OBSERVATION

Ventricular Wall Granulations and Draining of Cerebrospinal Fluid in Chronic Giant Hydrocephalus

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Background: In rare cases, adults with normal or almost normal cognition may have giant brain ventricles surrounded by a sliver of brain. Because the usual flow of cerebrospinal fluid (CSF) is interrupted in these individuals, they may develop alternative CSF pathways to preserve brain function.

Objective: To describe novel morphologic autopsy findings in a patient with chronic giant hydrocephalus that suggest the existence of alternative CSF draining pathways.

Design: Case report.

Setting: Autopsy study.

Patient: A 48-year-old man with chronic compensated hydrocephalus associated with a Dandy-Walker malformation.

Main Outcome Measure: Autopsy findings.

Results: We observed microscopic structures on the ventricular wall that may facilitate CSF resorption. Their histologic appearance, reminiscent of pacchionian granulations, showed the opposite relation in regard to CSF/blood compartments: whereas the core of a pacchionian granulation contains CSF and the granulation is bathed in blood of the venous sinus, the core of the ventricular granulation in our patient contained venules, with the granulation bathed in ventricular CSF.

Conclusions: These previously unreported (to our knowledge) ventricular wall granulations may facilitate draining of CSF into the venous system when CSF outflow from the ventricular system is occluded. The presence of these ventricular structures illustrates biologic adaptation to anomalous conditions and successful compensation.

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DEVELOPMENTAL VENTRICULOMEGALY may yield few clinical signs but has a striking appearance on magnetic resonance imaging (MRI).[1,2] Individuals such as the 44-year-old woman whose brain images are illustrated in **Figure 1** may lead normal lives. She did well in school, works as an administrator for a government agency, and speaks 7 languages. Her global IQ is 98, and her head circumference is abnormally large (62 cm). On MRI performed for an incidental headache, the lateral and third ventricles were markedly enlarged, and the sylvian aqueduct was occluded (Figure 1B). Although reliable data are lacking in similar subjects, cerebrospinal fluid (CSF) production likely continues, given the importance of CSF flow.[4,5] In symptomatic human hydrocephalus, the pressure of the retained CSF on the brain causes impaired arteriolar perfusion.[6] In the woman whose MRI is illustrated in Figure 1, despite the appearance of compression of the brain against the skull, arteriolar perfusion measured by the pulse arterial spin labeling technique was normal in both the white matter and the gray matter.[3] Brain metabolism as measured using positron emission tomography with fluorine-18 fluorodeoxyglucose was also normal (Figure 1E and F).[3]

The question arises as to how patients with occluded CSF outflow and giant hydrocephalus can compensate for this structural abnormality. In a man with Dandy-Walker malformation and similarly massive hydrocephalus, we observed microscopic structures on the wall of dilated ventricles that could facilitate absorption of CSF from the ventricles into

