

Expanding Cerebellar Lacunes Due to Dilatation of the Perivascular Space Associated With Binswanger's Subcortical Arteriosclerotic Encephalopathy

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An 80-year-old hypertensive woman developed right hemiplegia and died 24 hours after admission. Neuropathologic examination revealed multiple cerebral infarcts of various ages and diffuse subcortical arteriosclerotic encephalopathy. Clusters of asymptomatic "expanding" lacunes, due to dilatation of the perivascular spaces, were found in both dentate nuclei. These cavities, which presented as space-occupying lesions, were surrounded by a single layer of flattened cells and contained 1 or more sections of normal-looking arterioles. Such a topographic grouping of lacunes in the dentate nucleus has not been described previously. The mechanism of widening of the perivascular compartment remains unclear; its occurrence in a hypertensive patient and its association with typical Binswanger's subcortical arteriosclerotic encephalopathy and severe atherosclerosis with multiple infarcts suggest a common pathophysiologic mechanism possibly including an alteration of the blood-brain barrier. (*Stroke* 1987;18:1087-1092)

Cerebral lacunes are usually considered to be old, small, deep cerebral infarcts^{1,2} due to occlusive arterial lesions.^{3,4} However, old hemorrhages can be a cause of lacunes and have been recently reviewed.⁵ Dilatations of perivascular spaces, well known since the historic paper of Marie⁶ and the thesis of Ferrand,⁷ have been reemphasized recently as a possible mechanism of genesis of cerebral lacunes.^{8,9} To avoid the semantic confusion that surrounds the term cerebral lacune,¹⁰ a new neuropathologic classification has been proposed.^{11,12}

Lacunes due to dilatation of the perivascular space are usually asymptomatic.⁸ A new type of space-occupying lacune due to dilatation of the perivascular space was described as an "expanding cerebral lacune" by Poirier et al.⁹ In this initial report, the thalamo-mesencephalic "expanding lacunes" were responsible for clinical symptoms.

In this article, we report a new case of expanding lacune involving the cerebellum with three major points of interest: 1) the lesion was asymptomatic, presenting as an incidental autopsy finding, 2) the topographic grouping of lacunes in the dentate nuclei had never been described, and 3) the lacunes were associated with Binswanger's subcortical arteriosclerotic encephalopathy (SAE) and multiple cerebral infarcts. Such an association in a hypertensive patient suggests com-

mon pathogenetic mechanisms as the origin of these various lesions.

Report of a Case

An 80-year-old woman known to be hypertensive for many years had received various antihypertensive treatments. She suffered from left ventricular failure and coronary insufficiency. She was admitted to the hospital on March 8, 1983, because of dyspnea. Blood pressure was 170/100 mm Hg. She became somnolent, then comatose, and developed right hemiparesis 24 hours after admission and died within a few hours. Computed tomography (CT) scan was not obtained.

Postmortem examination revealed diffuse and severe atherosclerotic lesions in the thoracic and abdominal aorta and its main branches such as the carotid, iliac, coronary, and renal arteries. An old myocardial infarct involved the posterior part of the left ventricle.

The brain was sectioned after fixation for 1 month in 10% formalin. After horizontal section of the mesencephalon, the brain was cut in coronal slices and the cerebellum with the unseparated brainstem was cut in horizontal slices. Fourteen slices of the right and left cerebral hemispheres and 4 slices of the cerebellum and brainstem were embedded in celloidin. Several samples were embedded in paraffin. The sections were stained with hematoxylin and eosin, Loyez stain for myelin, Masson's trichrome, and Bodian silver impregnation combined with Luxol fast blue.

