Spontaneous CSF Leaks
Low CSF Volume Syndromes

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KEYWORDS

• Spontaneous CSF leak • Spontaneous intracranial hypotension (SIH)
• CSF hypovolemia • Orthostatic headaches • Diffuse patchy meningeal enhancement
• Acquired Chiari malformation • Epidural blood patch • Radioisotope cisternography

KEY POINTS

- Spontaneous intracranial hypotension nearly always results from spontaneous cerebrospinal fluid (CSF) leaks, typically at the spine level and only rarely from the skull base.
- The triad of orthostatic headaches, diffuse patchy meningeal enhancement, and low CSF pressure, although a diagnostic hallmark, may or may not be encountered because the variability in clinical presentations, imaging observations, and CSF findings is indeed substantial.
- The core pathogenetic factor is a decreased volume of CSF rather than its pressure.
- The anatomy of the leak may be complex. A preexisting dural weakness, usually in connection with an abnormality of the connective tissue matrix sometimes along with trivial traumas, may play an etiologic role.
- Slow-flow and fast-flow CSF leaks each present challenges on locating the actual site of the leak.
- Epidural blood patch (EBP) has emerged as the treatment of choice when conservative measures have failed. However, expect considerable variability in response to this treatment, and recall that the efficacy of EBP in spontaneous CSF leaks is substantially less than its efficacy in postlumbar puncture leaks.
- Surgery may be helpful in well-selected cases, when less invasive measures have failed and when the site of the leak has been definitely identified.

INTRODUCTION

About 2 decades ago, the first report on pachymeningeal gadolinium enhancement in spontaneous intracranial hypotension (SIH) appeared in the literature.[1] This relatively short interval has witnessed enormous progress while a much larger number of patients are now identified and a far broader clinical spectrum is recognized.[2]

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It is now known that almost all cases of SIH result from spontaneous cerebrospinal fluid (CSF) leaks, typically at the level of the spine. Spontaneous (nontraumatic) leaks at the level of the skull base occur only rarely.

A substantial variability in clinical, imaging, and CSF findings is also recognized, such as consistently normal CSF opening pressures in some of the patients, absent pachymeningeal enhancement or even essentially normal head magnetic resonance imaging (MRI) in some other patients, and yet absent headache in occasional patients. Decreased CSF volume (CSF hypovolemia), rather than decreased CSF opening pressure, seems to be the core pathogenetic factor as the independent variable, whereas CSF opening pressure, MRI findings, and clinical features seem to be variables dependent on the CSF volume.[3] The term *SIH* no longer seems broad enough to embrace all of these variables. Alternative terms, such as *CSF volume depletion*, *CSF hypovolemia*, or *spontaneous CSF leak*, have appeared in the literature and have been used interchangeably.[4,5]

Spontaneous CSF leak should not be equated with postdural puncture headaches. There are often substantial differences in the clinical features, response to treatment, and outcome in the two. In spontaneous CSF leak, the dural defect is often not a simple hole or rent. Many patients have a preexisting dural defect and display focal areas of dural attenuation, meningeal diverticula, or even focal zones of absent dura with nude arachnoid. These areas may weep CSF with variable rates or sometimes intermittently.

CSF DYNAMICS

The choroid plexus forms more than 75% of the CSF; the rest is secreted by the brain capillaries into the neuropil and enters the ventricles through the ependyma.[6] The rate of CSF formation in adults is 0.35 mL/min or about 500 mL/24 hr. CSF is absorbed by arachnoid villi into the cerebral venous sinuses and veins via a valvelike mechanism called bulk flow.[7,8] Normally, a minor portion of the CSF is absorbed into the cerebral vessels by simple diffusion. Recent studies suggest that a portion of the CSF is absorbed via the lymphatics of the region of the cribriform plate to the nasal submucosa.[9]

Although the rate of CSF formation is fairly constant, its volume is not. Based on old autopsy data, the total volume of the CSF was estimated to be about 500 mL. This figure has been, and continues to be, repeated in the literature. Tremendous variability in the size of the ventricles and the subarachnoid and cisternal spaces, especially in the young versus old, is obvious in modern head imaging. MRI volumetric studies point to substantial variations. The mean +/− standard deviation of cranial CSF for both sexes and for all people aged 24 to 80 years was noted to be 157 $\pm$ 59 SD; the number was smaller for women versus men and much smaller for young versus old patients.[10] Spinal CSF volume from T11-T12 to the sacral terminus was calculated to be 49.9 $\pm$ 12.1 SD[11]; the number is significantly smaller for obese versus nonobese patients.

In the horizontal position, the CSF pressure at lumbar, cisternal, and presumably intracranial or vertex levels are equal, measuring about 65 to 195 mm of water. In the vertical position, these pressures diverge. The vertex pressure becomes negative, whereas the lumbar pressure increases. Along the CSF axis, somewhere between the spinous processes of C7 and T5, there is a point referred to as the *hydrostatic independent point* where the CSF pressure remains unchanged whether patients are upright or supine.[12] The relationship between the CSF pressure and volume is exponential.[13] In experimental low-pressure headaches in human patients, it has been shown that withdrawal of approximately 10% of CSF will decrease the already negative vertex pressure by more than 40%.[14]

CAUSE

Spontaneous CSF leaks typically take place at the spinal dural sac at any level but more commonly at the thoracic level.[15] Posttraumatic and postsurgical CSF leaks (motor vehicle accidents [MVAs]; severe falls; blows to the head; cranial or spinal surgeries; ears, nose, and throat [ENT] surgeries) are not uncommon. However, spontaneous CSF leaks from the skull base are rare. Some of the patients with spontaneous CSF leaks may report occasional flow of clear fluid from the nose. It should not come as a surprise if such fluids do not prove to be CSF. A CSF leak leads to CSF volume depletion (CSF hypovolemia), which is also the pathogenetic core in overdraining CSF shunts and postsurgical CSF leaks. Reduced total body volume (true hypovolemic state) should also be expected to cause reduced CSF volume.

When the cause is discussed (**Box 1**), it is the spontaneous group that presents the real challenge. The exact cause of a spontaneous CSF leak often remains unclear. A preexisting dural weakness can lead to a CSF leak or sometimes render the dura more vulnerable to the effect of a trivial trauma. A minority of the patients may report a history of a previous trivial trauma (coughing, lifting, pushing, routine sport activities, and so forth). Evidence for a preexisting weakness of the dural sac has gained momentum. Dural abnormalities, meningeal diverticula, and CSF leaks have been noted in Marfan syndrome.[16–18] Stigmata of connective tissue disorder are seen in a minority of the patients with spontaneous CSF leaks.[19] Single or multiple meningeal diverticula are noted frequently in patients with spontaneous CSF leaks and in certain heritable disorders of connective tissue.[20–23] Dural ectasia is a common feature of Marfan

Box 1
Cause of CSF hypovolemia or CSF leaks

1. True hypovolemic state (reduced total body water)
2. CSF shunt overdrainage
3. Traumatic CSF leaks
   a. Overt injuries (MVAs, sports injuries, brachial plexus avulsions)
   b. Iatrogenic (postdural puncture, postepidural catheterization)
   c. Postsurgical (cranial or spinal surgeries, ENT surgeries)
4. Spontaneous CSF leaks
   a. Unknown cause
   b. Preexisting dural sac weakness
   c. Meningeal diverticula
   d. Evidences disorders of connective tissue matrix
      - Marfan syndrome or marfanoid features
      - Joint hypermobility
      - Retinal detachment at young age
      - Abnormalities of elastin and fibrillin in dermal fibroblast cultures
      - Familial occurrence of spontaneous CSF leaks
5. Trivial trauma (perhaps in the setting of preexisting dural weakness)
6. Herniated disks, spondylotic spurs

syndrome.[24,25] Familial occurrence of spontaneous CSF leak in the setting of familial joint hypermobility and aortic aneurysms is yet another testimony on the role of dural weakness based on a disorder of connective tissue matrix in some of the spontaneous CSF leaks (**Fig. 1**).[26] Uncommonly, a spondylotic spur or herniated disk may penetrate the dura and cause a CSF leak.[27–29] Sometimes, with brachial plexus avulsions, a tear in a nerve root sleeve may lead to CSF leakage.[30]

