J Neurosurg 117:615–628, 2012

Intracranial hypotension producing reversible coma: a systematic review, including three new cases

A review

Joshua J. Loya, B.A.,[1,2] Stefan A. Mindea, M.D.,[1] Hong Yu, M.D.,[1] Chitra Venkatasubramanian, M.D.,[3] Steven D. Chang, M.D.,[1] and Terry C. Burns, M.D., Ph.D.[1]

Departments of [1]Neurosurgery, [2]Epidemiology, and [3]Neurology & Neurological Sciences, Stanford University School of Medicine, Stanford, California

Intracranial hypotension is a disorder of CSF hypovolemia due to iatrogenic or spontaneous spinal CSF leakage. Rarely, positional headaches may progress to coma, with frequent misdiagnosis. The authors review reported cases of verified intracranial hypotension–associated coma, including 3 previously unpublished cases, totaling 29. Most patients presented with headache prior to neurological deterioration, with positional symptoms elicited in almost half. Eight patients had recently undergone a spinal procedure such as lumbar drainage. Diagnostic workup almost always began with a head CT scan. Subdural collections were present in 86%; however, intracranial hypotension was frequently unrecognized as the underlying cause. Twelve patients underwent one or more procedures to evacuate the collections, sometimes with transiently improved mental status. However, no patient experienced lasting neurological improvement after subdural fluid evacuation alone, and some deteriorated further. Intracranial hypotension was diagnosed in most patients via MRI studies, which were often obtained due to failure to improve after subdural hematoma (SDH) evacuation. Once the diagnosis of intracranial hypotension was made, placement of epidural blood patches was curative in 85% of patients. Twenty-seven patients (93%) experienced favorable outcomes after diagnosis and treatment; 1 patient died, and 1 patient had a morbid outcome secondary to duret hemorrhages. The literature review revealed that numerous additional patients with clinical histories consistent with intracranial hypotension but no radiological confirmation developed SDH following a spinal procedure. Several such patients experienced poor outcomes, and there were multiple deaths. To facilitate recognition of this treatable but potentially life-threatening condition, the authors propose criteria that should prompt intracranial hypotension workup in the comatose patient and present a stepwise management algorithm to guide the appropriate diagnosis and treatment of these patients.
(http://thejns.org/doi/abs/10.3171/2012.4.JNS112030)

Key Words • **coma** • **cerebrospinal fluid leak** • **epidural blood patch** • **intracranial hypotension** • **magnetic resonance imaging** • **subdural hematoma**

The syndrome of intracranial hypotension was first described in detail by Leriche in 1920; it results from leakage of CSF through a spinal dural breach into surrounding tissues.[29,38] As a relatively uncommon entity, intracranial hypotension has remained a diagnostic challenge and is frequently misdiagnosed. Contributing to the diagnostic challenge is the diversity of potential presentations, ranging from simple headaches to vertigo, cranial nerve palsies, or even obtundation and coma. Although most patients with intracranial hypotension follow a benign course, in rare cases intracranial hypotension has been reported to mimic serious neurodegenerative conditions such as frontotemporal dementia or parkinsonism.[27,39,49] One report even described spontaneous acute quadriplegia secondary to intracranial hypotension;[53] associated tonsillar herniation has in rare cases caused brainstem Duret hemorrhages and morbid outcomes.[13,48] Additionally challenging is that findings on axial head CT scans may mimic primary chronic SDH or cerebral edema, with the diagnosis often not made until further workup with MRI studies reveals the pathognomonic features of intracranial hypotension.

Intracranial hypotension may be iatrogenic, resulting from persistent spinal CSF leakage following procedures including spinal anesthesia, lumbar drainage, or spine surgery. Mild spinal CSF leakage is common, leading to the well-recognized postdural puncture headache, the incidence of which has been correlated with the needle size used;[12] however, persistent spinal CSF leakage or high rates of flow can lead to chronic symptoms and complications, including ICH. Indeed, fatal subdural hemorrhage

Abbreviations used in this paper: CTM = CT myelogram; EBP = epidural blood patch; GCS = Glasgow Coma Scale; ICH = intracranial hemorrhage; ICP = intracranial pressure; LP = lumbar puncture; MRIM = MRI myelogram; SDH = subdural hematoma.

has been reported after spinal anesthesia with needles even as small as 27 gauge.[11] Spinal CSF leaks may also develop spontaneously, leading to a syndrome of spontaneous intracranial hypotension. The incidence of spontaneous intracranial hypotension has been estimated at 1 in 20,000, although frequent misdiagnosis may make the condition more common than widely appreciated.[33,51] Risk factors for spontaneous intracranial hypotension are not well understood, and the site of leakage is often never identified. However, CSF leaks have frequently been shown to develop from rupture of dural diverticula.[55] Connective tissue disorders such as Ehlers-Danlos II, Marfan, and polycystic kidney disease have been associated with increased risk of intracranial hypotension.[51,52] Rarely, the dura mater may be physically eroded by spinal osteophytes.[8,22,66,68] Intracranial hypotension presenting as severe depression of mental status or coma is unusual but has been reported multiple times in the literature (Table 1).

Although the diverse features of intracranial hypotension have been thoroughly reviewed elsewhere,[15,35,40,43,51] the diagnosis and management of this entity as a primary cause of coma have not previously been reviewed in detail. We provide a systematic review of the published reports describing intracranial hypotension as a verified cause of coma. Clinical, radiological, diagnostic, and treatment data are compiled and a management algorithm is proposed. Finally, we discuss the implications of numerous reports of ICH after spinal procedures wherein intracranial hypotension was probably present but either not recognized or not treated, sometimes with devastating outcomes. We begin by describing 3 cases of intracranial hypotension–associated coma that have not been previously reported in the literature.

New Cases

Case 1

This 64-year-old Hispanic woman presented initially with 10 days of nausea, vomiting, and headaches. She was found to have a clival chordoma causing compression of the cervicomedullary junction (Fig. 1A). A lumbar drain was used for a transsphenoidal debulking of the tumor. Intraoperatively, a dural defect was noted and repaired with Duragen, Tisseel, and a vascularized septal flap. Postoperatively, her lumbar drain was kept clamped, and she awoke appropriately, following commands; an MRI study revealed the anticipated postoperative changes. Shortly thereafter, CSF rhinorrhea was noted and her lumbar drain was opened to drain 15 ml/hour. The patient's cognitive state subsequently deteriorated, requiring reintubation. Her mental status thereafter fluctuated widely—at times she briskly followed commands, and at other times she was unarousable. Multiple attempts at extubation failed. Follow-up MRI studies obtained on postoperative Day 7 revealed new effacement of the basal cisterns, flattening of the pons, sagging of the posterior fossa, and engorgement of the venous sinuses consistent with intracranial hypotension (Fig. 1B).

Her lumbar drain was clamped, and she was maintained in the reverse Trendelenburg position; however, she failed to make a full cognitive recovery and continued to demonstrate CSF rhinorrhea. On postoperative Day 9 she was taken back to the operating room for exploration. No discrete CSF leak was identified; however, the closure was revised and reinforced with an abdominal fat graft. A tracheostomy was also performed at this time, given the patient's multiple difficult reintubations. Postoperatively no further CSF leak was noted, her lumbar drain remained clamped, and her mental status steadily improved to baseline over the subsequent 36 hours. Follow-up MRI studies revealed resolution of intracranial hypotension findings (Fig. 1C), and she was subsequently discharged to a skilled nursing facility.

Case 2

This 59-year-old Taiwanese woman had a history of clear cell renal carcinoma status post–left nephrectomy. She had spinal metastases from T-12 to L-3 at the time of her presentation and was treated with radiotherapy and sunitinib for long-term control. Approximately 1 year after diagnosis, she presented with altered mental status, fever, coffee-ground emesis, and bleeding from her eyes, nose, and mouth. Workup revealed a urinary tract infection, neutropenia, and pancytopenia, which were ultimately attributed to Evans syndrome, a rare autoimmune hemolytic disorder. She was treated with antibiotics, steroids, and plasmapheresis, and the sunitinib was discontinued.

