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Negative-pressure and low-pressure hydrocephalus: the role of cerebrospinal fluid leaks resulting from surgical approaches to the cranial base

Report of 3 cases

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Object. Negative-pressure and low-pressure hydrocephalus are rare clinical entities that are frequently misdiagnosed. They are characterized by recurrent episodes of shunt failure because the intracranial pressure is lower than the opening pressure of the valve. In this report the authors discuss iatrogenic CSF leaks as a cause of low- or negative-pressure hydrocephalus after approaches to the cranial base.

Methods. The authors retrospectively reviewed cases of low-pressure or negative-pressure hydrocephalus presenting after cranial approaches complicated with a CSF leak at their institution.

Results. Three patients were identified. Symptoms of high intracranial pressure and ventriculomegaly were present, although the measured pressures were low or negative. A blocked communication between the ventricles and the subarachnoid space was documented in 2 of the cases and presumed in the third. Shunt revisions failed repeatedly. In all cases, temporary clinical and radiographic improvement resulted from external ventricular drainage at subatmospheric pressures. The CSF leaks were sealed and CSF communication was reestablished operatively. In 1 case, neck wrapping was used with temporary success.

Conclusions. Negative-pressure or low-pressure hydrocephalus associated with CSF leaks, especially after cranial base approaches, is difficult to treat. The solution often requires the utilization of subatmospheric external ventricular drains to establish a lower ventricular drainage pressure than the drainage pressure created in the subarachnoid space, where the pressure is artificially lowered by the CSF leak. Treatment involves correction of the CSF leak, neck wrapping to increase brain turgor and allow the pressure in the ventricles to rise to the level of the opening pressure of the valve, and reestablishing the CSF route. *(DOI: 10.3171/2011.6.JNS101504)*

Key Words • **cerebrospinal fluid** • **hydrocephalus** • **negative pressure** • **leak** • **low pressure** • **neck wrapping**

Negative-pressure and low-pressure hydrocephalus cases are clinical entities distinct from other types of hydrocephalus. Both entities are defined by the presence of very low or negative ICP and ventriculomegaly. The presentation is quite rare and has been described in patients with subarachnoid hemorrhage,[5,21,29,32] intraventricular hemorrhage,[21] lumbar puncture,[9] meningitis,[21] posterior fossa tumors, congenital aqueductal stenosis, spinal arachnoid cysts,[39] hemispherectomy,[7] and normal-pressure hydrocephalus.[4,5,28,29,35] Patients with low- or negative-pressure hydrocephalus frequently undergo multiple shunt revisions, without success in reversing the signs of ventriculomegaly. The neurological clinical course is insidious. Patients show a declining level of consciousness and function, with decreases in areas such as appetite, energy, speech, motor function, and balance. Although low pressure is the cornerstone of the definition, the clinical picture is similar to ventriculomegaly associated with high ICP symptoms in that they share signs and symptoms such as low level of consciousness, headaches, vomiting, and cranial neuropathies.[29,35,39]

Abbreviations used in this paper: CSAS = cortical subarachnoid space; ECF = extracellular fluid; ETV = endoscopic third ventriculostomy; EVD = external ventricular drain; ICP = intracranial pressure; VP = ventriculoperitoneal.

The underlying pathophysiology leading to ventriculomegaly with low ICP and symptoms resembling intracranial hypertension is complex. In this report we describe 3 patients who developed negative- or low-pressure hydrocephalus after undergoing a cranial approach for treatment of a ruptured posterior inferior cerebellar artery aneurysm, a vermian cavernous malformation, and a dissecting aneurysm of the left internal carotid artery terminus. These patients developed CSF leaks and required VP shunt placement at some point in their clinical course.

Case Reports

We retrospectively reviewed 3 cases of negative- or low-pressure hydrocephalus complicating cranial base approaches with CSF leaks at our institution. Each case is described and the origin and course of treatment for this condition are discussed.

