Low-pressure Hydrocephalus in Children: A Case Series and Review of the Literature

Zachary S. Smalley, BSc*
Garrett T. Venable, BSc*
Stephanie Einhaus, MD‡§
Paul Klimo, Jr, MD, MPH‡§¶

*College of Medicine, University of Tennessee Health Science Center, Memphis, Tennessee; ‡Department of Neurosurgery, University of Tennessee Health Science Center, Memphis, Tennessee; §Semmes-Murphey Neurologic and Spine Institute, Memphis, Tennessee; ¶Le Bonheur Children's Hospital, Memphis, Tennessee

Correspondence:
Paul Klimo, Jr, MD, MPH,
Semmes-Murphey Neurologic and Spine Institute,
6325 Humphreys Blvd,
Memphis, TN 38120.
E-mail: pklimo@semmes-murphey.com

Received, October 6, 2015.
Accepted, November 12, 2016.
Published Online, December 22, 2016.

BACKGROUND: Low-pressure hydrocephalus (LPH) is a rare phenomenon characterized by a clinical picture consistent with elevated intracranial pressure (ICP) and ventricular enlargement, but also a well-functioning shunt and low or negative ICP.
OBJECTIVE: To report our experience in evaluating this challenging problem.
METHODS: Patients with LPH were identified from several sources, including institutional procedural databases and personal case logs. Electronic medical records were reviewed to collect demographic, clinical, surgical, and radiographic data to determine the presence of LPH. Each patient's clinical course, including presentation, management, and outcome, is reported.
RESULTS: Thirty instances of LPH were identified in 29 patients. Eleven cases (37.9%) of LPH were after lumbar puncture (LP), and 19 cases (62.1%) occurred without any preceding spinal procedure. Among the post-LP patients, conservative measures alone were successful in 3 cases (27%); lumbar blood patch was successful in 2 cases (18%); and 6 cases (55%) required external cerebrospinal fluid (CSF) drainage. Of the spontaneous cases, 5 patients did not receive the full spectrum of treatment because of terminal prognosis. Of the remaining 14 patients, 11 (78.6%) required external CSF drainage. Post-LP patients required fewer days of external CSF drainage (median, 4 [range, 0-12] vs median, 11 [range, 0-90]) and had a shorter hospital stay (median, 2 [range, 2-16] vs median, 8 [range, 0-26]).
CONCLUSION: This study represents the largest series of LPH. Although its pathophysiology remains a mystery, there are a variety of management options. Multiple procedures and a protracted hospital stay are often required to successfully treat LPH.

KEY WORDS: Low-pressure hydrocephalus, Shunt malfunction, Ventricular shunt

Neurosurgery 80:439–447, 2017 DOI:10.1093/neuros/nyw046 www.neurosurgery-online.com

Dr Harold L. Rekate, in a 2009 paper, defined hydrocephalus as "an active distention of the ventricular system of the brain resulting from inadequate passage of cerebrospinal fluid (CSF) from its point of production, within the cerebral ventricles, to its point of absorption into the systemic circulation."[1] Signs and symptoms of de novo, or shunted, high-pressure hydrocephalus in children are, to some degree, age and pathology specific. This clinical picture is usually accompanied by dilation of the ventricles with or without transependymal CSF migration. There is a small subset of patients who have a clinical picture of increased intracranial pressure (ICP) with ventricular dilation but who, paradoxically, are found to have a normally functioning shunt (when a shunt is present) with low or even subatmospheric ICP. This rare clinical syndrome has been called low-pressure hydrocephalus (LPH) or a "negative-pressure" hydrocephalic state.

There are only a few reports on LPH in the literature.[2-5] A review of the literature suggests that there appears to be 2 primary etiologies: a primary cerebral vs a lumbar dural process. Pang and Altschuler were the first to report LPH in a case series of 12 shunted children who had ventriculomegaly and symptoms of hydrocephalus with normal-to-low ICP, which they believed to be due to altered compliance of the brain parenchyma in chronically shunted patients.[3] Alternatively, there are reports describing LPH after lumbar puncture or intradural spine surgery.[2,6,7] It has been proposed that the mechanism of LPH in this subset of patients is preferential drainage of the cortical subarachnoid space through a lumbar dural defect, which allows the ventricles

to enlarge while maintaining low ICP.[8] We report our experience evaluating and treating children with LPH.

METHODS

The institutional review board of our university approved this study. Since this study is a retrospective review, patient consent was not needed. Cases were identified by several resources, including a recently created shunt-surgery-specific database, a separate prospective neurosurgery procedural database maintained by the Neuroscience Center at our hospital, and review of personal case logs.

Only patients whose LPH required hospitalization from 2010 through 2014 were included in this study. LPH was strictly defined as marked ventricular dilation on computed tomography (CT) or magnetic resonance imaging (MRI) – compared with the child's baseline ventricular size, with or without transependymal flow – with corresponding symptoms of presumed elevated ICP or shunt malfunction (if one was present), but with low pressures (defined as <10 mm Hg or cmH20 or subatmospheric). The pressure was determined by shunt tap or surgical exploration, during which CSF could be aspirated easily without any resistance (ie, to rule out a proximal catheter malfunction) and distal flow was normal, or by an indwelling ICP monitor (ie, an external ventricular drain [EVD] or bolt).