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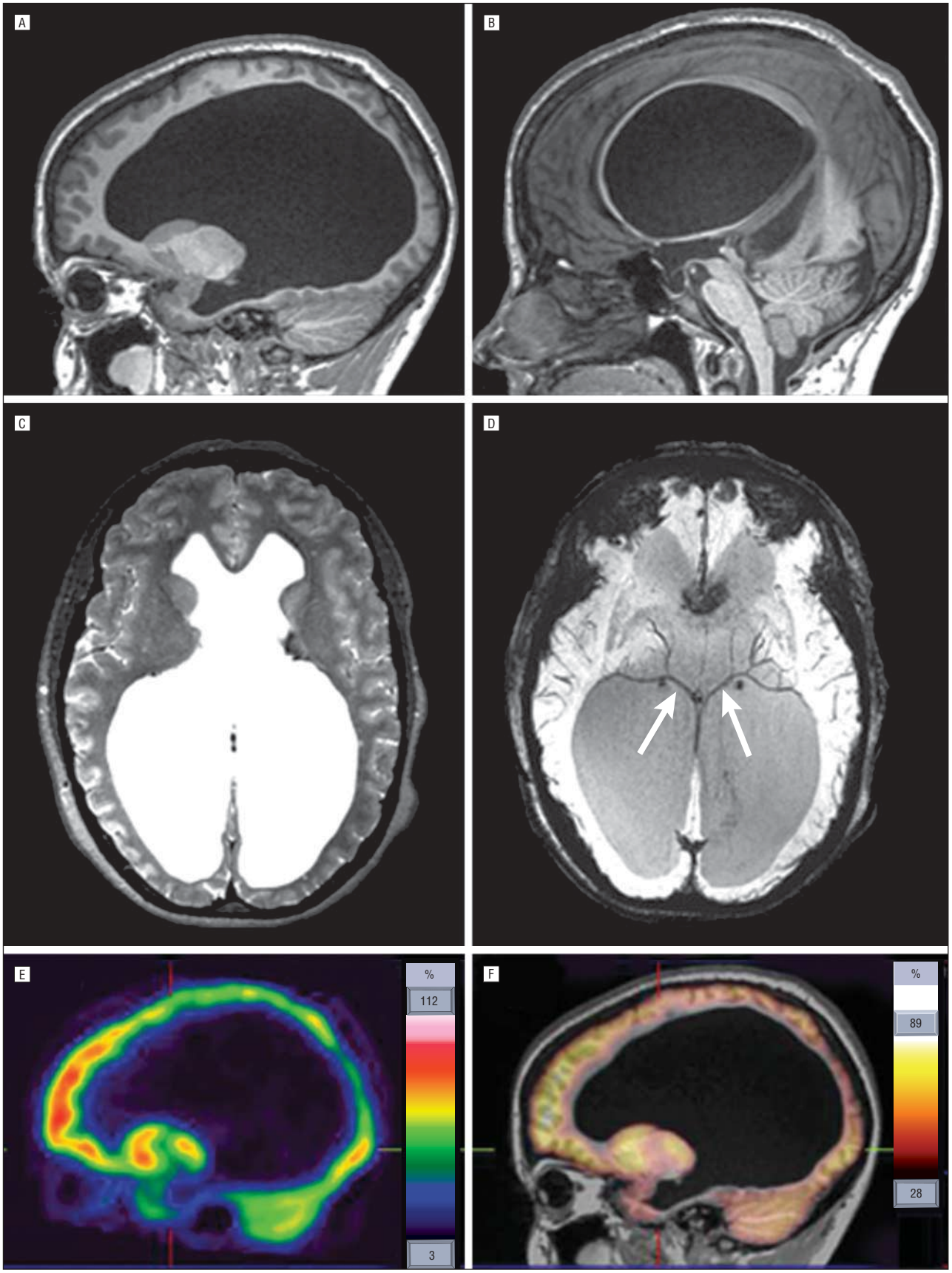

Figure 1. Brain images of an administrator who speaks 7 languages.[3] Magnetic resonance (MR) images and positron emission tomography (PET) with fluorine-18 fluorodeoxyglucose images are from a 44-year-old woman with giant hydrocephalus and normal cognition. Shown are T1-weighted lateral (A) and midline (B) sagittal MR images. C, T2-weighted axial MR image. D, Susceptibility-weighted axial MR image. The thalamostriate veins draining the ependymal veins (arrows) are similarly prominent in the brain of our other patient with a Dandy-Walker malformation (Figure 2A). E, Sagittal PET image at the level of A. F, Result of superimposing A and E.