Results

Multiple infarcts of various ages were found. A recent infarct involved the superficial territory of the left middle cerebral artery (MCA) and an older one the white matter of the left temporal lobe; an old infarct had destroyed the deep territory of the left MCA; watershed infarcts bilaterally involved the cerebellum at

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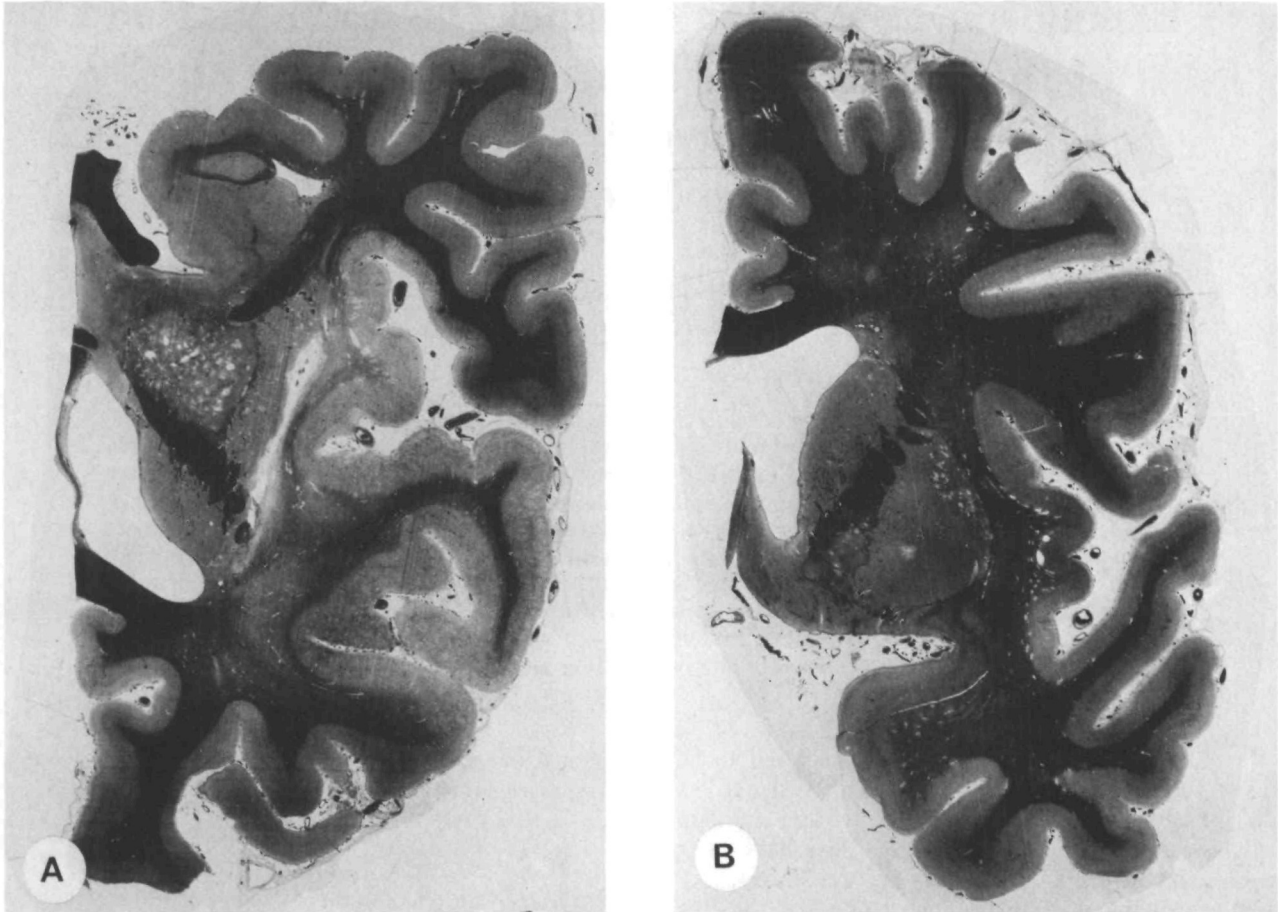


FIGURE 1. Coronal section of left hemisphere through the amygdala (A) and anterior part of the globus pallidus (B) showing spotty demyelination of the centrum ovale sparing the internal capsule and corpus callosum. Loyez stain.

the junction of the territories supplied by the posterior inferior cerebellar arteries and the superior cerebellar arteries. The basilar artery showed severe atherosclerotic lesions.