The following data points were collected for each patient: gender; age at time of LPH; details of the patient's hydrocephalus history, including the etiology and duration that shunt was present prior to LPH; details of the LPH, including preceding event(s), if applicable; and management. Etiology of hydrocephalus was based upon a review of the clinical and radiographic information available. LPH cases were classified as postprocedural or spontaneous.

Statistical Analysis

Data for all LPH cases were pooled to calculate descriptive statistics for the entire sample. All continuous data were found to be nonparametric and are presented as median (range). We also planned a priori to compare the cases by putative etiology (ie, postprocedural vs spontaneous). All data were analyzed using SPSS software (SPSS Statistics for Windows, Version 21.0., IBM, Armonk, New York).

RESULTS

Our search identified 29 patients who experienced 30 cases of LPH over a 5-yr period, yielding an incidence of 6 cases/yr, and an estimated 2.6% of our shunt surgery volume (average of 230 shunt operations per year during the study period). Table 1 presents the demographical information of each case. Out of the 29 patients, 27 were children less than 18 yr of age, with a median age of 5 yr (range, 0.42-26). Sixteen patients were male (55%) and 13 were female (45%). The underlying cause of their original hydrocephalus included 20 cases secondary to neoplasm (69%), 7 cases from posthemorrhagic hydrocephalus of prematurity (24%), 1 case of posterior fossa hemorrhage (3.5%), and 1 congenital malformation (3.5%). At the time of LPH development, 27 patients had a ventriculoperitoneal shunt (93%), 1 patient had a ventriculoatrial (VA) shunt (3.5%), and 1 patient (3.5%) had LPH as the initial manifestation of her hydrocephalus. This last patient was a 14-yr-old female with neurofibromatosis type 1 who developed a posterior fossa hemorrhage of unknown etiology 3 months after resection of bilateral C1 and C2 intra- and extradural neurofibromas, resulting in lethargy and quadraventricular hydrocephalus. Upon insertion of an EVD, her pressure was noted to be low, and she required subatomospheric drainage for a number of days in order to decompress her ventricles.

The most common presenting symptom was lethargy (59%), followed by nausea and vomiting (49%) and headache (31%) (Table 2). LPH developed spontaneously in 19 cases (63%) and following lumbar puncture (post-LP) in 11 (37%) cases (Figure 1). Management of each patient differed based on severity of symptoms, initial neurological exam, and the putative etiology of the low-pressure state. All patients, except those young children that died (see below), eventually recovered back to their neurological and radiographic baseline.

Post-LP LPH

Each post-LP LPH patient's clinical course and management is summarized in Table 3.

Among the post-LP cases, all patients developed symptoms of LPH within 24 hours of their LP, 5 patients (45.5%) had recent chemotherapy and/or radiation, 2 (18.2%) had remote chemotherapy and/or radiation, and 1 (9.1%) had both recent and remote chemotherapy or radiation. Eight patients (42.1%) of the spontaneous cases had recent chemotherapy and/or radiation, and 2 (10.5%) had remote chemotherapy or radiation.

Eleven patients with existing functioning shunts experienced post-LP LPH (Table 3). Conservative measures, including cervical wrap, enforced recumbency, serial shunt tapping, and downgrading a programmable valve setting alone or in combination, were successful in 3 cases (27.3%). When conservative measures failed to improve symptoms, 4 patients (36.4%) underwent a lumbar blood patch. The lumbar blood patch was successful in 2 of these 4 patients, while the other 2 required external CSF drainage. Four patients were managed immediately with external drainage due to severity of symptoms and initial neurological exam. CSF was aggressively removed until ventricular size decreased or normalized, and the child was back to his or her neurological baseline. Five patients had their shunt externalized alone, and 1 had both an EVD and shunt externalized. Among the 6 patients (54.5%) requiring external drainage, the median duration of external drainage was 3 days (range, 2-13). The final procedure in these 6 children were: (1) shunt internalization without valve change (2, 33.3%); (2) shunt internalization with valve change (2, 33.3%); (3) 1 endoscopic third ventriculostomy (ETV) with removal of shunt (16.7%); and (4) 1 distal catheter placed into the pleural space without valve change (16.7%). Those requiring more than conservative measures had a median of 2 procedures (range, 1-5). Patients with post-LP LPH had a median hospital stay of 2 days (range, 2-16).