On the morning of hospital Day 2, the patient became increasingly confused and somnolent. Head CT scans revealed small bilateral extraaxial collections and effacement of the third ventricle and suprasellar cistern. Brain MRI studies revealed diffuse dural enhancement, bilateral thin holohemispheric subdural hygromas, engorged dural sinuses, and downward displacement of the brainstem and cerebellum, with tonsillar herniation; findings that are consistent with intracranial hypotension (Fig. 2 left). A radionuclide cisternogram demonstrated some increased radiotracer activity anterior to the cervical and upper thoracic spine but did not reveal a clear site of extravasation. The CSF was xanthochromic, with elevated protein, but otherwise normal. The patient was maintained flat in bed for 72 hours, during which time her lethargy and confusion improved to near baseline. Head-of-bed elevation to 30° was then performed, whereupon she became stuporous within 30 minutes, requiring Trendelenburg position to recover. A CTM demonstrated contrast pooling in Tarlov cysts bilaterally at C4–7 and L1–2, but no definitive contrast extravasation (Fig. 2 right). A 30-ml EBP was placed under fluoroscopic guidance at L3–4, and after 24 hours of flat bed rest, she tolerated raising the head of the bed, with no recurrence of symptoms. She remained neurologically normal at her 2-month follow-up visit.

Case 3

This 32-year-old man had a history of acute T-cell lymphoma in complete remission. Approximately 6 months after completion of chemotherapy, and shortly after starting Coumadin for a peripherally inserted central catheter–related thrombus, he presented to the emergency department with a 4-day history of severe headaches that

TABLE 1: Overview of reported cases of intracranial hypotension and coma*

Case No.	Authors & Year	Age (yrs), Sex	Possible Associated Mechanism &/or Risk	Presenting Symptoms	Worst GCS or MS Score	Imaging Findings†	Subdural Fluid Evac & MS Outcome	IC Hypo Txs	Outcome	Leak Site Identified‡
1	Holmes, 1953 (Case 1)	73, F	spontaneous (fall from standing)	HA, incontinence	unarousable	SDH (no imaging)	surgical evac, trans imp	IV distilled H_2O	FR	ND
2	Nakajima et al., 1996	56, F	spontaneous (dancing/ aggressive head shaking)	HA, ortho AMS	decerebrate	bilat SDH	surgical evac, trans imp; re-evac × 2	flat bed rest	FR	ND
3	Beck et al., 1998	40, F	spontaneous	ortho HA, seizure, N/V	obtunded	bilat hygromas, DDE, PF coning, TH	no evac	EBP	FR	no (CTM)
4	Binder et al., 2002	43, M	spontaneous	ortho HA, CN VI palsy	obtunded	bilat hygromas, DDE, PF coning, TH	surgical evac, no imp	EBP × 2 & ITSI§	FR	no (CTM)
5	Evan & Mokri, 2002	42, M	spontaneous	ortho HA	obtunded	bilat hygromas, DDE, TH	no evac	EBP	FR	ND
6	Terajima et al., 2002	48, F	spontaneous	ortho HA, LOC	LOC requiring intubation	bilat SDH, DDE, downward herniation	surgical evac, no imp	EBP	FR	yes (MRI); T3–4
7	Whiteley et al., 2003	62, M	spontaneous	ortho HA, diplopia	GCS 7	bilat hygromas, DDE, TH	surgical evac, trans imp; re-evac × 1	EBP w/ ITSI	FR	ND
8	Bloch & Regli, 2003	38, F	lumbar drain for aneurysm clipping	HA, CN VI palsy	lethargy requiring intubation	herniation of corpus callosum, PF coning, TH	NA	EBP	FR	ND
9	Samadani et al., 2003 (Case 1)	42, F	lumbar drain for aneurysm clipping	AMS	decerebrate	bilat transtentorial herniation	NA	EBP	FR	ND
10	Kashmere et al., 2004	49, M	spontaneous (Hx of PT, neck manip, & RT/op for oropharyngeal SCC)	ortho HA, continuous hiccups, N/V	GCS 6	bilat hygroma, bilat SDH, DDE, PF coning, TH	biopsy performed; worsened afterward	EBP	FR	no (RNM)
11	Weisfelt et al., 2004	51, M	spontaneous	HA, AMS, ataxia	GCS 5	bilat hygromas, DDE, PF coning, TH	no evac	ITSI w/ imp, EBP	FR	yes (CTM)
12	Tsai et al., 2005	69, M	spontaneous	ortho HA, N/V	obtunded	bilat SDH, DDE, PF coning, TH	no evac	EBP × 2	FR	yes (MRIM); T7–9
13	Kremer et al., 2005	64, M	intrathecal chemo for Hodgkins lymphoma	AMS, CN III palsy, lt hemiparesis	GCS 3	bilat hygromas, DDE, PF coning, TH	no evac	EBP	no imp; died of pneumonia	ND
14	Sayer et al., 2006	62, M	spontaneous (severe cough for 2 mos)	nonortho HA, fatigue, slowed mentation	GCS 8	bilat SDH, DDE, PF coning, TH	surgical evac, trans imp; pneumocephalus evac × 2, bifrontal craniotomy	EBP	FR	ND
15	Akkawi et al., 2006	66, M	spontaneous	ortho HA, CN III & VII palsy, plegia, paresthesia	obtunded	bilat hygromas	surgical evac, no imp	EBP × 3,§ ITSI	FR	no (CTM)

(continued)

TABLE 1: Overview of reported cases of intracranial hypotension and coma* *(continued)*

Case No.	Authors & Year	Age (yrs), Sex	Possible Associated Mechanism &/or Risk	Presenting Symptoms	Worst GCS or MS Score	Imaging Findings†	Subdural Fluid Evac & MS Outcome	IC Hypo Txs	Outcome	Leak Site Identified‡
16	Zada et al., 2007	44, M	spontaneous	HA, ortho AMS, CN III palsy, N/V	obtunded	bilat hygromas, DDE, PF coning	no evac	EBP§	FR	yes (CTM); C1–3 & T6–10
17	Schievink et al., 2007	68, M	spontaneous	ortho HA & AMS	GCS 6	bilat SDH, DDE, PF coning	no evac	fibrin glue,§ EBP	FR	yes (CTM); level NR
18	Chi et al., 2007	43, M	spontaneous (Hx of spontaneous IC hypo 2 mos prior, resolved)	ortho HA, nausea, dizziness	GCS 3	bilat SDH, DDE, PF coning, transtentorial herniation	occipital craniectomy & evac, no imp	EBP	poor; DHs, multi infarcts	yes (MRIM); C1–3 & T-10
19	Mathew & Komotar, 2008 Case 1	36, F	lumbar drain for aneurysm clipping	AMS	GCS 5	subdural hygroma, PF coning	no evac	EBP	FR	ND
20	Case 2	26, M	lumbar drain for aneurysm clipping	ortho HA, CN III palsy	obtunded	SDH, PF coning, subfalcine herniation	no evac	EBP	FR	ND
21	Case 3	62, F	lumbar drain w/ craniotomy for SAH	AMS	obtunded	transtentorial herniation, PF coning	NA	EBP	near FR	ND
22	Aghaei Lasboo et al., 2008	46, M	spontaneous (heavy lifting; back strain)	ortho HA	GCS 4	bilat SDH, DDE, PF coning, TH	no evac	fibrin glue & ITSI;§ ITSI, EBP, & fibrin glue; EBP × 3	FR	yes (CTM); T2–7
23	Ferrante et al., 2009	62, M	spontaneous	ortho HA & AMS, N/V	GCS 5	bilat SDH, DDE, PF coning	surgical evac, no imp	EBP × 3	FR	no (CTM)
24	Sayao et al., 2009	58, M	spontaneous (distant Hx of whiplash from MVA)	frontotemporal dementia	GCS 3	bilat hygromas, DDE, PF coning	no evac	EBP w/ ITSI	FR	yes (CTM, MRIM); C-2
25	Schievink et al., 2009	44, F	spontaneous (aneurysm clipping w/o lumbar drain; Hx of PKD)	HA, CN III palsy, hemiparesis	GCS 6	SDH	surgical evac, no imp	surgical repair,§ EBP	FR	yes (CTM); T-5
26	Veeravagu et al., 2011¶	36, M	spontaneous, due to ventral T1–2 osteophyte	ortho HA & AMS, diplopia, N/V, tinnitus, vertigo	GCS 7	bilat SDH, DDE, PF coning, TH	surgical evac, trans imp	surgical repair,§ EBP × 2, ITSI	FR	yes (CTM); T1–2
27	present study Case 1	64, F	lumbar drain, clival chordoma resection, CSF rhinorrhea	AMS	GCS 7	venous sinus engorgement, PF coning	NA	surgical repair	near FR	ND

(continued)

TABLE 1: Overview of reported cases of intracranial hypotension and coma* *(continued)*