Case 1

This 61-year-old man with a ruptured left posterior inferior cerebellar artery aneurysm presented with a severe subarachnoid hemorrhage with a bilateral intraventricular contribution. The aneurysm was clipped through a far-lateral craniotomy, and due to ventricular blood casts, bifrontal EVDs were placed to treat his posthemorrhagic hydrocephalus. A CT scan obtained on the 2nd postoperative day demonstrated normal ventricle size and a fluid collection adjacent to the craniectomy site resembling a pseudomeningocele. On the 5th postoperative day, CT showed that the size of the ventricles had increased and the size of the fluid collection was stable. Given concerns about underdrainage, the catheter from the right frontal horn was replaced.

On postoperative Day 8, the patient became febrile, and CSF studies revealed a high cell count and leukocytosis. An evaluation for infectious diseases revealed meningitis caused by a gram-negative rod. Antibiotic therapy, tailored to infectious diseases consultations and CSF cultures, was initiated and the bifrontal EVDs were replaced on the 20th postoperative day.

The patient was extubated on the 11th postoperative day. A CT scan obtained the same day showed ventriculomegaly and a stable fluid collection as described previously in the subcutaneous tissue at the craniectomy site. The ventriculomegaly noted on the CT scan was attributed to an obstructed right frontal EVD catheter. Subsequently, the catheter was replaced with a right parietooccipital VP shunt. The patient was discharged in good condition.

Two days later he was acutely readmitted due to a decreased level of consciousness. A CT scan of the head revealed ventriculomegaly (Fig. 1A). The shunt was not working and the workup gave us the impression of a distal shunt failure, so treatment was initiated. The shunt was revised, but the patient's symptoms and ventriculomegaly did not improve. As a part of his workup, an attempt was made to place a lumbar drain. During the placement of the drain, however, it was extremely difficult to obtain adequate CSF flow. The question of a significant block between the cortical subarachnoid space (CSAS) and spinal subarachnoid space was raised. A nuclear scan using infusion of Tc-99m DTPA in the shunt showed that the radionucleotide tracer progressed no further than the patient's occiput, indicating the presence of an obstruction.

The patient underwent a VP-to-ventriculopleural shunt conversion, but his hydrocephalus still failed to resolve. At this point, suspicion for negative-pressure hydrocephalus was further explored and confirmed. A subatmospheric EVD (draining to gravity) was placed.[29] Neck wrapping with an elastic bandage to increase venous pressure in the head resulted in smaller ventricles and complete resolution of the hydrocephalus (Fig. 1B). Removal of the neck wrap resulted in the return of his ventriculomegaly (Fig. 1C). The patient was followed up with serial CT scans, which demonstrated resolving hydrocephalus. The drain was then clamped, and 12 days later a shunt revision to a Codman-Hakim VP shunt set at 30 mm H_2O was performed.

During the next 6 years, the patient underwent multiple shunt revisions. In 2009 the patient was admitted due to increased lethargy, dyspnea, and confusion, and an iatrogenic Chiari malformation was diagnosed. His far-lateral craniotomy was reexplored to clear scar tissue in the area and to seal the CSF leak that was presumed to be the cause of his pseudomeningocele. Thereafter, the patient underwent a shunt revision to a programmable ventriculoatrial shunt at 30 mm H_2O without an antisiphon device. He recovered well. According to the charts, the last follow-up was 2 months after the last intervention. At this time point the patient was readmitted due to a shunt infection without any indications of previous episodes of negative-pressure hydrocephalus or headaches.

Case 2

This 67-year-old man had a history of a vermian cavernous malformation extending into the fourth ventricle and a dural arteriovenous fistula, which had been embolized and irradiated with the Gamma Knife. The patient underwent a suboccipital craniotomy down to C-1 for the excision of the vermian cavernous malformation. Due to bleeding from the floor of the fourth ventricle, cottonoid packing was used; closure of the craniotomy was inadequate.

Postoperatively, the patient developed a cerebellar stroke with subsequent cerebellar swelling, which required reopening of the suboccipital craniotomy and removal of the cottonoid and bone flap. The cerebellum was partially resected to reduce the pressure in the posterior fossa, after which a CSF leak developed. After an adequate recovery, the patient was discharged for rehabilitation. Ten days later he returned with signs and symptoms of hydrocephalus, and a CT scan showed ventriculomegaly. When draining CSF at 20 cm below head level we saw a decrease in ventricular volume and improvement in the neurological condition. A VP shunt and ICP monitor were placed and indicated the presence of negative-pressure hydrocephalus. A CT scan repeated 3 days later did not show any difference in the size of his ventricles. A retrocerebellar pseudomeningocele related to a CSF leak was present, and the patient underwent surgical exploration of the craniectomy to seal the leak. Postoperative CT scans showed no change in the size of his ventricles.