TABLE 1. Characteristics of Children with LPH

Patient identifier	Age (yr)/sex	Etiology hydrocephalus	Etiology of LPH	Total months with shunt/ months since last revision	Management of existing hydrocephalus at onset of LPH
1	24/F	PHHP	Post-LP	289/20	VP shunt
2	7/M	Medulloblastoma	Post-LP	1/–[a]	VP shunt
3	1.42/F	Medulloblastoma	Post-LP	11/7	VP shunt
4	3/F	ATRT	Post-LP	9/1	VP shunt
5	14/F	Medulloblastoma	Post-LP	1/0.13	VP shunt
6	3/M	Tectal plate glioma	Post-LP	3/–	VP shunt
7	4/M	Ependymoma	Post-LP	2/–	VP shunt
8	5/M	Medulloblastoma	Post-LP	2/–	VP shunt
9	14/M	Medulloblastoma	Post-LP	6/4	VP shunt
10	6/M	Medulloblastoma	Post-LP	10/4	VP shunt
11	4/M	Medulloblastoma	Post-LP	7/–	VP shunt
7	4/M	Ependymoma	Spontaneous	12/10	VP shunt
12	5/M	Ependymoma	Spontaneous	32/0.73	VP shunt
13	0.42/F	ATRT	Spontaneous	0.13/–	VP shunt
14	1.58/M	ATRT	Spontaneous	7/5	VP shunt
15	14/F	Posterior fossa hemorrhage	Spontaneous	–	None
16	11/M	Tectal plate glioma	Spontaneous	55/–	VP Shunt
17	3/M	Medulloblastoma	Spontaneous	6/–	VP shunt
18	0.75/F	ATRT	Spontaneous	2/0.13	VP shunt
19	14/F	Dandy–Walker malformation	Spontaneous	178/0.13	VP shunt
20	1.42/F	Ependymoma	Spontaneous	1/0.2	VP shunt
21	3/M	Medulloblastoma	Spontaneous	3/0.4	VP shunt
22	10/F	PHHP	Spontaneous	121/0.4	VP shunt
23	5/F	PHHP	Spontaneous	60/24	VA shunt
24	6/M	PHHP	Spontaneous	76/–	VP shunt
25	2/M	ATRT	Spontaneous	0.27/–	VP shunt
26	26/M	PHHP	Spontaneous	311/0.07	VP shunt
27	4/F	PHHP	Spontaneous	50/43	VP shunt
28	1.42/F	PHHP	Spontaneous	12/0.03	VP shunt
29	5/M	Pineoblastoma	Spontaneous	2/0.03	VP shunt

Abbreviations: ATRT, atypical teratoid rhabdoid tumor; LPH, low-pressure hydrocephalus; PHHP, posthemorrhagic hydrocephalus of prematurity; VA, ventriculoatrial.
[a]No revision since initial placement.

TABLE 2. Presenting Sign and Symptoms of LPH by Etiology

Symptom	Overall (n = 29)	Post-LP (n = 11)	Spontaneous (n = 19)
Lethargy	17 (59%)	7 (64%)	10 (55%)
Headache	9 (31%)	4 (36%)	5 (28%)
Nausea/vomiting	14 (48%)	7 (64%)	7 (39%)
Agitation	4 (14%)	–	4 (22%)
Bradycardia	5 (17%)	–	5 (28%)
Failure to thrive	2 (7%)	–	2 (11%)
Other[a]	4	3	1

[a]Others include dizziness, dysconjugate gaze, decerebrate posturing, seizure, and slurred speech.

Spontaneous LPH

Nineteen patients had spontaneous LPH (Table 4). One patient (no. 7) had 2 episodes of LPH, 1 following an LP, and 1 spontaneously. Five (26.3%) young children (median age, 1.58 yr [range, 0.42-3]) with progressive and metastatic embryonal tumors (4 atypical teratoid rhabdoid tumors and 1 medulloblastoma) developed spontaneous LPH. Aggressive treatment was usually not pursued, given their terminal prognosis; all were discharged with palliative care, 4 of whom died within 1 mo of discharge.

Of the remaining 14 patients in the spontaneous group, 2 patients (14.3%) were successfully managed with conservative measures alone, and 1 patient (7%) was successfully managed with shunt valve revision alone. Eleven (78.6%) children required some form of CSF drainage (shunt externalization or EVD) to drain CSF aggressively until ventricular size decreased or normalized and the child was back to their neurological baseline. Eight patients had their shunt externalized alone, 1 had an EVD alone, and 2 had both an EVD and shunt externalized. Median time of external CSF drainage was 9 days (range, 2-90). The final procedure in these 11 children were: (1) shunt internalization without valve change (6, 54.5%); (2) shunt