CLINICAL MANIFESTATIONS

Headache

The most common clinical manifestation is orthostatic headache, a headache in the upright position relieved in recumbency.[31–33] The interval from change in posture (erect or recumbent) to the appearance of headache or relief from it is classically assumed to be a few minutes; but in many patients, it is much longer. The headache may be throbbing, but often it is not and is described as a pressure sensation that can range from dull to very severe. It is often, but not always, bilateral and can be frontal, fronto-occipital, holocephalic, or occipital. At this juncture, 2 points need emphasizing: (1) Not all patients with an orthostatic headache have CSF leaks, although

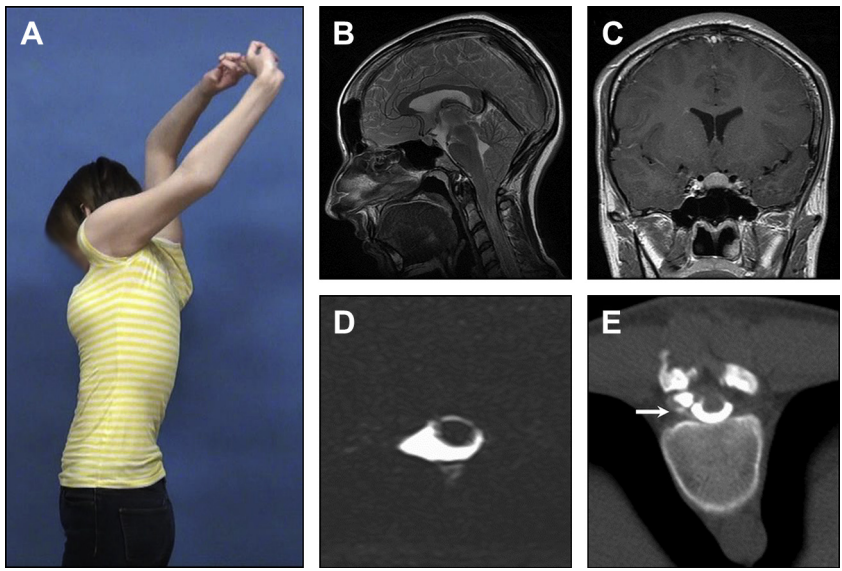

Fig. 1. (*A*) Young woman with joint hypermobility and strong family history of the same as well as aortic aneurysms presented with orthostatic headaches. (*B*) Head MRI on sagittal view shows descent of the cerebellar tonsils, flattened anterior pons, near obliteration of prepontine cistern, and crowded posterior fossa. (*C*) Coronal gadolinium enhance shows little for abnormal gadolinium enhancement, but there is pituitary engorgement and obliteration of the perichiasmatic cistern. Lower imaging panels: (*D*) Axial, heavily T2-weighted spine MRI that shows a meningeal diverticulum. (*E*) Hyperdynamic computed tomography myelography shows this to be a leaking meningeal diverticulum (*arrow*). Patient had a younger and an older sister; both had joint hypermobility and leaking meningeal diverticula, both were also seen in the past by the author,[26] and both had responded to surgical treatment of the meningeal diverticula, as did this patient. (*From* Mokri B. Unpublished data, with permission of Mayo Foundation; and *Courtesy of* Mayo Clinic, Rochester, MN, with permission.)

the large majority does. (2) Not all headaches related to CSF leaks are orthostatic. The variability is indeed substantial (Box 2). Sometimes, especially with chronicity, the orthostatic features of a typically orthostatic headache may dampen; and it may gradually transform into a lingering chronic daily headache.

Manifestations Other than Headaches

The clinical manifestations of SIH-CSF hypovolemia apart from headaches are listed in Box 3. Of these, neck and interscapular pain, cochleovestibular manifestations, and perhaps nausea are far more common than others. The level of the spine pain may not necessarily correspond to the level of the leak, and indeed it often does not.

Mechanisms of Clinical Manifestations

One consequence of a decrease in CSF volume is sinking of the brain. This outcome leads to traction or distortion of the anchoring or supporting pain-sensitive structures of the brain[34,35] and, therefore, to the headaches that are orthostatic or have some orthostatic features. The dilatation of intracranial venous structures also plays a likely role in the pathogenesis of headaches in CSF hypovolemia.

Traction, distortion, or compression of some of the cranial nerves, some of the structures or lobes of the brain, brainstem, mesencephalon, and diencephalon are thought to be responsible for the various cranial nerve palsies as well as many central nervous system manifestations seen in this disorder.[34] Cochleovestibular manifestations (tinnitus, hearing change, dizziness) may be related to traction on the eighth cranial nerve; but an alternative and perhaps a more plausible mechanism is altered pressure in the perilymphatic fluid or of the inner ear.[36] Galactorrhea, which may occur only rarely, and an increase in prolactin have been attributed to traction on or distortion of the pituitary stalk.[37] Dilatation of epidural venous plexus or traction and distortion of nerve roots are thought to be the cause of radicular symptoms.[38]

Diagnosis

For CSF examination, expect considerable variability in CSF findings (Table 1).

Box 2
Headache in intracranial hypotension (CSF leak–CSF hypovolemia)

- Orthostatic headaches (present in upright position, relieved in recumbency)
- Neck or interscapular pain or a lingering nonorthostatic headache preceding the orthostatic headache (by days or weeks)
- Orthostatic headache gradually evolving into lingering nonorthostatic chronic daily headaches (transformed orthostatic headaches)
- Nonorthostatic chronic daily headaches from start
- Exertional headaches[84]
- Acute thunderclaplike onset of orthostatic headaches[85]
- Second-half-of-the-day headaches (often with some orthostatic features)[85]
- Paradoxic orthostatic headaches (present in recumbency, relieved when upright)[86]
- Intermittent headaches of intermittent leaks
- The acephalgic form (where patients have no headache and present with other clinical manifestations of the CSF leak – CSF hypovolemia)

Box 3
Nonheadache manifestations of CSF leak–CSF hypovolemia

- Neck or interscapular pain (common), low back pain (much less common)
- Cochleovestibular manifestations, including tinnitus, change in hearing (muffled, distant, distorted, or echoed hearing, even hearing loss), and dizziness (vertigo, woozy, or lightheaded feelings)
- Nausea, less commonly emesis, often orthostatic
- Diplopia, often horizontal and caused by unilateral or bilateral sixth cranial nerve palsy,[15] less commonly third and fourth cranial nerve palsies[87]
- Visual complaints including blurred vision, photophobia, superior binasal visual field defect[88]
- Facial numbness or numb feeling, unilateral or bilateral
- Galactorrhea[37]
- Labyrinthine hydrops[36]
- Radicular upper limb symptoms[38]
- Stupor, diencephalic compression[89]
- Coma[90]
- Parkinsonism, ataxia, bulbar weakness[91]
- Frontotemporal dementia[92]
- Encephalopathy[93]
- Gait unsteadiness[94]
- Trouble with sphincter control
- Bibrachial amyotrophy[80]
- Cognitive difficulties
- Chorea[95]

Radioisotope Cisternography

Indium-111 is the radioisotope of choice. It is introduced intrathecally via a lumbar puncture, and its dynamic is followed by sequential scanning at various intervals of up to 24 or even 48 hours. Normally by 24 hours, but often even earlier, abundant radioactivity can be detected over the cerebral convexities.[39–41] In CSF leaks, the radioactivity typically does not extend much beyond the basal cisterns; therefore, at 24 hours or even 48 hours, there is paucity of activity over the cerebral convexities (**Fig. 2**). This abnormality is the most common cisternographic abnormality in CSF leaks. The detection of parathecal activity pointing to the level or approximate site of the leak, although more desirable, is less common. Meningeal diverticula or dilated nerve root sleeves, if large enough, may appear as foci of parathecal activity that may not be reliably distinguishable from sites of a CSF leak (**Fig. 3**). Computed tomography myelography (CTM) typically enables the differentiation. Early appearance of radioactivity in the kidneys and the urinary bladder (in less than 4 hours vs 6–24 hours) is another fairly common finding, indicating that intrathecally introduced radioisotope has been extravasated and has entered the systemic circulation, with subsequent renal clearance and early appearance in the urinary bladder. This cisternographic abnormality, however, is not always a very reliable indication of a CSF leak because

