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Commentary

Neuroradiologic Screening for Brain Metastases—Can Quadruple Dose Gadolinium Be Far Behind?

Lawrence E. Ginsberg and Frederick F. Lang

Sze et al in this issue of *American Journal of Neuroradiology* (see page 821) renew the controversy surrounding the best way to screen for brain metastases. This remains very relevant to the practice of neuroradiology and to all of those involved in the care of cancer patients. Will this article put to rest the question of how best to image this patient population? Likely not. Will and should it prevent the next researcher from giving even higher doses of the same or different contrast agents, or employing some other pulse sequence in an attempt to get to the ultimate goal of unearthing the very last or smallest metastasis? Probably not. Imaging guidelines are necessary, however, as is an understanding of the current medical and surgical issues in dealing with metastatic disease to the brain.

Of course, the treatment approach at each institution will govern how brain metastases are managed. At The University of Texas M. D. Anderson Cancer Center, we screen some 3500 patients for metastatic brain tumor and treat approximately 1000 patients per year. We rely on the expertise of physicians from multiple disciplines in order to apply several treatment modalities effectively, including surgery, stereotactic radiosurgery, conventional radiotherapy, and chemotherapy. Initial planning relies heavily upon whether the patient can be treated surgically. The decision to operate is influenced by many factors including the patient's medical and neurologic condition, the sensitivity of the particular histology to radiation therapy or chemotherapy, the extent of disease elsewhere, and, most importantly, the size, number and accessibility of the lesion(s). This last factor is most relevant to the neuroradiologist, because neuroimaging ultimately seeks to provide clinicians with an accurate assessment of the number, location and size of the cerebral metastases so that the most appropriate treatment is given to the patient.

For the patient with only one apparent metastasis detected with CT or single-dose, spin-echo MRI, surgical resection is the preferred treatment assuming other factors are favorable. Two randomized prospective trials have shown this approach to be more efficacious than whole-brain irradiation alone (1, 2). Additionally, these patients are traditionally given adjuvant whole-brain radiation therapy (WBRT) in order to treat radiographically undetectable disease and to minimize local recurrence. Radiation toxicity may adversely affect the quality of survival, however, so we have increasingly withheld WBRT at the M.D. Anderson Cancer Center, with the rationale that new lesions can be treated as they appear. In this subgroup of patients, increased imaging sensitivity is crucial. If only one metastasis is discovered in the patient, then there is increased confidence that surgery is the correct course, and WBRT may be withheld. Conversely, if a larger contrast dose or more sensitive pulse sequence were to detect other metastases, treatment could potentially be drastically altered.

Treatment options for patients with multiple brain metastases have changed significantly in recent years. The previously held belief that multiple metastases should be treated simply with WBRT has been challenged. In a study from our institution, surgical resection in patients with a limited number of brain metastases (typically 2–4 lesions) produced survival rates similar to patients with resected single metastases provided that all the lesions were resected and none were left behind (3). The advent of radiosurgery has also provided a simple, effective, noninvasive and cost-effective method of treating surgically inaccessible lesions, thereby expanding the therapeutic options available to patients with multiple metastases (4, 5). Imaging modalities that detect other metastases that are small and, more often than not, unresectable, will unquestionably alter the treatment algorithms for patients with multiple metastases. Questions also arise. For example, should surgery be withheld for a patient with a symptomatic, accessible 2-cm frontal lesion, and a 5-mm basal ganglia lesion that is detected only with the more sensitive imaging technique? Our approach might well be to resect the larger lesion surgically and apply radiosurgery to the inaccessible lesion. All of the above suggests that increasingly sensitive neuroimaging is necessary to detect the full extent of metastatic disease prior to treatment.

How then to best image the patient with known or suspected metastases to the brain or patients being screened for metastases? Sze et al make a case for

Departments of Diagnostic Radiology (LEG) and Neurosurgery (FFL), The University of Texas M. D. Anderson Cancer Center, Houston, Texas

Address reprint requests to: Lawrence E. Ginsberg, M.D., Diagnostic Radiology, Box 57, UT M. D. Anderson Cancer Center, 1515 Holcombe Blvd. Houston, TX 77030, e-Mail: lginsberg@di.mdacc.tmc.edu

selective use of triple-dose gadolinium in certain patients, particularly those in whom single-dose studies are equivocal, or in whom only one resectable lesion is seen. This is inconvenient to say the least because it requires physician monitoring of each case or additional imaging for some patients. Additionally, the increased costs of extra gadolinium are considerable, and probably not justified despite some soft evidence suggesting greater cost effectiveness as reported by Mayr et al (6). Sze et al and the other major reports describing the use of triple-dose gadolinium chelates in the evaluation of metastases to the brain, cite no cases in which completely "normal" images of the brain obtained with single-dose contrast later proved to harbor metastases after administration of triple-dose contrast (7, 8). Such cases, though, are certainly possible. We do not perform triple-dose post-contrast MRI at M.D. Anderson Cancer Center.

We feel the best answer at this time is magnetization transfer (MT) post-contrast imaging. In this technique, a saturation pulse is applied that targets hydrogen protons associated with complex macromolecules; the ensuing interactions result in signal loss from most non-enhancing structures, thus allowing greater conspicuity of enhancement. MT imaging has been well-described (9–12). MT with single-dose gadolinium administration has been shown to be roughly equivalent to triple dose post-contrast spin-echo imaging in terms of lesion conspicuity and detection (13, 14). The technique is not associated with greater costs. MT pulse sequences are widely available, and other than a small time penalty or increased background noise, has little significant downside. In addition, reports have demonstrated that post-contrast images with MT provide improved detection of enhancement in a variety of other diseases such as primary brain tumors, infectious and demyelinating disease, and stroke (9, 14–16). For these reasons, we advocate using MT pulses on all post-contrast brain MRI and feel that this is likely to provide adequate radiologic information in the work-up of the patient with brain metastases and indeed all patients.

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