REVIEW ARTICLE

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Spontaneous Intracranial Hypotension

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Spontaneous intracranial hypotension is a condition characterized by a lower-than-normal volume of cerebrospinal fluid (CSF) because of leakage of CSF through the dural membrane at one or multiple sites. The loss of CSF results in displacement of cerebral structures, causing headache and other neurologic symptoms.[1] The term "spontaneous" in relation to the disorder is used to differentiate it from intracranial hypotension caused by CSF leaks of known cause, such as craniospinal trauma, spinal surgery, or most commonly, lumbar puncture or spinal anesthesia. Although CSF pressure in this disorder, as measured by manometry during lumbar puncture, may be normal,[2] it is often lower than normal (with the normal value considered to be 6 to 25 cm of water, or 4.4 to 18.4 mm Hg), and the term "hypotension" continues to be used. Spontaneous intracranial hypotension assumes clinical importance as a treatable cause of headache and other manifestations, including dizziness, mental dullness, and behavioral changes, but the variability in clinical presentation makes diagnosis difficult.[1]

Pathophysiological Features

A CSF leak within the spinal column is the most common identifiable cause of spontaneous intracranial hypotension.[3] The mechanism underlying headache and neurologic manifestations is presumed to be downward displacement of cerebral structures and traction or distortion of pain-sensitive nerve endings in the cranial dura and its vasculature. Skull-base CSF leakage from the posterior cranial fossa into the soft tissues of the neck may rarely cause spontaneous intracranial hypotension, but skull-base CSF leaks resulting in CSF rhinorrhea or otorrhea have not been shown to cause spontaneous intracranial hypotension.[4]

Imaging of the spine and intraoperative observations have identified three types of spontaneous spinal CSF leaks (Fig. 1; Fig. S1 in the Supplementary Appendix, available with the full text of this article at NEJM.org; and Videos 1 through 4, available at NEJM.org).[3] One type is due to a linear tear in the dura located ventral to or posterolateral to the spinal cord. A second type is associated with leakage at sites of simple meningeal diverticula (Tarlov cysts) or with diffuse dilatations of the dural sac (dural ectasia), as occurs, for example, in ankylosing spondylitis. The third type, which is still being characterized, has been attributed to a spinal CSF–venous fistula. Spinal CSF–venous fistulas consist of abnormal communications between the CSF-containing spinal subarachnoid space and adjacent veins and usually are associated with meningeal diverticula. Spontaneous spinal CSF leaks can occur at multiple sites, although this is uncommon.[5]

Videos showing digital-subtraction myelography are available at NEJM.org

An underlying connective-tissue disorder may facilitate a rent in the dura that results in spontaneous intracranial hypotension, but with the exception of Marfan's and Ehlers–Danlos syndromes, such disorders are rarely identified. Spinal osteophytes or calcified disk herniations may abrade or penetrate the dura, causing a dural tear, and typically result in ventral spinal leaks.[6]