Table 1
CSF findings in spontaneous CSF leaks

Opening pressure	It is often low, occasionally atmospheric, or rarely even negative. It is sometimes within normal limits even on repeated taps despite active CSF leak.[96] Sometimes in the same patient, variable CSF opening pressures may be recorded in different occasions. This variability may be related to variability in the rate of the flow of the leak.
Color	It is often clear, occasionally xanthochromic, and sometimes blood tinged. Note that difficult and traumatic taps are not unusual when CSF opening pressure is very low. Engorgement of the epidural venous plexus is also a contributory factor.
Protein concentration	It may be normal or high. Values of up to 100 mg/dL are not uncommon, and protein concentrations as high as 1000 mg/dL have been rarely observed.[15]
Leukocyte count	It may be normal, but a lymphocytic pleocytosis of up to 50 cells per square millimeter is not uncommon, and higher counts are not rare. Counts as high as 222 cells per square millimeter have been documented.[15,97]
Erythrocyte count	It may be normal or elevated (sometimes considerably, in connection with traumatic taps).
Cytology and microbiology	It is normal/negative.
Glucose concentration	It is never low.

inadvertent partial extradural injection of the radioisotope or, more commonly, extravasation of the intrathecally introduced radioisotope through the dural puncture site may also lead to an early appearance of radioactivity in the urinary bladder. Furthermore, the early appearance of radioactivity in the urinary bladder should not be misinterpreted as evidence of increased CSF reabsorption[39,40] because the radioisotope in CSF leaks hardly reaches the cerebral convexities to be reabsorbed.

Head CT

The usual head CT is of limited value in the evaluation of spontaneous CSF leaks. Infrequently, it may show subdural fluid collections or increased tentorial enhancement.[35]

Head MRI

Head MRI subnormalities are listed in **Box 4**.

Diffuse pachymeningeal enhancement without leptomeningeal enhancement is the most common MRI abnormality. This abnormality is typically linear, uninterrupted, non-nodular, bilateral, and both supratentorial and infratentorial. It may vary from thick to quite thin (**Fig. 4**).[15,42–44]

The descent or sinking or sagging of the brain and brainstem is manifested by the descent of the cerebellar tonsils, often below the foramen magnum, sometimes mimicking type 1 Chiari malformation.[45] (**Fig. 5**), decrease in size of prepontine and perichiasmatic cisterns (see **Fig. 4**), inferior displacement and flattening of the optic chiasm, and crowding of the posterior fossa (see **Figs. 4** and **5**). The descent and distortion of the brainstem may be manifested by an increase in the anteroposterior diameter of the pons and by the downward displacement of the iter below the incisural line. The iter is the cephalad opening of the aqueduct of Sylvius seen on midline

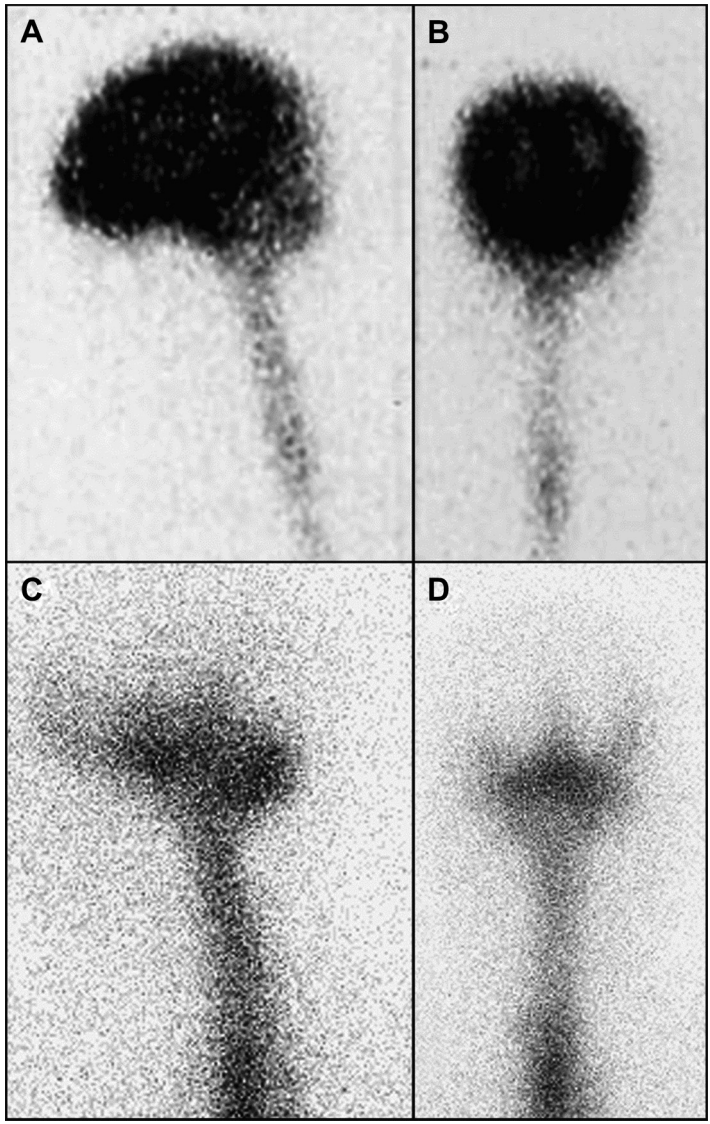

Fig. 2. Indium-111 radioisotope cisternography 24-hour images. (*A*, *B*) Normal study: (*A*) lateral view, (*B*) anteroposterior view. Note that there is plenty of radioactivity over the cerebral convexities at 24 hours. (*C*, *D*) Patient with active CSF leak: (*C*) lateral view, (*D*) posteroanterior view. Note paucity of radioactivity over the cerebral convexities at 24 hours.

sagittal image. The incisural line is the line drawn in midsagittal view between the anterior tuberculum sellae to the point of the junction of the straight sinus, inferior sagittal sinus, and the great vein of Galen.[44] Sometimes the descent of the brainstem and iter may be apparent while the cerebellar tonsils are still above the foramen magnum.

Subdural fluid collections may be bilateral or unilateral and are typically noted over the cerebral convexities (Fig. 6). They are often, but not always, thin and without compression of the underlying brain or effacement of the underlying sulci. These

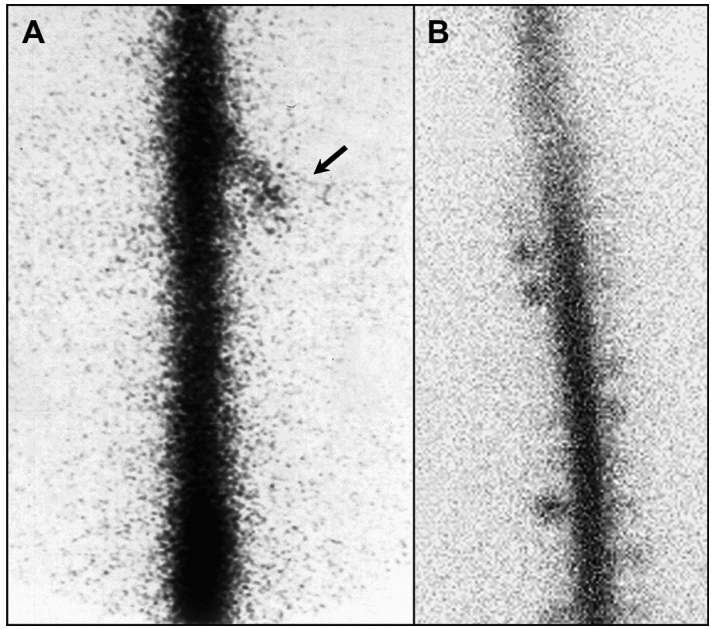

Fig. 3. (*A*) Parathecal activity (*arrow*). This activity may be seen in association with focal CSF leaks, dilated nerve root sleeves, or meningeal diverticula. Differentiation typically calls for additional studies, such as computed tomography myelography (CTM). (*B*) Multiple areas of parathecal activity often related to multiple dilated nerve root sleeves, multiple meningeal diverticula, or both. In this case, no active leak was detected on detailed CTM. Although such lesions may sometimes cause CSF leaks, such a cisternographic appearance should not be automatically labeled as a CSF leak or, worse, multiple areas of a CSF leak.

