



Discover Generics

Cost-Effective CT & MRI Contrast Agents

 FRESENIUS
KABI

[WATCH VIDEO](#)

AJNR

Subcortical Arteriosclerotic Encephalopathy: CT Spectrum and Pathologic Correlation

Preston R. Lotz, William E. Ballinger, Jr. and Ronald G. Quisling

AJNR Am J Neuroradiol 1986, 7 (5) 817-822

<http://www.ajnr.org/content/7/5/817>

This information is current as
of June 3, 2025.

Subcortical Arteriosclerotic Encephalopathy: CT Spectrum and Pathologic Correlation

Preston R. Lotz^{1,2}
William E. Ballinger, Jr.³
Ronald G. Quisling¹

Because of recent papers suggesting that subcortical arteriosclerotic encephalopathy (SAE) (Binswanger's disease) is more common than historically assumed, this investigation was initiated to assess the frequency of SAE, to gauge the reliability of CT in making this diagnosis, and to assess the strength of the correlation between SAE and arterial hypertension. Of 202 autopsied patients in a 17-month period, 82 had undergone antemortem CT. Of these, 20 had CT findings thought to represent varying degrees of the disease spectrum of SAE. Microscopy confirmed this diagnosis in 18 cases. The pattern of diminished attenuation in the white matter was periventricular in 16 patients (marked asymmetry in one) and limited to an isolated focus somewhat removed from the ependyma in two. Among the 16 with periventricular disease, the extent of the process by CT appeared mild in nine, moderate in five, and severe only in two. There were two false positive CT diagnoses of SAE. Among a control group of 10 patients with normal white matter by CT, seven had some microscopic evidence of SAE, although it was generally less severe than in those with positive CT scans. Subcortical arteriosclerotic encephalopathy is common and can be identified in its various forms by CT with a high degree of reliability.

Subcortical arteriosclerotic encephalopathy (SAE), or Binswanger's disease, is a sometimes dementing illness for which chronic arterial hypertension has been implicated as a major pathogenetic factor [1-6]. It had been considered to be rare, but recent reports suggest that it is fairly common [7-11]. Illustrations of CT images in this disorder have been restricted almost exclusively to severe cases [7, 9, 12-15]. The CT appearance of the advanced cases, specifically excessive periventricular radiolucency, is well known, but lesser degrees of involvement are less well appreciated.

The histologic abnormalities in SAE have been described in numerous small series and case reports, and include demyelination, axonal loss, and fibrous or "hyalinoid" thickening of the walls of small arteries in the deep cerebral white matter [2, 4, 5, 7, 12, 16-20]. The discovery of these typical findings in the postmortem examination of the brain of a patient with relatively modest periventricular lucency by CT in October 1982, prompted a prospective evaluation of autopsied patients whose CT scans suggested the presence of such changes to determine their frequency, the reliability of CT in detecting their presence, and the frequency of chronic arterial hypertension in affected patients.

Materials and Methods

During the 17 months from January 1983 through May 1984, the formalin-fixed brains of all autopsied patients whose antemortem cerebral CT studies showed abnormal radiolucent areas in the deep white matter thought likely to represent SAE were subjected to microscopic examination of suspicious areas. Those brains severely damaged by infarction or affected by cerebral edema of any cause between the antemortem scan and the patient's death were excluded.

This article appears in the September/October 1986 issue of *AJNR* and the December 1986 issue of *AJR*.

Received October 9, 1985; accepted after revision April 4, 1986.

Presented at the annual meeting of the American Society of Neuroradiology, Boston, June 1984.

¹ Department of Radiology, Veterans Administration Medical Center and Shands Teaching Hospital, University of Florida College of Medicine, Gainesville, FL 32602.

² Present address: Watson Clinic, P.O. Box 1429, Lakeland, FL 33802. Address reprint requests to P. R. Lotz.

³ Department of Pathology, Veterans Administration Medical Center and Shands Teaching Hospital, University of Florida College of Medicine, Gainesville, FL 32602.