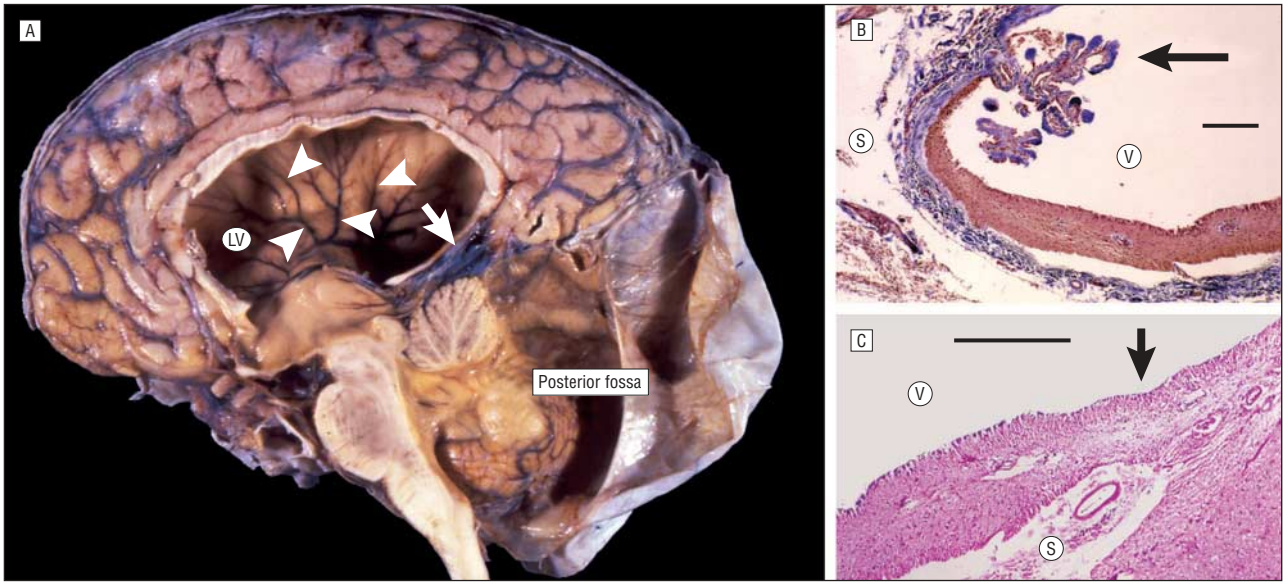

Figure 2. Brain images of our patient with a Dandy-Walker malformation. A, Mediosagittal view of the brain. The ependymal veins (arrowheads) and the internal cerebral veins (arrow) draining them are unusually large. Also shown are light micrographs of the choroid plexus (B, horizontal arrow) and the point where the ventricle normally communicates with the subarachnoid space (C, vertical arrow) through the foramen of Luschka, absent here. LV indicates lateral ventricle; S, subarachnoid space; V, ventricle; and scale bars, 1 mm (Masson trichrome [B] and hematoxylin-eosin [C]).

the venous system, normalizing CSF flow by an alternate route.

REPORT OF A CASE

A 48-year-old man had an IQ of 90 and an enlarged head circumference (67 cm). Since childhood, he had experienced occasional seizures, controlled with phenytoin treatment, but was gainfully employed and had served in the military. At age 48 years, a posterior fossa tumor was suspected because he had developed ataxia and nystagmus. A pneumoencephalogram (performed in 1978) revealed massive hydrocephalus. A ventriculoperitoneal shunt was placed. Within a few days, he developed peritonitis, followed by brief meningitis, which was treated and rendered sterile. However, hematemesis and bronchopneumonia led to his death. After written informed consent was obtained from the next of kin, an autopsy was performed.

The unfixed brain and meninges, partially drained, weighed 1660 g. Once fixed in 10% formalin solution, the brain with its coverings was sectioned in the sagittal plane (**Figure 2**A). After obtaining 1-cm-thick coronal sections of the right hemisphere, tissue blocks were obtained for histologic examination from the following: medulla, thalamus, hippocampi, middle frontal gyrus, caudate nucleus, calcarine cortex, cerebellar hemispheres, posterior fossa cyst wall, wall of the lateral ventricle, putamen and globus pallidus, junction of the cyst with the medulla, paraventricular cerebellar white matter, cerebellar remnants of the inferior vermis, and third ventricular wall at the level of the mammillary bodies. Paraffin-embedded 5-μm tissue sections were cut and stained with hematoxylin-eosin.[7] Selected sections were stained with Masson trichrome, elastica–van Gieson, and periodic acid–Schiff.[7]

