Vascular Dementia — Still Overdiagnosed

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THE NOTION THAT SLOWLY progressive dementia in the elderly is the result of chronic diffuse brain hypoxia is largely discredited — Alzheimer disease has nothing to do with cerebral arteriosclerosis. Nonetheless, it is still widely believed that many elderly people are demented on a cerebrovascular basis, most often in the form of ‘‘multi-infarct dementia.’’ Such a term does not refer to the circumscribed intellectual disturbances which follow single large infarcts in the territories of major cerebral vessels. Rather it denotes more global cognitive loss in the presumed presence of several lesions, often deep lacunes, none of which would alone be expected to cause intellectual impairment. In fact, many clinicians believe that when a demented patient has symptoms or signs of stroke (as reflected, for example, in the Hachinski Ischemic Score), cerebrovascular disease can be presumed to be either causing or contributing to the dementia, and on such an assumption rest a number of well-known clinical studies. Perhaps, therefore, one should ask upon what basis such an assumption is made.

Tomlinson, Blessed, and Roth have provided the most persuasive pathological evidence to date that stroke does cause dementia in the elderly. Comparing 50 brains of demented old people to brains of undemented controls, they concluded that half had what today is called senile dementia of Alzheimer type (SDAT). 17% had either definite or probable arteriosclerotic dementia, and 18% had a combination of the two diseases. The authors stressed a number of important details, however. First, of the 9 patients considered to have arteriosclerotic dementia, three had between 60 and 82 ml volume of infarction, and the other six had volumes of 101 to 412 ml; only one of the controls had more than 60 ml of infarction, and none had more than 100 ml. Second, the authors did not deal with ‘‘the possibility of ischaemic lesions affecting areas of brain likely to be particularly important in relation to producing features of dementia’’ — possibly relevant to the fact that three patients with lesions of 60 to 82 ml had dementia, whereas the single control with such a degree of infarction did not. Third, four of the nine cases of mixed arteriosclerotic dementia and SDAT also had more than 100 ml of softening; the other five did have volumes of infarction (mean 38.8 ml) encountered in several controls, suggesting to the authors that the presence of either disorder might lower the threshold for clinical expression of the other. Moreover, softening of mild to moderate degree was present in 19 of the 25 patients considered to have SDAT of sufficient severity to explain the dementia alone. (How many of these patients, or those whose dementia was of ‘‘mixed’’ type, had had symptoms or signs of stroke — i.e., a high ‘‘Ischemic Score’’ — was not determined.) Fourth, multiple small diencephalic infarcts were seen in both demented and non-demented subjects, and among those with arteriosclerotic dementia were never the only or even the major lesions. Fifth, ‘‘The sample was not a truly random one.’’ Thirty-four of the 50 demented patients, including eight of the nine with arteriosclerotic dementia and all 9 with mixed arteriosclerotic dementia and SDAT, were male, yet 15 of the 25 with SDAT were female. Since, in another survey, the authors had found dementia to be twice as frequent among women as among men, arteriosclerotic dementia was probably overrepresented in their series. As they noted, ‘‘... conclusions could not be drawn from this sample about the prevalence of the various types of dementing process in old age.’’

Thus, the frequency of arteriosclerotic dementia among old people cannot be determined from the data of Tomlinson, Blessed, and Roth. Their major finding, however, is one that seems to have been ignored by other investigators, namely that arteriosclerosis causes dementia only when there are large total volumes of brain infarction, usually of more than 100 ml. Smaller lesions, including multiple small subcortical infarcts, are unlikely to cause dementia. Such a conclusion would have come as no surprise to C. Miller Fisher, who two years earlier had expressed his view that lacunes were overrated as a cause of progressive dementia, and that when they occurred in large enough numbers (Marie’s ‘‘l'état lacunaire’’) to cause cognitive loss, there was usually pseudobulbar palsy, with dysarthria, dysphagia, bradykinesia, and gait disturbance. Paraphrasing Boyd, Fisher commented that ‘‘... lacunes lick the psyche and bite the soma, just opposite to senile dementia. ’’ Moreover, for them to appear in large numbers is unusual; of Fisher’s 114 consecutive patients with lacunes at autopsy, only nine had more than 10, and dementia, with or without pseudobulbar palsy, was rare. Fischer recently has reiteratd this point: ‘‘... one rarely (if ever) encounters the lacunar clinical state as described [by Marie].’’