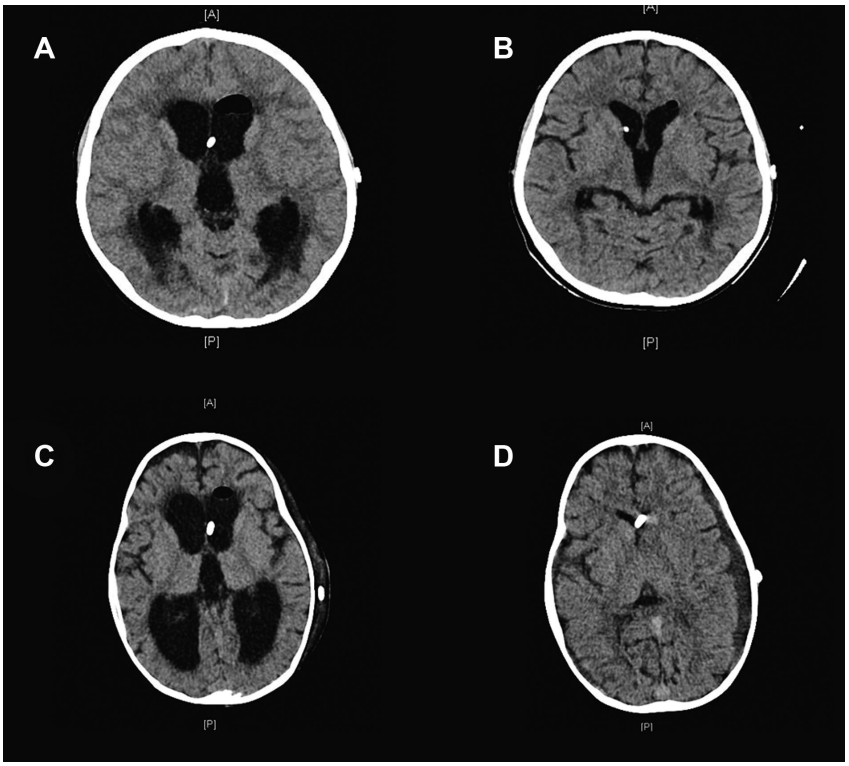

FIGURE 1. *CT images of patients presenting with post-LP (**A**, **B**) and spontaneous LPH (**C**, **D**). The demographic and procedural details are provided in Tables 1, 3, and 4. **A**, Post-LP patient (no. 9) immediately after EVD was placed showing dilated ventricles with transependymal flow. **B**, Post-LP patient (no. 9) with new baseline ventricular size 1 mo after ETV. The tip of the Ommaya reservoir catheter is seen in the right frontal horn. **C**, Spontaneous patient (no. 20) with persistently dilated ventricles after initially undergoing complete shunt revision, then valve revision to low-pressure flow regulated valve without antisiphon device. **D**, Shunt was externalized and eventually reinternalized after brain compliance normalized. CT demonstrates small ventricles 1 mo after reinternalization.*

internalization with valve change (3, 27.3%); and (3) distal catheter placed either in the atrium or pleural space with or without valve change (2, 18.2%). For the spontaneous group as a whole, the median number of interventions was 2 (range, 0-9) and the median duration of hospital length of stay was 8 days (range, 2-26).

DISCUSSION

LPH is a rare and challenging problem to recognize and manage. We categorized our cases as either post-LP (ie, a planned, intentional lumbar puncture in all of our patients, n = 11) or spontaneous (n = 19). Eleven patients (58%) in the latter group had an unplanned event, such as shunt malfunction or infection, intracranial hemorrhage, or symptomatic hyponatremia within 30 days preceding the onset of LPH. Eight (42%) patients had no preceding events. It is our belief that these preceding events somehow altered brain compliance leading to the development of LPH.

LPH can develop in any patient with active or treated hydrocephalus from any number of etiologies, such as intracranial hemorrhage (eg, aneurysmal subarachnoid hemorrhage), chronic compensated hydrocephalus or shunted hydrocephalus, intracranial infection, or brain tumors.[5,9] LPH has also been reported after cranial surgery complicated by a skull-base CSF leak.[10,11] To our knowledge, we are reporting for the first time that LPH may occur in young, terminally ill children with progressive and metastatic (ie, leptomeningeal) embryonal tumors. At the time of this manuscript preparation, all of these patients except 1 died within 1 month of the onset of LPH. We believe that recent or concurrent brain radiation and/or chemotherapy, in conjunction with a functioning shunt, may

TABLE 3. Management and Outcomes of Post-LP Cases of Low-Pressure Shunt Malfunction

Patient identifier	History of radiation (R) or chemotherapy (C)[a]	Intervention	Outcome
1	–	Conservative measures only	D/C on HD 2 at baseline[b]
2	Recent (R)	1. Lumbar blood patch 2. Shunt externalized, 4 d 3. Shunt internalized	D/C on HD 10 at baseline after internalization
3	Remote (C)	1. Lumbar blood patch 2. ETV 3. Returned to hospital 7 d later 4. Shunt externalized, 2 d 5. Shunt internalized with nonprogrammable low pressure valve	D/C on HD 16 at baseline
4	Remote (R), recent (C)	1. Shunt externalized, 2 d 2. Shunt internalized with nonprogrammable low pressure valve	D/C on HD 6 at baseline
5	–	1. Lumbar blood patch	D/C on HD 2 at baseline
6	–	Conservative measures only	D/C on HD 2 at baseline
7	Remote (R)	1. Shunt externalized, 2 d 2. Shunt internalized	D/C on HD 4 at baseline
8	–	1. Shunt externalized, 4 d 2. Distal shunt revision (peritoneal to pleural)	D/C on HD 10 at baseline
9	Recent (R), recent (C)	1. Shunt externalized, 1 d 2. EVD, 12 d 4. Removal of shunt	D/C on HD 15 at baseline
10	Recent (C), remote (R)	Conservative measures only	D/C on HD 2 at baseline
11	Recent (C), recent (R)	1. Lumbar blood patch	D/C on HD 2 at baseline

Abbreviations: D/C, discharged; ETV, endoscopic third ventriculostomy; EVD, external ventricular drain; HD, hospital day.
[a]Recent is defined as within 6 mo of low-pressure hydrocephalus presentation. Remote is greater than 6 mo from presentation.
[b]"Baseline" defined as patient's neurological function and ventricular size prior to onset of low-pressure hydrocephalus, except patient no. 9 who was successfully treated with ETV with new baseline ventricle size (see Figure 1).

predispose a child to develop LPH, either spontaneously or after a lumbar puncture.