Consequently, CT ventriculography was scheduled

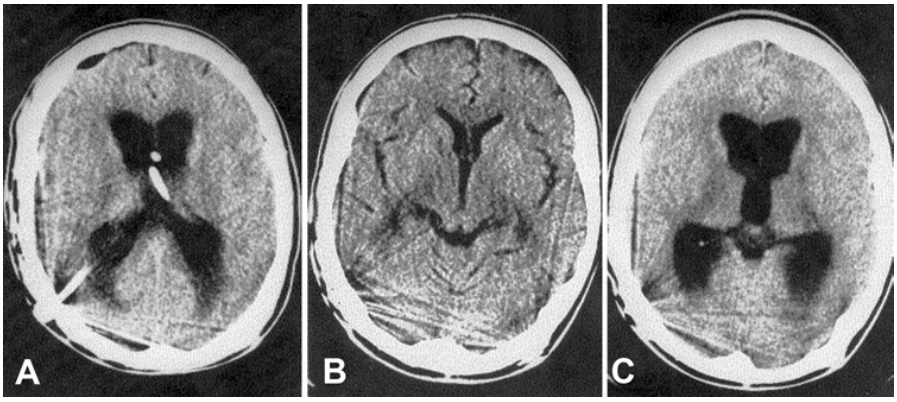

Fig. 1. Case 1. **A:** A CT scan obtained on postoperative Day 5 showing ventriculomegaly. **B and C:** CT scans showing resolution of the ventriculomegaly after neck wrapping **(B)** and recurrence of ventriculomegaly when the neck wrap is removed **(C)**.

to identify any points of blockage along the CSF pathways. There was no communication between the ventricles and the posterior subarachnoid space; therefore, the patient underwent placement of an EVD and an ETV to reestablish it. Postoperatively, the patient exhibited signs of ETV failure. The patient's condition declined for 6 weeks. After long conversation with his wife, treatment was withdrawn.

Case 3

This 56-year-old woman presented to the emergency room with an extensive subarachnoid hemorrhage. Diagnostic angiography revealed a dissecting aneurysm of the left internal carotid artery terminus and a right posterior communicating artery aneurysm. The aneurysms were treated by surgical clipping via an orbitozygomatic craniotomy. Ultimately, the patient required shunt placement and was discharged to a skilled nursing facility in stable condition.

Fourteen months after the initial surgical clipping of the aneurysms, the patient returned to our institution with symptoms of hydrocephalus, ventriculomegaly, and concerns about shunt failure (Fig. 2 left). Shunt revision failed to reverse her persistent ventriculomegaly and symptoms of hydrocephalus. After revision of the shunt, a skull defect at the site of the orbitozygomatic craniotomy into the frontal sinus was identified and a CSF leak was present (Fig. 2 right). The repair of the skull base defect CSF leak resulted in recovery and partial reversal of her clinical picture of hydrocephalus.

Discussion

Low-pressure and negative-pressure hydrocephalus cases are complex and rare clinical entities. These 3 representative cases come from a total of 20 or fewer cases of negative-pressure hydrocephalus in a neurosurgical practice of 25 years that has included approximately 7500 shunt procedures. Clinical suspicion for low- or negative-pressure hydrocephalus should be high when patients with enlarged ventricles have repeated "shunt failures" that do not improve with shunt revisions, and present with a CSF leak and loss of patency between the ventricles and the cortical subarachnoid space. The clues to understanding the changes in ventricular size in these types of hydrocephalus are transmantle pressure and brain turgor, the intrinsic property of the brain to resist distortion. Selective drainage of the CSAS when a CSF leak is present is also a key step in the evolution of events.