AJNR 7:817-822, September/October 1986

0195-6108/86/0705-0817

© American Society of Neuroradiology

The degree of white matter alteration by CT was graded subjectively by a neuroradiologist as mild, moderate, or severe, based on the extent of involvement rather than on the degree of radiolucency. The arteries of and near the circle of Willis were examined for atherosclerosis. Each brain was sectioned in a plane approximating that of the antemortem CT study. Specimens were taken from regions in the deep white matter identified as having abnormally low attenuation by CT. This included the white matter anterolateral to the frontal horns and posterolateral and superior to the trigones of the lateral ventricles in almost every case. Some overlying subcortical white matter, cerebral cortex, and ependyma were included in each specimen. Four sections were obtained from each specimen, one for each of four stains: hematoxylin and eosin (H and E), Masson trichrome (for collagen), Luxol Fast Blue with H and E (for myelin), and modified Seiver-Munger silver stain (for axons). The sections were examined for demyelination, axonal loss, and arterial/arteriolar wall thickening by a neuropathologist. The changes were graded as normal (−), mild (1+), moderate (2+), or severe (3+), based largely on the intensity of staining.

Ten brains from patients over 50 years old whose antemortem CT scans indicated no abnormal periventricular lucency to suggest the presence of SAE were subjected to the same sectioning and gross and microscopic examination in order to reveal the frequency of the disease changes of SAE in the presence of a normal CT scan. Bilateral sections from the same location already described adjacent to the frontal horns and trigones were obtained from each brain.

For both the abnormal and normal groups, the cardiac weight, thickness of the left ventricular wall, degree of coronary atherosclerosis, and evidence of myocardial infarction were recorded from the general autopsy data. Microscopic sections of the renal parenchyma in both patient groups were reviewed, and fibrous thickening of intrarenal small arteries and arterioles was graded on the same scale as were the cerebral vessels.

The charts of all patients were reviewed for evidence of chronic arterial hypertension, dementia, and factors that might have contributed to dementia or damage to the cerebral white matter. Any of the following could confirm the presence of chronic arterial hypertension: at least 3 recorded systolic pressures in excess of 150 mm Hg; at least 3 recorded diastolic pressures in excess of 90 mm Hg; left ventricular hypertrophy by postmortem examination (either simply recorded as such or recorded as a left ventricular mural thickness of at least 14 mm) in the absence of left ventricular outflow obstruction; or at least moderate arteriolar nephrosclerosis of the fibrous type typically caused by hypertension.

Results

The brains of 202 patients came to postmortem examination during the study period. Antemortem CT scans were available in 82 patients, 20 of which were deemed to have at least one area of diminished attenuation in the cerebral white matter suspicious for SAE. The CT scans were obtained within 1 month of death in 10 cases, between 1 and 6 months prior to death in four, between 6 and 12 months before death in four others, and from 12 to 26 months before death in two. The autopsy findings confirmed a diagnosis of SAE in 18 of the 20 suspected cases. These brains consistently showed the triad of demyelination, loss of axons, and fibrous thickening of the walls of small arteries in affected areas of the white matter, with the exception of one in which there was no demonstrable axonal loss in the specimens taken. The ages of these 18 individuals ranged from 56 to 93 years, with a mean age of 75 years. One case proved to have an occult

focus of metastatic carcinoma (the lucency on CT presumably being edema). The last had demyelination and axonal loss with normal small arteries, but also had an aqueductal subependymoma that had caused an obstructive hydrocephalus.

Of the 18 patients with SAE, the demyelination was wholly periventricular in 15, limited to focus separated from the ependyma by apparently normal white matter in two, and a combination of these two patterns in one (Figs. 1–5). One of the 15 patients with a purely periventricular pattern had a striking asymmetry from side to side (Fig. 4).

The brains with normal white matter by CT exhibited generally far fewer changes, but seven did show some evidence of SAE. The ages of the CT-normal patients ranged from 54 to 89 years, with a mean age of 74 years. The microscopic findings in both groups (abnormal and normal white matter by CT) are given in Table 1. Loss of axons was less dramatic than the demyelination in both groups.

Arteriolar nephrosclerosis generally correlated with the degree of arteriolar sclerosis in the white matter (Table 2). The frequencies of systemic arterial hypertension, dementia, cerebral atherosclerosis, infarction in the brain, and myocardial infarcts in the two groups of patients is presented in Table 3. Among the abnormal group with periventricular demyelination, nine had involvement judged to be mild, five moderate, and two severe. There was no apparent correlation between the occurrence of dementia and the extent of the CT changes.

Discussion

The discovery of 18 cases of SAE among 82 autopsied patients with antemortem CT studies attests to its recently reported prevalence in the population over 50 years of age [7–11]. That more mild examples than moderate and severe cases combined should be encountered is in keeping with our day-to-day observations in cerebral imaging in a population of veterans.