Clinical Assessment and Management

Although LPH is a fairly rare occurrence, neurosurgeons should be aware of its variable presentation and management. Clinically, it is nearly indistinguishable from high-pressure hydrocephalus or shunt malfunction. Children with LPH are not infrequently taken to the operating room for a presumed high-pressure shunt malfunction and then are found to have a working shunt, or they have an unexpectedly low ICP after replacing the ventricular catheter. Further surgical interventions are often needed in order to successfully treat LPH. Therefore, a high index of suspicion is necessary when shunted children present with signs and symptoms of shunt failure and ventriculomegaly with a history of chemotherapy and/or radiation therapy; recent shunt revision or procedure involving spinal durotomy, notably lumbar puncture; or a skull-base CSF leak. In addition to these historical clues, patients with LPH should have shunts that rapidly refill when pumped or aspirate easily when tapped with normal distal runoff.

The management of LPH is dependent on the etiology of the LPH and the severity of presentation. Furthermore, LPH is a rare occurrence, and the patients in this report were managed by 4 pediatric neurosurgeons, each with their own management style. Therefore, we could not apply a unifying treatment "protocol." However, the general principles employed were: attempt to repair lumbar CSF leak if one was present (blood patch) and maximize CSF removal either through the existing shunt (eg, neck wrap, externalizing) or by placing an EVD. Unlike high-pressure shunt malfunction, it is the distended ventricles, often with transependymal edema, that cause the patient's signs and symptoms in LPH. As evidenced in this report, it is not unusual for patients to undergo multiple procedures before being discharged. Initial treatment options for patients with mild post-LP LPH includes bed rest and cervical wrap, although both of these interventions can be difficult to sustain in children. We were able to successfully ameliorate symptoms in 2 children with post-LP LPH with the use of an epidural blood patch. For

TABLE 4. Management and Outcomes of Spontaneous Cases of Low-Pressure Shunt Malfunction

Patient identifier	History of radiation (R) or chemotherapy (C)[a]	Significant event preceding LPH[b]	Intervention	Outcome
7	Recent (R)	–	Conservative measures only	D/C on HD 2 at baseline[c]
12	Remote (R)	Hyponatremia following cervical wound debridement	1. Shunt externalized, 9 d 2. Distal shunt revision (peritoneal to pleural)	D/C on HD 20 at baseline
13	Recent (C)	–	Conservative measures only	Patient died 33 d after discharge
14	Recent (R), recent (C)	–	Conservative measures only	Patient died 1 d after withdrawal of care
15	–	Posterior fossa hemorrhage	1. EVD, 19 d 2. ETV, failed 3. Ventriculoatrial shunt placed with nonantisiphon programmable valve	D/C on HD 26 at neurological baseline
16	Remote (C)	–	1. Shunt externalized, 7 d 2. EVD, 6 d 3. Shunt internalized with programmable valve	D/C on HD 8 at neurological baseline
17	Recent (C), recent (R)	–	Conservative measures only	D/C to hospice care, still alive
18	Recent (C)	Trapped 4th ventricle from metastatic ATRT	1. Endoscopic fenestration of loculated hydrocephalus	Patient died 3 d after discharge
19	–	Shunt malfunction	1. Shunt revision with programmable valve	D/C on HD 3 at baseline
20	–	Shunt malfunction	1. Total shunt revision 2. Shunt revised with low pressure valve 3. Shunt externalized, 9 d 4. Shunt internalized	D/C on HD 20 at baseline
21	Recent (R)	Shunt malfunction	1. Shunt externalized, 8 d 2. Shunt internalized with programmable valve	D/C on HD 9 at baseline
22	–	–	Conservative measure only	D/C on HD 2 at baseline
23	–	Shunt malfunction	1. Distal shunt revision (atrial to pleural) 2. Shunt externalized, 5 d 3. Shunt internalized with nonprogrammable low-pressure valve	D/C on HD 14 at baseline
24	–	Shunt malfunction	1. Proximal shunt revision 2. Proximal shunt revision with externalization, 3 d 3. Shunt internalized	D/C on HD 4 at baseline
25	Recent (C)	–	Conservative measures only	Patient died 32 d after discharge
26	–	Shunt malfunction	1. Shunt externalized, 24 d 2. Proximal shunt revision 3. EVD, 22 d 4. Revision of EVD 5. Endoscopic septum pellucidotomy 6. Revision of EVD 7. Revision of EVD 8. Hemispherectomy 9. Total shunt revision	D/C on HD 26 at baseline
27	–		1. Proximal shunt revision 2. Shunt externalized, 11 d 3. Shunt internalized	D/C on HD 18 at baseline

TABLE 4 *Continued.*

Patient identifier	History of radiation (R) or chemotherapy (C)[a]	Significant event preceding LPH[b]	Intervention	Outcome
28	–	Shunt malfunction	1. Shunt revision (proximal and change to nonprogrammable medium pressure valve) 2. Shunt externalized, 2 d 3. Shunt internalized	D/C on HD 5 at baseline
29	Recent (R)	Shunt infection	1. Shunt externalized, 90 d 2. Shunt internalized	D/C on HD 3 with shunt externalized, shunt internalized 3 mo later