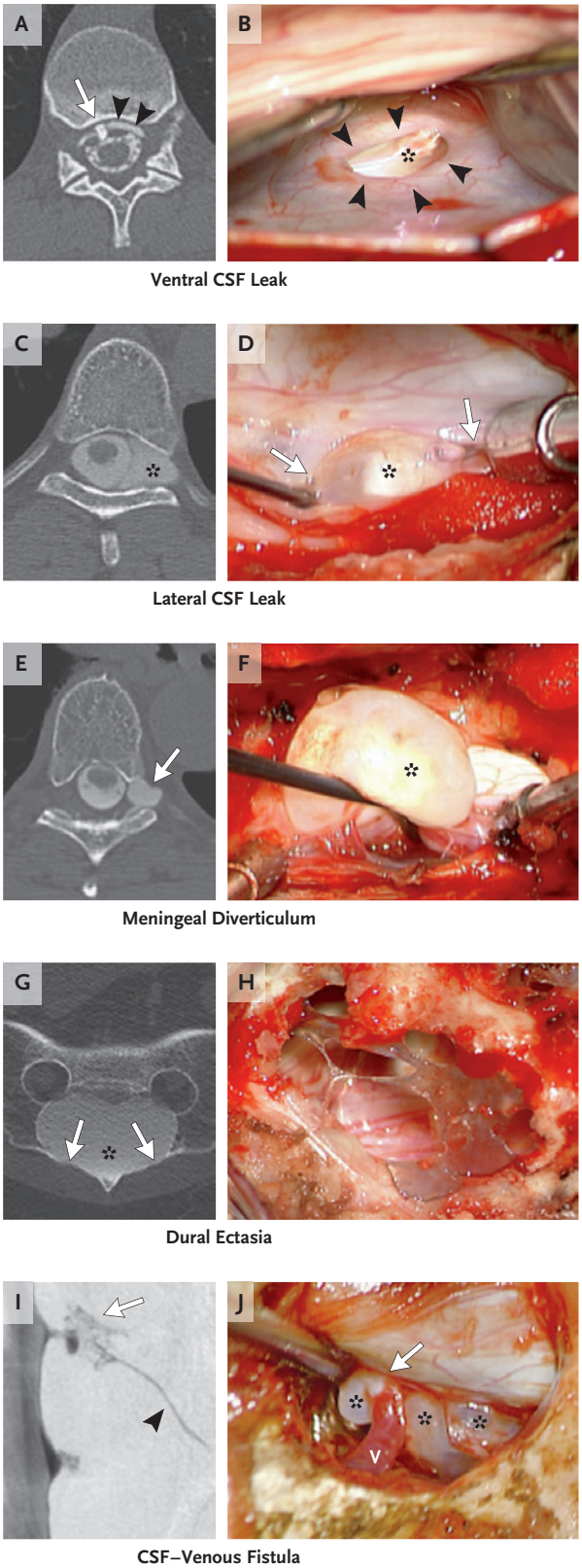

Figure 1. Types of Spontaneous Spinal Cerebrospinal Fluid (CSF) Leaks.

Ventral CSF leaks (type 1a) are ventral to the spinal cord and are usually associated with an osteophyte or calcified disk herniation. A computed tomographic (CT) myelogram (Panel A) shows an osteophyte penetrating the dura (arrow) and the ventral extradural CSF collection (arrowheads). An intraoperative photograph (Panel B, posterior intradural view) shows the ventral dural tear (arrowheads), with the jagged edge of the osteophyte (asterisk) penetrating the dura. Lateral CSF leaks (type 1b) usually cause the underlying arachnoid to billow through the dural tear. A CT myelogram (Panel C) shows a lateral extradural CSF collection (asterisk). An intraoperative photograph (Panel D) shows the cranial and caudal extent (arrows) of the lateral tear, with arachnoid billowing through the tear (asterisk). CSF leaks associated with simple meningeal diverticula are type 2a leaks. These diverticula generally arise from the nerve-root sleeve; multiple meningeal diverticula are common, but the CSF leak is usually from just one of the diverticula. A CT myelogram (Panel E) shows contrast material within a diverticulum (arrow). An intraoperative photograph (Panel F) shows the extent of the meningeal diverticulum (asterisk) dissected from the common thecal sac. CSF leaks associated with complex meningeal diverticula or dural ectasia (type 2b) may involve any spinal segment, but the sacrum is the most common site. A CT myelogram (Panel G) shows the sacral dural ectasia (asterisk) and associated bony erosion (arrows). An intraoperative photograph (Panel H) shows the bony erosion and extreme thinning of the dura, which may complicate surgical repair. CSF–venous fistulas (type 3) do not result in an extradural CSF collection, and special imaging is required to detect these fistulas. A digital-subtraction myelogram (Panel I, anteroposterior view) shows a CSF–venous fistula (arrow) with a prominent draining vein (arrowhead). An intraoperative photograph (Panel J, posterior view) shows meningeal diverticula (asterisks), the site of the CSF–venous fistula (arrow), and the draining vein (V).

