REVIEW ARTICLE

CONTINUUM AUDIO INTERVIEW AVAILABLE ONLINE

Spontaneous Intracranial Hypotension

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ABSTRACT

PURPOSE OF REVIEW: **Spontaneous intracranial hypotension is a disorder caused by spinal CSF leakage. This article reviews the clinical presentation, diagnosis, and treatment of spontaneous intracranial hypotension.**

RECENT FINDINGS: **The hallmark symptom of spontaneous intracranial hypotension is acute orthostatic headache; however, clinical presentations can be heterogeneous. New evidence shows that lumbar puncture is not always necessary or sufficient to establish the diagnosis. Some patients may have normal opening pressure, which suggests that insufficiency of CSF volume (hypovolemia) rather than CSF pressure might be the underlying mechanism. Several neuroimaging modalities can aid in diagnosis and localization of the CSF leakage, including brain MRI, spinal MRI, CT myelography, digital subtraction myelography, and radionuclide cisternography. Complications, such as subdural hematoma, can lead to a change in the headache pattern and potentially life-threatening consequences. Conservative treatments, such as fluid supplementation, can provide temporary relief; however, epidural blood patches, especially targeted ones, are more effective and definitive. For patients with refractory spontaneous intracranial hypotension, surgical repair of spinal CSF leakages should be considered.**

SUMMARY: **Brain and spinal MRIs are important for the diagnosis and treatment of patients with spontaneous intracranial hypotension. Early treatment with epidural blood patches may be considered to shorten the disease duration and minimize the potential risk of complications.**

CITE AS:
CONTINUUM (MINNEAP MINN) 2021;27(3, HEADACHE):746–766.

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RELATIONSHIP DISCLOSURE:
Dr Wang serves as an associate editor for *Cephalalgia*, *Headache*, and the *Journal of Headache and Pain* and as a consultant to the advisory boards of Daiichi Sankyo Company, Limited; Lilly; and Novartis AG. Dr Wang has received research/grant support from Allergan/AbbVie Inc; the Brain Research Center, National Yang Ming Chiao Tung University from The Featured Areas Research Program within the framework of the Higher Education Sprout Project by the Ministry of Education in Taiwan; Lilly; Novartis AG; Taipei Veterans General Hospital; Taiwan Ministry of Technology and Science; and Taiwan Headache Society.

UNLABELED USE OF PRODUCTS/INVESTIGATIONAL USE DISCLOSURE:
Dr Wang discusses the unlabeled/investigational use of theophylline for the treatment of postdural puncture headache.

INTRODUCTION

Spontaneous intracranial hypotension is a disorder related to spinal CSF leakage.[1-3] According to the *International Classification of Headache Disorders, Third Edition* (*ICHD-3*), a diagnosis of spontaneous intracranial hypotension requires the presence of low CSF pressure (<60 mm CSF) and/or evidence of a CSF leak on imaging.[4] However, typical presentations could occur in the absence of decreased CSF pressure, suggesting that inadequate CSF volume (ie, CSF hypovolemia) could be more important than inadequate CSF pressure (ie, CSF hypotension) in the underlying pathophysiology.[5,6] In particular, a 2016 study reported that the CSF pressure was less than 60 mm CSF in only 34% of confirmed cases of spontaneous intracranial hypotension, and a positive correlation seemed to exist between CSF

pressure and disease duration.[7] Therefore, a CSF pressure of greater than 60 mm CSF in a patient with a prolonged course does not necessarily exclude the possibility of spontaneous intracranial hypotension.

The classic presentation of spontaneous intracranial hypotension is acute orthostatic headache, but the diagnosis can sometimes be challenging as some patients may present with atypical initial presentations, such as cochleovestibular manifestations, cranial nerve palsies, personality changes, or even movement disorders.[1,8] Based on these symptoms, brain imaging (rather than spinal imaging) is usually part of the initial diagnostic workup, which could lead to diagnostic delays, especially when brain CT or noncontrast brain MRI is arranged. Although the diagnostic entity includes the term *spontaneous*, a significant proportion of patients report a history of trivial trauma or strenuous physical activities before the onset. Patients may also develop orthostatic headaches or other symptoms resembling spontaneous intracranial hypotension after spinal anesthesia or diagnostic lumbar punctures. In the presence of such iatrogenic causes, a diagnosis of postdural puncture headache is made according to the *ICHD-3* diagnostic criteria. When the headache associated with CSF leakage occurs after a procedure or trauma, it is termed CSF fistula headache. In such cases, the headache syndrome typically remits after successful management of the CSF fistula.[4]

KEY POINTS

- **Spontaneous intracranial hypotension is a disorder related to spinal CSF leakage. Acute orthostatic headache is the most common clinical presentation, but some patients may present with nonheadache symptoms.**
- **The female to male ratio of spontaneous intracranial hypotension is about 2:1, and it typically occurs in patients in their midthirties to midfifties.**

CLINICAL PRESENTATION AND DEMOGRAPHICS

The most common and important presentation of spontaneous intracranial hypotension is acute orthostatic headaches.[1] Spontaneous intracranial hypotension has a female preponderance, with a female to male ratio of about 2:1, and it typically occurs in patients in their midthirties to midfifties.[9] Patients may have some accompanying nonheadache symptoms. However, some patients may present with a wide variety of predominantly nonheadache symptoms; therefore, a delay in diagnosis may occur, which can range from days to even more than a decade.[10] Misdiagnosis is not uncommon in spontaneous intracranial hypotension but may lead to potentially life-threatening consequences because of complications, such as subdural hematoma, uncal herniation, sinus thrombosis, brainstem ischemia, and Duret hemorrhage.

Headache Symptoms

According to the *International Classification of Headache Disorders, Second Edition* (*ICHD-2*) criteria (2004), the so-called orthostatic headache in patients with spontaneous intracranial hypotension should develop after they assume an upright posture and improve after they lie down.[4,11] However, the temporal relationship between headache and postural changes is somewhat variable. According to an early report, up to 24% of patients lacked a typical orthostatic headache.[12] In addition, in patients who have developed complications such as subdural hematoma or cerebral venous thrombosis, a change in the headache pattern may be seen.[13-15] The postural component of headache can be lost. In some cases, a paradoxical postural headache, in which the headache gets worse in the supine position, may develop.