The accuracy of CT in distinguishing SAE from other causes of low attenuation in the white matter was 90% (18 of 20) in this limited series. The false positive diagnosis of focal SAE in a patient with a nonenhancing metastasis is an error that we believe can be avoided in most cases by recognizing the typically more subcortical than subependymal location of the lucency and by subsequently using a higher dose of contrast agent and delayed CT imaging. Our other false positive case, a patient with a chronic aqueduct obstruction previously shunted, represents a rather rare circumstance, although we know of no way to distinguish the pattern of periventricular lucency in this case from that due to arteriolar sclerosis. Because of these factors and the experience gained during the 17-month period of study, we feel that our false positive rate in the diagnosis of SAE by CT is currently below 5%.

Based on the finding of at least minimal evidence of SAE in seven of our 10 cases with normal CT scans, it seems apparent that there exists a significant false negative diagnosis rate in cases at the mild end of the disease spectrum. It is therefore possible that cases appearing to be early or mild by CT are not so in terms of their clinical and pathologic evolution. MR holds promise for greater sensitivity than CT in detecting early cases of SAE [8, 11, 21].

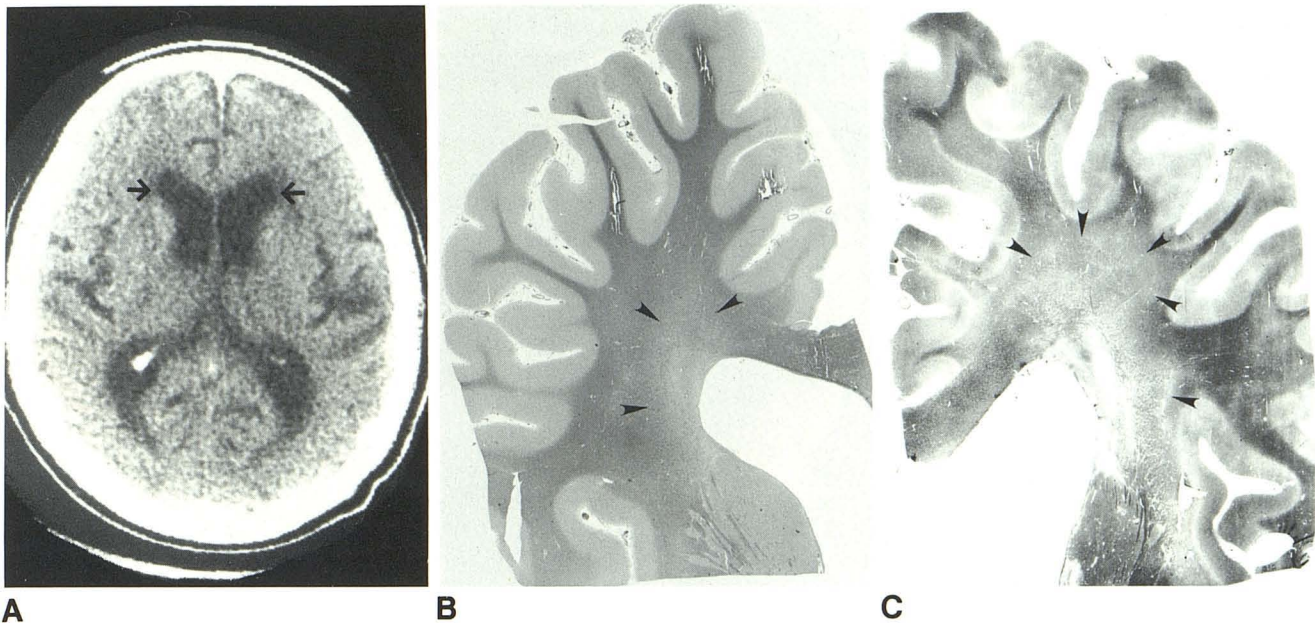


Fig. 1.—Mild periventricular form of subcortical arteriosclerotic encephalopathy. **A**, CT image showing abnormal lucencies (arrows) in white matter adjacent to frontal horns, small but quite apparent on left, barely detectable on

right. **B** and **C**, Right and left quadrant sections, respectively, of brain (Luxol Fast Blue stain) showing areas of demyelination (arrowheads) somewhat larger than depicted by CT. Transitions to normal white matter are ill-defined.

