From: Jeffrey Epstein <jeevacation@gmail.com>
To: melanie <[redacted]>
Subject: Re: melanie has sent you an UpToDate topic
Date: Fri, 08 Mar 2013 23:55:24 +0000

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great

On Fri, Mar 8, 2013 at 6:43 PM, melanie <[redacted]> wrote:

> JEE - read through this article. It is the most comprehensive that I could find related to low CSF pressure headaches.
>
> Perhaps there is something in here that will resonate, or at least it will tell us that this ISN'T what she's got.
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> Pathophysiology, clinical features, and diagnosis of spontaneous low cerebrospinal fluid pressure headache
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> Literature review current through: Feb 2013. &#124 This topic last updated: Jan 17, 2013.
>
> INTRODUCTION AND TERMINOLOGY — The production, absorption, and flow of cerebrospinal fluid (CSF) play key roles in the dynamics of intracranial pressure. Alterations in CSF pressure can lead to neurologic symptoms, the most common being headache. Most often, the headaches associated with low CSF pressure are orthostatic and occur after lumbar puncture, but similar headaches occur with spontaneous low CSF pressure due to spinal CSF leaks and with CSF shunt overdrainage. In addition, trauma, surgery, and other medical conditions have also been associated with low CSF pressure headache [1].
>
> Spontaneous low CSF pressure headache is being recognized with increasing frequency. Orthostatic headache, low CSF pressure, and diffuse meningeal enhancement on brain magnetic resonance imaging (MRI) are the major features of the classic syndrome. However, some cases have nonorthostatic headache, normal CSF pressure, or no evidence of diffuse meningeal enhancement [2].
>
> Our understanding of this syndrome is still evolving, and historically a number of terms have been used to describe it:
>
> - Spontaneous (or idiopathic) low CSF pressure headache
> - Spontaneous (or primary) intracranial hypotension
> - Low CSF volume headache
> - Hypoliquorrhoeic headache
> - Aliquorrhea
> - CSF leak headache

- CSF hypovolemia
- CSF volume depletion

This topic will discuss the pathophysiology, epidemiology, clinical features, and diagnosis of spontaneous low CSF pressure headache. Treatment is discussed separately. (See "Treatment and prognosis of spontaneous low cerebrospinal fluid pressure headache".)

Post-lumbar puncture headache is also discussed separately. (See "Post-lumbar puncture headache".)

PATHOPHYSIOLOGY — In the intact craniospinal vault, the brain is supported by the cerebrospinal fluid (CSF), such that a brain weight of 1500 g in air is only 48 g in CSF [3]. As the CSF pressure decreases, there is a reduction in the buoyancy of the brain's supportive cushion. As a result, the brain "sags" in the cranial cavity, causing traction on the anchoring and supporting structures of the brain [4-7].

Cause of headache — Traction on pain-sensitive intracranial and meningeal structures, particularly sensory nerves and bridging veins, is thought to cause headache and some of the associated symptoms [6]. In the upright position this traction is exaggerated, hence the postural component of the headache. Secondary vasodilation of the cerebral vessels to compensate for the low CSF pressure may contribute to the vascular component of the headache by increasing brain volume [5]. Because jugular venous compression increases headache severity, it seems likely that venodilation is a contributing factor to the headache.

CSF hypovolemia, rather than CSF hypotension per se, has been proposed as the underlying cause of the headache syndrome [2], as patients with normal CSF pressure have been described who have clinical and radiographic features that are otherwise typical of orthostatic headache [2,8-10]. In this paradigm, the CSF pressures, clinical manifestations, and imaging abnormalities of the syndrome are thought to be variables dependent on CSF volume [11]. Some authors [12] have therefore advocated the name "CSF hypovolemia syndrome" for the constellation of symptoms associated with CSF leakage.

An alternative hypothesis is that spinal loss of CSF results in an increased compliance at the caudal end of the spinal CSF space, and the abnormal distribution of craniospinal elasticity causes the headache syndrome [13]. This explanation is compatible with the observation that spinal sites of CSF leakage commonly produce orthostatic headache, whereas cranial sites of CSF leakage (eg, seen with spontaneous CSF rhinorrhea or CSF otorrhea) are less likely to do so.

