Diffusion-Weighted Imaging Hyperintensities in Intracerebral Hemorrhage: Microinfarcts or Microbleeds?
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As reported in “Predictors of Highly Prevalent Brain Ischemia in Intracerebral Hemorrhage,”1 a high prevalence of diffusion-weighted imaging hyperintense lesions (DWIHLs) in patients with spontaneous intracerebral hemorrhage is being recognized. These lesions have strong associations with subclinical markers of small vessel disease (SVD) such as cerebral microbleeds (CMBs).1–3 In view of the restricted diffusion of these lesions, they are presumed to be ischemic in nature; however, in the absence of any direct pathological correlation, this remains unverified.

A number of other intracerebral processes display restricted diffusion. Of most interest is acute/subacute hemorrhage, which displays restricted diffusion most notably within its diamagnetic oxyhemoglobin (hyperacute) and extracellular methemoglobin (late–subacute) states.4,5 Both of these byproducts of hemoglobin breakdown do not have the classic hypointense signal attributed to blood on T2*-weighted gradient echo (GRE) images and may go unnoticed.

We are currently characterizing the prevalence and determinants of SVD in a population of young stroke patients. Thus far, we have isolated 3 patients presenting with spontaneous intracerebral hemorrhage who were observed to have remote incident DWIHLs. They all have high CMB burden.

FIGURE: Restricted diffusion-weighted imaging (DWI) hyperintensities. Magnetic resonance imaging obtained in 44-year-old (Patient 1, A–E) and 49-year-old (Patient 2, F–J) men, performed 1 and 7 days, respectively, following symptom onset. DWI (b = 1,000) and apparent diffusion coefficient maps (A, B and F, G) demonstrate restricted diffusion of 3 lesions remote from the site of primary intracerebral hemorrhage. A micro diffusion-weighted imaging hyperintense lesion (DWIHL) within the right caudate (arrows) of Patient 1 is surrounded by cerebral microbleeds best seen on gradient echo (GRE) image E. This area is hyperintense on fluid attenuated inversion recovery (FLAIR), GRE, and T1-weighted images (C, D, E), with a rim of hypointensity on the GRE image. Patient 2 has a small DWIHL in the left frontal lobe (arrows) and another adjacent to the left splenium (arrowheads). The frontal lesion displays characteristics similar to those of the lesion mentioned above (H, I, J). The posterior lesion is hyperintense on FLAIR (H) and GRE (I) images, but does not display a rim of hypointensity on the GRE image and was isointense on T1-weighted images (not shown). The caudate and posterior lesions were undetectable on computed tomography, whereas the larger frontal lesion was visualized as hyperdense (not shown).
and severe white matter hyperintensities on magnetic resonance imaging (MRI). Interestingly, some of these DWIHLs have imaging characteristics suggestive of hemorrhage. The Figure demonstrates 2 lesions with imaging characteristics of late–subacute hemorrhage (hyperintense on both T1- and T2-weighted images with a hypointense rim on GRE images) in 2 patients. Conversely, the imaging characteristics (isointense on T1-weighted and hyperintense on T2-weighted images without a hypointense rim on GRE images) of the left hemispheric DWIHL adjacent to the splenium (see Fig. F–I) could be attributed to either subacute infarct or hyperacute oxyhemoglobin. Accordingly, only a follow-up MRI outside of the acute/subacute period could elucidate the true nature of this lesion.

These images suggest the intuitive concept that CMBs undergo similar imaging evolution as their macrohemorrhage counterparts. In view of these observations, it would be of great interest to see the imaging evolution of DWIHLs on sequential MRIs within the DECIPHER protocol outlined within this article.1 If incident small/micro infarcts and hemorrhagic lesions were occurring concurrently, it would favor the first or third “putative mechanisms” put forth by the authors, ahead of overly aggressive blood pressure (BP) lowering. Nevertheless, hemodynamic fluctuations may still play a role with acute rise in BP to compensate for increasing intracranial pressure, rupturing remote fragile diseased vessels, leading to CMBs, with subsequent aggressive lowering of BP, resulting in ischemic infarction.

Potential Conflicts of Interest
Nothing to report.

References

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Reply
Ravi Menon, MD and Chelsea Kidwell, MD

We thank the authors for their letter and interest regarding our study.1 They raise a number of interesting questions including whether any of the remote diffusion-weighted image (DWI) lesions detected in the acute intracerebral hemorrhage (ICH) setting could in fact represent small hemorrhages (eg, “acute” microbleeds) rather than true ischemic lesions.

In our Differences in the Imaging of Primary Hemorrhage Based on Ethnicity or Race (DECIPHER) analysis, we utilized a consistent, comprehensive methodology for lesion characterization. By reviewing information from all sequences, including T2*-weighted imaging, we took care to exclude from the analysis any DWI lesion with characteristics suggestive of any stage of hemorrhage. A number of studies have shown that within minutes to hours of hemorrhage onset, a rim of hypointense signal is typically seen on gradient-echo images.2,3 Moreover, many other clinical and laboratory papers attest to the sensitivity of T2*-weighted sequences for discriminating some signature of blood breakdown products in hematomas of all ages.4,5 Although it is certainly possible that a small number of lesions in our series may have been captured that actually represent a brief transition period when hemorrhage may not be differentiated from ischemia on magnetic resonance imaging sequences (due to insufficient T2 shortening and/or lack of paramagnetic properties), it is unlikely that this accounts for the vast majority of lesions.

It is also important to note that signal characteristics in the region of the hematoma rim and interior should be interpreted with extreme caution on other sequences (eg, DWI and apparent diffusion coefficient) in the presence of paramagnetic blood breakdown products due to magnetization gradients on T2*-weighted sequences. Due to the potential of artifacts in this setting, particularly at tissue interfaces, it is unclear whether such regions can be accurately interpreted as restricted diffusion due to ischemia.

We are in the process of analyzing serial imaging data regarding the temporal evolution of both small remote ischemic lesions and microbleeds in our DECIPHER primary ICH cohort and look forward to publishing these findings in the future. We look forward to additional follow-up regarding the authors’ series and hope that these future studies provide additional insights into the underlying mechanism of these lesions. It is possible that our patients possess different vascular risk factors (mean age in DECIPHER was 60 years), but in our series of >100 patients, after evaluation of all established stroke risk factors, blood pressure lowering was most significantly correlated with ischemic lesion development, a finding also reported in other series.6

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