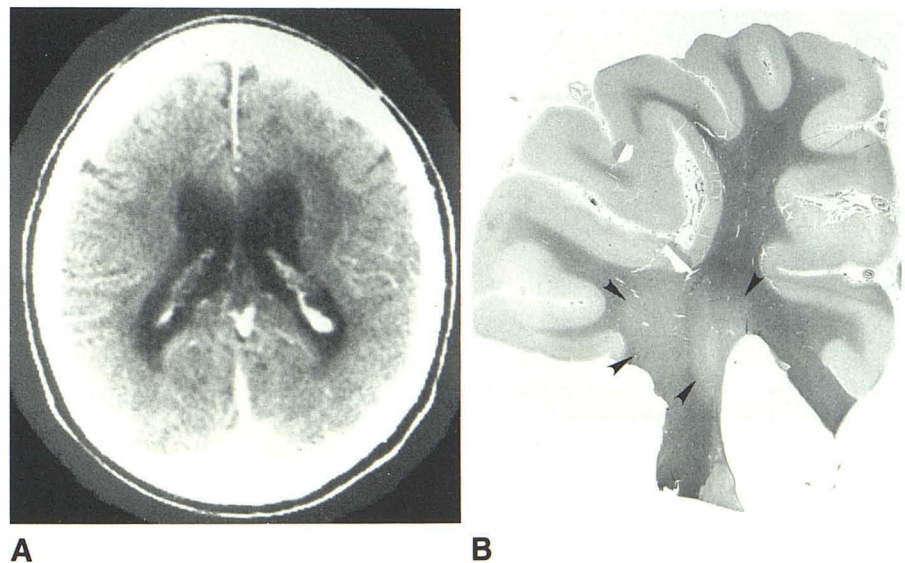


Fig. 2.—Moderate periventricular form of subcortical arteriosclerotic encephalopathy. **A**, CT section showing more extensive disease than in Figure 1A. **B**, Quadrant right frontal section (Luxol Fast Blue stain) showing greater degree and extent of demyelination (arrowheads) than in Figure 1B.

Discrete patches of low attenuation somewhat removed from the ventricular surface but not subcortical were identified in three of the 18 confirmed cases (Fig. 5). It seems entirely possible that such findings could be misconstrued as plaques of multiple sclerosis. This mistake appears even more likely with MR, given its greater likelihood of detecting such lesions on T2-weighted images. The radiologic distinction is likely to be a difficult one in many cases.

The periventricular lucency of SAE should not be mistaken for transependymal resorption of cerebrospinal fluid (TRCSF). We believe that the CT patterns of these two entities are sufficiently distinct to permit their separation by CT in nearly

every instance. TRCSF produces zones of lucency that are centered somewhat anterior to the angles of the frontal horns and have a fairly sharp transition to the normal density of white matter along their outer margin (Fig. 6). The lucencies frequently extend through the full thickness of the corpus callosum. The frontal lucencies of SAE, on the other hand, usually are centered directly at the angles of the frontal horn, seldom extend into the genu of the corpus callosum (and do so less completely and with a lesser degree of radiolucency when they do), and have less sharply defined margins with adjacent, normal white matter (Figs. 1, 2, 3). Sparing of the medial subependymal regions along the trigones and occipital