Case No.	Authors & Year	Age (yrs), Sex	Possible Associated Mechanism &/or Risk	Presenting Symptoms	Worst GCS or MS Score	Imaging Findings†	Subdural Fluid Evac & MS Outcome	IC Hypo Txs	Outcome	Leak Site Identified‡
	present study (continued)									
28	Case 2	59, F	spontaneous (Hx of RCC w/ spinal mets; Evans syndrome)	ortho AMS	obtunded	bilat hygromas, DDE, venous sinus engorgement, PF coning, TH	no evac	EBP	FR	no (RNM/CTM)
29	Case 3	32, M	spontaneous (Hx of T-cell lymphoma in remission; on Coumadin, last LP >2 mos prior)	HA, ortho AMS, CN III palsy	GCS 5	bilat SDH, PF coning, subfalcine herniation	trans imp	EBP	FR	no (MRI)

* AMS = altered mental status; chemo = chemotherapy; CN = cranial nerve; DDE = diffuse dural enhancement; DH = Duret hemorrhage; evac = evacuation; FR = full recovery; HA = headache; Hx = history; IC hypo = intracranial hypotension; imp = improvement; ITSI = intrathecal saline infusion; IV = intravenous; LOC = loss of consciousness; manip = manipulation; mets = metastases; MS = mental status; MVA = motor vehicle accident; multi = multiple; NA = not applicable; ND = not done; NR = not reported; N/V = nausea/vomiting; ortho = orthostatic; PF = posterior fossa; PKD = polycystic kidney disease; PT = physical therapy; RCC = renal cell carcinoma; RNM = radionuclide myelogram; RT = radiation therapy; SAH = subarachnoid hemorrhage; SCC = squamous cell carcinoma; TH = tonsillar herniation; trans = transient; Txs = treatments.

† All cases additionally showed effacement of basal cisterns. Only data shown or described in the original publication are included, but other findings are not excluded.

‡ Methodology of any myelographic investigation is given in parentheses. If nothing is listed, no such study was performed.

§ The most effective of the multiple listed treatments.

¶ At the time of writing, this case was included in an article submitted for publication.

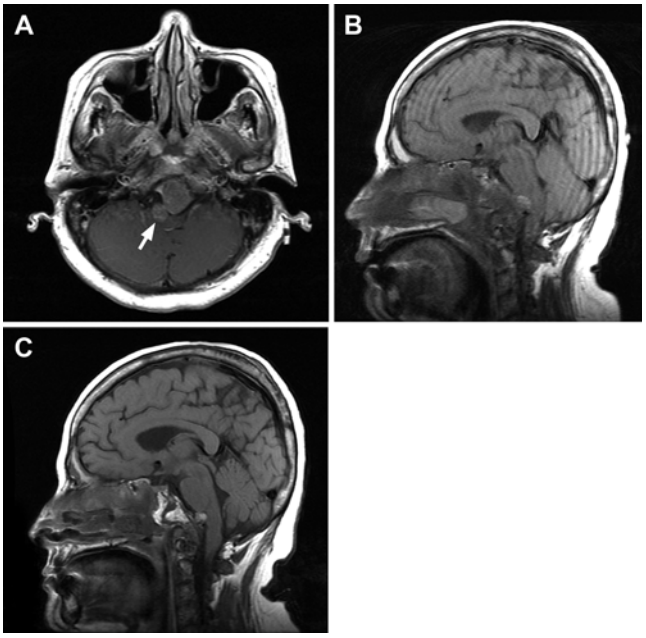

Fig. 1. Case 1. **A:** Preoperative axial T1-weighted postcontrast MRI study showing a lobular clival mass significantly deforming the ventral medulla *(arrow)*. **B:** Midline sagittal T1-weighted MRI study obtained on postoperative Day 7 with lumbar drain open demonstrating severe flattening of the pons against the clivus and sagging of the posterior fossa. **C:** Midline sagittal T1-weighted MRI study obtained after surgical reinforcement of the CSF leak, clamping of the lumbar drain, and resolution of symptoms demonstrating restoration of normal CSF spaces in the posterior fossa and basal cisterns.

were worse when lying flat. His last surveillance LP had been more than 2 months prior. Initial head CT scans revealed bilateral acute-on-chronic SDHs (rt > lt), with 2 mm of midline shift (Fig. 3A). His GCS score deteriorated to 11 by hospital Day 5, prompting bilateral bur hole evacuation of the SDH. Postoperatively his mental status transiently improved, but was back to GCS Score 11 by the next day. Follow-up head CT scans demonstrated stable postevacuation residual SDH. Workup included electroencephalography studies for seizures and LP for meningitis, both of which were normal.

On hospital Day 8 the patient's mental status declined further, and his pupils became anisocoric and sluggishly reactive, prompting intubation for airway protection (GCS Score 5T), administration of hypertonic saline, and placement of an external ventricular catheter, which revealed normal ICP. The MRI studies revealed effacement of the basal cisterns, flattening of the pons against the clivus, and caudal descent of the optic chiasm and diencephalon (Fig. 3B); however, intracranial hypotension was not diagnosed at that time. His mental status gradually improved, allowing for extubation; however, he followed a pattern of waxing and waning mental status (GCS Score 10–14). After 3 days it was noted that he seemed to improve while lying flat but worsened when upright, raising suspicion for intracranial hypotension. The patient was kept flat for 36 hours, during which time his mental status remained stable (GCS Score 14), yet he continued to fail subsequent head-of-bed tests. Follow-up brain MRI findings appeared stable, and this was read as consistent with intracranial hypotension. A full spine MRI series failed to localize a site of CSF leakage. The following day the patient received a 30-ml EBP at the level of L5–S1, after which he tolerated raising of the head of the bed and was able to be discharged within a few days. On 4-month follow-up the patient remained neurologically stable, and brain MRI studies revealed no evidence of intracranial hypotension (Fig. 3C).

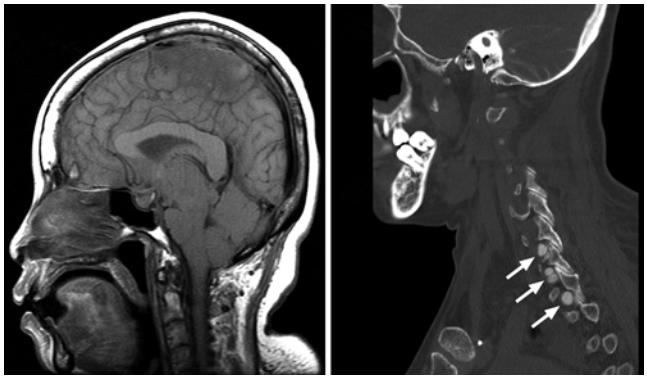

Fig. 2. Case 2. **Left:** Midline sagittal T1-weighted MRI study obtained at presentation showing posterior fossa crowding with pontine flattening and tonsillar herniation, consistent with intracranial hypotension. **Right:** Sagittal CTM demonstrating Tarlov cysts *(arrows)* at C6–7, C7–T1, and T1–2.

Systematic Review

Search Methods

We performed an English language literature PubMed search by using combinations of key words—including intracranial hypotension, intracranial hypovolemia, spinal CSF leak, lumbar drain, lumbar puncture, spinal anesthesia, epidural anesthesia, subdural hematoma, subdural hygroma, durotomy, herniation, Duret hemorrhage, overdrainage, and coma—to identify reports of patients with intracranial hypotension and coma or severe depression of mental state. Diagnosis of intracranial hypotension required demonstration of classic radiological signs, typically including MRI studies with sagittal cuts demonstrating "brain sag," with downward displacement of the diencephalon toward the posterior fossa and effacement of basal cisterns, stretching of the optic apparatus, and crowding or "coning" of the posterior fossa. Dural enhancement and venous engorgement were also frequently observed but not required. In some cases, including those treated before availability of MRI, intracranial hypotension was confirmed by direct measurement of ICP. Patients with confirmed intracranial hypotension were included for analysis if they demonstrated a GCS score of 8 or less, required intubation for airway protection due to impaired mental status, were obtunded, unarousable, or if other clear description was provided demonstrating profound depression of consciousness. Patients demonstrating only sleepiness or altered mental status without coma were excluded from analysis.