EPIDEMIOLOGIC FEATURES

Data from large community-based studies of the epidemiology of spontaneous intracranial hypotension are not available, but an estimate of the annual incidence is 4 to 5 cases per 100,000 population,[7] which is about half the incidence of aneurysmal subarachnoid hemorrhage. Although spontaneous intracranial hypotension can affect patients at any age, including children and adolescents, women between the ages of 35 years and 55 years are most often affected.[1,4]

CLINICAL MANIFESTATIONS

The cardinal symptom of spontaneous intracranial hypotension is a headache that worsens on

standing and subsides with lying down (orthostatic headache) (Table 1).[1] It is useful to ask patients how they feel on awakening, before getting out of bed, and whether the headache occurs soon after arising. The interval between standing and the onset of the headache is typically a minute or several minutes, but the headache can develop instantaneously, after a number of hours, or after a delay that extends into the afternoon ("second-half-of-the-day" headache). The orthostatic feature of the headache may lessen over time.[8] A few patients have a nonpositional or even reverse orthostatic headache (worse when the patient is recumbent).

The headache is usually holocephalic or bilaterally suboccipital but may be unilateral and occasionally has a throbbing component that simulates migraine. Valsalva maneuver–induced worsening of the headache has been reported to be common in patients with CSF–venous fistulas.[9]

Other neurologic manifestations can accompany or overshadow the headache and may become apparent only days or weeks after the onset of headache or even after the headache has resolved. Common aural symptoms are muffled hearing, pulsatile tinnitus, and hearing loss. Other symptoms that occur variably across patients are posterior neck pain or stiffness, nausea, vomiting, photophobia, and phonophobia, leading to a diagnosis of meningitis or migraine. Less common symptoms include facial pressure or paresthesias, diplopia (usually from sixth-cranial-nerve palsies), and tremor. Some patients report fatigue or difficulty with concentration and word finding, but the nonspecific nature of these symptoms makes them difficult to interpret and to attribute to the CSF leak.

In rare cases, coma and cerebral venous thrombosis occur days to months after the onset of spontaneous intracranial hypotension.[10,11] Coma is the result of extreme downward displacement of the midbrain and brain stem (brain sagging). Placing a comatose patient with spontaneous intracranial hypotension in the Trendelenburg position may result in improvement in the level of consciousness.[10] Superficial siderosis (hemosiderin deposits on the surface of the brain and spinal cord) and bibrachial amyotrophy (painless weakness and atrophy of the shoulders and arms) are potential long-term complications of spontaneous intracranial hypotension and are seen mostly in patients with chronic ventral spi-

Table 1. Clinical Manifestations of Spontaneous Intracranial Hypotension.*

Manifestations	No. of Patients (%)
Most common	
Headache	199 (98.5)
Orthostatic	188 (93.1)
Nonpositional	7 (3.5)
Reverse orthostatic	4 (2.0)
Common	
Vestibulocochlear symptoms	
Dizziness or vertigo	102 (50.5)
Muffled hearing or ear fullness	75 (37.1)
Tinnitus	56 (27.7)
Hypoacusis	53 (26.2)
Hyperacusis	12 (5.9)
Nausea and emesis	99 (49.0)
Disequilibrium	86 (42.6)
Posterior neck pain	69 (34.2)
Cognitive impairment	64 (31.7)
Fatigue	49 (24.3)
Phonophobia or photophobia	41 (20.3)
Visual blurring	36 (17.8)
Facial numbness, paresthesias, or pressure	32 (15.8)
Least common	
Interscapular pain	22 (10.9)
Dysgeusia	15 (7.4)
Low back pain	8 (4.0)
Behavioral-variant frontotemporal dementia	5 (2.5)
Bibrachial amyotrophy	3 (1.5)
Superficial siderosis†	3 (1.5)
Cerebral venous thrombosis	2 (1.0)
Diplopia with abducens-nerve palsy	2 (1.0)
Spinal cord herniation	2 (1.0)
Coma — GCS score, ≤8‡	1 (0.5)
Syringomyelia	1 (0.5)
Hemifacial spasm	1 (0.5)