The headache is usually bilateral, and the location of headaches can be variable. Some patients may have migrainelike features, such as nausea or phonophobia.[16,17] Cochleovestibular manifestations, including hypoacusis, Ménière-like syndrome, tinnitus, and dizziness, are not uncommon.[17-19] In an

Italian study, nausea (42%), neck stiffness (33%), and hypoacusis (25%) were commonly reported by patients, followed by tinnitus (18%) and photophobia (16%).[12] In comparison, nausea (73%) and vomiting (48%) seem more common in patients in Taiwan.[20] The headache of spontaneous intracranial hypotension can sometimes be triggered or aggravated by Valsalvalike maneuvers and resembles exertional or exercise headache.[21,22]

Of note, although orthostatic headache is the hallmark of spontaneous intracranial hypotension, not all orthostatic headaches are caused by spinal CSF leaks. Occasionally, patients with postural tachycardia syndrome or cervical spine lesions could present with a clinical picture indistinguishable from that of spontaneous intracranial hypotension.[23,24]

Most of the orthostatic headache or other symptoms associated with postural changes may be relieved after adequate treatment. However, some patients may have residual headache only in the afternoon (ie, second-half-of-the-day headache), which could be attributed to slow-flow leaks or residual symptoms in a patient who has been partially treated.[25] Therefore, care should be exercised when obtaining a history from a patient who has been partially treated (CSF leakage sites not completely sealed or the CSF pressure not yet normalized), as the clinical presentation could become atypical.

Nonheadache Symptoms

Nonheadache symptoms have also been reported in patients with spontaneous intracranial hypotension (**TABLE 11-1**[26-37]), and these symptoms may or may not be accompanied by headache.[3] Downward displacement of the brain is common in patients with spontaneous intracranial hypotension and is commonly attributed to decreased CSF volume and buoyancy. This change could lead to traction or compression of cranial nerves or brainstem structures, posterior fossa crowdedness, or traction of cerebral structures. Therefore, abducens nerve palsies,[30] oculomotor nerve or trochlear nerve palsies,[28] parkinsonism,[35] and other movement disorders have been reported. Cochleovestibular manifestations, such as dizziness, tinnitus, and hypoacusis, are frequently reported symptoms and may be caused by changes in perilymph pressure.[18] Also, some patients may present with personality changes or frontotemporal dementia–like symptoms.[33] Some patients may develop altered consciousness or even coma[31]; thus, spontaneous intracranial hypotension should be considered among the differential diagnosis of altered consciousness, particularly in the presence of posterior fossa crowdedness or uncal herniation.

ETIOLOGY AND SUSCEPTIBILITY

Studies have identified some predisposing factors for spontaneous intracranial hypotension, including hypermobility disorders such as dolichostenomelia (disproportionately long limbs), Ehlers-Danlos syndrome, and Marfan syndrome.[38,39] However, most patients do not have obvious stigmata of connective tissue laxity,[39] and genetic studies looking for mutations of connective tissue disorders in spontaneous intracranial hypotension were negative.[40,41] Spinal meningeal diverticulum, presumably associated with focal weakness in the dura, has been believed to be a predisposing factor for CSF leakage.[5,42] However, controversies arise based on recent findings. Spinal meningeal diverticula are uncommon in Taiwanese patients[43]; moreover, the prevalence of spinal meningeal diverticula did not differ between patients with

spontaneous intracranial hypotension and controls in a North American series.[44] Trivial trauma, which could lead to rupture of the preexisting dural weakness, is reported in a substantial minority of patients before the onset of spontaneous intracranial hypotension. In addition, osteophytes, diskogenic spurs, and other factors have been reported to be associated with spinal CSF leakage and should be considered in patients with spontaneous intracranial hypotension.[45-47] In such cases, surgical intervention to correct the underlying structural abnormality might be necessary in addition to the standard treatment of spontaneous intracranial hypotension. More evidence is needed for genetic factors and local structural variations to prove their roles in predisposition to the development of spontaneous intracranial hypotension.

DIAGNOSTIC INVESTIGATIONS

According to the *ICHD-3* criteria, spontaneous intracranial hypotension falls under the classification of headaches attributed to low CSF pressure (TABLE 11-2). In the *ICHD-2* criteria, spontaneous intracranial hypotension was defined as a

Clinical Manifestations of Spontaneous Intracranial Hypotension

TABLE 11-1

Headache and symptoms associated with headaches

- **Orthostatic headache**
- **Headache usually accompanied by**
  - Nausea
  - Vomiting
  - Hypoacusis
  - Neck stiffness or pain
  - Photophobia
  - Tinnitus
- **Migrainelike headache**[16]
- **Thunderclap headache**[26]
- **Headache mimicking benign exertional headache**[21]
- **Headache mimicking new daily persistent headache**[27]

Nonheadache symptoms

- **Diplopia due to oculomotor nerve palsy**[28] **and/or trochlear nerve palsy**[29]
- **Bilateral abducens nerve palsy**[30]
- **Ménière disease–like manifestations**[18]
- **Changes in consciousness or coma**[31]
- **Unsteady gait**[32]
- **Personality change, apathy, or frontotemporal dementia–like presentations**[33,34]
- **Movement disorders**
  - Parkinsonism[35]
  - Chorea[36]
- **Bibrachial amyotrophy, motor neuron disease–like presentations**[37]

diffuse and/or dull headache that worsens within 15 minutes after sitting or standing, accompanied by at least one of the following associated symptoms: neck stiffness, tinnitus, hypoacusis, photophobia, or nausea. In addition, objective evidence should be derived from one of the following: typical brain MRI findings, radiologic evidence of CSF leakage, or CSF pressure less than 60 mm CSF.[11] In the *ICHD-3* criteria (TABLE 11-3), the diagnosis of spontaneous intracranial hypotension requires the presence of a headache that has developed in temporal relation to the low CSF pressure (<60 mm CSF) and/or evidence of CSF leakage on imaging. Also, a diagnosis of spontaneous intracranial hypotension requires the absence of a procedure or trauma known to cause CSF leakage. As mentioned above, the clinical presentation of spontaneous intracranial hypotension can be atypical.[21,22,25] Therefore, headache features and associated symptoms are no longer included in the *ICHD-3* criteria.[4] However, the *ICHD-2* criteria are, in fact, more informative, as the criteria give some clinical clues to remind clinicians how typical cases present. In both the *ICHD-2* and *ICHD-3* criteria, lumbar puncture is not mandatory, particularly in the presence of radiologic evidence of spinal CSF leakage.

Based on neuroimaging and intraoperative findings, Schievink and colleagues[9] proposed a classification system for spinal CSF leaks (FIGURE 11-1). Aside from dural tear (type 1) and meningeal diverticulum (type 2), CSF-venous fistula (type 3) is a newly proposed type of CSF leak. CSF-venous fistula is a direct communication between the spinal subarachnoid space and epidural venous plexus; hence, the extravasated CSF will be directly shunted into the venous circulation. Currently, the identification of CSF-venous fistulas requires dynamic CT myelography or digital subtraction myelography; spinal MRI is not capable of identifying them. Patients with more than one etiology or those who do not fit into types 1 through 3 are classified as having an indeterminate/unknown (type 4) CSF leak.[9,48]

TABLE 11-2 ***ICHD-3* Diagnostic Criteria for Headache Attributed to Low CSF Pressure**[a]

Headache attributed to low CSF pressure

A Any headache[b] fulfilling criterion C

B Either or both of the following:

- **1** Low CSF pressure (<60 mm CSF)
- **2** Evidence of CSF leakage on imaging[c]

C Headache has developed in temporal relation to the low CSF pressure or CSF leakage, or led to its discovery[d]

D Not better accounted for by another *ICHD-3* diagnosis

CSF = cerebrospinal fluid; *ICHD-3 = International Classification of Headache Disorders, Third Edition*.