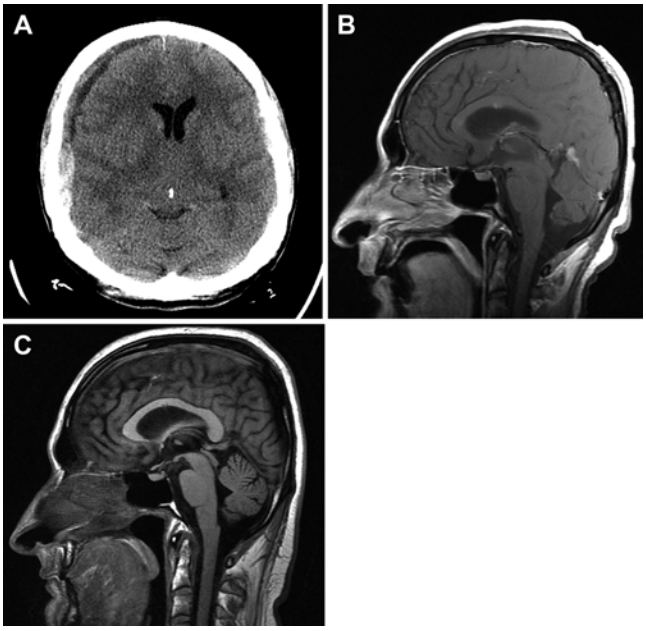

Fig. 3. Case 3. **A:** Axial CT scan showing bilateral mixed-density subdural fluid collection (rt > lt) with mild (2-mm) midline shift. **B:** Midline sagittal T1-weighted MRI study obtained after addition of contrast material showing flattening of the pons against the clivus and descent of the midbrain characteristic of intracranial hypotension. **C:** Midline sagittal T1-weighted FLAIR MRI study showing resolution of intracranial hypotension findings, with a wider prepontine cistern at the 4-month follow-up visit.

Results

Twenty-six patients described in 24 publications met inclusion criteria and were analyzed in conjunction with the 3 patients described above. The details of each case are presented in Table 1; findings are summarized in Table 2. The average age of patients with intracranial hypotension and coma was 51 years, with a male proportion of 62%. There were 22 cases (76%) of spontaneous intracranial hypotension, and 7 (24%) with a history of recent spinal procedures, including lumbar drainage in 6 patients and intrathecal chemotherapy in 1 patient. One other patient had a distant history of LP more than 2 months prior to symptom onset. A history of orthostatic headache was noted in 14 patients (48%). Orthostatic alteration of mental status was documented in 7 patients (24%), though the positionality of headache or altered mental status was not evaluated in all cases. Cranial nerve palsies were reported in 10 patients (34%; including 2 cases in which diplopia was reported but the cranial nerve was not specified), with cranial nerve III and VI palsy being most frequently documented.

All cases with sagittal views demonstrated at least some component of pontine flattening, with sagging of the posterior fossa or effacement of the basal cisterns. Additionally, 19 (66%) demonstrated herniation, with tonsillar herniation accounting for 13 (68%) of these. Twenty-five patients (86%) demonstrated at least some accumulation of subdural fluid. Diffuse dural enhancement was reported in 18 cases (62%). Imaging was performed to identify the site of CSF leakage in 17 patients (59%), with the leak identified in 10 (59%) of these. A CTM was the study most frequently used to identify the source of spinal CSF egress.

Of the 25 patients with a subdural fluid collection, an SDH was diagnosed in 14 (56%). Of the 12 patients who underwent subdural fluid/SDH evacuation, 6 demonstrated some transient improvement in mental status prior to varying degrees of subsequent redeterioration. The remaining 6 patients experienced no benefit at any time and either remained stable or experienced further neurological deterioration postoperatively (Table 1). Three underwent multiple surgeries for repeat evacuation.

One or more EBPs were used in 26 patients (90%), with subsequent resolution of symptoms in 22 (85%) of these. When the EBP failed, percutaneous injection of fibrin glue or surgery proved ultimately effective. In the

TABLE 2: Summary of reported findings in intracranial hypotension–associated coma

Characteristic or Finding	Value*
demographic	
male	62
average age in yrs	51
clinical	
orthostatic HA	48
orthostatic AMS	24
CN palsy	34
imaging	
subdural fluid collection	86
SDH if fluid collection	56
hygroma if fluid collection	48
diffuse dural enhancement	62
effacement of basal cisterns	86
PF coning	72
effacement of basal cistern or coning	93
herniation (any)	66
tonsillar herniation if herniation present	68
treatment attempts	
EBP	90
surgical repair	10
percutaneous fibrin glue	7
subdural evac if fluid collection present	48
effective treatments	
EBP if attempted	85
surgical repair if attempted	100
percutaneous fibrin glue if attempted	100
full or near full recovery	93
CSF leak investigation	
leak site identified	34
leak identification attempted	59
leak identified if attempted	59
iatrogenic	24

* All values are expressed as percentages, except for the average age.

first 2 reported cases, improvement ultimately occurred after a period of conservative therapy, the first being treatment with intravenous distilled water. All other patients each received treatment aimed at directly stopping the CSF leak, typically via EBPs, with or without other therapies as needed. In patients with SDH who did not undergo surgery, each improved (with the exception of 1 who succumbed to pneumonia). Intrathecal saline infusion was used to help stave off downward herniation in 7 (25%), with variable outcomes.

Discussion

Clinical Presentation

The most common symptom of intracranial hypotension is orthostatic headache, which is present in more than 90% of diagnosed cases.[58] In this review we found that 76% of patients had a documented history of headache, which was known to have been exacerbated in the upright position in two-thirds of these. The patient in Case 3 was atypical in that his headache was worse lying flat, although such paradoxical headaches have previously been reported.[36] If the patient's subsequent mental status deterioration is predominantly a result of spinal CSF leakage leading to excessive brain sag, with posterior fossa crowding causing brainstem compression or ischemia, Trendelenburg positioning should improve mental status and provide confirmation of the diagnosis. Among the patients reviewed, positional changes in mental status were only documented in 24%. The reluctance to place a comatose patient in a flat or head-down position due to risk of aspiration may have impeded clinical diagnosis in some cases, leading to diagnosis only after MRI studies were obtained. Therefore, the reliability of this feature of intracranial hypotension in patients presenting with coma remains to be directly evaluated. Patients whose neurological examination fails to improve when they are placed in the Trendelenburg position, as well as those who respond incompletely to EBP treatment, may additionally be suffering direct neurological symptoms as a result of intracranial hypotension complications, including large extraaxial collections, venous infarction, or parenchymal hemorrhage.

Cranial nerve palsies are among the most common focal neurological deficits associated with intracranial hypotension, occurring in 34% of the cases reviewed here. Pupillary dilation, generally interpreted as a grave prognostic indicator in the comatose patient, may result from traction on the third cranial nerve in the setting of low ICP. Therefore, patients with intracranial hypotension and very poor scores on neurological examinations (including GCS Score 3) with signs of brainstem dysfunction and fixed, dilated pupils may in fact have an excellent prognosis. This fact is of particular importance, because there have been some reported cases in which intracranial hypotension was suspected wherein care was withdrawn despite, in retrospect, a potentially favorable prognosis.[17,32]

Seventy-six percent of cases reviewed, including 2 of our 3 new reports (Cases 2 and 3) were categorized as spontaneous due to the absence of any iatrogenic cause for CSF leakage. However, "spontaneous" leaks may frequently be preceded by some event such as blunt trauma, physical straining, severe coughing fits, or aggressive cervical manipulation (Table 1) that could conceivably act on a preexisting dural weakness such as a Tarlov cyst or area of dural erosion. Case 3 is considered spontaneous despite a history of LPs, because symptom onset occurred acutely, more than 2 months after his most recent LP.

Twenty-four percent of cases reviewed, including one of our newly reported cases (Case 1), were associated with a lumbar drain. Although significant complications of lumbar drains are unusual, intracranial hypotension severe enough to cause brainstem dysfunction, acute SDHs, and tension pneumocephalus have been reported even during or following standard, uncomplicated lumbar drainage.[9,17,34,41] Cases of acute lumbar CSF overdrainage have additionally been reported, either during cranial surgery to facilitate brain relaxation, or due to an error in lumbar drain management. In some cases, such acute overdrainage has led to an acute herniation syndrome, with devastating brainstem hemorrhage.[46,48] Because the focus of this review is the syndrome of persistent intracranial hypotension associated with coma, such cases of acute CSF overdrainage are not included in Table 1. Nevertheless, they serve to emphasize the potentially devastating outcomes of spinal CSF overdrainage.