Abbreviations: D/C, discharged; ETV, endoscopic third ventriculostomy; EVD, external ventricular drain; HD, hospital day; IVH, intraventricular hemorrhage; LPH, low-pressure hydrocephalus.
[a]Recent is defined as within 6 mo of LPH presentation. Remote is greater than 6 mo from presentation.
[b]All preceding events occurred within 30 d of LPH presentation.
[c]"Baseline" defined as patient's neurological function and ventricular size prior to onset of LPH.

more severe presentations, the goal is to rapidly increase CSF output in order to decrease the ventricular volume. This can be achieved by externalizing a shunt and lowering the collection bag to promote siphoning (which, of course, will only work if the patient's valve does not have an antisiphon device), repetitive shunt pumping, or placing and setting an EVD at a low or negative level relative to the baseline drainage site.[12,13] Typically, these maneuvers will quickly improve the patient's clinical and radiographic picture; CSF drainage should be continued until both return to baseline. The time course of clinical improvement will parallel or even precede the improvement in ventricular size. After a period of clinical stabilization for a few days, we gradually start to elevate the CSF collection bag to determine whether brain compliance has normalized, which is done by assessing the patient's neurological status and repeating their CT scan. Once the optimal pressure range needed by that patient has been determined, options thereafter include replacing the shunt into the same distal compartment with the same valve, assuming the viscoelastic properties of the brain have returned to baseline; replacing the existing valve with a fixed low pressure or programmable one (in order to achieve greater CSF flow initially and then adjusting as the brain compliance normalizes); or placing the shunt in a low to negative pressure site, such as the pleural cavity or the atrium. Some have reported success with valveless shunts and larger diameter custom peritoneal distal catheters.[5,14,15] ETV is an excellent treatment option for LPH in those patients whose original hydrocephalus etiology would have made them a candidate for an ETV, as was the case for patient no. 9 in our series.[16]

Proposed Mechanisms of LPH

Several theories have been postulated to explain the development of low or negative pressure hydrocephalus, and all use terms such as "brain turgor," "viscoelastic," "compliance," and "elasticity" as a means to describe the brain's ability to respond to or resist (in terms of volume) deformational forces (in terms of pressure).[17] A compliant brain will allow greater change in volume for an increase in pressure than a less compliant one; elastance is the inverse of compliance.

One of the earliest descriptions of LPH was in 1994 by Pang and Altschuler.[3] Their hypothesis was that "intermittent shunt malfunction" may lead to a disruption of the normal relationship between the ventricular pressure and ventricular wall tension, which leads to changes in the viscoelastic modulus of the brain secondary to extravasation of extracellular water from the brain parenchyma, thus increasing brain compliance. They believe that the extracellular water is the only mobile pool that can be "wrung" out of the brain sponge to accommodate the ventricular distention. This hypothesis was based on the theory proposed by Hakim et al, who stated that increases in ventricular dilation create radial cortical stress that forces extracellular water from the brain parenchyma.[18] Altered compliance allows the persistence of ventriculomegaly, even though ICP is low and it is the stretching of brain tissue, which results in symptoms. The authors believed that "bioatrophic changes" in the brain secondary to diffuse brain trauma, infarcts, ischemic states, or radiation damage could lead to altered compliance and predispose to the development of a low-pressure state. Pang and Altschuler recorded changes in compliance in 3 patients via measurement of pressure–volume indices by CSF mock infusion during and after resolution of LPH. The patients had a statistically significant decrease from peak low-pressure state to resolution.[3]

In 2013, Preuss et al introduced a "pulsatile vector" theory in which they hypothesized CSF flow is driven by pulsatile arterial flow.[19] The flow initiates 3 intracranial directional forces that serve to drive CSF through the ventricles as well as subarachnoid and spinal CSF to the convexities of the brain surface, where it is reabsorbed. The authors believed the maintenance of fluid

flow is dependent on a precise synchronization of these vectors and appropriately low venous pressure to allow for reabsorption in the arachnoid villae. Any disturbance allows for development of hydrocephalus. Distention of the floor of the fourth ventricle puts stress on both the brainstem and area postrema, leading to many of the symptoms seen – bradycardia, diplopia, mydriasis, and nausea/vomiting.[7] This theory has yet to be experimentally confirmed.

When considering LPH after spinal procedures, the cause appears to be iatrogenic preferential CSF drainage from the lumbar theca. Of their 12 patients, Pang and Altshuler reported 2 patients who presented following a lumbar puncture.[3] They hypothesized that CSF leakage from the lumbar theca decreased the subarachnoid pressures and increased the transmantle pressure gradient between the ventricles and cortical subarachnoid space, thus promoting ventricular dilatation.[3] In 1999, Dias et al reported on a series of 2 patients with low-pressure shunt failure following lumbar puncture. They proposed that shunt failure is secondary to CSF leakage from the lumbar cistern, which reduces ICP below the opening pressure of the shunt valve, rendering the shunt nonfunctional despite being structurally intact. Continued CSF production leads to dilation of the ventricles even though the ICP is negative.[2] Khorasani et al, in their work on the treatment of slit ventricle syndrome, first noted that insertion of a lumboperitoneal shunt preferentially drains the cerebral subarachnoid space, thus allowing ventricular enlargement via establishment of a pressure gradient between the ventricles and cerebral subarachnoid.[8] Additionally, Tubbs et al report in a series of 5 patients who experienced shunt failure after intradural spinal surgery at a mean of 5 postoperative days, although it is unclear if their 5 cases were due to LPH.[20] It stands to reason that a defect in the lumbar dura following a lumbar puncture or a surgically created lumbar durotomy would create a similar loss of CSF from the lumbar space and subsequent drainage of the cerebral subarachnoid space, which would promote ventriculomegaly. However, it should be noted that while spinal CSF loss predisposes to LPH, many shunted children undergo an LP or other intradural spinal procedure (eg, detethering) without developing LPH.