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[b] Headache attributed to low CSF is usually but not invariably orthostatic. Headache that significantly worsens soon after sitting upright or standing and/or improves after lying horizontally is likely to be caused by low CSF pressure, but this cannot be relied upon as a diagnostic criterion.

[c] Brain imaging showing brain sagging or pachymeningeal enhancement, or spine imaging (spine MRI, or MRI, CT or digital subtraction myelography) showing extradural CSF.

[d] Evidence of causation may depend upon onset in temporal relation to the presumed cause, together with exclusion of other diagnoses.

Lumbar Puncture

Demonstration of low CSF pressure (<60 mm CSF) through lumbar puncture is part of the diagnostic criteria. However, lumbar puncture may not be necessary for all patients with suspected spontaneous intracranial hypotension, as CSF hypotension (ie, <60 mm CSF by the criteria) may not necessarily be present. An earlier study showed that 83% of patients with spontaneous intracranial hypotension had low or unmeasurable CSF pressures (n = 40).[49] However, in a 2013 study (n = 106), only 34% of confirmed spontaneous intracranial hypotension cases had CSF pressure less than or equal to 60 mm CSF, and 21% of patients even had CSF pressure greater than 120 mm CSF.[44] The discrepancies may be because of increasing recognition of this disease entity and growing understanding of neuroimaging findings, which lead to increasing diagnostic rates; hence, patients with atypical symptoms or minimal spinal CSF leaks can be diagnosed and incorporated into the analysis. Because the demonstration of nondecreased CSF pressure does not rule out the diagnosis of spontaneous intracranial hypotension and because lumbar puncture can be technically challenging in the presence of shrunken dura (which is common in spontaneous intracranial hypotension) and introduces additional dural defects that could potentially exacerbate CSF leakage, the diagnostic value of lumbar puncture becomes questionable, especially when evidence of spinal CSF leakage is demonstrated by brain or spinal neuroimaging studies.

Brain MRI Findings

As orthostatic headache is the most characteristic symptom of spontaneous intracranial hypotension, brain imaging is commonly part of the initial diagnostic workup. Brain CT is often nondiagnostic, as is noncontrast brain MRI; therefore, precontrast and postcontrast brain MRI should be arranged when spontaneous intracranial hypotension is clinically suspected. A variety of brain MRI findings have been described, with different diagnostic utilities and corresponding underlying mechanisms (**CASE 11-1**). Generally, they can be grouped into cerebral venous-related and brain descent–related signs (**TABLE 11-4**).[50]

TABLE 11-3 *ICHD-3* Diagnostic Criteria for Headache Attributed to Spontaneous Intracranial Hypotension[a]

Headache attributed to spontaneous intracranial hypotension	
A	Headache fulfilling criteria for headache attributed to low CSF pressure, and criterion C below
B	Absence of a procedure or trauma known to be able to cause CSF leakage[b]
C	Headache has developed in temporal relation to occurrence of low CSF pressure or CSF leakage, or has led to its discovery[c]
D	Not better accounted for by another *ICHD-3* diagnosis

CSF = cerebrospinal fluid; *ICHD-3 = International Classification of Headache Disorders, Third Edition*.

[a] Reprinted with permission from Headache Classification Committee of the International Headache Society, Cephalalgia.[4] © 2018 International Headache Society.

[b] Headache attributed to spontaneous intracranial hypotension cannot be diagnosed in a patient who has had a dural puncture within the prior month.

[c] Dural puncture to measure CSF pressure directly is not necessary in patients with positive MRI signs of leakage such as dural enhancement with contrast.