Box 4
Head MRI abnormalities in spontaneous CSF leak–CSF hypovolemia

1. Diffuse pachymeningeal enhancement
2. Descent or sinking or sagging of the brain
   a. Descent of the cerebellar tonsils (may mimic Chiari I malformation)
   b. Descent of brainstem or mesencephalon (occasionally without descent of cerebellar tonsils)
   c. Distortion and increase in anteroposterior diameter of the brainstem, flattening of anterior pons
   d. Descent of the iter below the incisural line
   e. Obliteration of some of the basal cisterns (ie, prepontine, perichiasmatic)
   f. Crowding of the posterior fossa
   g. Flattening of the optic chiasm
3. Subdural fluid collections (typically hygromas, infrequently hematomas)
4. Engorgement/enlargement of pituitary (may mimic pituitary tumor or hyperplasia)
5. Engorged cerebral venous sinuses
6. Decrease in size of the ventricles (sometimes referred to as ventricular collapse)

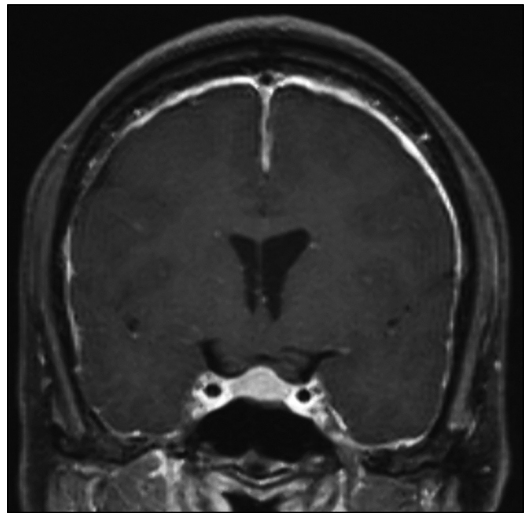

Fig. 4. Head MRI, T1-weighted gadolinium-enhanced coronal view at the level of the sella. Note diffuse pachymeningeal enhancement, enlarged pituitary, flattened optic chiasm, and near obliteration of the perichiasmatic cistern.

collections are usually hygromas but may show various signal intensity depending on the fluid protein concentration. Subdural hematomas can form and can become large enough to compress and shift the brain and become symptomatic. This, however, occurs uncommonly.

Pituitary engorgement and enlargement may mimic pituitary hyperplasia or tumor.[46,47] It may assume a domed appearance with the descended and flattened optic chiasm draped on it (see **Fig. 3**).

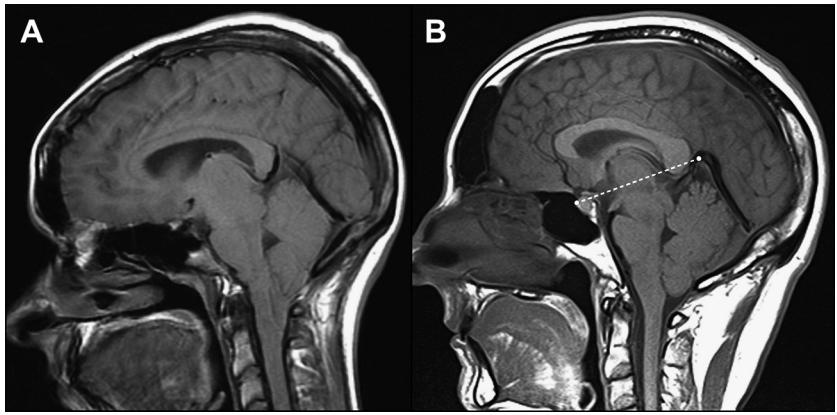

Fig. 5. (*A*, *B*) Head MRI, T1-weighted sagittal views. (*A*) Note descent of the cerebellar tonsils below the foramen magnum resembling Chiari I, crowded posterior fossa, increase in anteroposterior diameter of the brainstem, and decrease in prepontine cistern. (*B*) Descent of the cerebellar tonsils and flattening of the anterior pons. Also note descent of the iter (cephalad opening of the aqueduct of Sylvius) below the incisural line (*dashed line*) (see text) pointing to the descent of the brainstem.

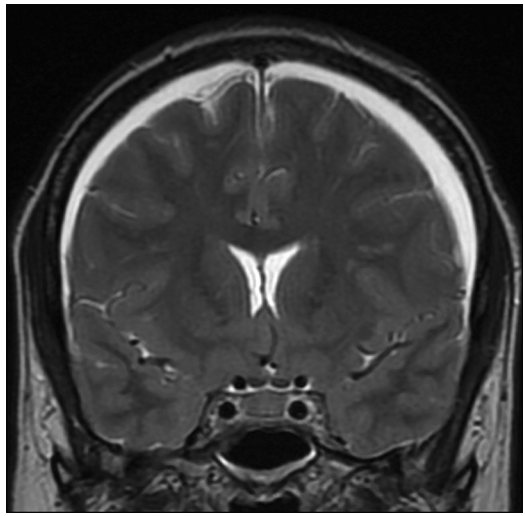

Fig. 6. Head MRI, T2-weighted unenhanced coronal view. Bilateral subdural fluid collections. Also note enlarged pituitary and obliteration of parasellar-perichiasmatic cistern caused by sinking of the brain.

Engorgement of cerebral venous sinuses (Fig. 7)[48] as well as decreased ventricular size (ventricular collapse) may be obvious, but often is not so obvious, and can best be appreciated in retrospect when images of the symptomatic phase are compared with postrecovery images.

In MR study of the brain in CSF leaks, this author has been helped most by T1-weighted gadolinium-enhanced coronal images at the level of the sella and by T1-weighted midline sagittal images. The latter can show the descent of the cerebellar tonsils and brainstem and its related distortions and crowding of the posterior fossa. The former can show a variety of abnormalities, including diffuse pachymeningeal enhancement, subdural fluid collections, pituitary engorgement, flattening of optic chiasm, decrease in perichiasmatic cistern; additionally, particularly when prerecovery and postrecovery images are compared, engorgement of cerebral venous sinuses

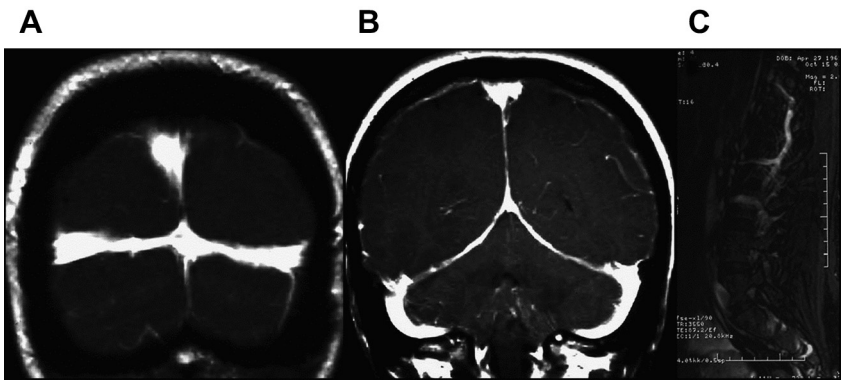

Fig. 7. (*A*, *B*) Engorgement of cerebral venous sinuses and (*C*) epidural venous plexus. Also note the very thin pachymeningeal enhancement.

may become more apparent and a previously unrecognized ventricular collapse may come to attention. These imaging changes are reflected schematically in the drawings of Fig. 8. This statement reflects personal preference and is not at all intended to diminish the high value of a complete study and other sequences but to simply emphasize that head MRI for evaluation of the CSF leaks should serve the clinician best when it includes T1 sagittal and T1 gadolinium enhanced coronal images.