Diffuse, often spotty, myelin loss involved the centrum ovale (Figure 1) mainly on the left side, the white matter of the gyri, the internal and external capsules, the cerebellar white matter, and the pons; it spared the corpus callosum. Microscopic examination of the white matter showed edema, swollen oligodendroglia, spongiosis, incomplete loss of myelin, and astrocytic

gliosis with Rosenthal's fibers. There were numerous dilations of the perivascular spaces; they occasionally contained edema fluid and/or lipid or hemosiderin-laden macrophages. Some of them were large, forming macroscopic lacunes.

Similar lacunes, corresponding to dilatation of the perivascular space, varying in size from 0.1 to 5 mm², were also present bilaterally in the caudate nucleus, globus pallidus, putamen (Figure 2), and thalamus. The cortex was spared. These cavities, like those in the white matter, were round, regular, and lined by a sin-

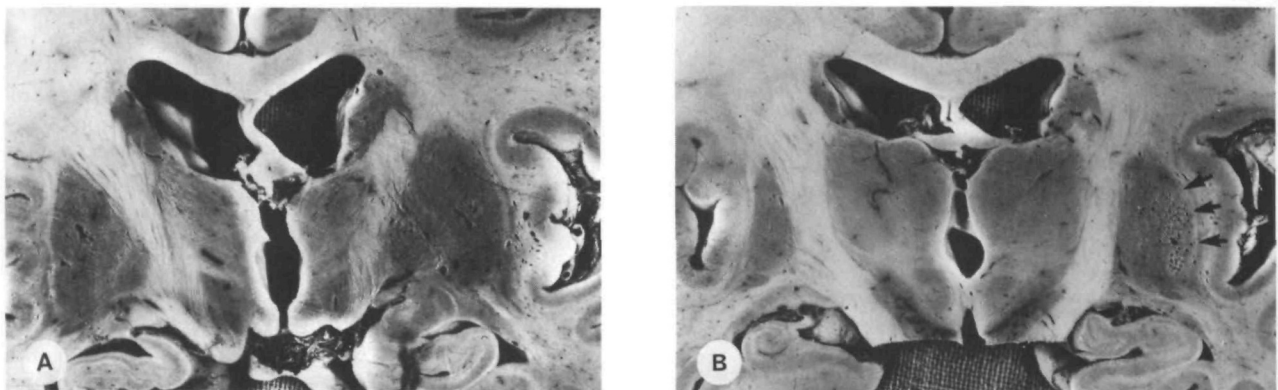


FIGURE 2. Coronal section of cerebral hemispheres through the mamillary bodies (A) and red nuclei (B). A: Type IIIa lacunes in both lenticular nuclei. B: Type IIIa lacunes or status cribrosus (arrows) in right putamen.

gle layer of epithelium-like cells (Figure 3). Each contained 1 or more sections of healthy-looking small arteries or arterioles. The surrounding parenchyma showed various degrees of edema, spongiosis, and reactive astrocytic gliosis with Rosenthal's fibers (Figure 3A). In the putamen, some of these cavities contained abnormal vessels that showed fibrosis of the wall, intimal thickening (Figure 3B), and hyalinization, which rarely narrowed the lumen. There was no amyloid angiopathy. The perforating arteries showed severe atherosclerotic lesions narrowing the lumen.

Lacunae of another type, corresponding to a small, deep infarct with irregular borders surrounded by marked astrocytic gliosis and containing residual tissue fragments and lipid-laden macrophages, were present in the lentiform nuclei but not in the white matter.

In the cerebellum, clusters of lacunae of various sizes due to dilatation of the perivascular space showed a characteristic grouping in the dentate nuclei (Figure 4A) involving the hilum of the left dentate nucleus in

particular (Figure 5). Some of the cavities overlapped the lamina, and very few were located outside the dentate nucleus. The largest cavity was a $5 \times 4 \text{ mm}^2$ cystic lesion located in the inferior part of the hilum of the left dentate nucleus (Figure 4B), which forced back the surrounding structures but did not destroy any tissue. A well-individualized small artery crossed the cavity, which was otherwise completely empty (Figure 4B).