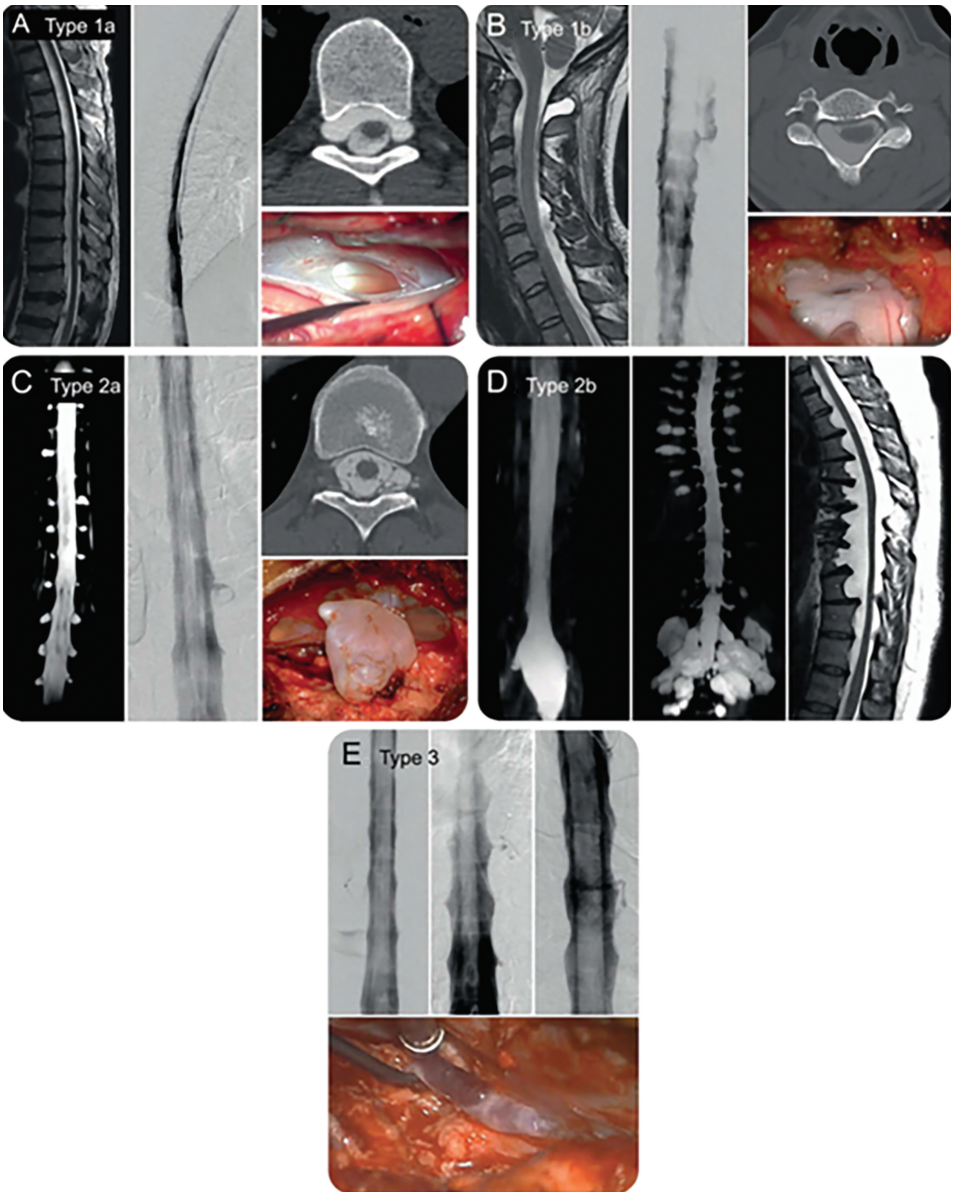

FIGURE 11-1

Classification of spontaneous spinal CSF leaks. *A*, Type 1a CSF leak: Sagittal T2-weighted MRI shows an extensive ventral fluid collection throughout the thoracic spine (*left panel*). Digital subtraction myelography (DSM) shows a ventral CSF leak at the T10-T11 level (*middle panel*). Post-DSM CT shows a ventral CSF collection (*right upper panel*). Intraoperative photograph shows a ventral dural tear measuring 6 mm (*right lower panel*). *B*, Type 1b CSF leak: Sagittal T2-weighted MRI shows an extensive dorsal fluid collection from C1-C2 to T1-T2 (*left panel*). DSM shows a posterolateral CSF leak at the C5-C6 level (*middle panel*). Post-DSM CT shows a posterolateral CSF collection (*right upper panel*). Intraoperative photograph shows a posterolateral dural tear measuring 2 mm (*right lower panel*). *C*, Type 2a CSF leak: Three-dimensional magnetic resonance (MR) myelogram shows several simple thoracic meningeal diverticula (*left panel*). DSM shows a CSF leak at the T11-T12 level outlining the meningeal diverticulum (*middle panel*). Post-DSM CT shows the meningeal diverticulum associated with extradural contrast (*right upper panel*). Intraoperative photograph shows the thin-walled meningeal diverticulum (*right lower panel*). *D*, Type 2b CSF leak: Three-dimensional MR myelograms show lumbosacral dural ectasia (*left panel*) and complex sacral cysts and multiple proximal and distal thoracic meningeal diverticula (*middle panel*). Sagittal T2-weighted MRI shows extensive thoracic dural ectasia (*right panel*). *E*, Type 3 CSF leak: DSMs show thoracic CSF-venous fistulas (*upper panels*). Intraoperative photograph shows a single venous channel draining CSF from the lateral common thecal sac (*lower panel*).

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CEREBRAL VENOUS-RELATED SIGNS. According to the Monro-Kellie doctrine, the sum of the volumes of brain tissue, vessels, and CSF is constant. The decrement of CSF volume during CSF leakage is compensated by the vascular structures because the brain tissue is presumably constant. Since the venous walls are more elastic than the walls of the arteries, intracranial venous structures can be dilated to a greater extent than the arteries.[51] Contrary to prior belief, a study by this author's group showed that brain tissue volume did not remain constant during CSF leakage but, indeed, slightly decreased (0.85%).[52]

The cerebral venous-related signs of spontaneous intracranial hypotension include diffuse pachymeningeal enhancement, the venous distension sign, and pituitary hyperemia (or pituitary enlargement). Diffuse pachymeningeal enhancement is the most well-recognized finding on postcontrast brain MRI and results from pachymeningeal venous dilation and increased contrast transit time (**FIGURE 11-2**). However, a number of other conditions can also present with pachymeningeal enhancement, such as pachymeningitis in granulomatous diseases, breast cancer metastasis, prostate cancer metastasis, secondary central nervous system lymphoma, and meningiomas.[53] Diffuse pachymeningeal enhancement in spontaneous intracranial hypotension is typically a homogeneous thickening of the dura, whereas pachymeningeal enhancement in the other conditions can be localized or heterogeneous. It is worth noting that diffuse pachymeningeal enhancement can be absent in a proportion of patients, especially when the timing of brain MRI is suboptimal.[54] In a study comparing patients with spontaneous intracranial hypotension with and without diffuse pachymeningeal enhancement, it was found that patients without diffuse pachymeningeal enhancement had shorter symptom duration (6.5 ± 4.4 days compared to 20.4 ± 16.3 days, $P<.001$).[55] However, another study concluded that patients without diffuse pachymeningeal enhancement had longer symptom duration (45.3 ± 59.0 weeks compared to 15.1 ± 33.0 weeks, $P=.002$).[56] The results of these two studies are not contradictory because the time scales are different. Taken together, diffuse pachymeningeal enhancement is present within a particular time window, and the absence of diffuse pachymeningeal enhancement does not exclude spontaneous intracranial hypotension from the differential diagnosis, especially when the postcontrast brain MRI is obtained too early (ie, <1 week) or too late (ie, >45 weeks).

The venous distension sign of the dominant transverse sinus (a convex rather than concave shape) has both high sensitivity and high specificity for spontaneous intracranial hypotension.[57] Pituitary gland hyperemia or enlargement is also commonly noted and could be misinterpreted as pituitary adenoma or tumor (**FIGURE 11-2**).[2] The diagnostic value of pituitary gland enlargement or hyperemia was challenged in a 2019 report.[58] In addition to alterations in the intracranial venous system, the size of superior ophthalmic veins may also serve as a useful guide in patients with spontaneous intracranial hypotension. A positive correlation is seen between the size of superior ophthalmic veins and intracranial pressure, and patients with spontaneous intracranial hypotension typically showed collapsed superior ophthalmic veins, the size of which recovered after treatment.[59,60]

BRAIN DESCENT–RELATED SIGNS. Downward displacement of brain structures is common in patients with spontaneous intracranial hypotension because of CSF leakage. Signs include closure of the midbrain-pons angle,[20] narrowing of the angle between the vein of Galen and the straight sinus,[61] flattening of the pons,[62]

KEY POINTS

- Diagnostic investigations for spontaneous intracranial hypotension include postcontrast brain MRI and spinal neuroimaging, such as spinal MRI, CT myelography, digital subtraction myelography, and radionuclide cisternography. Lumbar puncture is not always necessary or sufficient for diagnosis.
- Spinal CSF leaks can be classified as dural tear, meningeal diverticulum, or CSF-venous fistula. CSF-venous fistula is a direct communication between the spinal subarachnoid space and epidural venous plexus. The identification of CSF-venous fistulas requires dynamic CT myelography or digital subtraction myelography; spinal MRI is not capable of identifying them.
- Normal CSF pressure (>60 mm CSF) does not exclude the diagnosis of spontaneous intracranial hypotension. Insufficiency of intracranial CSF volume (ie, hypovolemia) may be more important in the pathophysiology of spontaneous intracranial hypotension.
- Brain neuroimaging findings in patients with spontaneous intracranial hypotension include cerebral venous-related signs and brain descent–related signs.

tonsillar descent, and posterior fossa crowdedness.[1] These brain MRI signs reflect the downward displacement of brain structures at different levels or brain structural deformities. The measurements of brain descent–related signs, including the midbrain-pons angle,[20] mamillopontine distance, height of the suprasellar cistern, diameter of the prepontine cistern, angle between the vein of Galen and the straight sinus, and venous hinge, could reflect the severity of brain sagging or deformity (CASE 11-2).[58] Among these signs, closure of the midbrain-pons angle is associated with poorer response rates to the first epidural blood patch.[20] These neuroimaging findings are helpful not only for diagnosis but also for prediction of treatment response.

