Imaging Advances Boost Microbleed Detection

BY DOUG BRUNK

SAN DIEGO — Various T_2*-weighted MRI techniques are improving the ability to detect microbleeds, which are clear markers of hypertensive vasculopathy, cerebral amyloid angiopathy, and other underlying small vessel disease.

In fact, the more clinicians like Dr. Steven M. Greenberg look for them, the more they're finding.

"At some point we will not be able to get any more sensitive," Dr. Greenberg said at the International Stroke Conference. "The brain is not one big microbleed. There will be some limit to how many we pick up, but for now the harder we look the more we find."

Dr. Greenberg, a neurologist with the Hemorrhagic Stroke Research Program at Massachusetts General Hospital and Harvard Medical School, Boston, noted that advances in detection are coming at a time when the incidence of hypertensive vasculopathy and cerebral amyloid angiopathy are expected to rise as the Baby Boom generation continues to age. "These are not the only causes of microbleed, but these two processes are common and highly age associated," he said. "With the aging of the population these have become important entities."

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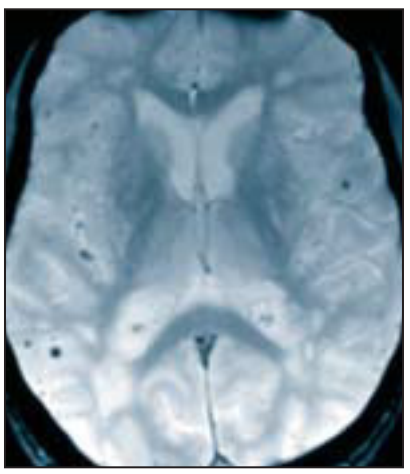
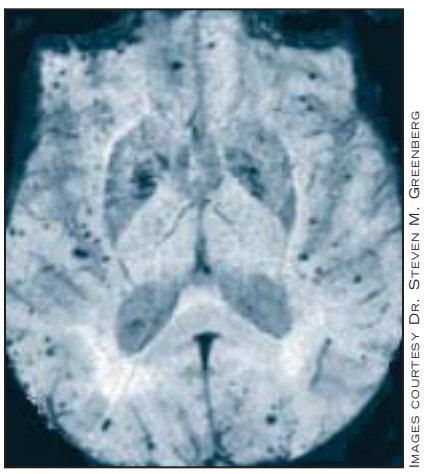
DR. GREENBERG

Histology remains the accepted standard for detecting microbleeds, but Dr. Greenberg considers MRI superior to pathology from a practical standpoint because it has "tremendous sampling ability. Because of the sensitivity of MRI for iron deposits, we're able to get a full survey of the brain. While we'll never be able to replace the specificity of pathology for either identifying the bleeds themselves or the vascular diseases that go along with them, the sensitivity of MRI will supersede what is practical in an autopsy exam."

Compared with conventional T_2-weighted MRI, T_2*-weighted MRI does not use a refocusing pulse, "so the dephasing caused by the paramagnetic iron is accentuated by the T_2*-weighted technique," Dr. Greenberg explained. "Lesions that are entirely invisible on T_2 sequence become highly visible on the T_2* technique. So until you've looked with a T_2* technique you really haven't done a proper test to look for microbleeds."



T2*-weighted, standard slice shows microbleeds in a 74-year-old woman.



A thin slice from the same woman identifies many more microbleeds.

IMAGES COURTESY DR. STEVEN M. GREENBERG

The most common microbleed mimics seen on MRI include mineral deposits, flow voids, bone/air artifacts, cavernous malformations, metastatic melanoma, and diffuse axonal injury.

According to detection criteria outlined by a group of experts including Dr. Greenberg, microbleeds should be black on T_2*-weighted MRI; blooming on T_2*-weighted MRI; devoid of signal hyperintensity on T_1- or T_2-weighted sequences; round or ovoid rather than linear; at least half surrounded by brain parenchyma; and be distinct from other potential mimics such as iron/calcium deposits, bone, or flow void; and should have a clinical history that excludes traumatic brain injury (Lancet Neurol. 2009;8:165-74).

The best clue to underlying disease may be location, Dr. Greenberg said. A deep hemispheric/brainstem pattern is suggestive of hypertensive vasculopathy while a strictly lobar pattern is suggestive of cerebral amyloid angiopathy.