Radiological and Diagnostic Studies

Head CT Scans. Intracranial hypotension is difficult to demonstrate definitively on routine axial head CT scans. Reported findings include effacement of the basal cisterns out of proportion to the size of any extraaxial collection, as well as third ventricular collapse and diffuse edema. Given the inability to appreciate pontine flattening or descent of the diencephalon without sagittal views, CT scanning rarely, if ever, leads to definitive diagnosis. Therefore, the diagnosis of intracranial hypotension depends heavily on clues from the patient's history, with further imaging studies obtained based on clinical suspicion.

Brain MRI Studies. The MRI studies provided the definitive diagnosis for 90% of the patients in this review. The findings of intracranial hypotension as evaluated by MRI studies are well described.[21,63] Given decreased CSF volume, the brain settles or "sags" down onto the cranial floor. Resultant changes include effacement of the basal cisterns; stretching or flattening of the optic apparatus; and descent of the thalamus toward the posterior fossa, with effacement of the third ventricle, flattening of the pons against the clivus, crowding of the posterior fossa, venous engorgement, dural enhancement, pituitary enhancement, and accumulation of subdural fluid collections.[1] Settling of the cerebral convexities away from the cranially adherent dura mater places tension on distended subdural veins, which may rupture and cause unilateral or bilateral hematomas.[10,54] As intracranial hypotension progresses, the posterior fossa becomes increasingly crowded, with structures settling down toward the foramen magnum, frequently with tonsillar herniation. Mul-

tiple descriptive terms have been used to describe these changes on MRI studies, including "brain sag" and "posterior fossa coning." Brain shifts relative to the immobile tentorium and foramen magnum may result in transtentorial and tonsillar herniation, respectively. Additionally, asymmetrical subdural fluid collections or hemorrhage may prompt midline shift and subfalcine herniation in some cases.

Published case series of intracranial hypotension reported subdural collections in anywhere from 10% to 80% of cases, with SDH present in approximately 40% of these.[27,43,51,54] By comparison, subdural fluid collections were present in 86% of the comatose patients with intracranial hypotension who were reviewed, with SDH diagnosed in 56% of these, probably representing the advanced pathophysiological effects of intracranial hypotension in patients who have progressed to coma.

Brain imaging studies may reveal additional complications of intracranial hypotension, including tension pneumocephalus in patients with prior cranial surgery, infarcts secondary to vascular compression with herniation, and brainstem (Duret) hemorrhage due to acute downward herniation. Other rare complications such as obstructive hydrocephalus secondary to cerebellar hemorrhages and venous sinus thrombosis and infarction have also been reported.[16] Therefore, a wide variety of intracranial findings can be consistent with an underlying diagnosis of intracranial hypotension.

Myelography Studies. A search for the site of spinal CSF leakage is frequently undertaken in patients with intracranial hypotension. However, empirical treatment with an EBP is often successful even if the exact site of the CSF leak is unknown[51] and may thereby help avoid an unnecessary diagnostic procedure. Nevertheless, an EBP targeted to a known CSF leak has a higher likelihood of being effective than one performed empirically, or "blind."[14] The CTM and MRIM are the most sensitive and frequently used studies to localize a spinal CSF leak. Postmyelogram CTs may be obtained shortly after contrast infusion to detect brisk leaks and in a delayed manner to identify the site of slow leaks. Radionuclide myelography or cisternography has a lower sensitivity but can be attempted in patients with occult CSF leaks not visualized by other means. Despite a vigilant search, the site of persistent leakage may remain occult in 35%–50% of cases.[51]

Lumbar Puncture. Lumbar puncture is frequently performed in the workup of patients with coma of unclear origin, and in intracranial hypotension may reveal a mild lymphocytic pleocytosis and slightly elevated protein.[27,35] Care is warranted when the lumbar cistern is punctured for LP or myelography, given the potential for further exacerbation of CSF hypovolemia from these additional spinal dural punctures.[4,34] Decompression of the thecal sac from prior spinal CSF leakage may preclude CSF access in some cases. In patients not already intubated, but for whom intracranial hypotension is suspected, the patient should be maintained flat during and following the procedure, with resources available to secure the airway if necessary.

Treatment Procedures

In Fig. 4, we summarize our suggested algorithm for the management of intracranial hypotension and coma. This treatment algorithm is based on the sum of anecdotal evidence compiled from published reports of intracranial hypotension presenting with coma, with a focus on timely diagnosis, complication avoidance, and treatments targeted toward the underlying disorder. In this section, we discuss the decision-making process and management at each stage of diagnosis and treatment of intracranial hypotension.

Acute Management. Perhaps the greatest barrier to appropriate management of patients with intracranial hypotension is misdiagnosis, with primary SDH being the most common working diagnosis reached. The airway should be secured early in any patient with coma; death from pneumonia is a documented though avoidable complication of intracranial hypotension.[25] Probably the fastest and simplest way to improve mental status in intracranial hypotension is by placing the patient in the Trendelenburg position. This simple maneuver relieves pressure on the brainstem and may rapidly improve cognitive status. Slow recovery may occur following severe or prolonged brainstem compression, or if ischemic or hemorrhagic injury has occurred.[13,27] Adequate hydration is among the standard treatments for any post-LP headache, and should be provided. Some have reported rapid improvement in mental status with intrathecal saline infusion to reverse the downward herniation. What additional benefit this yields over placing the patient in the Trendelenburg position, however, is not clear, and reported outcomes have been mixed.[1,2,7,64,65]

Epidural Blood Patch. Definitive treatment of intracranial hypotension requires the spinal CSF leak to be sealed (Fig. 4). Placement of an EBP remains the most common and effective treatment for intracranial hypotension. Case series have shown a single EBP to be an effective treatment in 36%–90% of patients with intracranial hypotension.[6,20,59] In our review of comatose patients, EBPs were successful in reversing the comatose state in 85%. After EBP, swift recovery of mental status often ensued within a matter of minutes, although in several cases multiple EBPs were required. Some have proposed that an appropriate treatment algorithm should involve, at first, an empirical 10- to 20-ml autologous EBP at the thoracolumbar junction, with subsequent Trendelenburg positioning to improve distribution throughout the epidural space. If symptoms persist, additional injections at other levels with volumes up to 100 ml have been proposed, with a period of days between injections to avoid excessive epidural compression.[51] Failure to recover after treatment with EBPs should raise suspicion for not only persistent CSF leakage, but other underlying injury, ranging from brainstem contusion to venous infarct or meningitis. Restoration of the basal cisterns, with decreased posterior fossa crowding and movement of the pons away from the clivus, should provide evidence of successful EBP placement.