Spinal Imaging Findings

Decreased intracranial CSF pressure or volume, or both, is the consequence of spinal CSF leakage; therefore, localization of spinal CSF leaks provides diagnostic clues and a therapeutic guide.

CASE 11-1

A 30-year-old man presented to a headache clinic with a severe headache that developed after playing basketball and had persisted for about 1 month. The pain was located at the bilateral temple and occipital regions; was throbbing in quality; and was accompanied by phonophobia, photophobia, and vomiting. The patient rated it 10 out of 10 on the numeric rating scale. His headache worsened immediately after standing up and improved within 5 minutes after lying down. He was a surgeon and could not perform surgery because the headache was unbearable after standing for a while. He had no past history of primary headache disorders, such as migraine.

Neurologic examination did not show any abnormal findings. Postcontrast brain MRI showed diffuse pachymeningeal enhancement, pituitary hyperemia, and flattening of the pons (FIGURE 11-2). Spinal MRI disclosed spinal CSF leaks at the T2-T3 level. The patient received analgesics and hydration with normal saline 3000 mL/d for 3 days, but the headache persisted. A targeted epidural blood patch with 21 mL autologous blood was performed at the T2-T3 level, and the orthostatic headache partially improved. Another targeted epidural blood patch with 21 mL autologous blood was done 3 days later. However, the patient's orthostatic headache changed paradoxically to worsening while lying down and improving with sitting up after the second epidural blood patch. He received acetazolamide 250 mg 2 times a day, and his headache totally subsided 3 days later.

SPINAL CT FINDINGS. CT myelography has been considered the gold standard in the localization of spinal CSF leaks. This imaging procedure involves the injection of iodinated contrast material into the thecal sac, followed by whole-spine axial CT. The distribution of CSF is visualized, and CSF extravasation can be localized.[2,63] In addition, CSF pressure can be directly measured. However, localization of high-flow (or fast-flow) CSF leaks may be challenging, as the contrast medium may spread throughout the epidural space quickly before acquisition of the CT myelogram.[63] One solution is the use of ultrafast dynamic CT myelography, which involves serial acquisition of the images immediately after the intrathecal injection of the contrast medium.[64,65] However, it is not clear whether spinal CSF leaks visualized on CT myelography colocalize with dural defects. According to a study comparing intraoperative findings with CT myelography, only a minority of patients had active CSF leakage at the locations of CSF leaks identified on CT myelography.[66] Whether these "spinal CSF leaks" could

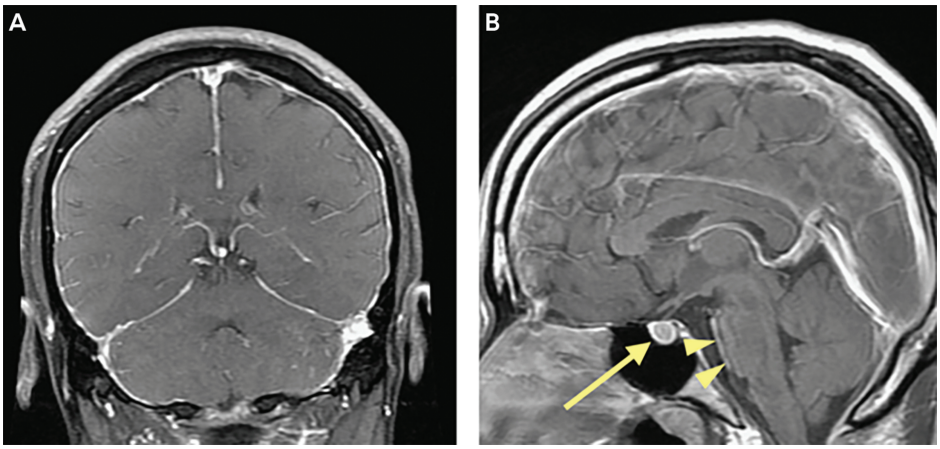

FIGURE 11-2
Imaging of the patient in CASE 11-1. *A*, Coronal postcontrast T1-weighted image shows diffuse pachymeningeal enhancement. *B*, Sagittal postcontrast T1-weighted image shows pituitary hyperemia (*arrow*) and flattening of the pons (*arrowheads*). These brain MRI signs are typical for spontaneous intracranial hypotension.

COMMENT

This patient's headache had features of migraine, including throbbing, photophobia, phonophobia, and vomiting. However, the acute orthostatic feature of his headache was a red flag for spontaneous intracranial hypotension. His brain MRI showed several typical features of spontaneous intracranial hypotension, including diffuse pachymeningeal enhancement, pituitary hyperemia, and flattening of the pons. This patient received two epidural blood patches and developed features of transient intracranial hypertension after the second. This phenomenon is called *rebound intracranial hypertension* and is one of the complications of epidural blood patch. Rebound intracranial hypertension is reversible; acetazolamide is helpful in patients with severe or intractable symptoms.

represent the final common pathways of CSF drainage rather than the active process of CSF leakage awaits further clarification. Weaknesses of CT myelography include its invasiveness and radiation exposure. The lumbar puncture required for intrathecal contrast administration could potentially exacerbate CSF leakage. More important, the amount of radiation exposure is considerable, especially for ultrafast dynamic CT myelography.[64]

SPINAL MRI FINDINGS. Spinal MRI can also be used for the diagnosis of spontaneous intracranial hypotension.[63] Conventional T2-weighted spinal MRI can reveal only indirect signs of spinal CSF leaks, such as epidural CSF collection, distention of epidural veins, and collapsed dura.[67,68] As spinal CSF leaks cannot be visualized directly, its clinical utility is limited.