Cause of low CSF pressure — In 1891 Quincke introduced the lumbar puncture (LP) [14], and in 1898 Bier suffered and was the first to report post-LP headache [15]. He proposed that ongoing leakage of cerebrospinal fluid (CSF) through the dural puncture site was the cause of the headache. This belief is still held today. It is thought that leakage of CSF through the dural rent made by the LP needle exceeds the rate of CSF production, resulting in low CSF volume and pressure [16]. (See "Post-lumbar puncture headache".)

The clinical syndrome of spontaneous low CSF pressure has been recognized for many years. The syndrome was first proposed in 1938 by Schaltenbrand [17,18], who termed it aliquorrhea, and described a headache syndrome virtually identical to that following LP. He proposed three possible mechanisms (decreased CSF production by the choroid plexus, increased CSF absorption, and CSF leakage through small tears) to explain the symptoms.

CSF leak — Today, the prevailing etiology is that of CSF leakage, which may occur in the context of rupture of an arachnoid membrane [19]. An underlying connective tissue disorder may result in dural weakness and play a role in the development of spontaneous low CSF pressure, as suggested by studies reporting abnormal connective tissue abnormalities in patients with spontaneous CSF leaks [20,21] and/or deficient fibrillin, elastin, or both in dermal fibroblast cultures from such patients [22]. Meningeal diverticula, often seen in patients with CSF leaks, may be related to this connective tissue problem [23], and meningeal diverticula have been described in patients with Marfan's syndrome [21].

A potential contributing factor to the development of spontaneous low CSF pressure is that of minor trauma or an inciting event, including a fall, a sudden twist or stretch, sexual intercourse or orgasm, a sudden sneeze, sports activity, or "trivial trauma" [24]. These relatively minor events may cause rupture of spinal epidural cysts (formed during fetal development) or perineural (Tarlov) cysts, or may cause a tear in a dural nerve sheath [19] with resultant cryptic CSF leakage.

Finally, degenerative disc disease and osseous spurs may rarely cause spontaneous low CSF pressure headache, presumably by causing dural tears [25-28].

Low venous pressure — An alternative hypothesis postulates that spontaneous intracranial hypotension results primarily from the lowering of venous pressure within the inferior vena cava system, amplified by the displacement of blood toward the heart that occurs due to the activation of leg muscles during standing and walking [29]. The lower pressure in the inferior vena cava leads to epidural venous hypotension and outflow of CSF along the spinal cavity, and in some cases precipitates actual CSF leaks from existing radicular arachnoid diverticula or cysts. In this paradigm, dural tears are not the cause of the condition but instead are a result of the low epidural pressure. Blood patching at the epidural lumbar space used to treat the condition does not work by sealing CSF leaks, but instead is effective because it disconnects the low-pressure epidural lumbar venous network that drains to the inferior vena cava and diverts venous return to the epidural thoracic and cervical venous network that drains to the superior vena cava.

This hypothesis has been challenged by experts who dispute a number of its assumptions regarding the anatomic and pathophysiologic characteristics of the spinal epidural veins [30]. In addition, the skeptics point out radiologic evidence that epidural veins are distended and the epidural sac is collapsed in patients with spontaneous intracranial hypotension prior to treatment, and that the epidural veins and dural sac return to normal proportions after treatment with blood patch [31]. These pre-treatment observations are best explained by CSF hypotension with dural sac collapse and expansion of the extradural space [30].

EPIDEMIOLOGY — There are few data regarding the incidence of low cerebrospinal fluid (CSF) pressure headache. In a systematic review published in 2006, the following observations were made [32]:

- The estimated annual incidence is 5 per 100,000
- The peak incidence is around age 40, but children and elderly are also affected
- Women are affected more frequently than men, with a female to male ratio of 2:1

The author concluded that spontaneous intracranial hypotension should be considered an important cause of new daily persistent headaches, particularly among young and middle-aged patients [32]. (See "New daily persistent headache".)

CLINICAL FEATURES — Postural headache is usually but not always the major manifestation of spontaneous low cerebrospinal fluid (CSF) pressure. Occasional patients report no headache, typically when other symptoms of low CSF pressure are predominant [32]. (See 'Associated symptoms and complications' below.)