Placement of an EBP can acutely raise ICP due to

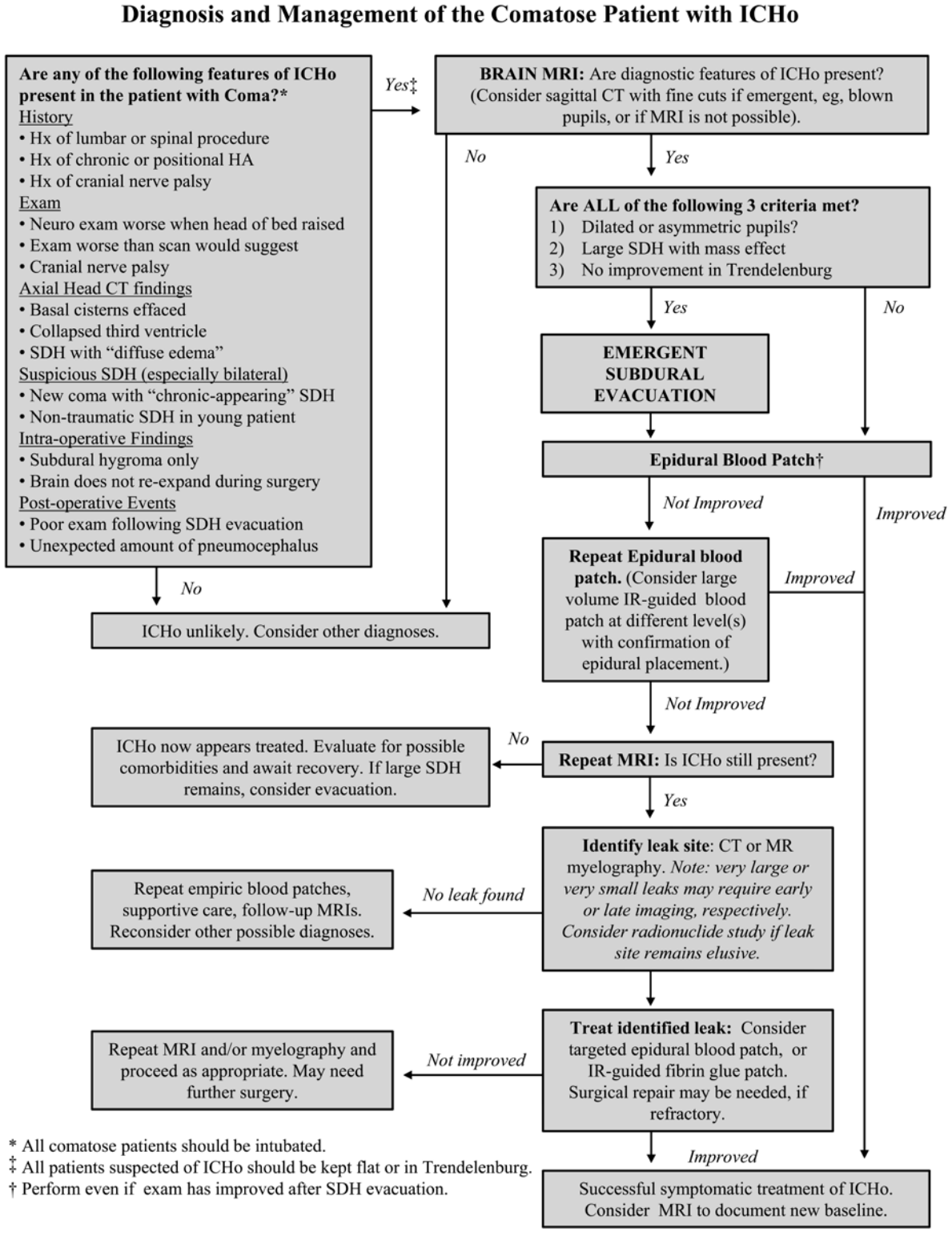

Fig. 4. Management algorithm for diagnosis and treatment of intracranial hypotension (ICHo) in the comatose patient. Hx = history; IR = interventional radiology.

mass effect of the blood on the lumbar cistern.[44] Although this is probably responsible for the almost immediate relief of headache in conscious patients and the frequently rapid improvement in mental status in comatose patients, some have argued against the use of EBP in the comatose patient with an ICH, due to concerns of further increased ICP.[3] To our knowledge, there has only been one published report of neurological deterioration as a result

of EBP, and this was in a patient with previously undiagnosed communicating hydrocephalus who was unknowingly dependent on spinal CSF leakage.[60] In almost all other cases with documented intracranial hypotension, EBP appears to be a safe and effective therapy, even in the setting of large SDHs.[54]

Epidural Fibrin Glue. If no improvement occurs after multiple properly placed EBPs, percutaneous fibrin glue has been used successfully to treat intracranial hypotension presenting with coma. This treatment is ideal if a site of EBP-refractory leak has been identified, and may enable avoidance of open surgical repair in up to half of such patients.[1,51,56]

Surgical Repair. Surgical exploration and repair may be appropriate for patients with refractory leakage from an identifiable site. Typically, leakage in spontaneous cases is from dural diverticula that may be repaired by suture, clipping, patching, or ligation. In cases of dural erosion by osteophytes, EBP is rarely successful, and open repair is generally ultimately required. Leakage of CSF into the thoracic cavity, such as following thoracic spine surgery, may prove to be a particular challenge, due in part to the ongoing negative intrathoracic pressure, and creative approaches to surgical repair may be needed.[16,42]

Evacuation of Subdural Collections. Difficult management questions arise in patients with intracranial complications of intracranial hypotension, such as large SDHs or intraparenchymal hemorrhages. Although these may be secondary to an underlying spinal CSF leak and may resolve spontaneously after correction of the intracranial hypotension,[18,45] clinical judgment is needed to decide when these complications themselves have become significant or even the sole contributors to the patient's ongoing comatose state. At some point, intracranial mass lesions may lead to a problem of increased rather than decreased ICP, necessitating surgical management.[16] Distinguishing between increased and decreased ICP states in these patients may be challenging, because both may result in a depressed level of consciousness, with impairment of cranial nerve function, including dilated pupils. We suggest that failure to improve after placement of the patient in the Trendelenburg position in the setting of a significant ICH with mass effect and pupil dilation should prompt emergency subdural evacuation. Consideration should be given to keeping the patient flat during and after the procedure to minimize pneumocephalus and reaccumulation of the subdural collection. After subdural evacuation, we recommend that the patient receive an empirical EBP to treat the presumed underlying cause of the subdural collection and to minimize the risk of reaccumulation (Fig. 4).

It should be noted that patients with a history of anticoagulation may be particularly at risk for poor outcomes from SDH. McHardy et al.[32] in 2001 presented a first report of SDH following lumbar drainage for prophylactic spinal cord protection during abdominal aortic aneurysm repair. The patient became unresponsive after being placed upright for the first time 2 days after lumbar drain removal. With a fixed and dilated pupil and a GCS score of 4, neurosurgical intervention was declined and the patient died. In a case series from Johns Hopkins, SDHs were reported in 8 patients (3.5%) undergoing lumbar drainage for thoracoabdominal aortic aneurysm repair.[17] Fifty percent (4 of 8) of these patients died, of whom only 1 underwent neurosurgical intervention, whereas the 4 surviving patients each underwent neurosurgical intervention. Subdural hematomas were associated with higher volumes of CSF drainage intraoperatively. Although radiological evaluation for ongoing intracranial hypotension was not performed in these cases, they may illustrate the potential consequences of failing to evacuate large symptomatic SDHs when needed after recent lumbar drainage.

If the patient improves with EBP treatment, even a significant SDH can be left to resolve spontaneously.[51,54] Intracranial pressure measurements were performed in 9 of the 12 patients reviewed who underwent subdural evacuation; none of these were found to have elevated ICP.[7,13,37,50,57,65] Thus, most of them probably did not need evacuation but were treated in part because intracranial hypotension was not diagnosed until after surgery. If the subdural fluid is observed intraoperatively to be under low pressure and the brain fails to reexpand on subdural evacuation, this may indicate persistent intracranial hypotension that will be incompletely treated with subdural evacuation alone. Opening the subdural space to air may promote pneumocephalus, further exacerbating the downward herniation.[50] Thus, care must be taken to ensure repair of the spinal CSF leak in conjunction with surgery to avoid further neurological deterioration or even death (Fig. 4). Of the 12 patients in our series who underwent evacuation, some improved transiently (possibly due to postoperative flat bed rest), but all patients soon reverted to their baseline level of coma or deteriorated even further after SDH evacuation. Reaccumulation of subdural fluid was the rule rather than the exception after surgery and led to additional procedures to reevacuate subdural fluid or air in 3 cases (Table 1).

A Larger Problem of Undiagnosed Intracranial Hypotension

Our inclusion criteria required not only coma, but that the diagnosis of intracranial hypotension be made, with confirmation by imaging findings or ICP monitoring. However, numerous other case reports and case series describe comatose patients in whom neither sagittal brain imaging nor ICP monitoring were performed, but whose clinical presentations suggest intracranial hypotension. Numerous procedures can lead to a syndrome of intracranial hypotension with potential for development of ICH and/or coma, including LP,[28] placement of a lumbar drain,[9,17,34,41] lumboperitoneal shunt,[30] baclofen pump,[26] spinal anesthesia,[70] epidural anesthesia with inadvertent durotomy,[70] myelography,[47] and spine surgery wherein CSF is encountered.[4,16] Several fatalities have been reported among patients with ICHs following spinal procedures, probably resulting from undiagnosed or untreated intracranial hypotension.[11,16,17,32,67]

Zeidan et al.[70] reviewed 47 reported cases of SDH after dural puncture during anesthesia procedures, in which most of the patients underwent surgical evacua-

tion. Among these 47 patients, only 6 were evaluated with MRI studies, and in these 6 the focus was on evaluation of the hematoma, with no case reports demonstrating a midsagittal MRI cut that would permit evaluation of ongoing intracranial hypotension. Eight of 47 patients had previously received EBPs for spinal headaches, but no patients received EBP after being found to have an SDH.[70] Most underwent SDH evacuation. Six patients died; 5 of these died after surgical evacuation of the SDH; the sixth died of acute respiratory arrest before surgery could be offered. Whether outcomes could have been improved with concurrent evaluation and treatment for persistent intracranial hypotension must remain a matter of speculation. Furthermore, the percentage of patients with "routine" chronic SDHs who may harbor an occult spinal CSF leak leading to undiagnosed spontaneous intracranial hypotension is entirely unknown. Schievink[51] recently described spontaneous resolution of chronic SDHs in 3 elderly patients who underwent anticoagulation therapy after treatment of underlying spontaneous CSF leaks. Therefore, spontaneous CSF leakage may warrant routine consideration in all patients with nontraumatic SDHs.