Heavily T2-weighted magnetic resonance myelography is an imaging technique that can be used to visualize spinal CSF leaks; it was demonstrated to be comparable to the gold standard CT myelography.[43,69,70] It is a noninvasive imaging technique and does not require IV or intrathecal contrast administration. Spinal CSF leakages seen on heavily T2-weighted magnetic resonance myelography can be divided into three types: high-cervical retrospinal CSF collections, epidural CSF collections, and periradicular leaks (**FIGURE 11-4**).[43,70] High-cervical retrospinal CSF collection is a well-known false localizing sign, and its presence does not indicate the location of dural tears.[71] After leakage from the dural tears, the extravasated CSF is distributed in the epidural space (ie, epidural collection) in the direction of gravity and is subsequently drained out of the spinal canal via the neuroforamina (ie, periradicular leaks). As demonstrated

TABLE 11-4 Brain MRI Signs of Spontaneous Intracranial Hypotension

Cerebral venous-related signs

- Diffuse pachymeningeal enhancement
- Venous distension sign
- Pituitary hyperemia (or pituitary enlargement)

Brain descent–related signs

- Closure of the midbrain-pons angle
- Narrowing of the angle between the vein of Galen and straight sinus
- Flattening of the pons
- Tonsillar descent
- Posterior fossa crowdedness

Measurements for brain descent

- Midbrain-pons angle
- Mamillopontine distance
- Height of suprasellar cistern
- Diameter of the prepontine cistern
- The angle between the vein of Galen and straight sinus
- Venous hinge

CASE 11-2

A 52-year-old man presented with pulsatile headache and drowsiness after 2 weeks of a weight-lifting program. The pulsatile headache was located at the bilateral temples and accompanied by photophobia, and the intensity was 8 to 9 out of 10. He also reported that he had been sleepy and lacked motivation over the previous 2 weeks. An initial brain MRI showed closure of the midbrain-pons angle (0 degrees), narrowing of the angle between the vein of Galen and the straight sinus, flattening of the pons, and posterior fossa crowdedness (FIGURE 11-3A). Magnetic resonance myelography showed periradicular leaks at C7-T1 and T1-T2, suggestive of the CSF leakage sites. After three targeted epidural blood patches, the patient finally recovered, and follow-up brain MRI showed widening of the midbrain-pons angle compared to the initial brain MRI (FIGURE 11-3B).

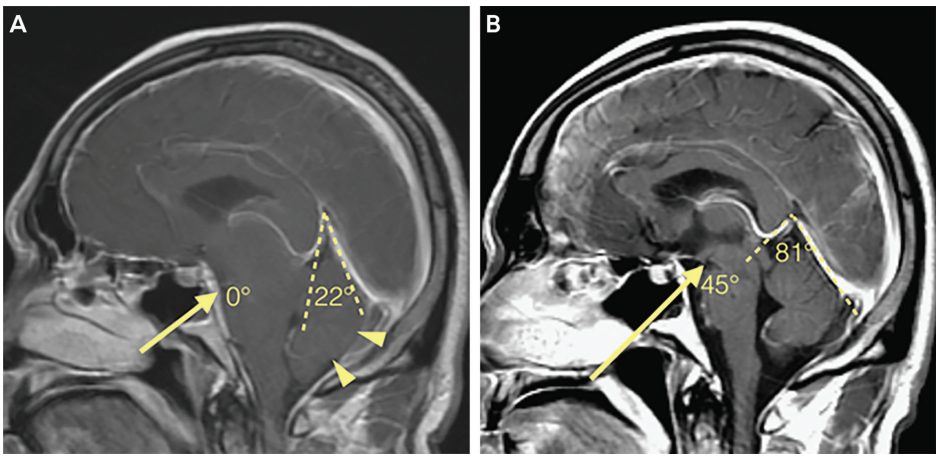

FIGURE 11-3

Imaging of the patient in CASE 11-2. *A*, Initial sagittal postcontrast T1-weighted image shows closure of the midbrain-pons angle (0 degrees, *arrow*), narrowing of the angle between the vein of Galen and the straight sinus (22 degrees), flattening of the pons, and posterior fossa crowdedness (*arrowheads*). *B*, Sagittal postcontrast T1-weighted image after recovery shows widening of the midbrain-pons angle (45 degrees, *arrow*) and the angle between the vein of Galen and the straight sinus (81 degrees) compared to the initial MRI. Also, the flattening of the pons and posterior fossa crowdedness have subsided.

COMMENT

Patients with spontaneous intracranial hypotension can present with nonheadache symptoms, including cognitive changes. Closure of the midbrain-pons angle, narrowing of the angle between the vein of Galen and the straight sinus, flattening of the pons, and posterior fossa crowdedness are brain descent-related signs of spontaneous intracranial hypotension. The symptoms of patients with closure of the midbrain-pons angle are more refractory to treatment, and these patients usually need more than one epidural blood patch.

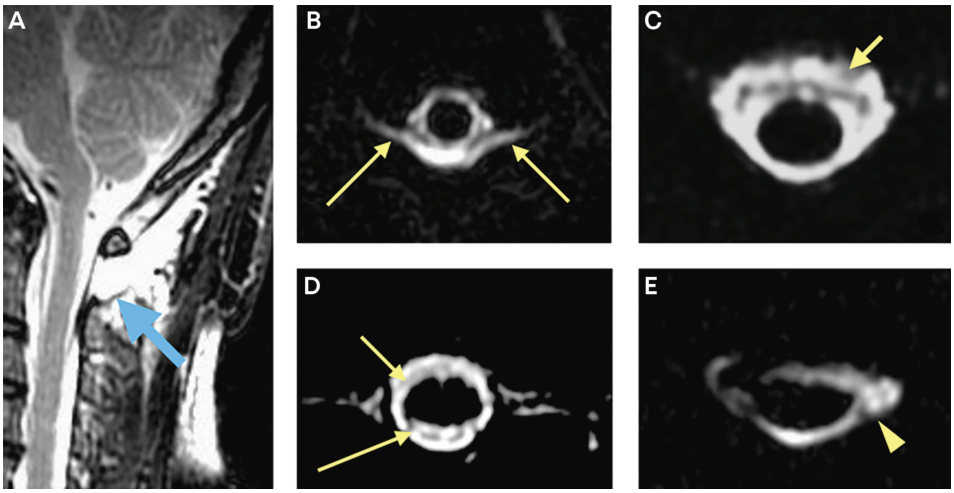

FIGURE 11-4

Spinal imaging signs of spontaneous intracranial hypotension. Spinal CSF leakage on heavily T2-weighted magnetic resonance myelography includes three different presentations: high cervical retrospinal CSF collection (*A, arrow*), periradicular leak (*B, arrows*), and epidural CSF collection (*C, D, arrows*). The length of the epidural collection could have prognostic value, and patients with extensive anterior (or ventral) epidural CSF collections (*C*) may require more than one epidural blood patching.[20] Some patients may have a spinal meningeal diverticulum (*E, arrowhead*).

in patients receiving lumbar puncture, about two-thirds of periradicular leaks are within three vertebral segments of the dural defect, presumably at the puncture sites (ie, L2-L3 level),[69] which makes them reasonable targets for an epidural blood patch since the injected blood can spread to the nearby segments.[72] The distribution of epidural CSF collection is much wider, based on which the exact location of dural tears cannot be ascertained.[69] However, the length of the epidural collection has prognostic value, and patients with extensive anterior (or ventral) epidural CSF collection may require more than one epidural blood patch.[20]