Role of Transmantle Pressure

Transmantle pressure is the differential pressure equal to the ventricular pressure minus the CSAS pressure, which reflects the pressure transmitted to the brain parenchyma.[27] The existence of transmantle pressure is hotly debated in the literature.[6,10,11,14,15,22–24,29,31,34,36,39] Reports in support of a minimal transmantle pressure gradient cite this factor as the initial event that facilitates the development of ventriculomegaly.[6,10,14,15,22–24,29,39] Other authors have been unable to measure a transmantle pressure gradient that could be used to interpret the induction of ventriculomegaly.[11,31,34,36]

There are many challenges in measuring a transmantle pressure gradient experimentally. In particular, it

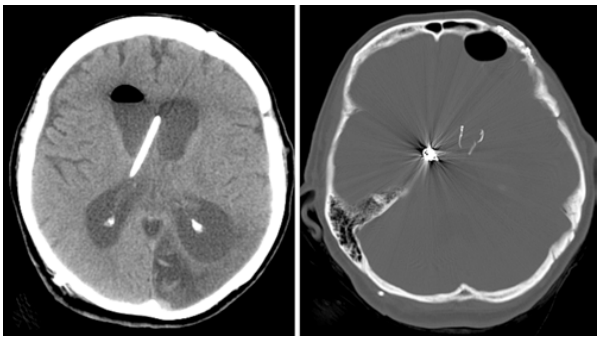

Fig. 2. Case 3. **Left:** A CT scan showing ventriculomegaly, raising the question of shunt failure in a patient with subarachnoid hemorrhage who developed hydrocephalus and was treated with a shunt. **Right:** A CT scan showing a skull base defect and a leak at the site of the craniotomy.

is difficult to measure a transmantle pressure gradient for the brain because it is difficult to isolate specific brain compartments. Furthermore, to study transmantle pressure, the experimental setup must have a sensor that measures both time and pressure with an adequate resolution for dynamic states of pressure. These difficulties were demonstrated by Rekate and McCormick[31] in a previous attempt.

We propose the theory, based on the observed cases, that in negative- and low-pressure hydrocephalus the blockage of CSF pathways between the ventricles and the CSAS and the presence of a CSF leak that communicates between the subarachnoid space compartment and atmospheric pressure establish a pressure gradient. These pressure gradients provide the basis for the creation of a transient and subtle transmantle pressure that leads to ventriculomegaly.[22,29,39]

The existence of a transmantle pressure in patients with blocked CSF pathways and a CSF leak could fill the gap in our understanding of the pathophysiology of hydrocephalus in these cases. When CSF communicates freely between the ventricles and the CSAS, the pressures are equally distributed. The transmantle pressure is near zero, and the ventricles maintain their size due to the pressure equilibrium. Ventriculomegaly can occur when the ventricular pressure is higher than pressure from the CSAS. This relationship can be observed whenever there is a block between the ventricles and CSAS and processes that increase the ventricular compartment pressure or that decrease the CSAS compartment pressure are at work.[17,19,29,32,39] In Case 1, posthemorrhagic events leading to blood products in the subarachnoid space and meningitis could probably provide the basis for an obstruction between the ventricular space and the CSAS as was confirmed by nuclear studies and intraoperative findings. In Case 2, posthemorrhagic events also occurred, and the level of obstruction at the posterior CSAS was confirmed by CT ventriculography. The next pathophysiological step is the creation of a transmantle pressure difference.

In all of our cases, a CSF leak was present postoperatively. Thus, the loss of fluid from the CSAS could lead to a lower CSAS pressure than ventricular pressure in compartments that are disconnected as in cases with blocked CSF circulation.[29] This is the equivalent of the CSAS acting as a "vacuum" for the ventricles because this space is selectively drained by a CSF leak.

The Role of Modified Brain Turgor

The role of brain parenchyma and its response concerning the various pressure differences that occur in this sequence of events cannot be overlooked. Brain parenchyma has viscoelastic properties and behaves in a biphasic fashion between 2 borderline states (a highly elastic state and a highly compliant state). Changes between the 2 states are easily observed whenever the most motile elements of the brain, which are the venous blood content and brain ECF, shift.[12,21,29,30,32,33,39]

Brain possesses the ability to resist or permit distortion due to changes in brain turgor. Brain turgor (Kb), a correction factor ranging from 0 to 1, describes the ability of the brain parenchyma to resist distortion due to applied pressures.[30] A value of 0 means that the brain shows no resistance to distortion so that a change in brain volume could not effectively change ICP. A brain turgor value of 1 signifies the opposite and thus refers to a more compliant brain.[30]

The features that characterize brain turgor are the brain parenchymal mass, the brain ECF, and the blood volume content.[30] In our cases, the ventricles were enlarged due to the presence of transmantle pressure created by a CSF leak in the CSAS and a block between the ventricles and CSAS.[29,30] Whether the viscoelastic properties and thus brain turgor (Kb) change in cases of negative- or low-pressure hydrocephalus complicating cranial approaches with CSF leaks is unknown.