Headache — The headache caused by low CSF pressure may be of sudden or gradual onset. Rarely, it starts as a thunderclap headache [23]. (See "Thunderclap headache".)

Headache pain with this syndrome is often described as an intense, throbbing, or dull pain that may be generalized or focal. However, headache severity is widely variable and ranges from mild to incapacitating [32]. Frontal pain is reported by patients as often as occipital and diffuse pain [24].

Headache relief is typically obtained with recumbency, usually within minutes. In rare cases associated with an asymmetric cervical CSF leak, headache relief occurs only with lying on one side of the body [33]. The headache is seldom relieved with analgesics. Exacerbating factors include erect posture, head movement, coughing, straining, sneezing, jugular venous compression, and high altitude [34].

During the course of the illness, the orthostatic features may disappear, and a chronic daily headache may develop [23]. On occasion, the postural component may not be present at all. Furthermore, paradoxical headache, worse with recumbency and better with the upright position, has been reported in rare patients with spontaneous low CSF pressure [35,36]. In other cases, the headache can mimic a primary headache syndrome, such as primary cough headache [37] or primary exertional headache [38]. These primary headache syndromes are discussed separately. (See "Primary cough headache".)

Most CSF leaks occur at the thoracic or cervicothoracic junction. Leakage of CSF into the petrous or ethmoidal regions or through the cribriform plate can also occur, and although overt CSF otorrhea and CSF rhinorrhea may result, it is not uncommon for the patient to swallow the fluid and be unaware of the leak.

Low CSF pressure headache may spontaneously resolve within two weeks [39]. In some cases, it lasts months or rarely years.

Associated symptoms and complications — In 1825, Magendie described vertigo and unsteadiness in a patient following the removal of CSF [40]. Today, the list of reported associated symptoms is varied and extensive. The most common associated symptoms with spontaneous low CSF pressure headache, reported in about half of patients, are [32]:

- Neck pain or stiffness
- Nausea
- Vomiting

Other associated symptoms include the following [32]:

- Change in hearing (eg, hyperacusis, echoing, or tinnitus) [2,14,24]
- Anorexia
- Vertigo
- Dizziness
- Diaphoresis
- Blurred vision
- Diplopia
- Transient visual obscurations [3]
- Photophobia
- Unsteadiness or staggering gait [16]
- Hiccups
- Dysgeusia [24]

Other rare symptoms associated with the syndrome are probably due to distortion or compression of brain and/or spinal cord structures. These rare manifestations (and associated central nervous system structures) are as follows [41]:

- Galactorrhea and hyperprolactinemia (pituitary stalk)
- Ataxia (posterior fossa)
- Quadriparesis (brainstem and upper cervical spinal cord) [36]
- Cerebellar hemorrhage (cerebellar bridging veins) [36]
- Parkinsonism [42] and chorea [43] (deep midline structures)
- Hypoactive, hypoalert behavior (pons and midbrain) [44]
- Stupor and coma (diencephalon) [45,46]

Except for hemorrhage, these manifestations are typically reversible with successful treatment of the CSF leak.

Subtle cognitive deficits may be associated with the syndrome and are typically reversible with successful treatment of the CSF leak [32]. Frank dementia is rare, but a case of reversible frontotemporal dementia attributed to low CSF pressure has been reported [47]. Another report described eight patients with

“frontotemporal brain sagging syndrome” (FBSS) who presented with progressive behavioral symptoms and cognitive dysfunction suggestive of behavioral variant frontotemporal dementia [48]. Atypical clinical features included headache and daytime somnolence. MRI in all cases revealed sagging of the frontal and temporal lobes with downward displacement of the cerebellar tonsils, swelling of the midbrain, flattening of the ventral pons and effacement of the basal cisterns. Two patients had pachymeningeal enhancement. Treatments directed at intracranial hypotension led to unsustained improvement in a few patients. Frontotemporal dementia is discussed separately. (See "Frontotemporal dementia: Clinical features and diagnosis".)

Examination — The neurologic examination is typically normal [39]. Unilateral or bilateral abducens palsies have been reported, as have visual field defects [3]. A slow pulse, or vagus pulse, has also been described [5].