Discussion

Neuropathologic examination showed various lesions in the brain of a hypertensive patient. Diffuse atherosclerosis and multiple cerebral infarcts were present; the most recent infarct found in the territory of the left MCA probably caused the hemiparesis and subsequent death of the patient.

The patient's medical history was very succinct, and no information on her previous mental status was available. However, her long history of hypertension, the macroscopic and microscopic appearance of the

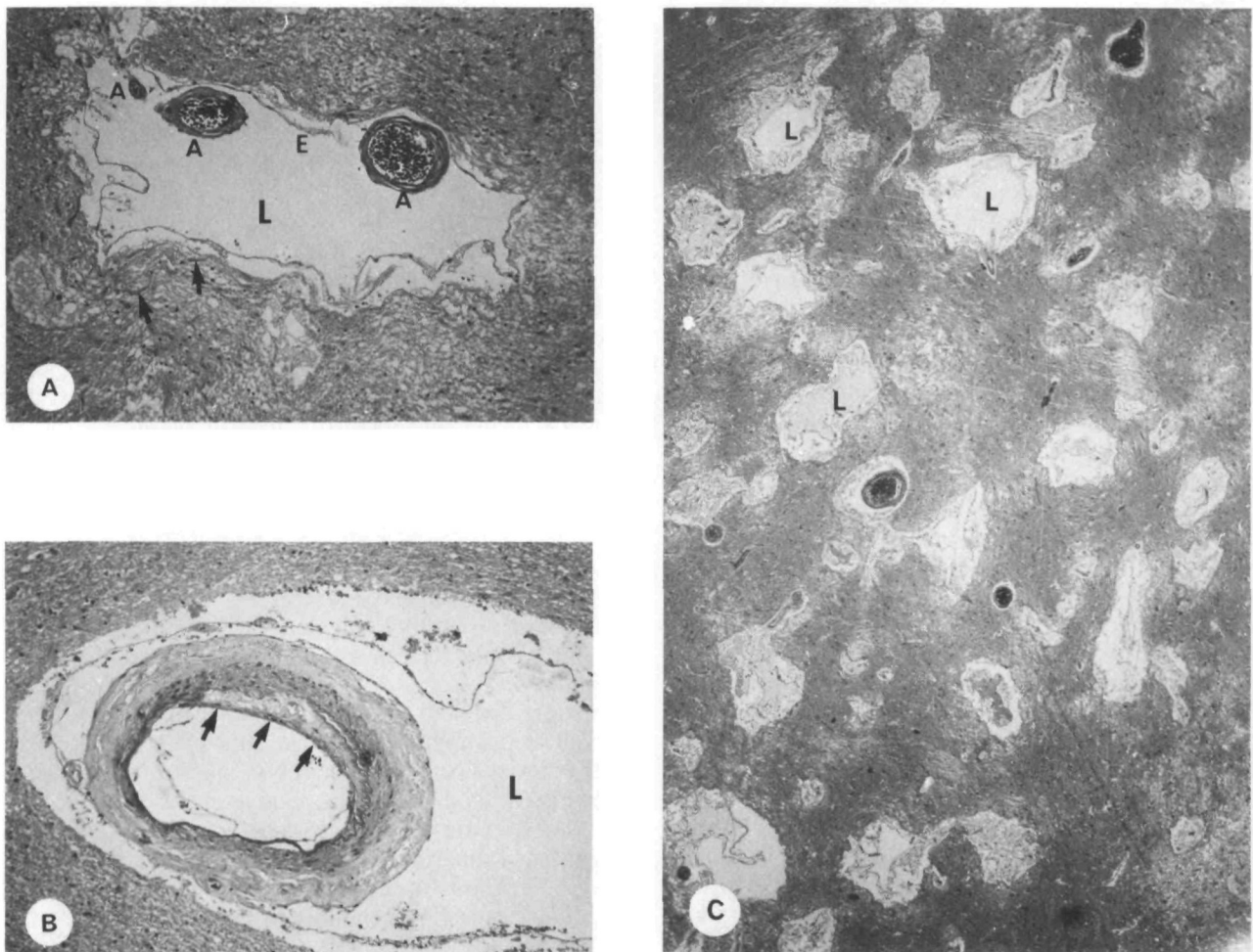


FIGURE 3. Microscopic appearance of the putamen. A: Type IIIa lacune (L) lined by a single-layered epithelium (E) and containing 3 sections of normal small arteries and arteriole (A). Surrounding parenchyma shows edema, spongiosis, and reactive astrocytic gliosis with Rosenthal's fibers (arrows). Hematoxylin and eosin stain, $\times 84$. B: Type IIIa lacune (L) containing