A mathematical model based on principles of bulk flow by Rekate et al confirmed that a reduction by even 2 mm in the mean thickness of the cortical subarachnoid space will cause an increase in ventricular volume by nearly 4.5 fold.[21] Preuss et al reported the case of an 8-yr-old boy with shunt-dependent hydrocephalus secondary to medulloblastoma who developed LPH following lumbar puncture. The authors used their "pulsatile vector" theory to explain the development of low pressure; even in this model, the primary event was identified as acute loss of subarachnoid CSF.[7]

Strengths and Limitations

Although this is the largest series of LPH, when studying any rare event or outcome, the study size predictably precludes robust statistical analysis. This series is no different. Additionally, with a similar presentation to high-pressure hydrocephalus or a high-pressure shunt malfunction, diagnosis is usually made during an initial invasive procedure (shunt exploration or revision or EVD placement) leading to an increased burden of procedures and operations and increasing the variability of initial management. A drawback of our study is that we present no unified management pathway or protocol. This is due to a number of factors, including the rarity of this phenomenon, the treatment preference(s) of the attending neurosurgeon, patient factors including the underlying etiology of the child's hydrocephalus (eg, amenable to ETV or not), the type of shunt (eg, flow regulated valve with or without antisiphon device), the putative etiology and severity of the child's LPH state, and, finally, the overall life expectancy of the child (eg, the infants with metastatic embryonal tumors). Nonetheless, the 2 principles that guided our initial management were to seal any CSF leak, if possible, and remove more CSF out of the ventricles in order to correct the ventriculomegaly. The final intervention(s) depended on whether the patient's brain compliance had normalized.

Further studies (human, animal, or computer models) are needed to elucidate the mechanisms behind the development of such changes in the structural integrity of brain parenchyma or the altered intracranial CSF flow dynamics that allow for the development of LPH spontaneously or after spinal durotomy, respectively. Although radiation, chemotherapy, and other diffuse brain afflictions are believed to contribute to alterations in brain compliance, no steadfast evidence currently exists. Further knowledge of this fascinating phenomenon could be achieved with the power of a multi-institute collaboration, such as the Hydrocephalus Clinical Research Network.

CONCLUSION

This study represents the largest case series of pediatric LPH, due in part to our high-volume brain tumor program. Within pediatric neurosurgery, LPH is a well-recognized yet rare phenomenon. The precise pathophysiology has not been elucidated but is likely due to more than one mechanism (ie, iatrogenic vs spontaneous). Management is dictated by the presence of a treatable inciting event, such as a CSF leak or infection, and the severity of symptoms, which in turn is directly due to the degree of ventricular distention. A high clinical suspicion is required to reduce or prevent the number of invasive interventions needed to ameliorate LPH.

Disclosures

The authors have no personal, financial, or institutional interest in any of the drugs, materials, or devices described in this article.

REFERENCES

1. Rekate HL. A contemporary definition and classification of hydrocephalus. *Semin Pediatr Neurol*. 2009;16(1):9-15.
2. Dias MS, Li V, Pollina J. Low-pressure shunt 'malfunction' following lumbar puncture in children with shunted obstructive hydrocephalus. *Pediatr Neurosurg*. 1999;30(3):146-150.