FINDINGS

The autopsy revealed a Dandy-Walker malformation. Some imaging and gross pathologic findings have been reported elsewhere (case I in the study by Masdeu et al[8]). The ventricles were markedly enlarged, with prominent ependymal veins (Figure 2A). Because the choroid plexus was present (albeit smaller than normal), it was assumed that CSF was being secreted into the ventricles (Figure 2A and B). The CSF drainage was compromised because the foramina of Luschka and Magendie had not been formed (Figure 2C). A pressure gradient was likely created by air entering the ventricles during pneumoencephalography, causing dehiscence in the cyst wall, formed of a thin layer of glial tissue lined with ependymal cells on the ventricular side and of an outer layer of arachnoid tissue (Figure 2B and C). Other than the cyst wall, the wall of the ventricles was mostly devoid of normal ependymal lining but showed no inflammatory changes (**Figure 3**A). In about 15% of the sampled ventricular wall, particularly adjacent to draining ependymal veins, there were clusters of venules separated from CSF in the ventricle by a thin layer of glial tissue (Figure 3B-D). On the ventricular wall of the frontal horns near the draining system of a prominent thalamostriate vein (Figure 2A), there were other peculiarly shaped structures. Protruding from the wall into the ventricular CSF, they contained a cluster of venules similar to the structures shown in Figure 3 but were larger (**Figure 4**). The venules were separated from CSF by a fluffy lining with staining characteristics similar to those of astrocytic tissue (Figure 4C and D). The base contained collagenous material similar to the adventitia of larger veins. It is possible that these structures derived from ependymal veins. Their base was rounded, but their ventricular aspect (in contact with