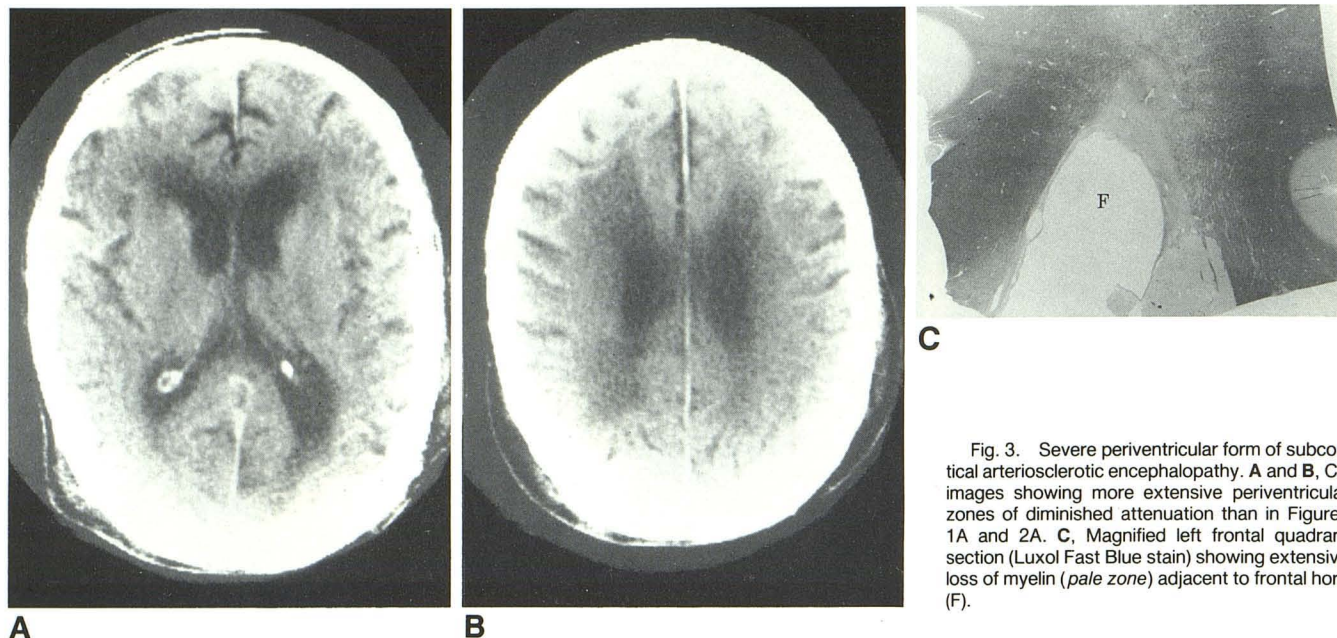


Fig. 3. Severe periventricular form of subcortical arteriosclerotic encephalopathy. **A** and **B**, CT images showing more extensive periventricular zones of diminished attenuation than in Figures 1A and 2A. **C**, Magnified left frontal quadrant section (Luxol Fast Blue stain) showing extensive loss of myelin (*pale zone*) adjacent to frontal horn (F).

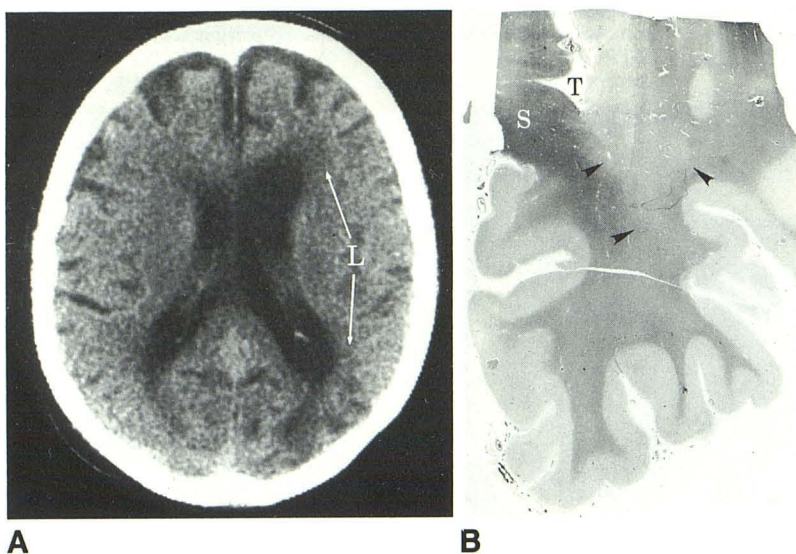


Fig. 4. Asymmetric periventricular form of subcortical arteriosclerotic encephalopathy. **A**, CT section showing moderate area of abnormal lucency (L) adjacent to left frontal horn and trigone with little or no involvement on right. **B**, Quadrant section (Luxol Fast Blue stain) including artefactually small left trigone (T) and splenium of corpus callosum (S) showing moderately extensive demyelination (*arrowheads*).