Cerebrospinal fluid analysis — The opening pressure with lumbar puncture (LP) in patients with spontaneous intracranial hypotension usually ranges from 0 to 70 mmH20 [4], whereas normal opening pressure is generally considered to be 60 to 200 mmH2O in adults and children; opening pressures up to 250 mmH2O may be normal in obese people. (See "Cerebrospinal fluid: Physiology and utility of an examination in disease states", section on 'Physiology of CSF formation and flow'.)

The opening pressure is in the normal range in some cases of proven spontaneous intracranial hypotension, especially if the measurement is made after a period of recumbency, or if the CSF leak is intermittent. Even within the same patient, the CSF pressure may vary from LP to LP.

In patients with spontaneous intracranial hypotension, LPs are often difficult. Repeated attempts may be needed to obtain CSF, and traumatic blood-tinged fluid may result. In addition, so-called "dry taps" may be encountered, requiring cisternal taps to collect the fluid. In rare instances, the CSF pressure is negative (below that of atmospheric pressure), and a sucking noise may be heard when the stylet is removed from the LP needle.

The CSF is typically clear and colorless. Common CSF abnormalities include a moderate lymphocytic pleocytosis (up to 50 cells/mm^3), the presence of red blood cells, and elevated protein (commonly up to 100 mg/dL) [8]. The CSF pleocytosis likely reflects a reactive phenomenon secondary to hydrostatic pressure changes [39]. The elevated protein may be related to lowered CSF pressure leading to disruption of normal hydrostatic and oncotic pressure across the venous sinus and arachnoid villi, resulting in the passage of serum protein into the CSF [39].

CSF cytology and microbiology is always normal and CSF glucose is never low [49].

Brain MRI — The advent of MRI has greatly improved the diagnosis of low CSF headaches. While brain and/or spine MRI is abnormal in most patients with spontaneous intracranial hypotension, a systematic review estimated that brain MRI remains normal in up to 20 percent of patients [32].

Prominent abnormal features on brain MRI include the following:

- Diffuse meningeal enhancement (DME) (image 1) [50]
- Subdural hematomas or hygromas, presumably from rupture of the bridging veins as the CSF volume decreases [40,51]
- "Sagging" of the brain, with cerebellar tonsillar herniation and descent of the brainstem mimicking a Chiari I malformation (image 2) [52]
- Engorgement of cerebral venous sinuses [53]
- Pituitary enlargement [54,55], flattening of the optic chiasm, and increased anteroposterior diameter of the brainstem
- Decrease in the size of cisterns and ventricles

The acronym SEEPS (for Subdural fluid collections, Enhancement of the pachymeninges, Engorgement of the venous structures, Pituitary enlargement, and Sagging of the brain) recalls the major features of spontaneous intracranial hypotension on brain MRI [32].

Meningeal enhancement involves the pachymeninges and spares the leptomeninges, without abnormal enhancement in the depth of the cortical sulci or around the brainstem (image 1) [8,50,56-58]. It is also contiguous (without skip areas), non-nodular, and involves both supratentorial and infratentorial compartments. The enhancement is often thick and obvious, but sometimes can be quite thin. Diffuse meningeal enhancement may improve or resolve with resolution of the headache.

Diffuse meningeal enhancement is believed to be secondary to vascular dilatation. According to the Monro-Kellie doctrine [59], any decrease in CSF volume must be compensated given the noncompressible nature of the skull. As a result, loss of CSF volume results in an increase in intracranial blood volume, and venous engorgement results in a greater concentration of gadolinium in the dural vasculature and interstitial fluid of the dura.

A minority of patients with spontaneous intracranial hypotension may present with swelling of the upper brainstem and diencephalon, but limited to absent DME and subdural fluid collections on MRI [60]. The upper brainstem swelling is hypothesized to be a manifestation of venous stagnation caused by downward stretching of the vein of Galen, which results in a functional stenosis where the vein of Galen joins the straight sinus.

Head CT — Head computed tomography (CT) in patients with CSF leaks is usually normal. However, subdural fluid collections or increased tentorial enhancement may be noted [61]. In addition, slit-shaped ventricles have been reported, with associated tight basal cisterns and scant CSF over the cortex [62]. These changes resolve after resolution of the headache and are believed to be secondary to brain edema, perhaps itself secondary to venous dilatation.