Conclusions

Intracranial hypotension is now a well-documented cause of coma, and one that is easily and frequently misdiagnosed. In our review of the literature, 26 patients with coma and well-documented intracranial hypotension were identified, in addition to 3 new cases from our own institution. Although evacuation of SDHs may be indicated in some patients, it is unnecessary in most cases and may lead to worsened outcomes. To help guide management, our proposed algorithm outlines factors that should prompt consideration of intracranial hypotension in the comatose patient and guides when to perform certain diagnostic or treatment interventions. The fact that a significant percentage of patients with SDHs after spinal procedures have morbid or fatal outcomes when a syndrome of ongoing intracranial hypotension was not recognized or treated underscores the importance of maintaining a high index of suspicion for intracranial hypotension in the comatose patient and effectively treating the underlying cause when diagnosed.

Disclosure

The authors have no conflict of interest to declare.

Author contributions to the study and manuscript preparation include the following. Conception and design: Burns, Loya. Acquisition of data: all authors. Analysis and interpretation of data: Burns, Loya. Drafting the article: Burns, Loya. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Burns. Statistical analysis: Loya. Administrative/technical/material support: Mindea, Yu, Venkatasubramanian, Chang. Study supervision: Burns, Mindea, Yu, Venkatasubramanian, Chang.

Acknowledgments

The authors thank Cindy H. Samos for editorial assistance and Elizabeth Hoyte for assistance with figure preparation.

References

1. Aghaei Lasboo A, Hurley MC, Walker MT, Surdell D, Song JK, Rosenow JM, et al: Emergent image-guided treatment of a large CSF leak to reverse "in-extremis" signs of intracranial hypotension. **AJNR Am J Neuroradiol 29:**1627–1629, 2008 (Erratum in **AJNR Am J Neuroadiol 31:**E38, 2010)
2. Akkawi N, Locatelli P, Borroni B, Agosti C, Pezzini A, Stefini R, et al: A complicated case of intracranial hypotension: diagnostic and management strategies. **Neurol Sci 27:**63–66, 2006
3. Amorim JA, Remigio DS, Damázio Filho O, de Barros MA, Carvalho VN, Valenca MM: Intracranial subdural hematoma post-spinal anesthesia: report of two cases and review of 33 cases in the literature. **Rev Bras Anestesiol 60:**620–629, 344–349, 2010
4. Andrews RT, Koci TM: Cerebellar herniation and infarction as a complication of an occult postoperative lumbar dural defect. **AJNR Am J Neuroradiol 16:**1312–1315, 1995
5. Beck CE, Rizk NW, Kiger LT, Spencer D, Hill L, Adler JR: Intracranial hypotension presenting with severe encephalopathy. Case report. **J Neurosurg 89:**470–473, 1998
6. Berroir S, Loisel B, Ducros A, Boukobza M, Tzourio C, Valade D, et al: Early epidural blood patch in spontaneous intracranial hypotension. **Neurology 63:**1950–1951, 2004
7. Binder DK, Dillon WP, Fishman RA, Schmidt MH: Intrathecal saline infusion in the treatment of obtundation associated with spontaneous intracranial hypotension: technical case report. **Neurosurgery 51:**830–837, 2002
8. Binder DK, Sarkissian V, Dillon WP, Weinstein PR: Spontaneous intracranial hypotension associated with transdural thoracic osteophyte reversed by primary dural repair. Case report. **J Neurosurg Spine 2:**614–618, 2005
9. Bloch J, Regli L: Brain stem and cerebellar dysfunction after lumbar spinal fluid drainage: case report. **J Neurol Neurosurg Psychiatry 74:**992–994, 2003
10. Brightbill TC, Goodwin RS, Ford RG: Magnetic resonance imaging of intracranial hypotension syndrome with pathophysiological correlation. **Headache 40:**292–299, 2000
11. Cantais E, Behnamou D, Petit D, Palmier B: Acute subdural hematoma following spinal anesthesia with a very small spinal needle. **Anesthesiology 93:**1354–1356, 2000
12. Carson D, Serpell M: Choosing the best needle for diagnostic lumbar puncture. **Neurology 47:**33–37, 1996
13. Chi NF, Wang SJ, Lirng JF, Fuh JL: Transtentorial herniation with cerebral infarction and duret haemorrhage in a patient with spontaneous intracranial hypotension. **Cephalalgia 27:** 279–282, 2007
14. Cho KI, Moon HS, Jeon HJ, Park K, Kong DS: Spontaneous intracranial hypotension: efficacy of radiologic targeting vs blind blood patch. **Neurology 76:**1139–1144, 2011
15. Chung SJ, Kim JS, Lee MC: Syndrome of cerebral spinal fluid hypovolemia: clinical and imaging features and outcome. **Neurology 55:**1321–1327, 2000
16. Cornips EM, Staals J, Stavast A, Rijkers K, van Oostenbrugge RJ: Fatal cerebral and cerebellar hemorrhagic infarction after thoracoscopic microdiscectomy. Case report. **J Neurosurg Spine 6:**276–279, 2007
17. Dardik A, Perler BA, Roseborough GS, Williams GM: Subdural hematoma after thoracoabdominal aortic aneurysm repair: an underreported complication of spinal fluid drainage? **J Vasc Surg 36:**47–50, 2002
18. de Noronha RJ, Sharrack B, Hadjivassiliou M, Romanowski CA: Subdural haematoma: a potentially serious consequence of spontaneous intracranial hypotension. **J Neurol Neurosurg Psychiatry 74:**752–755, 2003
19. Evan RW, Mokri B: Spontaneous intracranial hypotension resulting in coma. **Headache 42:**159–160, 2002
20. Ferrante E, Arpino I, Citterio A, Savino A: Coma resulting