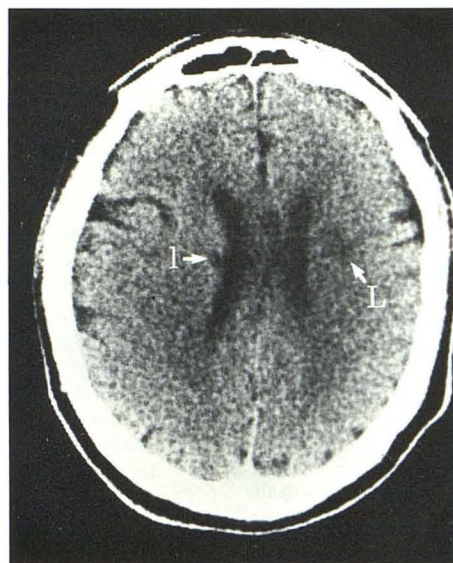
horns is a fairly consistent but not invariable finding with SAE, whereas TRCSF frequently produces sharply demarcated lucencies medial to the trigones and occipital horns. Given the prevalence of SAE, its coexistence in patients with various forms of hydrocephalus is to be expected. Decisions regarding the management of patients with hydrocephalus should not be based on the mistaken impression that transependymal migration of CSF is present when the zones of low attenuation seen at CT are really due to SAE. If there is doubt about the origin of periventricular lucencies, treatment decisions must be based wholly on clinical, laboratory, and other CT criteria.

In view of the loss of myelin and axons present with SAE, it seems reasonable to expect some degree of ventricular enlargement in affected individuals. Sporadic reports have indicated that this occurs [7, 13, 14, 17, 20, 22]. While the small number of patients in this series precluded a significant evaluation of this issue, we believe that many of these patients

have enlarged ventricles, and this may explain some cases of so-called deep cerebral atrophy.

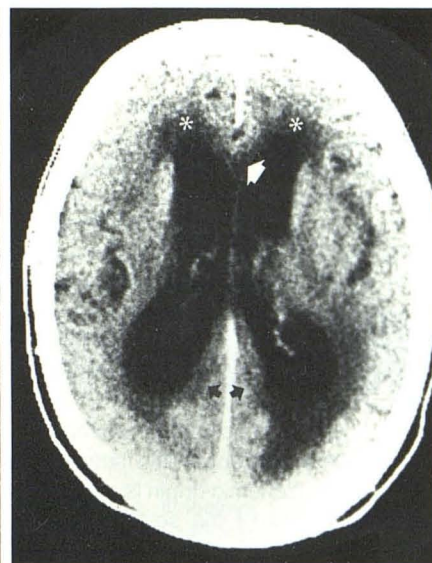
SAE, in its advanced form, can produce dementia and is called Binswanger's disease [1, 5-7, 9, 13, 14, 17, 22]. It has been considered uncommon [4, 23]. Recent papers have mentioned its clinically milder forms [7, 8, 11, 20, 21] and asymptomatic cases [11, 21]. Clinical evidence of dementia was noted in seven of our 16 cases with more than a solitary patch of SAE detected by CT (Table 3). Two of these seven had a postmortem tissue diagnosis of Alzheimer's disease, but three patients with mild SAE and two with moderate SAE had no other known explanations for their dementia. Interestingly, the two individuals with the most advanced SAE in this series had no record of an altered mental status. The presence of basal ganglionic and/or thalamic lacunae with SAE in nine of our 18 cases, and of small white-matter infarcts in seven, suggests a relationship between SAE and the lacunar

Fig. 5.—Patchy form of subcortical arteriosclerotic encephalopathy. CT image with patch of mild radiolucency (L) in left corona radiata and lacune (I) in subependymal region on right.



5

Fig. 6.—Transependymal resorption of subcortical arteriosclerotic encephalopathy. CT section in patient with hydrocephalus secondary to meningeal carcinomatosis showing lucent zones (asterisks) centered anterior to frontal horns with confluence in corpus callosum (white arrow) and extension of lucent zones medial to trigones and occipital horns (black arrows).



6

TABLE 1: Microscopic Findings in Abnormal and Normal Groups

	No. Patients by Pathologic Grade			
	—	1+	2+	3+
CT abnormal (n = 18)				
Arteriosclerosis	0	2	8	8
Demyelination	0	2	9	7
Loss of axons	1	9	8	0
CT normal (n = 10)				
Arteriosclerosis	3	4	2	1
Demyelination	3	7	0	0
Loss of axons	8	2	0	0

state [14, 17, 22]. It is entirely possible that dementia heretofore attributed to the lacunar state really has been due to coexisting, undiagnosed SAE. Similarly, the occurrence of cortical infarcts in 10 of our patients strongly suggests a relationship between these lesions and SAE, thereby further stimulating the speculation that in some cases of multiinfarct dementia, the dementia is actually partly or wholly due to the coexisting SAE.