Clearly, then, pathological evidence of stroke doesn’t necessarily mean that cerebrovascular disease has anything to do with a patient’s dementia, and in most instances it probably doesn’t. Yet many clinicians and pathologists have ignored the above data and assumed that if a demented patient has symptoms or signs of stroke, or autopsy evidence of cerebral infarction, then the dementia is at least partly vascular in origin. Such an inference is frequently made from pathological reports even when the size or location of the lesion(s) is not described. Oft-cited studies of this nature include those of Corsellis, who found ‘‘organic psychosis’’ among 167 elderly patients to be ‘‘asso-
cated with cerebral vascular changes" in 46 (28%) (of whom 20% had had focal neurological signs) and "associated with mixed vascular and senile changes" in 20 (12%) (of whom 25% had had focal neurological signs); Delay et al, who attributed dementia in old age to cerebrovascular disease in a quarter of cases and to mixed senile and arteriosclerotic disease in half; Sournander and Sjogren, who classified as "cerebrovascular dementia" 72 (23%) of their 318 cases (of whom, interestingly, was considered to have a mixture of SDAT and cerebrovascular dementia); Malamud, who found "arteriosclerotic brain disease" in 356 (29%) of 1225 cases and "mixed senile-arteriosclerotic disease" in 283 (23%); Todorov et al, who diagnosed "vascular dementia" in 132 (17%) of 776 cases and "combined senile-vascular dementia" in 250 (32%) (criteria for "vascular" in this study were simply "parenchymatous lesions of vascular origin"); and Jellinger, who attributed dementia in the elderly to cerebrovascular disease in 225 (22%) of 1009 cases and to "mixed senile and vascular origin" in 136 (13%). In this last study, "lacunar state" was the most frequently encountered change in patients with vascular dementia. There was also a high frequency of cerebrovascular lesions in patients classified as having "senile dementia" (i.e., SDAT) and of "senile parenchymal changes" in patients considered to have vascular dementia."

Even the absence of pathologic Alzheimer disease or other identifiable dementing illness may not warrant blaming dementia on vascular disease when only small infarcts are found at autopsy, for the cause of dementia is not always clear pathologically. Some of Marie's patients considered to have "l'etat lacunaire" may well have had normal pressure hydrocephalus; alcoholic cerebral atrophy was not recognized until the past decade; and demented patients have been found at autopsy to have lesions which defy classification. In fact, in two of Tomlinson, Blessed, and Roth's 50 cases, there were no visible lesions at all; others have also reported examples of dementia and "normal histology." Too often, pathologic evidence of stroke has been presumed the cause of dementia simply because an alternative diagnosis could not be conjured up.

If cerebrovascular or multi-infarct dementia is over-diagnosed pathologically, then obviously it is over-diagnosed clinically as well, and claims that a high "Ischemic Score" justifies a diagnosis of multi-infarct dementia must be viewed skeptically, even when at autopsy one or more strokes are found. A high "Ischemic Score" can identify patients who have had a stroke, but prior stroke doesn't necessarily mean that vascular disease caused or even contributed to the dementia. Yet that seems to be the underlying assumption of many investigators estimating etiologic prevalences or studying psychological, metabolic, or other clinical features in demented patients. When studies rest upon such shaky terrain, it is hardly surprising that their conclusions are conflicting. A high "Ischemic Score" does correlate with previous stroke, and cerebrovascular disease can cause dementia, either acutely, as after large infarcts, or more insidiously, as, infrequently, in "l'etat lacunaire" or, even more rarely, in such conditions asBinswanger disease, Takayasu arteritis, or primary cerebral amyloid angiopathy. Cerebrovascular disease may even play a role in some cases of normal pressure hydrocephalus. However, most patients considered demented on a vascular basis probably aren't. The conclusion of Tomlinson, Blessed, and Roth is as valid today as it was a dozen years ago: "Arteriosclerotic dementia is almost certainly overdiagnosed clinically."


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