Spine MRI abnormalities are listed in Box 5.

Extradural (or extra-arachnoid) fluid collections are fairly common.[15,49–51] These collections may be focal or extend along several spinal levels (Fig. 9). They only uncommonly enable the determination of the exact site of the CSF leak. Also uncommon, although not rare, is the detection of extravasated fluid into the paraspinal soft tissues. This fluid often occurs across fewer levels and may point to the site or the approximate site of the leak. Heavily T2-weighted spine MRI or the so-called heavily T2-weighted MR myelography[52] provides cleaner and nicer images but, in the author's experience, has not been notably superior to the usual but high-quality spine MRIs and certainly, for the detection of the site of the CSF leakage, has not been a substitute for CTM. It should be noted that in patients with typical clinical and head MRI findings, the real question is not if there is extradural fluid but, instead, where the fluid is leaking from. To answer this question, CTM and its versions (dynamic and hyperdynamic CTM) remain the dependable method of choice (see Fig. 1).

Meningeal diverticula (single but often multiple that may vary in size) and also dilated nerve root sleeves are fairly common in spontaneous CSF leaks. Spinal dural enhancement,[43] engorgement of epidural venous plexus, and engorgement of intradural spinal veins may be seen.[53]

Mechanism of MRI Abnormalities

In exploring the mechanism of MRI abnormalities in the setting of decreased CSF volume, the principles of the Monro-Kellie doctrine have to be considered. According to

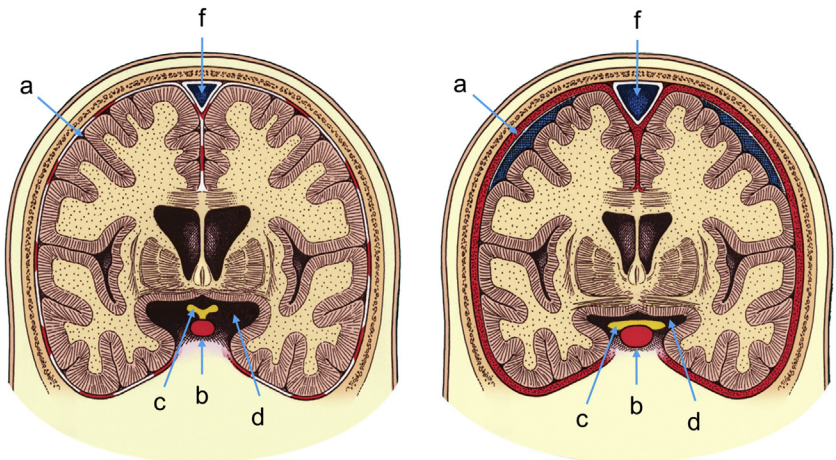

Fig. 8. Gadolinium-enhanced head MRI (see text). Left (normal). Right (during active CSF leak). (*a*) pachymeninges. (*b*) pituitary gland. (*c*) optic chiasm. (*d*) prechiasmatic cistern. (*f*) superior sagittal sinus indicating extraarachnoid fluid collections in blue, over the cerebral convexities. Contrast with images on Fig. 12 (*A, D*). (*From* Mokri B. Unpublished data, with permission of Mayo Foundation; and *Courtesy of* Mayo Clinic, Rochester, MN, with permission.)

Box 5
Spine MRI abnormalities in spontaneous CSF leaks-CSF hypovolemia

- Extra-arachnoid fluid collections that may be focal or frequently extend along several spinal levels
- Extra-dural extravasation of fluid toward paraspinal soft tissues
- Meningeal diverticula, single or multiple; various sizes at various levels
- Spinal dural enhancement
- Engorgement of epidural venous plexus
- Engorgement of intradural spinal veins

this doctrine, "with intact skull, the sum of volumes of brain plus CSF plus intracranial blood is constant."[54] Therefore, an increase or decrease in one will result in a decrease or increase in one or both of the remaining two. In the case of a decrease in CSF volume, given the fact that the brain is basically nonexpandable, it is an increase in the intracranial blood volume that has to compensate for a decrease in CSF volume (**Fig. 10**). Therefore, an intracranial venous hypervolemia occurs with such changes as dilatation of cerebral venous sinuses, engorgement of the pituitary, and diffuse meningeal engorgement. Because leptomeninges have blood-brain barriers and pachymeninges do not, it is only the pachymeninges that enhance with gadolinium.[55] Another volume compensatory mechanism is the collection of subdural fluids.

Similarly, spinal pachymeningeal enhancement can be seen on spine MRI. However, at the spine level, in contrast to the skull, there is an epidural space containing adipose and soft connective tissue as well as the epidural venous plexus. In CSF hypovolemia, a relatively mild collapse of the dural sac may take place that, in turn, leads to the dilatation of the epidural venous plexus. Engorgement of the intradural veins may also be encountered.[53]

Other consequences of CSF volume loss include a decrease in the size of the ventricles sometimes referred to as ventricular collapse and the descent of the brain with such MRI changes as the descent of the cerebellar tonsils; crowding of the posterior fossa; decrease in the size of some of the basal cisterns (ie, prepontine or perichiasmatic cisterns); descent of the brainstem and iter, which is not uncommonly accompanied by deformity; and an increase in the anteroposterior diameter of the brainstem.

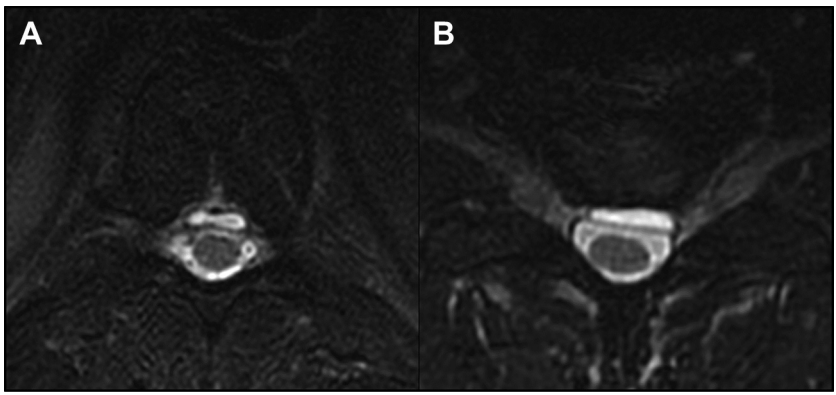

Fig. 9. Spine MRI, axial views (*A*, *B*). Elongated ventral extra-arachnoid fluid collection. This collection had extended across several spinal levels.