The first proposed theory assesses the role of venous brain-blood shifts and the subarachnoid space in changing the brain viscoelasticity in cases of negative- or low-pressure hydrocephalus. This theory uses indirect evidence to support the role of venous blood shifting in this context. It is based on observations and reversal of the clinical picture in this specific subgroup of patients derived from the application of a cervical tourniquet (neck wrapping) to patients with altered brain viscoelasticity.[30,32] Veins act as highly compressible structures whereas the blood within them behaves as an incompressible fluid. In patients with negative- or low-pressure hydrocephalus associated with a CSF leak and no communication between the ventricles and the subarachnoid space, the evolved transmantle pressure could act as the factor that decreases the diameter of the cerebral venous network and drives part of the cerebral venous blood volume out of the cerebrum.

This shift of cerebral venous blood volume decreases brain turgor.[30,32] Therefore, the brain becomes less stiff and more vulnerable to deformation forces. The cycle of events creates a feedback loop in which the transmantle pressure initially may lower brain turgor. Lower brain turgor would make the brain more susceptible to the effects of transmantle pressure until a new equilibrium is reached and ventriculomegaly reaches its peak.

The second proposed theory involves a shift in brain ECF in cases of low-pressure hydrocephalus as a key step in changing brain viscoelasticity. In their series of patients with low-pressure hydrocephalus, Pang and Altschuler[29] showed that 3 children had an increased pressure-volume index measured at the peak of their symptoms and ventricular volume. No data about the presence of a CSF leak or a pseudomeningocele were reported in this series. Pang and Altschuler proposed that the observed increase in the pressure-volume index could be attributed to a highly compliant brain at the peak of ventriculomegaly.

Ventriculomegaly increases cortical radial pressure,[15] and the brain acts like a sponge that is "squeezed." A percentage of ECF exits the brain, and a final state of a highly compliant viscoelastic material is reached, demonstrating increased brain turgor (Kb). Peak radial cortical pressure is present when equilibrium is established. According to Pang and Altschuler[29] and Hakim et al.,[15] these events explain why it is difficult to treat ventriculomegaly in cases of low- or negative-pressure hydrocephalus.

Another possibility is that prolonged ventriculomegaly changes the structure of brain parenchyma and

diminishes its recoil properties.[29] Unfortunately, there is no direct evidence for the loss of ECF in patients with negative- or low-pressure hydrocephalus because no measurements of brain water content or MR imaging diffusion-weighted studies are available for these patients. Del Bigio and Bruni[8] reported mostly loss of brain water content in hydrocephalic rabbits or no changes depending on the methods used to assess the ECF content of the brain. Numerous studies, however, have reported increases in brain water content in cases of high- or normal-pressure hydrocephalus.[2,3,13,18,20,25,38] Still, other studies have reported no changes in brain ECF.[37]

Interpretation of the Clinical Picture

The neurological clinical course is insidious. These patients show a declining level of consciousness and function (decreased appetite, energy, speech, motor function, and balance). Headaches, vomiting, and cranial neuropathies are common. Classic signs and symptoms of high ICP are observed in patients with low-pressure hydrocephalus, so the source and the cause should be further clarified to reveal the shared pathophysiology.[5,7,9,16,21,26,28,29,32,35,39]