Intrathecal gadolinium-enhanced magnetic resonance cisternography (myelography) is gaining interest for the detection of spinal CSF leaks. It involves intrathecal administration of gadolinium followed by T1-weighted spinal MRI. The method was demonstrated to have superior detection rates for spinal CSF leaks as compared to CT myelography and is therefore increasingly being used in the diagnosis of spontaneous intracranial hypotension.[73] However, a number of issues remain. The gadolinium contrast medium has not been approved for intrathecal use. More important, as with other invasive neuroimaging techniques, lumbar puncture is necessary for intrathecal contrast administration and may introduce additional dural defects. It may not be easy to tell whether the detected gadolinium leakage results from the spontaneous intracranial hypotension itself or from the lumbar puncture meant for contrast administration, especially when the localized CSF leaks are in the vicinity of the upper lumbar regions. In fact, a study by this author's group showed post–lumbar puncture CSF leakages were not restricted to puncture levels and may spread to nearby, or even remote, levels.[69]

DIGITAL SUBTRACTION MYELOGRAPHY. Digital subtraction myelography is a powerful tool to detect the location of spinal CSF leaks. This procedure requires a

fluoroscopic-guided lumbar puncture and intrathecal injection of a contrast medium.[74] After the intrathecal injection, the procedure table is tilted head down so that extravasation of the contrast medium through the dural defects can be visualized in real time. The major advantage of digital subtraction myelography is the detection of high-flow (or fast-flow) CSF leaks. However, digital subtraction myelography requires the patient's cooperation and is relatively invasive.

RADIONUCLIDE CISTERNOGRAPHY. Radionuclide cisternography has been commonly used in the detection of spinal CSF leakages, although it is no longer suggested by the *ICHD-3*.[4] It requires intrathecal injection of an iodinated tracer (indium 111 diethylenetriamine pentaacetic acid [^{111}InDTPA]), followed by sequential scanning immediately and at 1, 2, 4, and 24 hours and sometimes 48 hours.[75] The findings of radionuclide cisternography can be divided into direct and indirect evidence of spinal CSF leaks. Direct evidence is increasing radioactivity at parathecal regions near the leakage sites. Indirect evidence includes paucity of activity over the cerebral convexities and the radioactivity usually not extending beyond the basal cisterns.[75] Early radioactivity at the kidney and bladder is also indirect evidence, but this finding may be confounded by systemic reuptakes of leaked iodinated tracer from the lumbar puncture site.[75] The major disadvantage of radionuclide cisternography is the suboptimal spatial and temporal resolution; an advantage is the longer duration of sequential scanning, which may be helpful in individuals with extremely slow-flow CSF leaks.[63]

COMPLICATIONS

The most common complication of spontaneous intracranial hypotension is subdural hematoma. According to recent studies, subdural hematoma can be demonstrated in about 20% to 25% of patients with spontaneous intracranial hypotension who underwent their first brain imaging study after symptom onset.[13,20] Patients with subdural hematoma may have neurologic deficits or worsening headaches, and a large subdural hematoma may cause herniation and even mortality.[13] In patients with spontaneous intracranial hypotension with subdural hematoma, surgical intervention (ie, a burr hole) should be considered when the thickness of the subdural hematoma is greater than or equal to 10 mm or they show cognitive deterioration, and the CSF leakage should be adequately treated simultaneously with either epidural blood patches or surgical repair.[15]

Other complications include cerebral venous thrombosis, bibrachial amyotrophy, and superficial siderosis.[1] Cerebral venous thrombosis has been reported and is an uncommon complication of spontaneous intracranial hypotension.[76,77] The underlying mechanism behind cerebral venous thrombosis in spontaneous intracranial hypotension can be explained by the Virchow triad.[76] Following the Monro-Kellie doctrine, cerebral venous dilation occurs during spinal CSF leaks, resulting in slowing cerebral venous flow velocity, which causes a hypercoagulable state and venous thrombosis.[14] Bibrachial amyotrophy is a rare complication, and the underlying mechanism is compression from the ventral extradural CSF collection.[37,78] Superficial siderosis is a remote but rare complication of spontaneous intracranial hypotension, but the underlying mechanism linking spinal CSF leaks and repetitive subarachnoid hemorrhage remains unknown.[1,79] In some situations, the spinal dural defects caused by the spinal cord herniation may be the bleeding points, and this bleeding from dural lacerations may be the reason for the superficial siderosis.[80] In addition, brain

KEY POINTS

- The Monro-Kellie doctrine states that the sum of the volumes of brain tissue, vessels, and CSF within the skull is constant. The decrement of CSF volume during CSF leakage is compensated by the dilation of intracranial venous structures. Cerebral venous-related signs of spontaneous intracranial hypotension include diffuse pachymeningeal enhancement, the venous distension sign, and pituitary hyperemia (or pituitary enlargement).
- Brain descent–related signs reflect the downward displacement of brain structures or brain structural deformities in patients with spontaneous intracranial hypotension. Among these signs, closure of the midbrain-pons angle is associated with a poorer response to the first epidural blood patch. These neuroimaging findings are helpful not only for diagnosis but also for prediction of treatment response.
- Localization of spinal CSF leaks by spinal neuroimaging can provide clues for diagnosis and guide therapeutic interventions.
- Heavily T2-weighted magnetic resonance myelography can be used to visualize spinal CSF leaks; it was demonstrated to be comparable to the gold standard CT myelography. It is a noninvasive imaging technique and does not require IV or intrathecal contrast administration.

sagging following spinal CSF leaks may cause traction of the cerebellar veins and then subarachnoid hemorrhage, which may, in part, explain the reason for the superficial siderosis.[81]

TREATMENT

The treatment of spontaneous intracranial hypotension includes conservative observation, medications, epidural blood patch, or surgical repair.[1] Because of limited clinical studies, no consensus currently exists on how to treat these patients. FIGURE 11-5 provides an algorithm of treatment strategies.

Conservative Treatments

Conservative treatment strategies include strict bed rest, adequate hydration, analgesics, and abdominal binders. One study analyzed eight patients with spontaneous intracranial hypotension who received conservative treatment, including absolute bed rest and IV hydration.[82] The study showed that only three out of eight patients totally recovered immediately after conservative treatments; two patients completely recovered after 6 to 8 months, and the three remaining patients had persistent mild headaches. Currently, no controlled studies have investigated the efficacy of conservative treatments. Considering the devastating complications (eg, subdural hematoma) and disabling symptoms of spontaneous intracranial hypotension, epidural blood patch or even surgical repair should be considered when patients do not improve after conservative strategies. In the author's practice, targeted epidural blood patch is usually performed as early as possible even without conservative treatments.