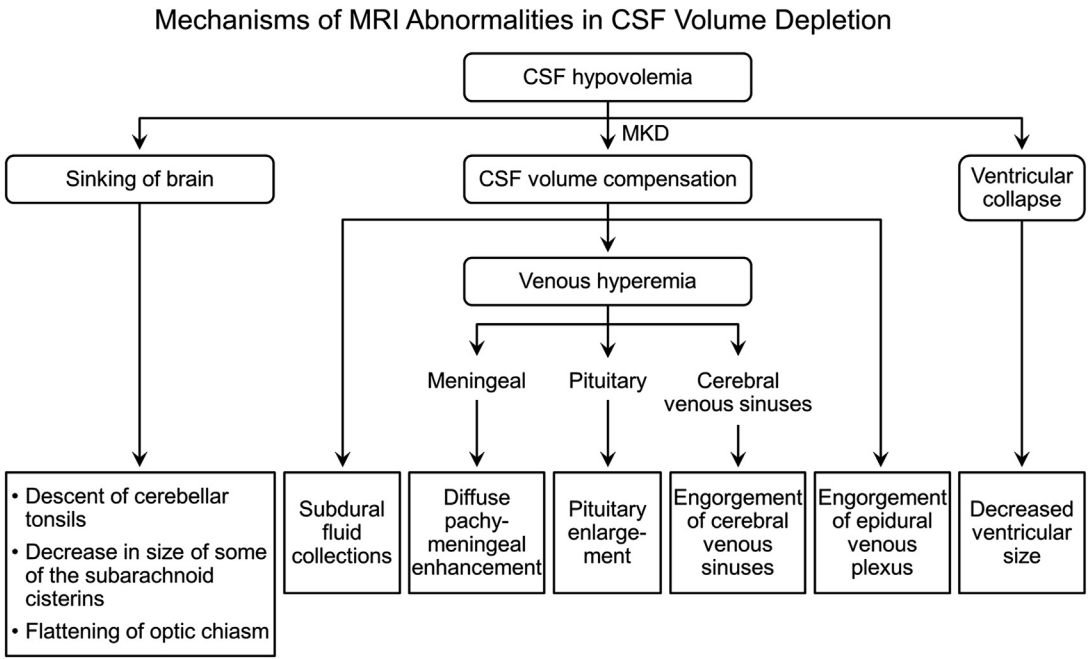

Fig. 10. Diagram intended to show mechanisms of various head MRI abnormalities in CSF leaks (see text). MKD, Monro-Kellie Doctrine.

Myelography/CTM

This study may show several abnormalities and also provides an opportunity to measure CSF opening pressure. The following abnormalities may be detected:

- Extra-arachnoid fluid, which may be quite focal or could extend across several vertebral levels or even several spinal levels, such as from cervical all the way to the lumbar level
- Meningeal diverticula, single or multiple, various sizes, different levels, may or may not be the site of CSF leakage even when large
- Extradural egress of contrast extending into the paraspinal soft tissues

The rate of the CSF leak may vary from patient to patient and, in the same patient, from one encounter to the next. CTM is more reliable than other imaging studies for locating the exact site of the CSF leakage (see **Fig. 9**). When an attempt is made to locate the site of the CSF leak, the two extremes of rapid flow or slow flow each present substantial challenges.

In rapid-flow leaks, after the initial myelogram and by the time patients are taken for the CT scanning, enough contrast has been extravasated epidurally to extend across several vertebral levels making it virtually impossible to determine the actual site of the CSF leakage. This obstacle is overcome by proceeding with high-speed CT scanning of the spine right after the intrathecal injection of the contrast and bypassing the myelographic phase. This technique, known as *dynamic CTM*,[56] and its variations, as well as digital subtraction myelography,[57] have been very helpful in locating the site of the leakage in high-flow leaks.

In slow-flow CSF leaks, several maneuvers have been tried including

- Another CT scanning can be obtained after a delayed period of three to four hours.
- Positive pressure myelography which involves intrathecal injection of fluid to elevate CSF pressure from low to normal levels before injection of contrast in order to increase the likelihood of CSF-contrast extravasation. The results have been variable and not enough to generate strong enthusiasm.
- Gadolinium myelography is essentially a spine MRI after intrathecal injection of gadolinium.[58] This maneuver is sometimes helpful in detecting the site of a slow-flow CSF leak but not as much as initially hoped. This maneuver is an off-label use of gadolinium and should be considered only when the diagnosis of a CSF leak is highly suspected[59] and when the site of the CSF leak has not been detected by other diagnostic techniques, such as CTM.

Overall, locating the site of the CSF leak in slow-flow CSF leaks often remains problematic and sometimes quite frustrating for patients and the physicians.

Treatment

The treatment modalities advocated for patients with spontaneous CSF leaks are listed in **Table 2**. Fortunately, the leak stops in some of the patients regardless of any treatments.

Bed rest has traditionally been recommended. Nevertheless, because many of the patients have significant orthostatic symptoms, at least initially, they tend to stay recumbent much of the time anyway.

Another traditionally recommended measure is hydration, which is often an overhydration because many patients are not dehydrated. Its effectiveness has not been clearly established. The efficacy of caffeine and theophylline has been demonstrated

Table 2
Treatment of spontaneous CSF leaks

Conservative measures	• Bed rest (Typically, patients with substantial orthostatic headaches tend to remain reclined much of the time anyway.) • Coffee • Hydration or, more accurately, overhydration because the large majority are not dehydrated • Time (might be the most important element)
Medications	• Analgesics (It is often, but not always, impractical because the effect of analgesics in the upright position may be only partial and many patients become completely or substantially headache free in recumbency.) • Caffeine • Theophylline • Corticosteroids
Abdominal binder	• Binders • Corsets
Epidural injections	• Homologous blood epidural blood patch: targeted, distant, bilevel, multilevel, blind (at lumbar level) • Fibrin glue (fibrin sealant) • Fibrin glue and blood
Surgical repair of the leak	• Surgical closure (not always possible) • Reinforcement with muscle and/or fibrin sealant
Other measures in special situations	• Epidural saline infusions (uncertain, unpredictable efficacy or durability; risk of infection) • Intrathecal fluid injection (for quick CSF volume replacement) in rare instances of progressing obtundation, stupor, or coma from descent and compromise of brainstem and midbrain • Epidural infusion of dextran (rarely practiced) • Intravenous saline infusions

in some studies[60]; but this efficacy often, although not always, is nonimpressive and of doubtful durability.

Some patients may report various degrees of symptom control from corticosteroids, but a few points need emphasizing:

- Not all patients respond to corticosteroids and indeed most may not.
- Even when effective, the effect is often partial and of doubtful durability.
- Considering the potential side effects of corticosteroid therapy, especially for extended periods of time, such treatment does not seem to be a long-term solution.

Intrathecal fluid infusions or epidural infusions of crystalloids (eg, saline) or colloids (eg, dextran) produce varying results[61–65] but can be considered with limited expectations and for a limited period in patients who fail repeated epidural blood patches (EBP) and when surgery is not an option. There is, however, concern about the possibility of the introduction of infection in prolonged infusions as well as the probability of catheter failures.

EBP is the treatment of choice in patients who fail an initial trial of conservative management.[66,67] The effect of EBP is twofold: (1) an early (sometimes almost immediate) effect related simply to volume replacement resulting from dural tamponade and (2) a latent effect, which results from sealing the leak. In spontaneous CSF leaks, the

success rate with each EBP is approximately 30%.[67] Many patients require more than one EBP. The success rate is significantly more impressive for postlumbar puncture headaches whereby the first EBP gives relief in the vast majority and a second one in nearly all cases. This difference is likely a consequence of one or more of the following factors:

- In postlumbar puncture headaches, the level of the EBP is typically the same as the level of the leak, whereas in spontaneous CSF leaks, the EBP may be distant from the actual site of the leak.
- The anatomy of the leak in many patients with spontaneous CSF leaks is more complicated than a simple hole or rent produced by spinal tap needles.
- In spontaneous CSF leaks, the dural defect commonly is in the anterior aspect of the dural sac or in the nerve root sleeve or the axilla of the nerve root sleeve.
- Spontaneous CSF leaks may take place from multiple sites at different levels, and some patients who have spontaneous CSF leaks may fail even multiple EBPs.

Sometimes epidural injection of fibrin glue[68,69] may be carried out translaminar or transforaminal, depending on the situation at hand. Sometimes a combination of epidural injection of fibrin glue and homologous blood is considered. Epidural injections of blood or fibrin glue may be single level, bilevel, or even multilevel. They may be targeted, distant from the site of the leak, or could be blind EBPs (when the site of CSF leak has not been determined). These injections are typically placed at the lumbar level.