Four approaches have been proposed for interpreting the clinical picture: neural tissue stretching, altered cerebral perfusion, brain herniation related to ventriculomegaly, and pressure differences between the ventricles and subarachnoid space.[1,15,16,21,27,29,32,39] The dilated frontal horns could probably affect the integrity of the pyramidal tracts as they course around the horns. Differences in the integrity of white matter tracts have been observed on diffusion tensor MR imaging in children with hydrocephalus before and after shunt placement.[1] The dilation of the third ventricle could account for patients' memory problems. High cortical radial pressure could compromise cortical regional blood flow and lead to global confusion, altered affect, and psychomotor retardation.[15,29] Symptoms of decreased consciousness can be attributed to either brain herniation due to differences in craniospinal pressure or to low blood flow and compromised perfusion.[15,29,39] Evidence concerning the existence of a significant craniospinal pressure gradient leading to a gradual brain herniation can be drawn from Case 1. In this patient, we managed to identify an iatrogenic Chiari malformation caused by pressure differences. Ventricular pressure was constantly greater than pressure in the CSAS and spinal subarachnoid space, leading to tonsillar herniation.

Treatment Approaches

Our treatment algorithm in cases of low- or negative-pressure hydrocephalus involves the identification of the site of the CSF leak. To correct the ventriculomegaly and symptoms of increased ICP, the transmantle pressure should be eliminated by sealing the CSF leak and making the CSF pathways patent (by means of ETV or surgical exploration) or by increasing pressure in the subarachnoid space (by neck wrapping). Another critical step in abolishing the phenomenon is to revise the highly compliant brain to its prior state of elasticity. This procedure requires time so that the lost brain water content can be regained gradually.[29,30,32,39] External ventricular drainage, starting at a negative pressure and slowly and gradually approaching the zero pressure point (2–4 cm/day stabilized for 2–3 days) over a period of few days, is required.[29,30,32,39] In a series reported by Pang and Altschuler,[29] the mean time for reversing ventriculomegaly and related symptoms was 22.2 days. This procedure of negative-pressure brain drainage provides enough time for the brain to regain its recoil and to respond to differences in pressure. Another possible explanation could be that an EVD set to subatmospheric pressure helps create a lower ventricular drainage pressure than the drainage pressure created in the subarachnoid space in which pressure has been artificially lowered by the CSF leak. The pressure of the CSAS is then higher than the pressure in the isolated ventricular compartment. The evolution of the dynamic phenomenon continues with the ventricles "pushed" back to their initial sizes. Subsequently, the ventricular pressure gradually rises to near the opening pressure of the draining EVD.

Another question that should be answered is how did the neck wrapping in our Case 1 manage to reverse the patient's symptoms and ventriculomegaly? Neck wrapping causes 2 different actions: it increases subarachnoid space pressure and changes brain viscoelasticity.[30,32] Neck wrapping increases dural venous pressure and thus impedes the drainage of CSF from the subarachnoid space to the dural sinuses. The pressure of the subarachnoid space rises and the transmantle pressure that created the phenomenon is reversed. The brain is pushed inward. If a shunt or an EVD is present, the inward movement of the brain causes CSF to be displaced from the ventricles through the shunt or EVD, and the patient's clinical picture improves (Fig. 1B). Once a new pressure equilibrium has been established between the different CSF compartments, the ventricular pressure gradually reaches the opening pressure of the shunt so that the shunt works. Another less likely mechanism is modification of the brain's viscoelasticity. The venous drainage of the brain is blocked, the brain becomes stiffer, and more CSF egresses through a shunt or an EVD.[30,32]

Conclusions

Cranial approaches complicated with CSF leaks can manifest with difficult-to-treat negative- or low-pressure hydrocephalus. The symptoms often create confusion concerning the treatment approach because they are similar to the symptoms caused by increased ICP. The underlying pathophysiology, however, is completely different. In these cases the establishment of a transmantle pressure due to a CSF leak and a block in the communication between the ventricles and the subarachnoid space could initiate the development of the clinical entity. Changes in brain turgor follow and feed the phenomenon.

To treat low- and negative-pressure hydrocephalus, the CSF leak should be sealed, and the CSF communication between the compartments should be reestablished. Neck wrapping should be applied judiciously whenever a trial confirms a positive result. One of the most critical steps in treatment is the application of prolonged

subatmospheric-pressure extraventricular drainage of the brain in difficult-to-treat cases in an effort to regain the previous viscoelastic properties and recoil of the brain. In all cases, patience and clear identification of the various jigsaw-puzzle pieces are required to achieve the goal of treatment.

