magnetic susceptibility until the hematocrit exceeds 90% or is under 10% [1]. Therefore, dilution without lysis of intracellular methemoglobin does not greatly influence the selective T2 relaxation enhancement until it is under a hematocrit of 10%.
Intracellular methemoglobin has a powerful selective T2 relaxation enhancement in addition to its proton-electron dipolar-dipolar relaxation enhancement [2]. The proton density of intracellular methemoglobin or deoxyhemoglobin (hematocrit of 90% after plasma resorption) is similar to that of gray matter [1]. Therefore, purely intracellular methemoglobin is hyperintense on T1-weighted images, isointense or proton-density-weighted images, and quite hypointense on T2-weighted images (Fig. 1).

Panhyperintensity (on all spin-echo sequences) (Fig. 2) is a frequent finding in subacute and chronic hematomas. It is from the proton-electron dipolar-dipolar proton relaxation enhancement of dilute free methemoglobin. This relaxation causes a mild shortening of the T1 and T2 relaxation times, and the diluteness of the solution is responsible for a high proton density. The TRs used in spin-echo MR imaging are much longer than the TEs and usually are not much longer than the T1 relaxation times. The TEs are usually shorter than the T2 relaxation times. Therefore, the T1 shortening and high proton-density effects of dilute methemoglobin will dominate the spin-echo intensity pattern, resulting in panhyperintensity. Free, unbound Fe²⁺ ions also cause proton-electron dipolar-dipolar proton relaxation enhancement [2] and may also play a role in the panhyperintensity of dilute chronic hematomas.

Hyperintensity on T1-weighted images and isointensity on both proton-density- and T2-weighted images indicate a short T1 relaxation time and normal proton density and T2 relaxation time; that is, a proton-electron dipolar-dipolar proton relaxation enhancement without selective T2 proton relaxation enhancement or dilution. Free undiluted methemoglobin should have these properties.

If the hematocrit of intracellular methemoglobin is reduced by dilution without cell lysis (dilute intracellular methemoglobin) then the proton density will be elevated. The decrease in the proton-electron dipolar-dipolar relaxation enhancement is "compensated" by the increase in proton density until there is a great degree of dilution. The decrease in the selective T2 relaxation enhancement will only be evident if the hematocrit is drastically reduced (<10%) [1]. Therefore, the elevation of the proton density will be the most noticeable effect; that is, the T1-weighted image will remain hyperintense, the proton-density and T2-weighted images will become more intense (depending on the degree of dilution), but the T2-weighted image will still be significantly hypointense to the proton-density-weighted image (Fig. 2).

Intermediate states may exist. The intensity patterns of these states will vary between the patterns of the individual components. A combination of intracellular methemoglobin and deoxyhemoglobin will be variably hypointense on T1-weighted images. The proton-density- and T2-weighted images will not be affected because the proton densities and the T2 relaxation times are similar for intracellular methemoglobin and intracellular deoxyhemoglobin. Similarly, different
degrees of lysis of intracellular methemoglobin will result in variable T2-weighted image hypointensities because of the change in selective T2 proton relaxation enhancement caused by the variable decreases in the heterogeneity of the magnetic susceptibility. The T1-weighted and proton-density-weighted images will be relatively unaffected because both intracellular and undiluted free methemoglobin have similar proton-electron dipolar-dipolar proton relaxation enhancement and proton density. Various degrees of free methemoglobin dilution will cause the T1-weighted image to vary from hypointensity to isointensity, the proton-density-weighted image to vary from isointensity to hyperintensity and then back to isointensity, and the T2-weighted image to vary from isointensity to hyperintensity. As the free methemoglobin is diluted it loses its proton-electron dipolar-dipolar enhancement and its proton density increases to that of CSF. CSF has such long T1 and T2 relaxation times that on conventional spin-echo MR images with TRs less than 3000 msec it will be hypointense on T1-weighted images, mildly hypointense or isointense on proton-density-weighted images, and hyperintense on T2-weighted images. Of course other combinations may occur as well; for example, undiluted free deoxyhemoglobin and free methemoglobin. In this case there will be variable hyperintensity on T1-weighted images with isointensity on proton-density- and T2-weighted images.

Figure 6 illustrates the four possible methemoglobin states and Table 2 presents the functional relationships between the methemoglobin states and the resultant relaxation enhancements and proton density. In Table 2, the (Hct)(100 – Hct) factor is the heterogeneity factor [1]. The $1/T2^*$ on gradient-echo MR is proportional to the field gradient across the cell membrane and the $1/T2$ of spin-echo MR is proportional to the square of the field gradient. The gradient across the cell membrane is proportional to the difference in magnetic susceptibility across the cell membrane and to the field strength. The fractions in the equations result from the fact that methemoglobin has five and deoxyhemoglobin has four unpaired electrons per iron atom, and that the magnetic susceptibility is proportional to the number of unpaired electrons. Table 3 presents the patterns of the relative relaxation times and proton densities occurring in the various types of regions associated with subacute intracranial hematomas. Of course, mixtures will have patterns intermediate to their individual components.