abnormal but patent artery with fibrous intimal thickening (arrows). Hematoxylin and eosin stain, $\times 120$. C: Type IIIa lacunae (L), numerous, small, and lined by a single-layered epithelium. Hematoxylin and eosin stain, $\times 39$.

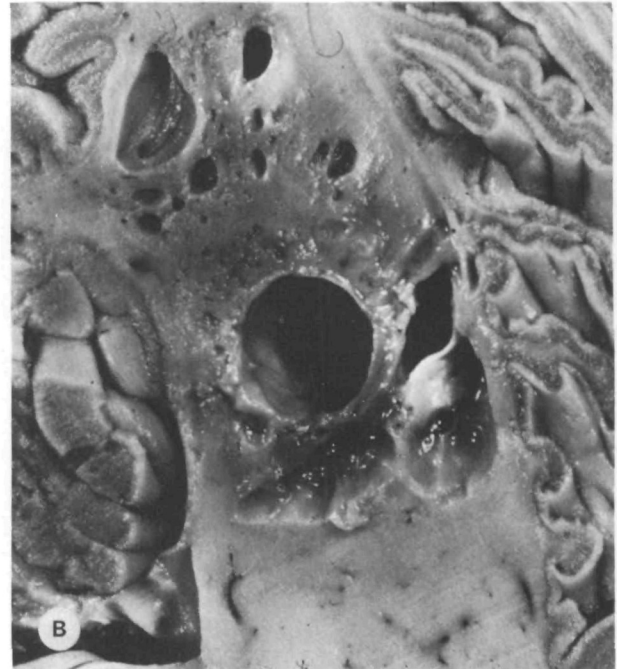
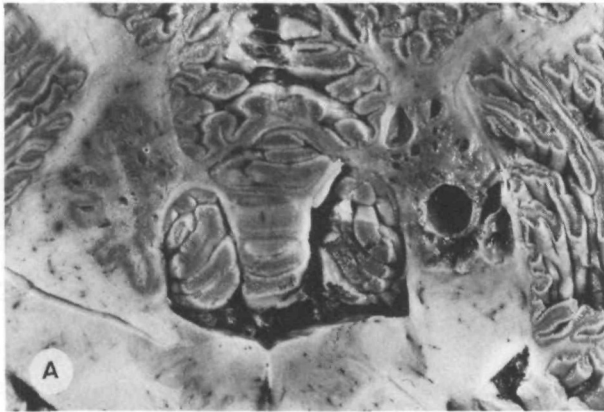


FIGURE 4. Horizontal sections of brainstem and cerebellum through dentate nuclei. A: Cluster of Type III lacunes of various sizes in dentate nuclei. B: Higher magnification of expanding lacune located in left dentate nucleus. The $5 \times 4\text{-mm}^2$ cystic lesion is round, regular, and has a smooth border; it is crossed by a small artery. This expanding cavity compresses surrounding structures.

cerebral white matter alterations, their association with numerous lacunes in the white matter and basal ganglia, and their sharp contrast to the almost-normal cortex were all typical of SAE.^{13,14}