In well-selected cases, surgery is effective and is considered for those patients who fail conservative measures and less invasive treatments such as EBPs[15,70] or when the anatomy of the leak has been such that the success of nonsurgical approaches has been predicted to be remote. The surgery is not always straightforward because the anatomy of the leak is not always simple.[71] The surgeon may encounter the extravasated CSF but may not be able to locate the site of the leak and, therefore, may have to pack the area with blood-soaked gelatin sponge muscle, or fibrin glue and hope for the best. The margins of dural defect may be so markedly attenuated that they may not yield to suturing. Sometimes the site of the leak and the dural defect is in the anterior aspect of the dura or the leak may be from a meningeal diverticulum or a defect or diverticulum of a nerve root sleeve. Each of these may have varying anatomic configurations and provide the surgeon with unpredicted challenges. It is essential, however, to try to locate the site of the CSF egress before surgery and to realize that a meningeal diverticulum, even when large, may not necessarily be the actual site of the CSF leakage. With careful selection, surgical results can be fulfilling.

COMPLICATIONS OF CSF LEAKS

Subdural Hematomas

These hematomas may complicate subdural hygroma or may be subdural hematomas right from the start. They may be thin and asymptomatic but can be large, become symptomatic, and compress the underlying brain. Symptomatic and expanding subdurals require surgical intervention.[72,73] Careful postoperative monitoring is important, watching for manifestations of increased sagging of the brain. Surgical creation of a skull defect will violate the Monro-Kellie principle and may lead to increased sinking of the brain (**Fig. 11**).[74] It is wise to address the treatment of CSF leakage at some point along with the treatment of the subdural hematoma.

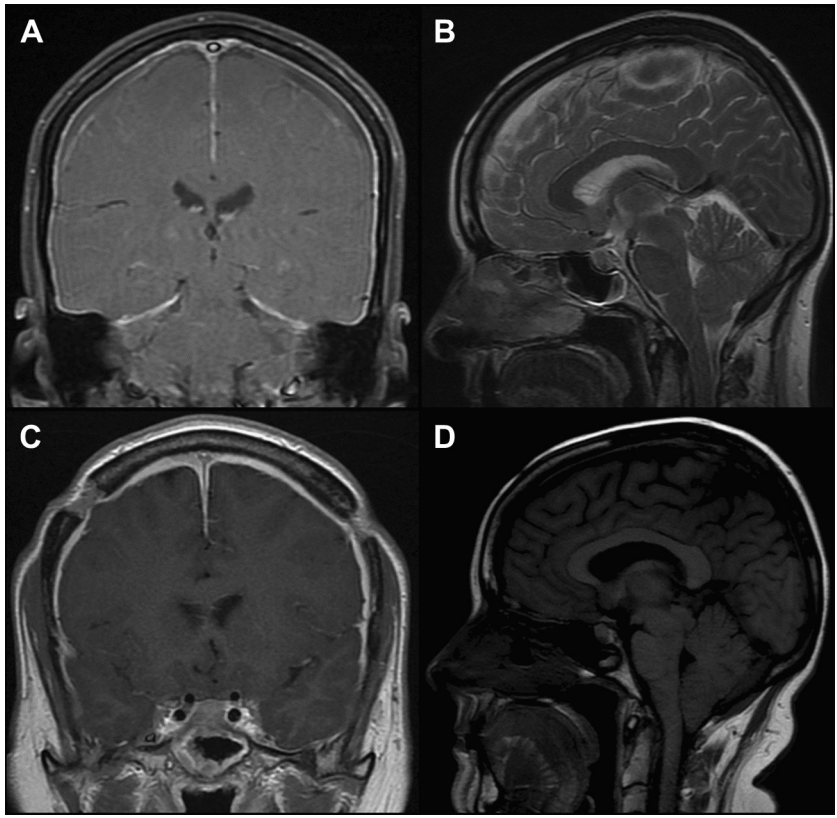

Fig. 11. Coronal (*A*) and sagittal (*B*) head MRIs in a patient with CSF leak and bilateral subdural collections. (*A*) Bilateral subdurals and diffuse pachymeningeal gadolinium enhancement. (*B*) Low-lying cerebellar tonsils. Patient had been subjected to bilateral burr hole evacuation of subdurals (*C*), but the leak had not been addressed. Note further descent of the cerebellar tonsils (*D*). (*From* Mokri B. Unpublished data, with permission of Mayo Foundation; and *Courtesy of* Mayo Clinic, Rochester, MN, with permission.)

Rebound Intracranial Hypertension

This complication is sometimes noted after a CSF leak has been successfully treated surgically or by EBP. Sometimes patients may present with recurrence of headache, although typically not an orthostatic headache, and sometimes even papilledema may be noted (**Fig. 12**).[75] This phenomenon is often a self-limiting phenomenon but may frustratingly take a long time to resolve. Acetazolamide is frequently helpful to decrease the symptoms. The true incidence of this rebound intracranial hypertension is likely higher than thought because some of the patients may be asymptomatic or minimally symptomatic.

Cerebral Venous Sinus Thrombosis

In patients with CSF leaks, change in headache characteristics within a short period of time may raise this possibility[76]; but fortunately, its incidence is very low. When cerebral venous sinus thrombosis develops, it calls for anticoagulation therapy.

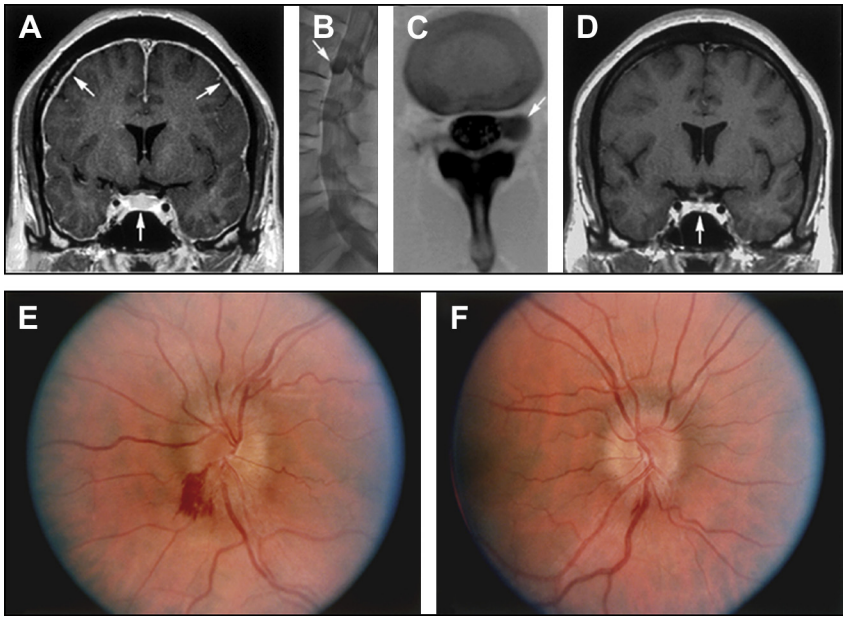

Fig. 12. Patient presented with orthostatic headaches. (*A*) Head MRI shows diffuse pachymeningeal enhancement (*upper arrows*) and enlargement of pituitary (*lower arrow*) and flattened optic chiasm. (*B*, *C*) CTM identifies leaking meningeal diverticulum (*arrow*). Surgical repair is followed by resolution of the orthostatic headaches and reversal of the head MRI abnormalities. (*D*) Also noted is mildly smaller size of the ventricles (on [*A*]), in retrospect pointing to presence of ventricular collapse, which also subsequently reversed (*B*). The *arrow* (*D*) points to reversal of pituitary enlargement and flattening of optic chiasm. The ventricular collapse is often subtle and is recognized retrospectively. Sometimes, however, it is quite obvious. This patient's extra-arachnoid/subdural symptoms resolved after surgery but later presented with a different type of headache and bilateral papilledema (*E*, *F*) as the result of rebound intracranial hypertension. (*From* Mokri B. Unpublished data, with permission of Mayo Foundation; and *Courtesy of* Mayo Clinic, Rochester, MN, with permission.)

Superficial Siderosis

This complication is a rare and remote complication of spinal CSF leaks.[77–79] It is frequently associated with elongated extra-arachnoid fluid collections, often ventral to the cord and along several vertebral levels.