DIAGNOSIS — The diagnosis of low cerebrospinal fluid (CSF) pressure headache should be considered in patients who present with positional orthostatic headache, with or without associated symptoms, perhaps in the setting of minor trauma, and in the absence of a history of dural puncture or other cause of CSF fistula. Low CSF pressure headache following a lumbar puncture (LP) rarely creates a clinical dilemma.

Confirmation of the diagnosis requires evidence of low CSF pressure by MRI (eg, pachymeningeal enhancement) or LP, and/or evidence of a CSF leak on neuroimaging studies, mainly computed tomographic (CT) myelography or, less often, radioisotope cisternography.

For patients with suspected CSF pressure headache, we recommend brain MRI with gadolinium to assess for the typical features. (See 'Brain MRI' above and 'Neuroimaging' below.)

Diagnostic criteria — Diagnostic criteria for "headache attributed to spontaneous (or idiopathic) low cerebrospinal fluid (CSF) pressure," as delineated in the second edition of the International Classification of Headache Disorders, are as follows [63]:

- A. Diffuse and/or dull headache that worsens within 15 minutes after sitting or standing, with at least one of the following (and fulfilling criterion D):
  - Neck stiffness
  - Tinnitus
  - Hypacusia
  - Photophobia
  - Nausea
- B. At least one of the following:
  - Evidence of low CSF pressure on MRI (eg, pachymeningeal enhancement)
  - Evidence of CSF leakage on conventional myelography, CT myelography, or cisternography
  - CSF opening pressure <60 mmH2O in sitting position
- C. No history of dural puncture or other cause of CSF fistula

- D. Headache resolves within 72 hours after epidural blood patching

A separate set of criteria exists for post-dural (post-lumbar) puncture headache.

Neuroimaging — The advent of brain MRI has greatly improved the diagnosis of low CSF headaches. Spine MRI, radioisotope cisternography, and CT myelography can be useful in evaluating patients with spontaneous low pressure headache, particularly when brain MRI is nondiagnostic. These imaging studies are generally not done in patients with post-lumbar puncture headache, where the diagnosis is more obvious.

The utility of head CT for confirming the diagnosis is limited, as head CT is often normal in patients with spontaneous low CSF pressure headache. However, head CT may suggest the diagnosis by demonstrating subdural fluid collections, slit-shaped ventricles, tight basal cisterns, scant CSF over the cortex, or increased tentorial enhancement [32]. (See 'Head CT' above.)

MRI of brain and spine — For patients with suspected low CSF pressure headache, we recommend obtaining brain MRI with gadolinium to assess for the typical features of the syndrome, which are diffuse pachymeningeal enhancement (image 1), "sagging" of the brain, tonsillar descent, and posterior fossa crowding (image 2). (See 'Brain MRI' above.)

While brain and/or spine MRI is abnormal in most patients with spontaneous intracranial hypotension, a systematic review published in 2006 estimated that brain MRI remains normal in up to 20 percent of patients [32]. A subsequent report evaluated 18 patients with spontaneous intracranial hypotension and found that the sensitivities of brain and spine MRI were 83 and 94 percent, respectively [31].

Spinal MRI may be helpful for confirming the diagnosis and for identifying the exact location of the CSF leakage. Such studies may reveal [49]:

- Extra-arachnoid fluid collections
- Collapse of the dural sac and engorgement of the epidural venous plexus
- Meningeal diverticula
- Extradural extravasation of fluid

In a series of 10 women who had characteristic orthostatic headache without a previous history of dural tear, spinal MRI revealed dilated cervical epidural veins [12]. The authors concluded that this finding is an indicator of CSF hypovolemia and can be used to differentiate spontaneous low CSF pressure from the other causes of diffuse meningeal enhancement.

Subtraction MRI employs rapid postprocessing image analysis of standard T2 and T1 MRI sequences in order to delineate the dural sac of the spinal cord and distinguish between fluid and fat. In a report of 17 patients with spontaneous intracranial hypotension, subtraction MRI of the spinal cord identified the epidural CSF fluid collection in all patients, although the site of the CSF leak was not detected [64]. Additional studies are needed to determine the sensitivity and specificity of this method.