The macroscopic cavities or lacunes had different microscopic appearances and corresponded to various pathologic processes. According to the neuropathologic classification proposed by Poirier et al,^{10,11} cerebral lacunes can be divided into 3 categories: Type I lacunes correspond to old, small, deep cerebral infarcts; they are irregular anfractuous cavities, devoid of any lining epithelium, and contain macrophages and small parenchymatous fragments, usually surrounded by marked astrocytic gliosis. Type II lacunes are old, small hemorrhages that are easily recognized by the presence of hemosiderin-laden macrophages and the iron pigmentation of their walls. Type III lacunes are due to dilatation of the perivascular space; they are round, very regular cavities and always contain 1 or 2 sections of an artery with a patent lumen and usually normal walls. The cavity is lined by a single layer of epithelial cells that correspond to the leptomenigeal cells forming the normal lining of the perivascular spaces.¹⁵ The surrounding parenchyma is usually depressed rather than destroyed. Apart from occasional Type I lacunes in the lentiform nuclei, most of the lacunes observed in our case were of Type III. Among this group, the multiple microscopic lacunes we observed in the white matter, basal ganglia, and dentate nuclei correspond to the status cribrus (*état criblé*) described by Durand-Fardel¹⁶ as many round, small holes (*criblures*), always containing a patent blood vessel and located in the hemispheric white matter (Type IIIa lacunes in the present classification¹¹). Some of the lacunes seen in the lentiform nuclei can be considered *lacunes de désintégration* (Type IIIb), which were first described by Marie,⁶ who claimed that

they were due to perivascular dilatation destroying the adjacent brain by a specific process he named *vaginite destructive*. Type IIIc lacunes⁸ are single subputaminal lacunes, known as solitary cavities, surrounding the lenticulostriate arteries at their entrance into the lentiform nucleus.⁶

The very unusual macroscopic appearance of the cluster of cavities found at the postmortem examination of the cerebellum might have been misleading. However, cerebral porosis¹⁷ or intraparenchymal neuroepithelial cysts¹⁸ were easily eliminated on microscopic grounds. In fact, these cerebellar cavities, like the multiple cavities disseminated throughout the white matter and most of those involving the basal ganglia, satisfied the histologic criteria of Type III lacunes according to the classification of Poirier et al.^{11,12} Moreover, the cystic lesions observed in the left dentate nucleus had all the features of Type IIIc or expanding lacunes: they formed round, regular cavities reaching a maximum of $5 \times 4\text{ mm}^2$; they were delineated by a single-layered, flat epithelium and contained a small artery with a patent lumen and normal walls; they looked like space-occupying lesions that compressed and thinned the adjacent parenchyma without destroying tissue; and they caused only reactive lesions such as astrocytic gliosis, spongiosis, swollen oligodendroglia, and myelin loss with edema.

Only 3 cases of similar space-occupying, "expanding," or Type IIIc lacunes have been previously reported.^{9,19,20} The first publication⁹ gave a precise description of expanding lacunes and reported the case of a 59-year-old nonhypertensive woman who developed progressive thalamic dementia. CT scan showed hydrocephalus and lacunar low densities in the mesencephalon and both thalami. Neuropathologic examination revealed space-occupying lacunes bulging into the third ventricle, squeezing the aqueduct, protruding

into the fourth ventricle, and situated in the territory of the paramedian mesencephalo-thalamic arterial pedicle. The cavities were round and regular and varied in size from 1 to 10 mm in diameter. Each cavity was lined by a single layer of epithelial-like cells. There

was no gliosis around the cavities except in the left thalamus. In almost all cavities, a normal small artery or arteriole was present. The vascular lumen was empty. Rare macrophages and lymphocytes were observed in the cavities. Multiple very small cavities of the same