from spontaneous intracranial hypotension treated with the epidural blood patch in the Trendelenburg position pre-medicated with acetazolamide. **Clin Neurol Neurosurg 111:**699–702, 2009
21. Forghani R, Farb RI: Diagnosis and temporal evolution of signs of intracranial hypotension on MRI of the brain. **Neuroradiology 50:**1025–1034, 2008
22. Hasiloglu ZI, Abuzayed B, Imal AE, Cagil E, Albayram S: Spontaneous intracranial hypotension due to intradural thoracic osteophyte with superimposed disc herniation: report of two cases. **Eur Spine J** [epub ahead of print], 2011
23. Holmes JM: Intracranial hypotension associated with subdural haematoma. **Br Med J 1:**1363–1366, 1953
24. Kashmere JL, Jacka MJ, Emery D, Gross DW: Reversible coma: a rare presentation of spontaneous intracranial hypotension. **Can J Neurol Sci 31:**565–568, 2004
25. Kremer S, Taillandier L, Schmitt E, Bologna S, Moret C, Picard L, et al: Atypical clinical presentation of intracranial hypotension: coma. **J Neurol 252:**1399–1400, 2005
26. Lad SP, Li G, Lin SC, Henderson JM: Intracranial hypotension from intrathecal baclofen pump insertion. A case report and review of the literature. **Stereotact Funct Neurosurg 86:** 75–79, 2008
27. Lai TH, Fuh JL, Lirng JF, Tsai PH, Wang SJ: Subdural haematoma in patients with spontaneous intracranial hypotension. **Cephalalgia 27:**133–138, 2007
28. Lee SJ, Lin YY, Hsu CW, Chu SJ, Tsai SH: Intraventricular hematoma, subarachnoid hematoma and spinal epidural hematoma caused by lumbar puncture: an unusual complication. **Am J Med Sci 337:**143–145, 2009
29. Leriche R: De l'hypotension du liquide céphalorachidien dans certaines fractures de la base du crâne et de son traitment par l'injection de serum sous la peau. **Lyon Chir 17:**638, 1920
30. Liao YJ, Dillon WP, Chin CT, McDermott MW, Horton JC: Intracranial hypotension caused by leakage of cerebrospinal fluid from the thecal sac after lumboperitoneal shunt placement. Case report. **J Neurosurg 107:**173–177, 2007
31. Mathew L, Komotar R: Epidural blood patch for severe postoperative intracranial hypotension. **J Neurosurg Anesthesiol 20:**49–52, 2008
32. McHardy FE, Bayly PJ, Wyatt MG: Fatal subdural haemorrhage following lumbar spinal drainage during repair of thoraco-abdominal aneurysm. **Anaesthesia 56:**168–170, 2001
33. Mea E, Chiapparini L, Savoiardo M, Franzini A, Grimaldi D, Bussone G, et al: Application of IHS criteria to headache attributed to spontaneous intracranial hypotension in a large population. **Cephalalgia 29:**418–422, 2009
34. Menon G, Bahuleyan B, Nair S: Acute subdural hematoma after transsphenoidal surgery. **J Clin Neurosci 16:**160–162, 2009
35. Mokri B: Spontaneous low cerebrospinal pressure/volume headaches. **Curr Neurol Neurosci Rep 4:**117–124, 2004
36. Mokri B, Aksamit AJ, Atkinson JL: Paradoxical postural headaches in cerebrospinal fluid leaks. **Cephalalgia 24:**883–887, 2004
37. Nakajima H, Sakai T, Aoki N, Takakura K: Bilateral chronic subdural hematomas associated with intracranial hypotension—case report. **Neurol Med Chir (Tokyo) 36:**647–649, 1996
38. Page F: Intracranial hypotension. **Lancet 1:**1–5, 1953
39. Pakiam AS, Lee C, Lang AE: Intracranial hypotension with parkinsonism, ataxia, and bulbar weakness. **Arch Neurol 56:** 869–872, 1999
40. Paldino M, Mogilner AY, Tenner MS: Intracranial hypotension syndrome: a comprehensive review. **Neurosurg Focus 15(6):**ECP2, 2003
41. Pepper JP, Lin EM, Sullivan SE, Marentette LJ: Perioperative lumbar drain placement: an independent predictor of tension pneumocephalus and intracranial complications following anterior skull base surgery. **Laryngoscope 121:**468–473, 2011
42. Raffa SJ, Benglis DM, Levi AD: Treatment of a persistent iatrogenic cerebrospinal fluid-pleural fistula with a cadaveric dural-pleural graft. **Spine J 9:**e25–e29, 2009
43. Rahman M, Bidari SS, Quisling RG, Friedman WA: Spontaneous intracranial hypotension: dilemmas in diagnosis. **Neurosurgery 69:**4–14, 2011
44. Ramsay M, Roberts C: Epidural injection does cause an increase in CSF pressure. **Anesth Analg 73:**668, 1991
45. Rudehill A, Gordon E, Rähn T: Subdural haematoma. A rare but life-threatening complication after spinal anaesthesia. **Acta Anaesthesiol Scand 27:**376–377, 1983
46. Ruiz-Sandoval JL, Campos A, Romero-Vargas S, Jiménez-Rodríguez MI, Chiquete E: Multiple simultaneous intracerebral hemorrhages following accidental massive lumbar cerebrospinal fluid drainage: case report and literature review. **Neurol India 54:**421–424, 2006
47. Sakurai K, Nishio M, Sasaki S, Ogino H, Tohyama J, Yamada K, et al: Postpuncture CSF leakage: a potential pitfall of radionuclide cisternography. **Neurology 75:**1730–1734, 2010
48. Samadani U, Huang JH, Baranov D, Zager EL, Grady MS: Intracranial hypotension after intraoperative lumbar cerebrospinal fluid drainage. **Neurosurgery 52:**148–152, 2003
49. Sayao AL, Heran MK, Chapman K, Redekop G, Foti D: Intracranial hypotension causing reversible frontotemporal dementia and coma. **Can J Neurol Sci 36:**252–256, 2009
50. Sayer FT, Bodelsson M, Larsson EM, Romner B: Spontaneous intracranial hypotension resulting in coma: case report. **Neurosurgery 59:**E204, 2006
51. Schievink WI: Spontaneous spinal cerebrospinal fluid leaks and intracranial hypotension. **JAMA 295:**2286–2296, 2006
52. Schievink WI, Gordon OK, Tourje J: Connective tissue disorders with spontaneous spinal cerebrospinal fluid leaks and intracranial hypotension: a prospective study. **Neurosurgery 54:**65–71, 2004
53. Schievink WI, Maya MM: Quadriplegia and cerebellar hemorrhage in spontaneous intracranial hypotension. **Neurology 66:**1777–1778, 2006
54. Schievink WI, Maya MM, Moser FG, Tourje J: Spectrum of subdural fluid collections in spontaneous intracranial hypotension. **J Neurosurg 103:**608–613, 2005
55. Schievink WI, Meyer FB, Atkinson JLD, Mokri B: Spontaneous spinal cerebrospinal fluid leaks and intracranial hypotension. **J Neurosurg 84:**598–605, 1996
56. Schievink WI, Moser FG, Pikul BK: Reversal of coma with an injection of glue. **Lancet 369:**1402, 2007
57. Schievink WI, Palestrant D, Maya MM, Rappard G: Spontaneous spinal cerebrospinal fluid leak as a cause of coma after craniotomy for clipping of an unruptured intracranial aneurysm. Case report. **J Neurosurg 110:**521–524, 2009
58. Sciubba DM, Kretzer RM, Wang PP: Acute intracranial subdural hematoma following a lumbar CSF leak caused by spine surgery. **Spine (Phila Pa 1976) 30:**E730–E732, 2005
59. Sencakova D, Mokri B, McClelland RL: The efficacy of epidural blood patch in spontaneous CSF leaks. **Neurology 57:** 1921–1923, 2001
60. Sperry RJ, Gartrell A, Johnson JO: Epidural blood patch can cause acute neurologic deterioration. **Anesthesiology 82:** 303–305, 1995
61. Terajima K, Oi Y, Ogura A, Sakai N, Takei M, Tamaki T, et al: Blood patch therapy for spontaneous intracranial hypotension: safe performance after epidurography in an unconscious patient. **AnesthAnalg 94:**959–961, 2002
62. Tsai PH, Wang SJ, Lirng JF, Fuh JL: Spontaneous intracranial hypotension presenting as mental deterioration. **Headache 45:**76–80, 2005
63. Watanabe A, Horikoshi T, Uchida M, Koizumi H, Yagishita T, Kinouchi H: Diagnostic value of spinal MR imaging in spontaneous intracranial hypotension syndrome. **AJNR Am J Neuroradiol 30:**147–151, 2009

64. Weisfelt M, van den Munckhof P, Majoie CB, Bouma GJ, Bosch DA: Reversal of acute neurological deterioration from spontaneous intracranial hypotension by lumbar subarachnoidal infusion with normal saline. **Arch Neurol 61:**444–445, 2004
65. Whiteley W, Al-Shahi R, Myles L, Lueck CJ: Spontaneous intracranial hypotension causing confusion and coma: a headache for the neurologist and the neurosurgeon. **Br J Neurosurg 17:**456–458, 2003
66. Witiw CD, Fallah A, Muller PJ, Ginsberg HJ: Surgical treatment of spontaneous intracranial hypotension secondary to degenerative cervical spine pathology: a case report and literature review. **Eur Spine J** [epub ahead of print], 2011
67. Wynn MM, Mell MW, Tefera G, Hoch JR, Acher CW: Complications of spinal fluid drainage in thoracoabdominal aortic aneurysm repair: a report of 486 patients treated from 1987 to 2008. **J Vasc Surg 49:**29–35, 2009
68. Yokota H, Yokoyama K, Noguchi H, Uchiyama Y, Iwasaki S, Sakaki T: Thoracic osteophyte causing spontaneous intracranial hypotension. **Cephalalgia 28:**396–398, 2008
69. Zada G, Pezeshkian P, Giannotta S: Spontaneous intracranial hypotension and immediate improvement following epidural blood patch placement demonstrated by intracranial pressure monitoring. Case report. **J Neurosurg 106:**1089–1090, 2007
70. Zeidan A, Farhat O, Maaliki H, Baraka A: Does postdural puncture headache left untreated lead to subdural hematoma? Case report and review of the literature. **Int J Obstet Anesth 15:**50–58, 2006

Manuscript submitted November 17, 2011.
Accepted April 25, 2012.
Please include this information when citing this paper: published online June 22, 2012; DOI: 10.3171/2012.4.JNS112030.

Address correspondence to: Terry C. Burns, M.D., Ph.D., Department of Neurosurgery, Stanford University School of Medicine, Edwards Building, Neurosurgery Mail Room, 300 Pasteur Drive, Stanford, California 94305-5487. email: tcburns@stanford.edu.