Advances in T_2*-weighted MRI techniques are leading to further improvements in detection rates. These include increasing the echo time, which allows greater time for the dephasing of the paramagnetic signal; thinner scanning sections, which increase the signal-to-noise ratio; increasing the magnetic field strength; and image postprocessing techniques such as susceptibility-weighted imaging, which "incorporates the phase shift as well as the magnitude effects of the iron deposits to increase their visibility."

Such advances in detection "will change our understanding of the prevalence of microbleed lesions," Dr. Greenberg said. "This is a story that has to play itself out before we'll know where we land.

"It's a growth area—one that we as researchers and clinicians need to better understand the implications of."

Dr. Greenberg disclosed that he has received grant and research support from the National Institutes of Health and the Alzheimer's Association. ■

Migraine With Aura in Midlife Linked to Later Stroke

BY MARY ANN MOON

Women who have migraine with aura in their middle years are more likely than others to show cerebellar "infarct-like lesions" on brain MRI in late life, according to a report in JAMA.

This link between migraine with aura and presumed occult stroke is independent of cardiovascular risk factors and CV disease history at either time period, said Ann I. Scher, Ph.D., of the Uniformed Services University, Bethesda, Md., and her associates.

These findings from a prospective longitudinal study are consistent with those of the recent cross-sectional CAMERA (Cerebral Abnormalities in Migraine, an Epidemiological Risk Analysis) study (JAMA 2004;291:427-34), "the only other study that measured infarcts on MRI, which also found the migraine-associated infarcts to be preferentially located in the cerebellum," the investigators noted.

As such, they confirm the previous findings and point to the need for additional research with sequential MRIs "to better establish the temporality and dose-response relationship between migraine with aura and brain infarcts," they added.

Several researchers cautioned, however, that without knowledge of the source or type of lesions that were seen and without any known clinical symptoms or consequences of the lesions, it is too early to say whether migraine has harmful effects on the brain.

Dr. Scher and her colleagues studied this issue using data from the Reykjavik Study, a population-based prospective assessment of cardiovascular disease in Iceland, which began in 1967. They examined data on a subset of 4,689 subjects who were middle-aged (average age, 51 years) at enrollment, when migraine data were collected, and were elderly (average age, 76 years) in 2002-2006 when brain MRI was performed.

'Infarct-like lesions' were significantly more prevalent in women who reported migraine with aura in midlife (31%) than in women who did not have migraine (25%).

There were 2,693 women and 1,996 men in this study. A total of 12% (6% of the men and 17% of the women) had migraine at midlife, including approximately 5% who had migraine without aura and approximately 8% who had migraine with aura.

"Infarct-like lesions" were significantly more prevalent in women who reported migraine with aura in midlife (31%) than in women who did not have migraine (25%), but no difference was found in prevalence among men.

Similarly, infarcts in the cerebellum, but not in cortical or subcortical locations, were more prevalent in women who reported migraine with aura in midlife (23%) than in women without headache (15%), but there was no difference in prevalence among men.

"However, we cannot rule out a possible increased risk for men [who have] migraine with aura, due to the relatively small number of [such] men in our sample," the investigators noted (JAMA 2009;301:2563-70).

In an editorial comment accompanying this report, Dr. Tobias Kurth and Dr. Christophe Tzourio of the University Pierre et Marie Curie, Paris, said these findings should be interpreted with caution (JAMA 2009;301:2594-5).

"In the absence of the source and the nature of 'infarct-like lesions' and the absence of clinical symptoms or consequences, it is premature to conclude that migraine has hazardous effects on the brain," they said.

"New studies examining the association of migraine with structural brain changes and brain function should improve understanding of the associations, and perhaps further unveil migraine-specific mechanisms," Dr. Kurth and Dr. Tzourio said.

Dr. Scher has served on advisory boards of Endo Pharmaceuticals and OrthoMcNeil Neurologics.

Dr. Kurth reported receiving funding from McNeil Consumer & Specialty Pharmaceuticals, Merck, and Wyeth Consumer Healthcare; serving as a consultant to i3 Drug Safety and World Health Information Science Consultants; and receiving honoraria from Genzyme, Merck, and Pfizer.

Dr. Tzourio reported receiving fees from Sanofi-Synthelabo and Merck Sharpe & Dohme.

The study was funded by the National Institutes of Health and several individual NIH institutes, as well as Hjartavernd (the Icelandic Heart Association), the Althingi (the Icelandic Parliament), and the Migraine Research Foundation. ■