White matter lesions and normal-pressure hydrocephalus: Binswanger disease or Hakim syndrome?

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White Matter Lesions and Normal-Pressure Hydrocephalus: Binswanger Disease or Hakim Syndrome?

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In 1894, Otto Binswanger [1] described a clinical form of dementia in the elderly characterized by subcortical white matter lesions, "enormously enlarged ventricles," normal cerebral cortex, and "severe atheromatosis of the arteries of the brain" and concluded, "It is very likely that the subcortical loss of fibers is caused by the deficiency of the blood supply resulting from arteriosclerosis." This condition is known variously as subcortical arteriosclerotic encephalopathy, subcortical ischemic leukoencephalopathy, lacunar dementia, and Binswanger disease [2]. The presence of periventricular, deep white matter infarctions (DWMI) that spare the arcuate subcortical fibers is the typical hallmark of this condition.

In 1964, Salomón Hakim [3] published in Bogotá, Colombia, the description of a clinical triad of gait apraxia, incontinence, and dementia in adults with hydrocephalus and "normal" CSF pressure. The most striking feature of the syndrome was the possibility of a return to normal function after CSF shunting. Despite widespread disagreement on the terminology, Hakim syndrome currently is known as normal pressure hydrocephalus (NPH).

I have pointed out the difficulties in clinically separating Binswanger disease from NPH [2]. In fact, both entities are characterized by prominent changes in ambulation, such as small-step gait (marche à petits pas), gait apraxia, and frequent falls. A subcortical type of dementia, with changes in mood, behavior, and personality, is common in both, as well as pseudobulbar palsy, emotional incontinence, and frontal lobe signs with loss of incentive, drive, and insight. Profound apathy and abulia may be observed in advanced cases of both Binswanger disease and NPH. In both entities, mutism, bradykinesia, rigidity, and dysarthria may lead to confusion with Parkinson disease. Finally, urinary urgency and incontinence are early occurrences in both conditions.

The radiologic similarities between Binswanger disease and NPH also are illustrated in the article by Bradley et al. [4] in this issue of the AJNR. In addition to the aforementioned near identity of the clinical presentation, another point of departure for their study was the well-documented clinicopathologic observation of the frequent occurrence of hypertension and cerebrovascular disease in cases of idiopathic NPH [5, 6].

In their case-control MR study, Bradley et al. compare the presence and degree of periventricular hyperintensity in 55 patients with treated and untreated NPH and in 62 consecutive age-matched control subjects more than 60 years old. A highly significant statistical association (p < .001) was found between DWMI and NPH when compared with controls.

A second group of cases included 78 consecutive patients with MR evidence of periventricular hyperintensity who were presumed to have DWMI (or various stages of Binswanger disease by Román's terminology). No patient in this group was considered to have NPH clinically, but the study ascertained the presence and degree of communicating hydrocephalus in these patients. Again, a smaller, but still significant, statistical association (p < .05) was found between DWMI and communicating hydrocephalus.

The main shortcoming of the study by Bradley et al. is the assumption that all cases that showed periventricular hyperintensity on MR studies had DWMI. A proportion of these...
patients probably have état criblé [7, 8]. This is the term used for a dilatation of Virchow-Robin perivascular spaces, usually with thinning and pallor of the perivascular myelin and shrinkage, atrophy, and isomorphic gliosis of the parenchyma around the blood vessel. Arteries and arterioles in état criblé are generally thickened and ectatic and have sclerotic walls that show changes of fibrohyalinosis and fail to stain with Congo red, indicating absence of amyloid angiopathy. Damage of the blood-brain barrier occurs with increase in the water content of perivascular tissues and astrocytes, which explains the increase in MR signal intensity [9]. Although état criblé may represent the morphologic substrate of a progressive loss of autoregulation of cerebral blood flow, and therefore may indicate an enhanced risk for the development of senile dementia of the Binswanger type [2], most authors consider état criblé a normal, asymptomatic change of aging cerebral arterioles [10].

Nonetheless, this important study by Bradley et al. provides an interesting hypothesis on the possible pathogenesis of NPH and also offers a glimmer of understanding of the possible reasons why tests fail to predict a successful shunting procedure. It is clear that the net effect of the ventricular dilatation appears to be an increase in intristitial pressure in the brain parenchyma, manifested mainly in the periventricular regions [11]. As the perfusion of the periventricular regions proceeds in a centripetal pattern from the surface of the brain toward the ventricles by means of long medulary arteries, an increase in the intraventricular pressure may result in an opposite gradient of centrifugal pressure capable of producing ischemia of the watershed periventricular white matter. This is the probable explanation for the presence of possible lesions of Binswanger disease in 95% of patients who have shunts placed because of Hakim syndrome. Another probable cause of periventricular white matter hyperintensity in NPH could be diffusion of CSF into these areas.

A loss of autoregulation of cerebral blood flow in the elderly is probably important in increasing the risk for watershed infarctions. Striking loss of reactivity of the cerebral blood vessels in response to IV acetazolamide can be shown by single-photon emission CT (SPECT) in elderly patients [12, 13], most likely resulting in DWMl during episodes of hypotension or cardiac arrhythmias.

A correlation between reversibility of NPH and increased aqueductal CSF velocities as a reflection of appropriate cerebral blood flow also is postulated by Bradley et al. [4]. This interesting concept incorporates previous ideas involving tensile strength, systolic pressure waves, and CSF circulation. Whether this test will be a more reliable index of therapeutic success remains to be demonstrated. However, the main importance of the article by Bradley et al. is to call attention to the much forgotten relationships existing between cerebral blood flow and CSF circulation and to the occurrence of ischemic periventricular lesions in patients with NPH and in elderly patients with communicating hydrocephalus. Extensive ischemic periventricular white matter lesions may signal the point of no return for surgical treatment of these patients. Therefore, early diagnosis and treatment of NPH would be advisable, before extensive ischemia occurs.

What, if any, is the etiologic relationship between arterial hypertension and NPH? The answer still eludes us. However, if arterial hypotension clearly results in decreased production of CSF, the missing link quite simply may be an increase in CSF production in hypertensive subjects leading to ventricular dilatation and manifested by increased aqueductal CSF velocity. Further research using new imaging techniques, such as SPECT and gated high-resolution MR imaging, should provide a better understanding of the pathogenesis, prevention, and treatment of the entities described by Binswanger and Hakim.

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