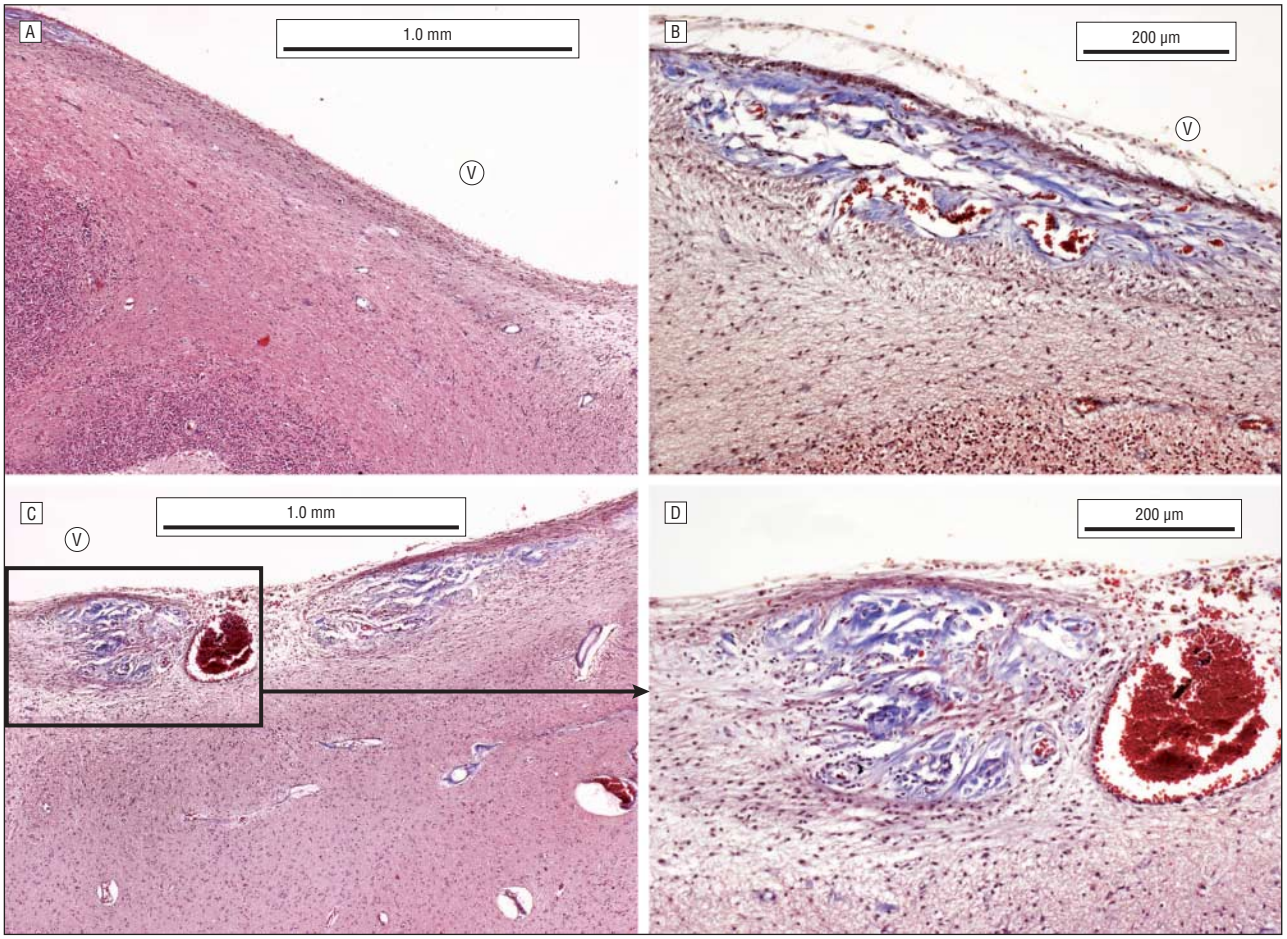

Figure 3. Wall of the fourth ventricle. A, Light micrographs stained with Masson trichrome showing that the normal ependymal lining of the fourth ventricle has been shorn and replaced by a lining of astrocytes. B-D, At places, there are clusters of venules near the ventricular fluid, separated from it by a layer of astrocytes. The wall of the venules has connective tissue, stained blue. Red blood cells in the venules are best seen at higher magnification (B and D [D shows details of boxed portion of C]). There is no ependymal inflammation, and the white matter is not edematous. V indicates ventricle.

CSF) was markedly folded, increasing the surface exposed to CSF and facilitating CSF resorption into the venous channels in the core of the structure (Figure 4).

COMMENT

Compensatory mechanisms in long-standing giant hydrocephalus are poorly understood.[4,9] In acute experimental hydrocephalus induced by outflow blockage, the ventricles initially expand and then stabilize.[10] The CSF absorption occurs through the wall of the dilated ventricles and, in experimental animals and probably in humans, through brain capillaries.[11,12] In an experimental model of chronic hydrocephalus, compensation is partly accomplished through vascular proliferation in the deep white matter, which increases CSF clearance by the transependymal route.[9,13] Oi and Di Rocco[11] stressed that transependymal drainage, referred to as the "minor CSF pathway," is the main route for CSF dynamics in lower mammals and during developing stages of the human brain. This pathway may become particularly prominent in subjects with obstructed outflow from the ventricles. The novel vascular structures on the ventricular wall in our patient may be hypertrophied remnants of this primitive system and may facilitate CSF flow from the ventricles into the venous system.[3] The higher osmotic pressure in the blood of the ventricular wall venules, compared with that in CSF, would favor the movement of water from ventricular CSF to venous blood.

The finding described herein is morphologic. The function of these ventricular wall structures can only be postulated from their location and type of tissue. Proof of their function would require visualization in a live subject of flow from the ventricle into the venous system. This flow is probably slow, unlike the flow visualized using techniques such as cardiac-gated phase-contrast cine MR imaging.[14] The flow could be studied by using soluble contrast ventriculography and computed tomography[11] or by using intraventricular gadopentate dimeglumine and MR imaging.[15]

It is unclear why the subependymal venous structures described herein have not been previously reported (to our knowledge) in humans. A possible reason is the location of the brain blocks routinely obtained for neuropathologic analysis, which usually do not include some of the regions in which we observed these changes. Even in our patient, we did not sample the ventricular wall extensively enough to obtain an exact measurement of the area covered by the structures we report. The percentage given in the "Findings" section is