* Data are from 202 consecutive patients with spontaneous intracranial hypotension, according to the modified International Classification of Headache Disorders, third edition (ICHD-III) criteria, who were evaluated between January 1, 2020, and December 31, 2020, at a single center.
† The number and percentage represent symptomatic patients. In patients with spontaneous intracranial hypotension, superficial siderosis is a fairly common finding on magnetic resonance imaging but, if mild, often does not cause symptoms.
‡ Scores on the Glasgow Coma Scale (GCS) range from 3 to 15, with lower scores indicating greater alteration of consciousness.

nal CSF leaks.[12,13] In one study, one or both of these complications affected almost 60% of such patients at 16 years of follow-up.[14] In some patients with spontaneous intracranial hypotension and frontal-lobe and temporal-lobe downward sagging, symptoms develop that are similar to the symptoms associated with behavioral-variant frontotemporal dementia (personality changes, altered behavior, and executive dysfunction).[15] These changes may be delayed for months or years after the onset of other symptoms of spontaneous intracranial hypotension. A source of CSF leakage is not found in most of these patients, despite extensive investigation.

Table 2. Modified ICHD-III Diagnostic Criteria for Spontaneous Intracranial Hypotension.*

A. Any headache attributed to low CSF pressure or CSF leakage that meets criterion C, below
B. Either or both of the following:
Low CSF pressure (<60 mm CSF)
Evidence of CSF leakage on imaging
C. Headache that developed in temporal relation to the low CSF pressure or CSF leakage or that led to its discovery
D. Headache not better accounted for by another ICHD-III diagnosis

* The modified ICHD-III criteria[16] also apply to patients who do not have headache but whose symptoms are best explained by spontaneous intracranial hypotension. Headache attributed to spontaneous intracranial hypotension cannot be diagnosed in a patient who, within the prior month, has had a procedure or trauma known to be able to cause CSF leakage.

DIAGNOSIS

The diagnostic criteria for spontaneous intracranial hypotension in the International Classification of Headache Disorders, third edition (ICHD-III), include evidence of typical findings on magnetic resonance imaging (MRI) of the head, CSF leak on spinal imaging, or low CSF pressure as measured by lumbar puncture (Table 2).[16] Gadolinium-enhanced MRI is most often used and typically shows enhancement of the pachymeninges (dura), as well as features of subdural fluid collections, engorgement of venous structures, pituitary enlargement, sagging of the brain, or reduction in the volume of the optic-nerve sheath subarachnoid space (Fig. 2).[1,17,18] Pachymeningeal enhancement is the most common and recognizable feature on imaging and has been attributed to secondary dilatation of the venous system in the cranial dura as a result of the lowered volume of CSF within the intracranial space (the Monro–Kellie doctrine). However, an estimated 20% of patients with spontaneous intracranial hypotension have normal findings on head MRI.[1]

The site of spinal CSF leakage can be determined in most patients but depends on the thoroughness of the investigation. Spinal imaging with MRI or computed tomographic (CT) myelography is usually performed for the initial evaluation of patients; such imaging can detect extradural spinal CSF collections, signifying CSF leakage in the spinal column.[17-19] Spinal MRI with special sequences that are sensitive for CSF (heavily T2-weighted magnetic resonance myelography) may not be inferior to conventional CT myelography for the detection of extradural CSF, and its use obviates lumbar puncture and exposure to ionizing radiation from CT.[20] Extradural spinal CSF collections are found in about half of all patients with spontaneous intracranial hypotension.[3,17] Specialized spinal imaging such as digital-subtraction myelography (see Video 4) or dynamic CT myelography may detect CSF–venous fistulas in patients without an extradural spinal CSF collection, mainly when MRI of the head shows the typical findings of spontaneous intracranial hypotension[21] but also occasionally when the head MRI is normal.[22]