Radioisotope cisternography — Radioisotope cisternography is particularly useful for identifying CSF leaks. It is usually obtained as the next step if a CSF leak is suspected and MRI is normal or nondiagnostic.

Since a lumbar puncture is required as part of the procedure, opening CSF pressure is measured, and CSF is sent for analysis at the same time. Placement of numbered cotton pledgets in the nose for subsequent detection of radioactivity aids in detection and localization of CSF leakage through the paranasal sinuses.

Normal CSF flow involves cephalad migration from the site of injection to the cerebral convexities and the sylvian fissures [5], and, therefore, the most common cisternographic abnormality in CSF leaks is the absence or paucity of activity over the cerebral convexities [65-67]. It is advisable to look for early accumulation within the bladder and kidneys, or leakage of isotope outside of the normal confines of the subarachnoid space.

Early soft tissue uptake of radioisotope may also be suggestive of CSF leak, perhaps reflecting unusually rapid uptake of the radioisotope into the bloodstream through the epidural venous plexus [11].

In a small retrospective study of patients with spontaneous CSF leaks, the diagnosis of intracranial hypotension was supported in all 10 patients who had radionucleotide cisternography, which showed early bladder accumulation of the nucleotide and reduced activity over the cerebral hemispheres, consistent with rapid uptake of the tracer in the bloodstream [68]. In addition, the location of the leaks was identified in 7 of the 10 patients with this method.

Iatrogenic CSF leak from the lumbar puncture is a potential complication of radioisotope cisternography [69].

CT myelography — Computed tomographic (CT) myelography is the best test to identify the site of the leak. CT myelography is most commonly used in order to localize the level of the spinal leak when treatment beyond epidural blood patch (such as surgery or fibrin glue injection) is contemplated.

Both early and delayed cuts should be obtained at each spinal level, since CSF leaks may be rapid or slow. In cases where radiocisternography or spinal MRI has identified the approximate level of the leak, focused CT cuts can be used to locate the source more precisely.

MR myelography — Preliminary evidence suggests that magnetic resonance (MR) myelography using heavily T2-weighted sequences may be an alternative to CT myelography for detecting the level of CSF leaks.

- In a report of 19 patients with spontaneous intracranial hypotension, the accuracy of MR myelography for demonstrating and localizing CSF leaks was similar to CT myelography [70].
- In a study involving 17 patients with spontaneous intracranial hypotension, characteristic imaging features of spontaneous intracranial hypotension were seen on initial brain MRI in 13 patients (76 percent), and abnormal CSF collections were seen on MR myelography in the four patients (24 percent) whose initial head MRI was negative [71]. The authors suggested that the combination of brain MRI and MR myelography may improve the early diagnostic rate for spontaneous intracranial hypotension.

Lumbar puncture — A lumbar puncture (LP) can document low CSF pressure in suspected cases of spontaneous low CSF pressure headache, and may be diagnostically useful when MRI is not available or is not tolerated. However, LP is generally not necessary in cases where MRI is consistent with low CSF pressure headache. There is also concern that dural puncture from the procedure could potentially worsen the low CSF pressure and exacerbate the syndrome. In addition, the opening pressure is normal in some patients with proven spontaneous intracranial hypotension. (See 'Cerebrospinal fluid analysis' above.)

Although current diagnostic criteria define low CSF pressure based upon measurements taken in the sitting position [63], we recommend using the lateral decubitus position for greater accuracy. To ascertain correct placement of the spinal needle, CSF flow should be observed either spontaneously, with gentle aspiration, or with Valsalva maneuver [14]. (See "Lumbar puncture: Technique; indications; contraindications; and complications in adults".)

Differential diagnosis — Patients who have CSF shunts placed for various neurosurgical indications may develop a syndrome identical to that of spontaneous intracranial hypotension, probably secondary to overdrainage (overshunting) of CSF [8].

Orthostatic headache in the absence of CSF leak may also be a manifestation of the postural tachycardia syndrome or orthostatic intolerance [72]. (See "Postural tachycardia syndrome".)

One case report described spontaneous orthostatic headache and a "dry tap" at lumbar puncture that was attributed to an intradural myxopapillary ependymoma [73].

