INTRODUCTION

Even with current clinical diagnostic methods, there continues to be considerable difficulty in diagnosing neurodegenerative diseases with confidence. Neuroimaging has the potential to improve dementia diagnosis further by going beyond its traditional role of simply excluding mass lesions and stroke and helping to distinguish specific dementing diseases. Considerable research indicates that magnetic resonance imaging (MRI) can identify early structural changes caused by Alzheimer’s disease (AD). MRI also can identify Creutzfeldt-Jakob disease (CJD) and frontotemporal dementia (FTD). Furthermore, molecular neuroimaging techniques reveal characteristic focal abnormalities in neurodegenerative diseases that are unrecognized by other methods. Although further research is needed to understand how the clinical potential of imaging can be optimally exploited, there is now sufficient experience to suggest ways in which neuroimaging can be incorporated into everyday diagnostic and treatment decisions about dementia.

STRUCTURAL IMAGING: CT AND MRI

Mass Lesions

The most obvious use of brain imaging is to identify a mass lesion. Brain tumors, subdural hematomas, and brain absesses all can cause dementia and are easily recognized with computed tomography (CT) and MRI. Although a few mass lesions will be identified during routine dementia evaluations, these days, most are found when a brain scan is obtained to evaluate focal neurological deficits rather than dementia. The most conspicuous exception is in elderly individuals in whom evaluations are delayed or incomplete. In our referral practice, we occasionally find unsuspected brain tumors and subdural hematomas with neuroimaging when previous physicians inappropriately presumed that an elderly patient had AD without considering other possibilities or incorrectly assumed that a scan must have been done previously. Fortunately, such diagnostic errors are becoming less common as physicians have learned that age is not an appropriate criterion for deciding whether to order brain imaging.

Mass lesions also may be recognized with neuroimaging first during a routine dementia evaluation, when a patient’s initial symptoms are misinterpreted as psychiatric. Frontal mass lesions may cause few obvious focal neurological signs, so brain imaging might not have been considered necessary. This error can be avoided by always obtaining a CT or MRI scan when disruptive behavioral and personality changes occur de novo in middle or late adulthood.

Mass lesions are especially likely when dementia has developed over less than a year. Although it may seem obvious that brain tumors, such as glioma or central nervous system lymphoma, can cause
rapidly progressive dementia, it is sometimes very difficult to obtain a consistent or accurate history
about the timing of symptom onset. When there is any reason to suspect a rapidly progressive demen-
tia, a particularly diligent review of image results is warranted.

Vascular Lesions

Cerebral infarcts are a common cause of dementia, and like AD, the incidence of vascular
dementia increases with age. Although stroke usually causes obvious clinical symptoms, imaging
has demonstrated that stroke often can be asymptomatic (1,2). Furthermore, by the time of a demen-
tia evaluation, patients with stroke may have substantial motor and sensory recovery, so that focal
deficits are no longer apparent. In addition, the severity of dementia may preclude a detailed neuro-
logical examination, making it impossible to identify subtle deficits by clinical examination alone.
For all of these reasons, structural imaging should be used routinely to look for evidence of cerebral
infarcts causing or contributing to dementia.

Structural imaging is quite sensitive in identifying stroke, so the major clinical challenge in this
use of neuroimaging is to interpret the significance of lesions that are found and whether they repre-
sent stroke (Fig. 1). White matter abnormalities are common in the elderly and do not always repre-
sent stroke (3). Increased signal on MRI may be caused by enlarged perivascular spaces, and AD itself
can cause white matter changes, perhaps due to Wallerian degeneration. On the other hand, the pres-
ence of extensive white matter abnormalities is associated with diminished cognitive performance in
otherwise healthy individuals (4,5). Dementia also can be seen in individuals with clear-cut, but silent,
infarcts. One of the ways to determine the significance of white matter lesions is to assess their extent
and location, and to consider the imaging results in the context of the patient history. The more exten-
sive the white matter abnormalities are, the more likely it is that they are contributing to the demen-
tia. The location is also important. Even small thalamic infarcts often cause cognitive impairment (6).
Furthermore, if the location of infarcts and white matter changes corresponds to the localization sug-
gested on the mental status exam, they are the likely explanation for the change in cognition (for exam-
ple, preponderant left hemisphere lesions in a demented patient with prominent language disturbance).
Finally, a sudden onset and stepwise decline in cognition suggests the diagnosis of vascular demen-
tia, which imaging can confirm (7,8).

White matter abnormalities and even clear stroke on neuroimaging alone is insufficient to exclude
AD. Lacunar and silent cortical infarcts are very common in the elderly, occurring in approximately
30% (9). In most cases, these strokes do not cause dementia. However, they may contribute to the sever-
ity of dementia in those with AD. Careful studies that have examined the combined effects of abnor-
mal white matter, brain infarction, and measures of cerebral atrophy including hippocampal size
consistently show stronger relations between brain atrophy measures and cognition than vascular fac-
tors. This supports the notion that AD pathology is often the primary factor for cognitive decline in
older individuals with concurrent cerebrovascular injury (10). The phenomenon of mixed AD and vas-
cular dementia is well recognized and stroke is found in approximately 30% of patients with AD at autops
y (11). One approach to identifying AD in patients who also have extensive vascular lesions is
to document a slow, progressive cognitive decline while demonstrating with neuroimaging that vas-
cular lesions have remained unchanged.

CT or MRI?

Although mass lesions are well visualized by both CT and MRI, MRI is preferable. It is more sen-
sitive in identifying focal structural abnormalities, especially in the temporal cortex, provides better
tissue contrast, and permits increased imaging flexibility by offering protocols that emphasize dif-
ferent tissue properties. For example, diffusion-weighted imaging can suggest that a vascular lesion
is recent, and fluid attenuated inversion recovery (FLAIR) imaging can highlight otherwise indistinct
white matter lesions. MRI also has some advantages in identifying particular dementing disorders, as