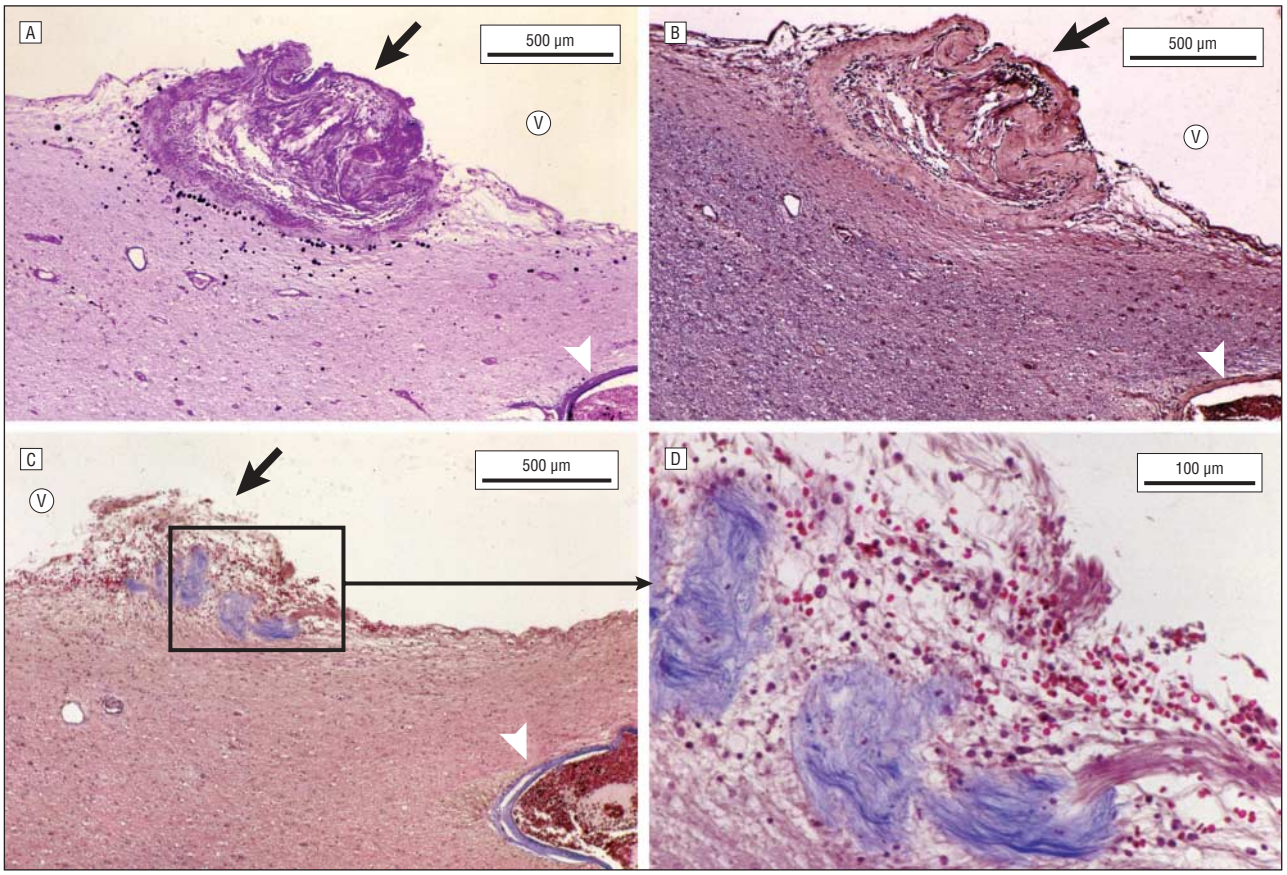

Figure 4. Wall of the lateral ventricle. A-D, Light micrographs showing peculiar clusters of venules and capillaries on the wall of the lateral ventricle (thick arrows) (D shows details of boxed portion of C). All micrographs were obtained from adjacent sections, as can be appreciated by comparing the venule in the right lower corner of each micrograph (arrowheads). The aspect of the cluster facing the ventricle (V) is markedly wrinkled, allowing for greater surface exposure. The base is formed by collagenous material, staining similarly as the wall of the venule (arrowheads) (periodic acid–Schiff [A], elastica–van Gieson [B], and Masson trichrome [C and D]).

based on a small sample of the ventricular wall and is a gross approximation. Similar to pacchionian granulations, poorly formed in infants and well formed in adults,[11] it is likely that these ventricular granulations develop over time in individuals with chronic hydrocephalus. Their absence in children may be another reason why they have not been previously reported in humans, as many autopsied hydrocephalus cases represent the pediatric age group.[4]

A general mechanism cannot be hypothesized on the basis of a single case. The ventricular wall structures we observed should not be assumed to explain functional compensation in other individuals with chronic giant hydrocephalus such as the woman described in the introduction of this article. However, we expect that a search for similar structures in other patients with well-compensated giant hydrocephalus may follow this report of our observation, with possible organization of a collaborative study. The development of these ventricular structures illustrates an adaptation by nature to unfavorable circumstances to circumvent a problem and to restore function.

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