Low CSF pressure, or pressure at the low end of the normal range, is not necessary for a diagnosis of spontaneous intracranial hypotension, since patients may have normal or even elevated CSF pressure.[1,2,23] Low opening CSF pressure, as measured by lumbar puncture (<6 cm of water), was retained as part of the ICHD-III criteria for the diagnosis of the disorder because it allows the diagnosis to be confirmed in health care settings that have limited access to imaging.

TREATMENT

Data from randomized trials are not available to guide the management of spontaneous intracranial hypotension. Depending on the severity of the symptoms, a practical approach includes a short course of conservative measures over a period of a few days or weeks, consisting of bed rest, high oral fluid intake, caffeine, and an abdominal binder. The main therapeutic maneuver in patients whose condition is not improved with

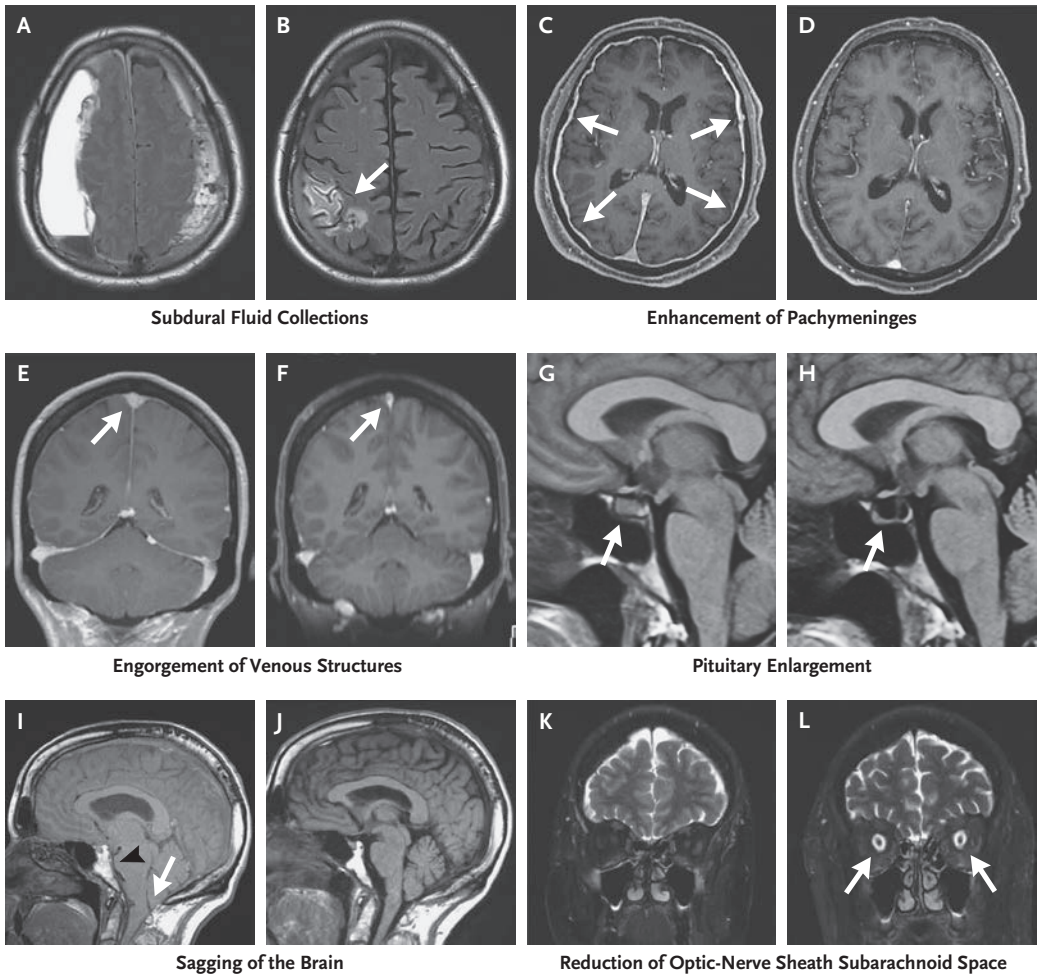

Figure 2. Head MRI Findings before and after Treatment in Patients with Spontaneous Intracranial Hypotension.

An axial MRI scan with fluid-attenuated inversion recovery (FLAIR) (Panel A) shows bilateral subdural hematomas, which resolved with treatment (Panel B). The presumed mechanism of subdural hematoma formation in spontaneous intracranial hypotension is tearing of bridging veins caused by brain sagging. A cerebral infarct (Panel B, arrow) developed as a result of cerebral venous thrombosis. Pachymeningeal enhancement, which is typically associated with intracranial hypotension, is evident on a pretreatment axial T1-weighted, gadolinium-enhanced MRI scan (Panel C, arrows), with resolution after treatment (Panel D). A coronal T1-weighted, gadolinium-enhanced MRI scan shows superior sagittal sinus engorgement (Panel E, arrow), which resolved after treatment (Panel F, arrow). Pituitary enlargement is seen on a sagittal T1-weighted MRI scan (Panel G, arrow), with resolution after treatment (Panel H, arrow). (The pituitary enlargement is apparent only as compared with a baseline, partially empty sella.) A sagittal T1-weighted MRI scan shows brain sagging (Panel I); the subarachnoid spaces are obliterated, with flattening of the pons (arrowhead) and downward displacement of the cerebellar tonsils, mimicking a Chiari malformation (arrow). The abnormalities resolved after treatment (Panel J). Reduction of the optic-nerve sheath subarachnoid space is evident on a coronal T2-weighted MRI scan (Panel K). The normal optic-nerve sheath subarachnoid space was restored with treatment (Panel L, arrows).