The relationship between systemic arterial hypertension and SAE is not clear. Hypertension might be the sole etiologic factor [3], a necessary but not the only causative agent [1, 2, 20, 22], or a contributing but nonrequisite element [14]. SAE has been said to occur in the absence of hypertension [7, 13, 24, 25]. Most patients in both of our groups were hypertensive (Table 3). Interestingly, the one patient in the normal CT group without any microscopic evidence of SAE was the only normotensive individual in that group. A large number of normal blood pressure recordings were available on this patient. It is unclear from these data whether SAE can occur in the absence of hypertension. That the arterial changes of SAE are due to exposure of vessel walls to intraarterial pressure over

TABLE 2: Correlation Between Cerebral and Renal Arteriosclerosis

Grade of arteriolar nephrosclerosis	No. of Patients			
	Grade of Arteriosclerosis in Cerebral White Matter			
	0	1+	2+	3+
Abnormal group*				
0				
1+		1	3	
2+		1	1	5
3+			3	2
Normal group**				
0	1			
1+	1	3	1	1***
2+			1	
3+		1		

* Insufficient data on two patients; therefore, n = 16.

** Insufficient data on one patient; therefore, n = 9.

*** Very focal, limited extent, but severe.

TABLE 3: Associated Findings in Abnormal and Normal Groups

	CT Diagnosis	
	Abnormal (n = 18)	Normal (n = 10)
Hypertension	17	9
Dementia	7*	2*
Moderate or severe cerebral arteriosclerosis**	9	3
Brain infarcts:***	16	1
Lacunar (basal ganglia and thalami)	9	1
White matter only	7	0
Cerebral cortical	10	0
Myocardial damage from coronary atherosclerosis	13	2

* Two had Alzheimer's disease.

** Based on autopsy findings.

*** Based on autopsy and CT findings.

time seems quite possible. That is, the greater the pressure and/or the life span of the individual, the more likely are these changes to be present. It follows that wholly normotensive persons would develop these changes if they lived long enough. This is of course speculative. By CT, several of our hypertensive patients with SAE only had normal blood pressure recordings in the months (or, at most, few years) preceding their deaths. It seems plausible that a reduced cardiac output may have contributed to the preterminal normotension. This phenomenon might explain the absence of hypertension in some reported cases of SAE. That other factors, including genetic ones, might contribute to the development of SAE is open to speculation, although Rothemunde and Frische [3] studied many factors and found a positive correlation with arterial hyalinosis only for long-standing arterial hypertension.

The ultimate pathogenetic factor very well may be ischemia. Although an ischemic origin is difficult to prove, it seems quite tenable in view of the severity of vascular changes in the territory of deep perforating arteries and the sparing of subcortical U-fibers, which are within the territory of supply of cortical branches [26].

It is highly uncertain whether the eight cases reported by Binswanger in 1894 [27] were all examples of the disease that has come to bear his name. Binswanger described a predominance of findings in the temporooccipital white matter, a distribution likewise mentioned by Farnell and Globus in 1932 [16]. These reports used autopsy data only. More recent literature, reporting the use of CT or MR to identify areas of involvement, illustrates the pattern seen in our patients, specifically that of predominant involvement near the frontal horns and superolateral to the trigones [7, 8, 14, 15].

SAE is being recognized increasingly by modern imaging methods. It is common, and can be diagnosed reliably, but much remains to be learned about its origin, especially regarding the role of arterial hypertension and about its importance as a cause of dementia and perhaps other disorders.