Disclosure

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Author contributions to the study and manuscript preparation include the following. Conception and design: Rekate, Filippidis. Analysis and interpretation of data: Rekate. Drafting the article: Filippidis, Kalani. Critically revising the article: all authors.

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References

1. Air EL, Yuan W, Holland SK, Jones BV, Bierbrauer K, Altaye M, et al: Longitudinal comparison of pre- and postoperative diffusion tensor imaging parameters in young children with hydrocephalus. Clinical article. **J Neurosurg Pediatr 5:**385–391, 2010
2. Anik Y, Demirci A, Anik I, Etus V, Arslan A: Apparent diffusion coefficient and cerebrospinal fluid flow measurements in patients with hydrocephalus. **J Comput Assist Tomogr 32:** 392–396, 2008
3. Aygok G, Marmarou A, Fatouros P, Young H: Brain tissue water content in patients with idiopathic normal pressure hydrocephalus. **Acta Neurochir Suppl 96:**348–351, 2006
4. Bannister CM: A report of eight patients with low pressure hydrocephalus treated by C.S.F. diversion with disappointing results. **Acta Neurochir (Wien) 27:**11–15, 1972
5. Clarke MJ, Maher CO, Nothdurft G, Meyer F: Very low pressure hydrocephalus. Report of two cases. **J Neurosurg 105:** 475–478, 2006
6. Conner ES, Foley L, Black PM: Experimental normal-pressure hydrocephalus is accompanied by increased transmantle pressure. **J Neurosurg 61:**322–327, 1984
7. Daniel RT, Lee GY, Halcrow SJ: Low-pressure hydrocephalic state complicating hemispherectomy: a case report. **Epilepsia 43:**563–565, 2002
8. Del Bigio MR, Bruni JE: Cerebral water content in silicone oil-induced hydrocephalic rabbits. **Pediatr Neurosci 13:**72–77, 1987
9. Dias MS, Li V, Pollina J: Low-pressure shunt 'malfunction' following lumbar puncture in children with shunted obstructive hydrocephalus. **Pediatr Neurosurg 30:**146–150, 1999
10. Dutta-Roy T, Wittek A, Miller K: Biomechanical modelling of normal pressure hydrocephalus. **J Biomech 41:**2263–2271, 2008
11. Eide PK, Saehle T: Is ventriculomegaly in idiopathic normal pressure hydrocephalus associated with a transmantle gradient in pulsatile intracranial pressure? **Acta Neurochir (Wien) 152:**989–995, 2010
12. Fried A, Shapiro K: Subtle deterioration in shunted childhood hydrocephalus. A biomechanical and clinical profile. **J Neurosurg 65:**211–216, 1986
13. Grasso G, Alafaci C, Passalacqua M, Morabito A, Buemi M, Salpietro FM, et al: Assessment of human brain water content by cerebral bioelectrical impedance analysis: a new technique and its application to cerebral pathological conditions. **Neurosurgery 50:**1064–1074, 2002
14. Hakim S, Adams RD: The special clinical problem of symptomatic hydrocephalus with normal cerebrospinal fluid pressure. Observations on cerebrospinal fluid hydrodynamics. **J Neurol Sci 2:**307–327, 1965
15. Hakim S, Venegas JG, Burton JD: The physics of the cranial cavity, hydrocephalus and normal pressure hydrocephalus: mechanical interpretation and mathematical model. **Surg Neurol 5:**187–210, 1976
16. Jurkiewicz J: Negative-pressure hydrocephalus. **J Neurosurg 85:**364–365, 1996
17. Khorasani L, Sikorski CW, Frim DM: Lumbar CSF shunting preferentially drains the cerebral subarachnoid over the ventricular spaces: implications for the treatment of slit ventricle syndrome. **Pediatr Neurosurg 40:**270–276, 2004
18. Kimelberg HK: Water homeostasis in the brain: basic concepts. **Neuroscience 129:**851–860, 2004
19. Le H, Yamini B, Frim DM: Lumboperitoneal shunting as a treatment for slit ventricle syndrome. **Pediatr Neurosurg 36:** 178–182, 2002