conservative measures is an epidural "blood patch," whereby autologous blood obtained by venipuncture is injected into the lumbar spinal epidural space. Immediate relief is sometimes obtained, presumably because of an immediate increase in CSF pressure caused by the epidural hematoma. Resolution of the CSF leak probably depends on the formation of a fibrin clot at the site of the dural tear. It is not necessary to identify the site of the CSF leak in order to achieve good results with a blood patch in the lumbar spine. Most patients do not require more than one or two epidural blood patches to obtain symptomatic relief.[1,24] Some studies have suggested a benefit

of the use of blood patches with higher rather than lower volumes of blood.[1,24]

For patients with persistent symptoms after blood patching, specialized spinal imaging with digital-subtraction myelography (Videos 1 through 4) or dynamic CT myelography may be necessary to localize the site of the CSF leak. This allows for treatment with directed epidural blood patching or glue injections to seal the site of the CSF leak or for microsurgical repair of the leak.[25-27] For CSF–venous fistulas, endovascular glue embolization has been used.[28] The durability of these different treatments has not been determined. One complication of successful CSF leak treatment is the development of rebound high intracranial pressure, which results in reverse orthostatic headaches; the high pressure is generally self-limiting.

SUMMARY

Spontaneous intracranial hypotension is a cause of headache and a variety of other neurologic manifestations. A causative CSF leak at the level of the spine can be detected in most patients, and several types of leaks have been identified. Epidural blood patching is successful in reducing or eliminating symptoms in most patients and can be used without localization of the leak. For cases that do not respond to blood patching, specialized spinal imaging is indicated to localize the site of the CSF leak, and several surgical and nonsurgical treatment options have become available, depending on the type of leak.

Disclosure forms provided by the author are available with the full text of this article at NEJM.org.

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