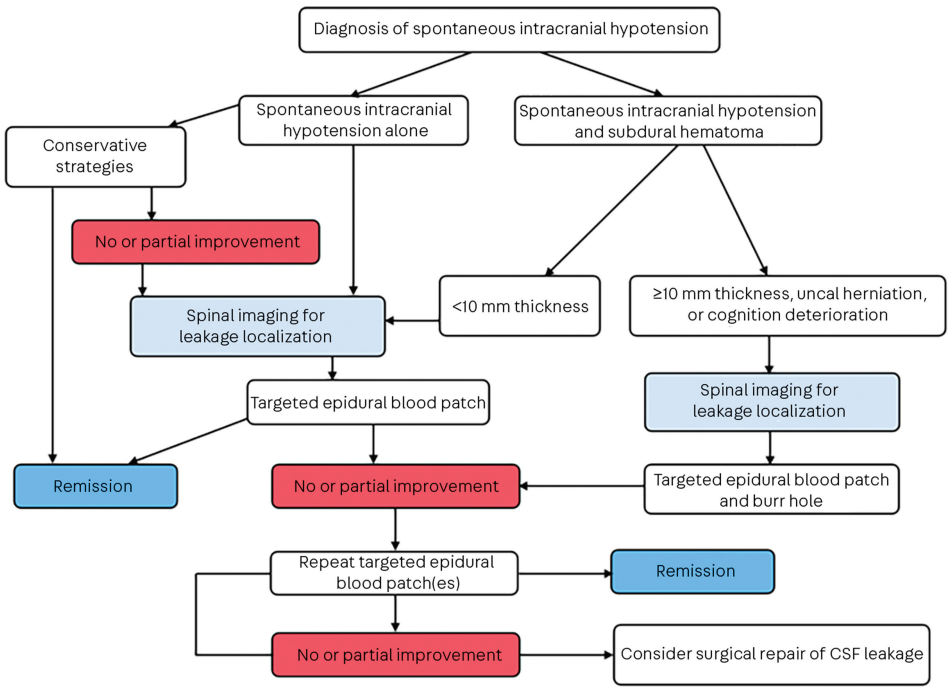

FIGURE 11-5
Algorithm of treatment strategies of patients with spontaneous intracranial hypotension.

Medications

The options for pharmacologic treatment include analgesics, caffeine, theophylline, and corticosteroids.[1] In animal models, caffeine can increase CSF production; thus, it may be helpful in CSF hypovolemia.[83] A double-blind placebo-controlled trial showed that caffeine could reduce headache severity in postdural puncture headache, but the effect was transient, and patients still needed epidural blood patch.[84,85] Theophylline may be another option. A randomized controlled trial in postdural puncture headache showed patients receiving 250 mg IV aminophylline had lower headache intensity 8 hours after the treatment compared with the placebo group.[86] In addition, some studies reported that greater occipital nerve block could improve postdural puncture headache.[87-89] To date, only case reports have shown the effectiveness of corticosteroids; however, one controlled study did not show any therapeutic benefit of corticosteroids in postdural puncture headache.[90,91]

Epidural Blood Patch

Currently, epidural blood patch is the treatment of choice for spontaneous intracranial hypotension. The underlying mechanism of epidural blood patch includes the early effect of direct compression of the dural sac and occupying of the epidural space by injected blood and the late effect of fibrosis and healing of the dural tears.[1] Patients usually improve immediately or within 1 day after the procedure whether or not the epidural blood patch is delivered in the vicinity of the dural tear. However, further observation is needed to ensure that the CSF leaks are adequately treated; repeat epidural blood patch is sometimes necessary for those with incomplete response. The epidural blood patch can be performed by an experienced anesthesiologist with or without the guidance of fluoroscopy or CT scan. Protocols are variable, with different injection techniques, blood amounts, and duration of bed rest after the treatment; therefore, the success rate after epidural blood patches is also variable.[1]

Epidural blood patches can be divided into blinded (lumbar) epidural blood patches and targeted epidural blood patches. The injection site of a blinded epidural blood patch is always at the lumbar level. After the injection, the Trendelenburg position is suggested by some experts to facilitate the spread of the injected blood to the thoracic and higher levels.[92] Targeted epidural blood patch involves delivery of blood to the leakage sites; hence, localization of spinal CSF leaks through adequate spinal neuroimaging is mandatory, which may require an experienced neuroradiologist.[93] Cho and colleagues[94] showed that the success rate of targeted epidural blood patch is higher than that of blinded lumbar epidural blood patch. Wu and colleagues[20] found that a larger amount of injected blood (≥22.5 mL) predicted a better response to the first epidural blood patch. Moreover, some neuroimaging findings, such as the length of ventral epidural CSF collections and a narrower midbrain-pons angle (<40 degrees), could also predict responsiveness. The possible side effects of epidural blood patch include rebound intracranial hypertension and radicular pain at the dermatome of injection; these conditions are usually transient and reversible.[1] Other rare side effects of epidural blood patch include arachnoiditis, transient bilateral paraplegia, and cauda equina syndrome.[95]

Considering the inefficacy of conservative treatment and the high rate of complications in patients with spontaneous intracranial hypotension, epidural blood patch (especially targeted epidural blood patch) is suggested to be used as early as possible.

KEY POINTS

- **Subdural hematoma is the most common complication of spontaneous intracranial hypotension, especially in patients who develop a change in their headache pattern.**
- **Purely conservative treatments for spontaneous intracranial hypotension (eg, fluid supplementation) are usually temporizing measures, and definitive treatment (eg, targeted epidural blood patches) is more effective. For patients with refractory spontaneous intracranial hypotension, surgical repair of the spinal leaks should be considered.**

Surgical Repair

Surgical approaches usually include partial or bilateral laminectomy, and the extent of bone removal depends on the presurgical spinal neuroimaging findings.[96] If the spinal CSF leak is extensive, laminectomy should be performed at more than one spinal level. Since the surgical approach is more invasive, surgery should be reserved for spontaneous intracranial hypotension refractory to at least three epidural blood patches or other less invasive treatment options. The dural tear or hole can be directly repaired by suture with or without fibrin glue coverage[2]; however, anaphylaxis to fibrin glue may occur. Leaking meningeal diverticula are usually ligated by suture or buttressed with muscle or absorbable gelatin compressed sponge. In some situations, a metal aneurysm clamp can be used for ligation.[66]

CONCLUSION

Spontaneous intracranial hypotension can be easily diagnosed based on acute orthostatic headache; however, it can also present atypically. Typical brain MRI studies are diagnostic for patients even without a lumbar puncture. Recent advances include spinal neuroimaging studies to localize leakage sites. Early use of targeted epidural blood patch may be warranted since conservative treatment in patients with spontaneous intracranial hypotension usually results in a prolonged disabling state. For patients with refractory spontaneous intracranial hypotension, surgical repair of the CSF leakage may be considered.

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