20. Leliefeld PH, Gooskens RH, Braun KP, Ramos LM, Uiterwaal CS, Regli LP, et al: Longitudinal diffusion-weighted imaging in infants with hydrocephalus: decrease in tissue water diffusion after cerebrospinal fluid diversion. Clinical article. **J Neurosurg Pediatr 4:**56–63, 2009
21. Lesniak MS, Clatterbuck RE, Rigamonti D, Williams MA: Low pressure hydrocephalus and ventriculomegaly: hysteresis, non-linear dynamics, and the benefits of CSF diversion. **Br J Neurosurg 16:**555–561, 2002
22. Levine DN: Intracranial pressure and ventricular expansion in hydrocephalus: have we been asking the wrong question? **J Neurol Sci 269:**1–11, 2008
23. Linninger AA, Sweetman B, Penn R: Normal and hydrocephalic brain dynamics: the role of reduced cerebrospinal fluid reabsorption in ventricular enlargement. **Ann Biomed Eng 37:**1434–1447, 2009
24. Linninger AA, Xenos M, Zhu DC, Somayaji MR, Kondapalli S, Penn RD: Cerebrospinal fluid flow in the normal and hydrocephalic human brain. **IEEE Trans Biomed Eng 54:**291–302, 2007
25. Massicotte EM, Buist R, Del Bigio MR: Altered diffusion and perfusion in hydrocephalic rat brain: a magnetic resonance imaging analysis. **J Neurosurg 92:**442–447, 2000
26. McCullough DC, Fox JL: Negative intracranial pressure hydrocephalus in adults with shunts and its relationship to the production of subdural hematoma. **J Neurosurg 40:**372–375, 1974
27. Miller JD: Volume and pressure in the craniospinal axis. **Clin Neurosurg 22:**76–105, 1975
28. Owler BK, Jacobson EE, Johnston IH: Low pressure hydrocephalus: issues of diagnosis and treatment in five cases. **Br J Neurosurg 15:**353–359, 2001
29. Pang D, Altschuler E: Low-pressure hydrocephalic state and viscoelastic alterations in the brain. **Neurosurgery 35:**643–656, 1994
30. Rekate HL: Brain turgor (Kb): intrinsic property of the brain to resist distortion. **Pediatr Neurosurg 18:**257–262, 1992
31. Rekate HL, McCormick J: Failure to demonstrate a brain transmissibility factor, in Marlin A (ed): **Concepts in Pediatric Neurosurgery.** Zurich: Karger, 1990, pp 235–242
32. Rekate HL, Nadkarni TD, Wallace D: The importance of the cortical subarachnoid space in understanding hydrocephalus. **J Neurosurg Pediatr 2:**1–11, 2008
33. Shapiro K, Fried A: Pressure-volume relationships in shunt-dependent childhood hydrocephalus. The zone of pressure instability in children with acute deterioration. **J Neurosurg 64:**390–396, 1986
34. Shapiro K, Kohn IJ, Takei F, Zee C: Progressive ventricular

enlargement in cats in the absence of transmantle pressure gradients. **J Neurosurg 67:**88–92, 1987
35. Singounas EG, Krasanakis C, Karvounis PC: Observations on the pathogenesis of low pressure hydrocephalus. Analysis of 25 cases. **Neurochirurgia (Stuttg) 19:**22–25, 1976
36. Stephensen H, Tisell M, Wikkelsö C: There is no transmantle pressure gradient in communicating or noncommunicating hydrocephalus. **Neurosurgery 50:**763–773, 2002
37. Tamaki N, Yamashita H, Kimura M, Ehara K, Asada M, Nagashima T, et al: Changes in the components and content of biological water in the brain of experimental hydrocephalic rabbits. **J Neurosurg 73:**274–278, 1990
38. Tourdias T, Dragonu I, Fushimi Y, Deloire MS, Boiziau C, Brochet B, et al: Aquaporin 4 correlates with apparent diffusion coefficient and hydrocephalus severity in the rat brain: a combined MRI-histological study. **Neuroimage 47:**659–666, 2009
39. Vassilyadi M, Farmer JP, Montes JL: Negative-pressure hydrocephalus. **J Neurosurg 83:**486–490, 1995

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