REFERENCES

- Hughes W, Dodgson MCH, MacLennan DC. Chronic cerebral hypertensive disease. *Lancet* **1954**;2:770-774
- Okeda R. Morphometrische Vergleichsuntersuchungen an Hirnarterien bei Binswangerscher Encephalopathie und Hochdruck-encephalopathie. *Acta Neuropathol (Berl)* **1973**;26:23-43
- Rothemunde E, Frische M. Klinisch-pathologische Studie zur Entstehung der intracerebralen Gefasshyalinose beim Hypertonie. *Arch Psychiatr Nervenkr* **1973**;217:195-206
- Burger PC, Burch JG, Kunze U. Subcortical arteriosclerotic encephalopathy (Binswanger's disease). A vascular etiology of dementia. *Stroke* **1976**;7:626-631
- Janota I. Dementia, deep white matter damage and hypertension: "Binswanger's disease." *Psychol Med* **1981**;11:39-48
- Tomonaga M, Hiroki Y, Tohgi H, Kameyama M. Clinicopathologic study of progressive subcortical vascular encephalopathy (Binswanger type) in the elderly. *J Am Geriatr Soc* **1982**;30:524-529
- Goto K, Ishii N, Fukasawa H. Diffuse white matter disease in the geriatric population. A clinical neuropathological and CT study. *Radiology* **1981**;141:687-695
- Bradley WG Jr, Waluch V, Brant-Zawadzki M, Yadley RA, Wycoff RR. Patchy, periventricular white matter lesions in the elderly: common observation during NMR imaging. *Noninvasive Med Imag* **1984**;1:35-41
- Zeumer H, Hacke W, Hundgen R. Subkortikale arteriosklerotische Enzephalopathie. Klinische, CT-morphologische, und elektrophysiologische Befunde. *Fortschr Neurol Psychiatr* **1981**;49:223-231
- Pullicino P, Eskin T, Ketonea L. Prevalence of Binswanger's disease. *Lancet* **1983**;1:939
- Brant-Zawadzki M, Fein G, Van Dyke C, Kiernan R, Davenport L, de Groot J. MR imaging of the aging brain: patchy white matter lesions and dementia. *AJNR* **1985**;6:675-682
- Rosenberg GA, Kornfeld M, Stovring J, Bicknell JM. Subcortical arteriosclerotic encephalopathy (Binswanger): computerized tomography. *Neurology (NY)* **1979**;29:1102-1106
- Zeumer H, Schonsky B, Sturm KWQ. Predominant white matter involvement in subcortical arteriosclerotic encephalopathy. *J Comput Assist Tomogr* **1980**;4:14-19
- Loizou LA, Kendall BE, Marshall J. Subcortical arteriosclerotic encephalopathy: a clinical and radiological investigation. *J Neurol Neurosurg Psychiatry* **1981**;44:294-304
- Valentine AR, Moseley IF, Kendall BE. White matter abnormality in cerebral atrophy: clinico-radiological correlations. *J Neurol Neurosurg Psychiatry* **1980**;43:139-142
- Farnell FJ, Globus JH. Chronic progressive vascular subcortical encephalopathy. *Arch Neurol Psychiatr (Chicago)* **1932**;27:593-604
- Olzowski J. Subcortical arteriosclerotic encephalopathy. Review of the literature on the so-called Binswanger's disease and presentation of two cases. *World Neurol* **1962**;3:359-375
- Jellinger K, Neumayer E. Progressive subcortical vasculare Encephalopathie Binswanger. Eine klinisch-neuropathologische Studie. *Arch Psychiatr Z Ges Neurol* **1964**;205:523-554
- Aronson SM, Perl DP. Clinical Neuropathological Conference. *Dis Nerv Syst* **1974**;35:286-291
- DeReuck J, Crevits L, DeCoster W, Sieben G, vander Eecken H. Pathogenesis of Binswanger chronic progressive subcortical encephalopathy. *Neurology (NY)* **1980**;30:920-928
- Erkinjuntti T, Sipponen JT, Iivanainen M, Ketonen L, Sulkava R, Sepponen RE. Cerebral NMR and CT imaging in dementia. *J Comput Assist Tomogr* **1984**;8:614-618
- Caplan LR, Schoene WC. Clinical features of subcortical arteriosclerotic encephalopathy (Binswanger's disease). *Neurology (NY)* **1978**;28:1206-1215
- Brust JCM. Dementia and cerebrovascular disease. In: Mayeux R, Rosen WG, eds. *The dementias*. New York: Raven Press, **1983**:131-147
- Maeda S, Nakayama H, Isaka K, Aihara Y, Nemoto S. Familial unusual encephalopathy of Binswanger's type without hypertension. *Folia Psychiatr Neurol Jpn* **1976**;30:165-177
- Tanaka M, Ikuta F, Oyake H. Report of a case of chronic progressive subcortical encephalopathy (Binswanger's disease) unassociated with hypertension. *Clin Neurol (Tokyo)* **1969**;9:398-404
- DeReuck J. The cortico-subcortical arterial angioarchitecture in the human brain. *Acta Neurol Belg* **1972**;72:323-329
- Binswanger O. Die Abgrenzung der allgemeinen progressiven Paralyse. *Klin Wochenschr (Berl)* **1984**;31:1103-1105, 1137-1139, 1180-1186