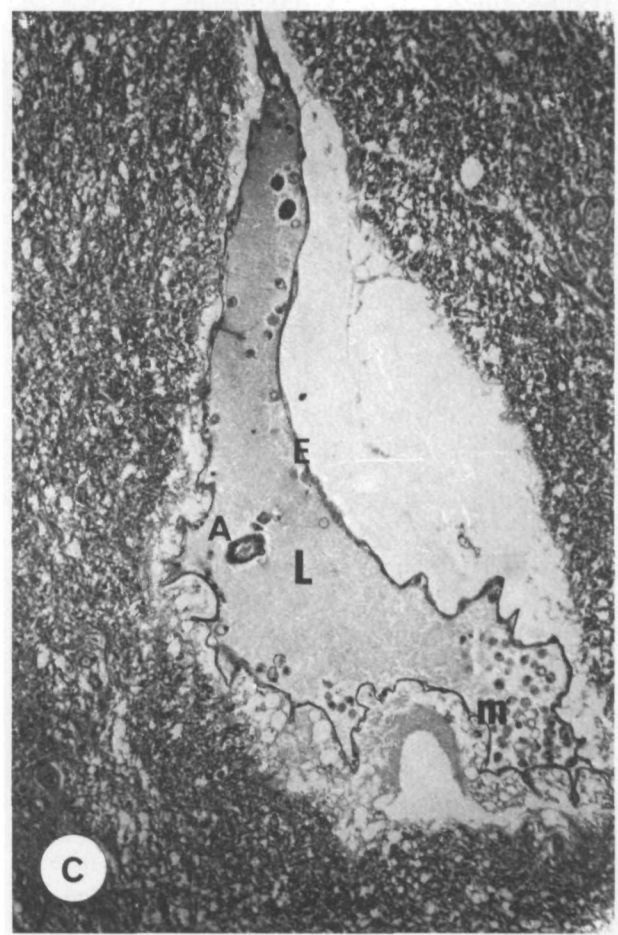
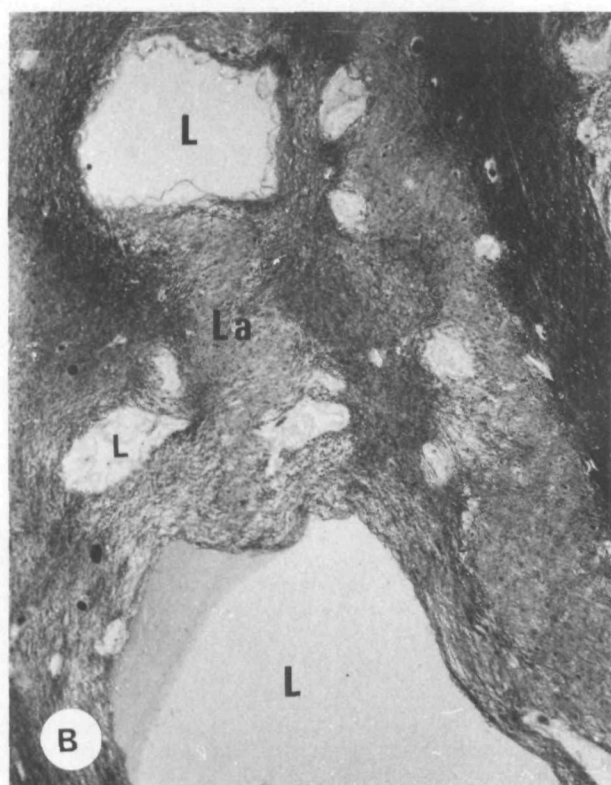
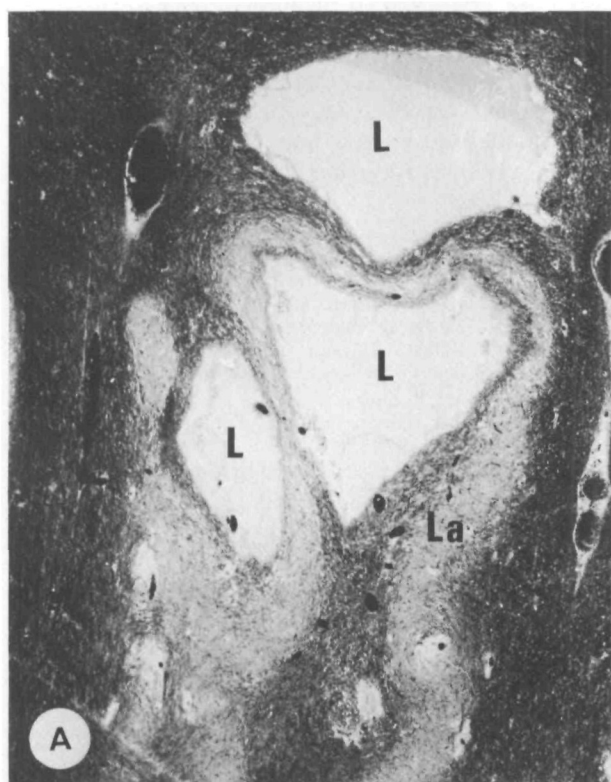