3. Pang D, Altschuler E. Low-pressure hydrocephalic state and viscoelastic alterations in the brain. *Neurosurgery*. 1994;35(4):643-655; discussion 655-646.
4. Vassilyadi M, Farmer JP, Montes JL. Negative-pressure hydrocephalus. *J Neurosurg*. 1995;83(3):486-490.
5. Akins PT, Guppy KH, Axelrod YV, Chakrabarti I, Silverthorn J, Williams AR. The genesis of low pressure hydrocephalus. *Neurocrit Care*. 2011;15(3):461-468.
6. Tubbs RS, Pugh J, Acakpo-Satchivi L, Wellons JC, Blount JP, Oakes WJ. Acute ventriculoperitoneal shunt malfunction following opening of the spinal subarachnoid space: a case series. *Childs Nerv Syst*. 2009;25(5):599-600.
7. Preuss M, Evangelou P, Hirsch W, et al. Acute two-compartment low pressure hydrocephalus-a case report. *Childs Nerv Syst*. 2013;29(12):2307-2310.
8. 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*. 2004;40(6):270-276.
9. 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*. 2002;16(6):555-561.
10. Daniel RT, Lee GY, Halcrow SJ. Low-pressure hydrocephalic state complicating hemispherectomy: a case report. *Epilepsia*. 2002;43(5):563-565.
11. Filippidis AS, Kalani YS, Nakaji P, Rekate HL. Negative-pressure and low-pressure hydrocephalus: the role of cerebrospinal fluid leaks resulting from surgical approaches to the cranial base Report of 3 cases. *J Neurosurg*. 2011;115(5):1031-1037.
12. Hunn BH, Mujic A, Sher I, Dubey AK, Peters-Willke J, Hunn AW. Successful treatment of negative pressure hydrocephalus using timely titrated external ventricular drainage: a case series. *Clin Neurol Neurosurg*. 2014;116:67-71.
13. Kalani MY, Turner JD, Nakaji P. Treatment of refractory low-pressure hydrocephalus with an active pumping negative-pressure shunt system. *J Clin Neurosci*. 2013;20(3):462-466.
14. Owler BK, Jacobson EE, Johnston IH. Low pressure hydrocephalus: issues of diagnosis and treatment in five cases. *Br J Neurosurg*. 2001;15(4):353-359.
15. Galbarriatu L, Rivero-Garvia M, Olivares M, Miranda D, Pomposo I, Marquez-Rivas J. Low-pressure hydrocephalus: indication for custom-made catheters? Technical report. *Acta Neurochir*. 2013;155(10):1981-1985.
16. Hamilton MG, Price AV. Syndrome of inappropriately low-pressure acute hydrocephalus (SILPAH). *Acta Neurochir Suppl*. 2012;113:155-159.
17. Rekate HL. Brain turgor (Kb): intrinsic property of the brain to resist distortion. *Pediatr Neurosurg*. 1992;18(5-6):257-262.
18. Hakim S, Venegas JG, Burton JD. The physics of the cranial cavity, hydrocephalus and normal pressure hydrocephalus: mechanical interpretation and mathematical model. *Surg Neurol*. 1976;5(3):187-210.
19. Preuss M, Hoffmann KT, Reiss-Zimmermann M, et al. Updated physiology and pathophysiology of CSF circulation-the pulsatile vector theory. *Childs Nerv Syst*. 2013;29(10):1811-1825.
20. Tubbs RS, Pugh J, Acakpo-Satchivi L, Wellons JC, 3rd, Blount JP, Oakes WJ. Acute ventriculoperitoneal shunt malfunction following opening of the spinal subarachnoid space: a case series. *Childs Nerv Syst*. 2009;25(5):599-600; discussion 601-595.
21. Rekate HL, Nadkarni TD, Wallace D. The importance of the cortical subarachnoid space in understanding hydrocephalus. *J Neurosurg Pediatr*. 2008;2(1):1-11.

Acknowledgments

The authors wish to thank Andrew J. Gienapp, BA (Department of Medical Education, Methodist University Hospital, Memphis, TN, and Department of Neurosurgery, University of Tennessee Health Science Center, Memphis, TN) for technical and copy editing, preparation of the manuscript for publishing, and publication assistance with this manuscript, and John Essary, MA (Department of Communications, Cumberland University, Lebanon, TN) for assistance in figure preparation.

COMMENT

The authors report on their experience with the largest reported group of patients with the rare condition low pressure hydrocephalus. This is diagnosed in patients who have symptoms of shunt malfunction or increased intracranial pressure in the setting of a working CSF shunt, low intracranial pressure, and marked ventricular enlargement.

This retrospective review identified 27 pediatric and 2 adult patients that exhibited this syndrome either after lumbar puncture ("post-LP," 11 patients) or no spinal procedure ("spontaneous," 19 cases). Patients with post-LP LPH were generally treated in a stepwise fashion, with: 1. simple methods to increase ventricular CSF drainage (cervical wrap, recumbency, serial shunt taps, decreasing programmable shunt valve opening pressures), 2. decrease thecal CSF loss with a lumbar blood patch, or 3. external ventricular drainage and subsequent shunt revision.

Of the 19 patients with "spontaneous" LPH, 8 had no preceding events and 11 had a recent event (within 30 days) that could have affected the shunt function or CSF dynamics, such as a shunt malfunction or infection, intracranial hemorrhage or hyponatremia. Those who were terminally ill were not treated for the LPH, the majority were treated with external ventricular drainage, and a few were treated with conservative measures alone.

This report sheds further light on this rare but clinically significant condition. It shows that patients with post-LP LPH have a less severe form of the disease that does not require as intense therapy, which is useful information to have when counselling a parent of a child with LPH. Those who had LPH not after any procedure or following recent non-spinal procedures (spontaneous group) required more prolonged and intense therapy. The subset of truly spontaneous cases of LPH all had aggressive CNS neoplasms that were not treated. This is the first description of such a group of LPH patients.

As there is much to learn about this disease, more detail regarding the cases in each group would have benefited the reader. The authors strived to provide more specifics about the management of these patients, however, I suspect that the necessary detail was hampered by the retrospective nature of the study. The authors mention that their endpoint for the patients undergoing external ventricular drainage is when "brain compliance has normalized," which was determined presumably by ventricles that do not enlarge when reaching EVD pressures above atmospheric. Aside from the patients who had malignant brain tumors without any primary procedure performed, it appears that, based on their results, patients with this problem can be expected to recover, however the long term outcomes of this condition are still unknown.

Philipp R. Aldana
Jacksonville, Florida