Misdiagnosis — The syndrome of spontaneous low CSF pressure headache has been under-recognized, in part because headache in general is a common ailment, and because patients with low CSF pressure headache

typically present with a normal neurologic examination. The diagnosis was often missed prior to the advancement of MRI imaging and the specific MRI findings associated with low CSF pressure headache. Even in the modern era of MRI availability, misdiagnosis is common [74].

Inappropriate and unnecessary clinical investigations may result if the diagnosis of spontaneous low CSF pressure headache is not considered. As an example, before diffuse meningeal enhancement on brain MRI was a recognized feature of spontaneous intracranial hypotension, patients with this finding were often subjected to extensive testing to rule out other causes such as meningeal carcinomatosis, meningitis, subarachnoid hemorrhage, neuroborreliosis, and neurosarcoidosis. (See 'Brain MRI' above.)

SUMMARY AND RECOMMENDATIONS

- The major features of the classic spontaneous low cerebrospinal fluid (CSF) pressure headache syndrome are orthostatic headache, low CSF pressure, and diffuse meningeal enhancement on brain MRI. (See 'Introduction and terminology' above and 'Clinical features' above.)
- The prevailing etiology is CSF leakage, which may occur in the context of rupture of an arachnoid membrane. An alternative hypothesis is that low CSF pressure is caused by epidural venous hypotension from the lowering of venous pressure within the inferior vena cava system. Most CSF leaks occur at the thoracic or cervicothoracic junction. An underlying connective tissue disorder may play a role in the development of CSF leaks. Other potential contributing factors are minor trauma, degenerative disc disease, and osseous spurs. (See 'Pathophysiology' above.)
- The estimated annual incidence of spontaneous low CSF pressure headache is 5 per 100,000, with a peak incidence around age 40 and a female to male ratio of 2:1. (See 'Epidemiology' above.)
- The headache caused by low CSF pressure may be sudden or gradual in onset, and severity is widely variable. The headache is typically relieved with recumbency and exacerbated with upright posture. Other headache patterns have also been reported with this syndrome. Commonly associated symptoms are neck pain or stiffness, nausea and vomiting, change in hearing, and photophobia. There is a varied and extensive list of additional associated symptoms. (See 'Clinical features' above and 'Headache' above and 'Associated symptoms and complications' above.)
- Traction on pain-sensitive intracranial and meningeal structures, particularly sensory nerves and bridging veins, is thought to cause headache and some of the associated symptoms. (See 'Pathophysiology' above.)
- Some rare but serious symptoms (eg, altered level of consciousness, parkinsonism) associated with the syndrome are probably caused by distortion or compression of brain and/or spinal cord structures. (See 'Associated symptoms and complications' above.)
- For patients with suspected low CSF pressure headache, we recommend brain MRI with gadolinium to assess for the typical features, which include diffuse meningeal enhancement (image 1), subdural hematomas or hygromas, sagging of the brain (image 2), engorgement of cerebral venous sinuses, and pituitary enlargement. Brain MRI remains normal in up to 20 percent of patients with low CSF pressure headache. (See 'Brain MRI' above.)
- The diagnosis of low CSF pressure headache should be considered in patients who present with positional orthostatic headache, with or without associated symptoms, perhaps in the setting of minor trauma, and in the absence of a history of dural puncture or other cause of CSF fistula. Confirmation of the diagnosis requires evidence of low CSF pressure by MRI or lumbar puncture and/or evidence of a CSF leak on CT myelography or radioisotope cisternography. Low CSF pressure headache following a lumbar puncture rarely creates a clinical dilemma. (See 'Diagnosis' above.)
- Diagnostic criteria for headache attributed to spontaneous low CSF pressure are discussed above. (See 'Diagnostic criteria' above.)
- Patients who have CSF shunts in place may develop a syndrome identical to that of spontaneous intracranial hypotension, probably secondary to overdrainage (overshunting) of CSF. (See 'Differential diagnosis' above.)
- Initial therapy for most patients with a confirmed diagnosis of spontaneous low CSF pressure headache consists of conservative measures and/or epidural blood path therapy. For patients who fail these treatments, additional options include continuous epidural saline infusion, epidural fibrin glue, or

surgical repair of the defect. Treatment of spontaneous low CSF pressure headache is discussed separately. (See "Treatment and prognosis of spontaneous low cerebrospinal fluid pressure headache".)

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