Bibrachial Amyotrophy

Another rare complication of CSF leaks, also often associated with elongated extra-arachnoid fluid collections, is painless bilateral weakness and atrophy of some of the upper limb myotomes. This complication often begins on one side before becoming bilateral. It may involve shoulder girdle myotomes, proximal upper limb myotomes, or distal upper limb myotomes (**Fig. 13**). It may mimic motor neuron disease.[80]

RECURRENCE OF CSF LEAKS

These recurrences are not rare and may occur with variable frequency and at variable intervals from a previous leak. There is paucity of reliable data regarding the incidence

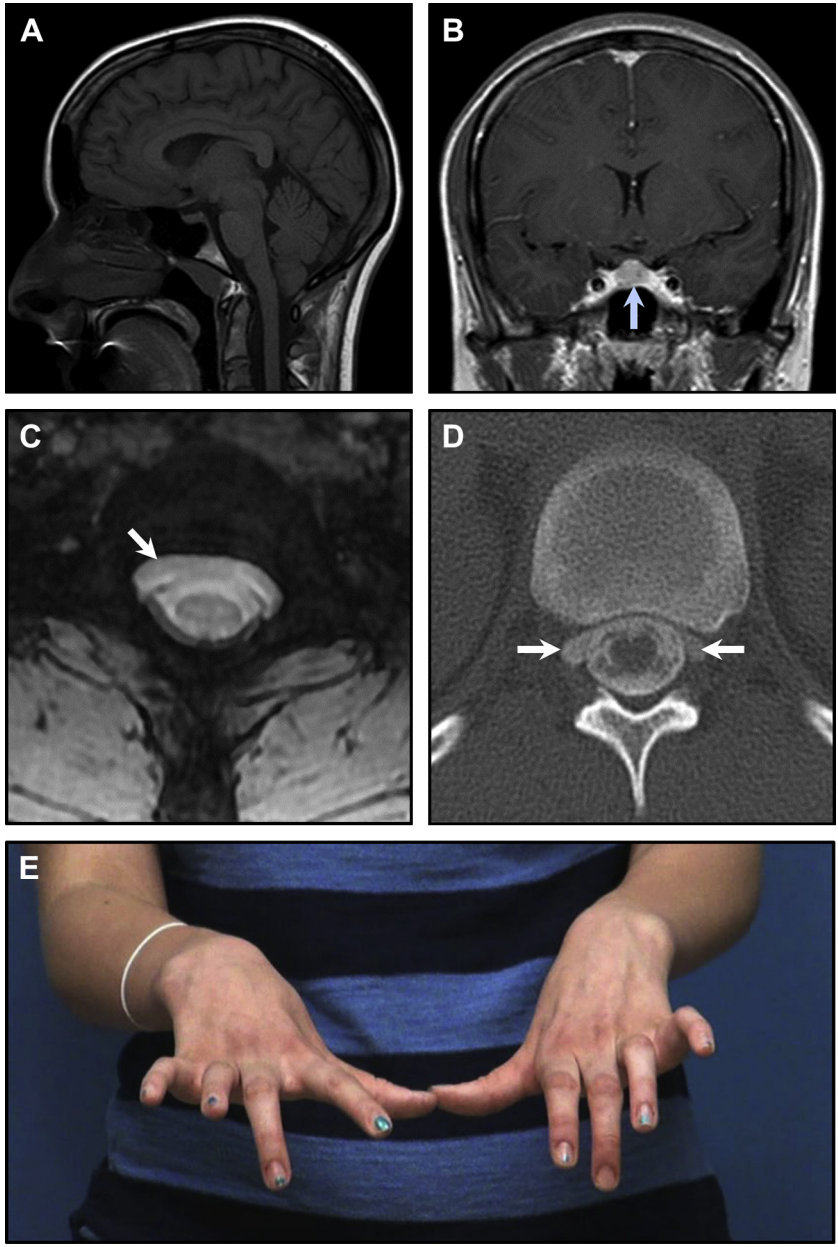

Fig. 13. Bibrachial amyotrophy in spontaneous CSF leak. Head MRIs: (*A*) sagittal view shows descent of cerebellar tonsils and brainstem, (*B*) enhanced coronal view shows enlarged pituitary (*arrow*) and obliteration of parasellar-perichiasmatic cistern. (*C*) Spine MRI shows ventral extra-arachnoid/extradural fluid collections (*arrow*) also seen in (*D*) CTM (*arrows*). The extra-arachnoid ventral fluid collection had extended across several cervical and thoracic levels. (*E*) The related bilateral distal upper limb muscle atrophy. The atrophic muscles were quite weak. She could not hold a pencil. (*From* Mokri B. Unpublished data, with permission of Mayo Foundation; and *Courtesy of* Mayo Clinic, Rochester, MN, with permission.)

of such recurrences, and information based on essentially surgical referrals may not be applicable to the entire group. Although not formally studied or proven, possibly those with stigmata of the disorders of the connective tissue matrix might be at a somewhat higher risk of recurrence.

ORTHOSTATIC HEADACHES WITHOUT CSF LEAK

As addressed earlier in the article, not all headaches of spontaneous CSF leaks are orthostatic. Similarly, not all orthostatic headaches are caused by CSF leaks. They have been noted in association with other conditions including

- Postural orthostatic tachycardia syndrome[81]
- After surgery for Chiari malformation
- The syndrome of the trephined[82]
- Increased compliance of dural sac[83]
- Occasional cases of colloid cyst of the third ventricle[31]

SUMMARY AND LESSONS OF THE PAST 2 DECADES

Schaltenbrand[31] described the spontaneous occurrence of the syndrome of intracranial hypotension in 1939, and he pointed out that the syndrome itself had been described in the French literature about 2 decades earlier. However, much of our current knowledge of this entity has been acquired in the past 2 decades, essentially in connection with the availability of MRI and its enormous impact on the recognition of this entity. The following are some of what has been recognized:

- SIH almost always results from spontaneous CSF leaks. The old theories of decreased CSF production or increased CSF absorption have never been substantiated.
- Decreased CSF volume (CSF hypovolemia) rather than decreased CSF pressure (CSF hypotension) is the core pathophysiologic factor as an independent variable, whereas CSF pressures, clinical manifestations, and imaging findings are variables that depend on the CSF volume.
- Most spontaneous CSF leaks occur at the spinal level, frequently on preexisting zones of dural weakness. As opposed to posttraumatic leaks, the spontaneous ones only rarely occur at the level of skull base, such as the cribriform plate.
- A significant minority of patients displays clinical stigmata of heritable disorders of the connective tissue matrix. These stigmata likely play an etiologic role in the formation of meningeal diverticula or zones of dural weakness and CSF leaks.
- Although the triad of orthostatic headaches, low CSF pressure, and diffuse pachymeningeal enhancement on head MRI is the hallmark of the diagnosis, expect substantial variability in just about every aspect of this entity, including CSF opening pressure (which may be normal), the clinical manifestations including headaches (broad clinical features, various headache types), and the imaging abnormalities (ie, absent pachymeningeal enhancement).
- The anatomy of spontaneous CSF leaks can be complex. One should not expect a simple hole or rent or equate the spontaneous CSF leak with the leaks that may occur after dural puncture or epidural catheterization.
- The rate of CSF leak can vary. Slow-flow and fast-flow CSF leaks each present diagnostic challenges when attempts are made to locate the site of the CSF leakage. Novel imaging techniques have helped enormously with locating the site of the fast-flow leaks, but the slow-flow leaks continue to remain challenging.

- EBP has emerged as the treatment of choice for those who fail the initial conservative measures. It can be targeted or distant, single level, bilevel, or, in selected cases, multilevel. Epidural fibrin glue injection also has utility in selected cases. Combined fibrin glue and EBP have been tried by some, but it is not a routine approach and needs particular considerations.
- It is expected that surgery is aimed at stopping the leak when less invasive measures, such as EBP, have failed or when the anatomy of the leak is such that the chance of nonsurgical success is predicted to be very slim. It is essential to determine the site of the leak before surgery is undertaken.

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