A report by Di Chiro et al. [3] demonstrated the evolution of intracranial hemorrhage in a monkey on high-resolution MR imaging at 0.5 T. Their images (interpreted in light of the importance of susceptibility heterogeneity) at days 2–3 were characteristic of intracellular deoxyhemoglobin; days 4–8, of intracellular methemoglobin; and days 5–15, of dilute free...
malignant melanoma, as well as of hemosiderin at 2 months.

Melanin is a free-radical trap and can chelate paramagnetic metal ions. The unpaired electrons of the free radicals and of the chelated metal ions and probably of associated methemoglobin are the source of melanin's paramagnetism [4, 5]. The major paramagnetic effect of significance to spin-echo MR imaging is the proton-electron dipolar-dipolar interaction [6]. In deeply pigmented melanomas without gross pathologic evidence of hemorrhage this interaction can cause sufficient proton relaxation enhancement to mimic methemoglobin's hyperintensity on T1-weighted images (Fig. 7). However, melanotic melanomas are not as hyperintense on T2-weighted images as free dilute methemoglobin is nor as hypointense as undiluted intracellular methemoglobin. Thus, melanotic melanomas may be difficult to distinguish from certain regions of subacute hematomas. Fat is hyperintense on T1-weighted images, isointense on proton-density images, and hypointense on T2-weighted images at high field strengths (1.5 T) (Fig. 1). It may also be difficult to differentiate it from regions of subacute hematomas or from melanotic melanomas. However, associated MR and clinical findings usually allow the differentiation of melanotic melanoma, fat, and subacute hematomas.

Rapid imaging by gradient echoes rather than by spin echoes has recently been introduced. Its sensitivity to T2* allows the effects of susceptibility heterogeneity to be detected at much lower field strengths [7, 8], at the cost of lower signal to noise and increased sensitivity to field gradients because of the magnet and the macroscopic susceptibility heterogeneity and chemical shifts. Although subacute hematomas have not yet been carefully studied by gradient-echo techniques, they should have characteristics similar to those observed on high-field spin-echo MR. One additional effect seen on gradient-echo techniques can be confusing. It is the peripheral hypointensity caused by the border between macroscopic regions of different susceptibilities, for example, dense calcium–soft tissue; air–soft tissue; fat–water; and deoxyhemoglobin, methemoglobin, or hemosiderin and soft tissue. These must be differentiated from marginal hemosiderin deposits around hemorrhagic lesions. Marginal hemosiderin deposits have both T2* shortening and T2 shortening on spin-echo images because of both macroscopic and microscopic susceptibility heterogeneity.

Our current clinical MR observations and previous in vitro models indicate that further subcategorization of subacute hematomas is possible on the basis of T1-, proton-density-, and T2-weighted images. However, melanotic melanomas and fat may be difficult to differentiate, by intensity patterns alone, from certain regions of subacute hematomas.

REFERENCES

# TABLE 3: Relative Relaxation Times and Proton Densities in Regions Associated with Subacute Intracranial Hematomas

<table>
<thead>
<tr>
<th>Region</th>
<th>Relaxation Time or Proton Density</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dilute intracellular methemoglobin*a</td>
<td>Decreased</td>
</tr>
<tr>
<td>Dilute (free) lysate (free) methemoglobin*a</td>
<td>Increased</td>
</tr>
<tr>
<td>Undiluted intracellular methemoglobin*a</td>
<td>Decreased</td>
</tr>
<tr>
<td>Undiluted (free) lysate (free) methemoglobin*b</td>
<td>Increased</td>
</tr>
<tr>
<td>Dilute intracellular deoxyhemoglobin</td>
<td>Decreased</td>
</tr>
<tr>
<td>Dilute intracellular and lysate (free) oxyhemoglobin; lysate (free) deoxyhemoglobin; or any dilute protein solution, edema, tumor, or CSF</td>
<td>Unchanged or increased</td>
</tr>
<tr>
<td>Intracellular deoxyhemoglobin or hemosiderin</td>
<td>Unchanged</td>
</tr>
<tr>
<td>Gray matter (standard) or undiluted (free) lysate (free) deoxyhemoglobin or oxyhemoglobin, or undiluted intracellular oxyhemoglobin</td>
<td>Unchanged or increased</td>
</tr>
<tr>
<td>Hemosiderin deposits ± calcifications</td>
<td>Unchanged</td>
</tr>
<tr>
<td>Very dense calcifications, dura, or flow void</td>
<td>Decreased</td>
</tr>
<tr>
<td></td>
<td>Decreased</td>
</tr>
</tbody>
</table>

*Can be mimicked by fat or melanin.

Note.—Undiluted = concentration equivalent to hematocrit of 90%.

---

**Fig. 7.—Nonhemorrhagic (pathologically proved) melanotic melanoma metastasis.**

A, Unenhanced CT scan shows high-absorption left frontal mass surrounded by low-absorption regions (edema).

B, T1-weighted image, TR = 600 msec, TE = 20 msec. Tumor is hyperintense because of proton-electron dipolar-dipolar proton relaxation enhancement of melanin.

C, T2-weighted image, TR = 2500 msec, TE = 80 msec. Tumor is mostly isointense with some regions of hypointensity. There is no peripheral hemosiderin ring. Surrounding edema is hyperintense.

---