FIGURE 5. Microscopic appearance of dentate nucleus. A, B: Cluster of Type III lacunes (L) of various sizes involving mainly the hilum of the dentate nuclei. Some cavities overlap the lamina (La) and very few lie outside the dentate nucleus. The largest cavities displace surrounding structures, causing thinning of the lamina. Loyer stain, $\times 27$. C: Type III lacune (L) lined by single-layered epithelium (E) containing sections of arteriole (A), edema fluid, and macrophages (m). Surrounding parenchyma showed edema and spongiosis. Masson's trichrome stain, $\times 130$.

type were also found in the left pallidum. The patient was not hypertensive, but a paramedian mesencephalic artery showed severe lesions of segmental necrotizing angiitis of unknown etiology.

The authors⁹ found a rather similar case¹⁹ in the literature; a 70-year-old normotensive patient had developed a progressive psycho-organic syndrome and strokes. Neuropathologic examination showed “massive cavities” in the basal ganglia of both cerebral hemispheres, bulging into the lateral ventricle. Macroscopic and microscopic appearances of these cavities looked quite similar to those of the present case despite the absence of mention by the author of any epithelium around the cavities. Pilleri¹⁹ termed the condition “status cavernosus,” which he attributed to an as yet unrecognized vascular process.

Two almost symmetrical “expanding cerebral lacunes” bulging into the lateral ventricles with characteristic macroscopic and microscopic features were also described²⁰ in a 66-year-old hypertensive patient who had been treated for normal pressure hydrocephalus and who died from a thalamic hemorrhage. One of these lacunes was demonstrated on CT scan. These lesions were associated with various types of cerebral lacunes.

In our case, as in the case reported by Derouesné et al,²⁰ the patient's medical history was very poor, and because of the multiplicity of lesions, no clinical signs could be precisely related to the expanding lacunes.

The particular topographic grouping of the lacunes in the cerebellar dentate nucleus in our case is very unusual and has not been previously reported; however, some similarity may exist between Type IIIc giant lacunes, which develop around the perforating arteries of the basal ganglia, and the cluster of cerebellar lacunes, which developed around small perforating arteries of the dentate nucleus, seen in our case.

The mechanisms involved in the formation of the Type III lacunes are not clearly understood and are probably multiple. Dilatation of perivascular spaces is observed in cerebral atrophy as a result of shrinking of brain parenchyma. In elderly hypertensive patients, it has been suggested that dilatation of perivascular spaces could result from the mechanical stress caused by high blood pressure on brain arterioles.²¹ The usual association, in the literature^{13,14} as well as in our case, of SAE with Type III lacunes suggests that a common pathophysiologic mechanism can explain the development of both lesions. Subarachnoid hemorrhage is generally believed to be caused by a disruption of the blood–brain barrier due to episodes of high blood pressure causing focal vasogenic brain edema and/or chronic hypoxia related to arteriolar arteriosclerotic changes.¹⁴ An abnormality of arterial wall permeability may also explain the dilatation of the perivascular space forming Type III lacunes.⁹ The presence of segmental necrotizing angiitis of the artery supplying the involved territory in the case of Poirier et al⁹ and of severe arteriosclerotic lesions in our case and that of Derouesné et al²⁰ support this hypothesis. Our patient was hypertensive for a long time and had a severe and

diffuse atherosclerotic disease causing a myocardial infarct and multiple cerebral infarcts. These degenerative arteriolar changes secondary to severe hypertensive disease (arteriolar segmental degeneration or lipohyalinosclerosis) are also responsible for lacunar infarcts (or Type I lacunes)¹ that are usually associated with SAE and Type III lacunes.¹⁴

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