Spontaneous Intracranial Hypotension

Spontaneous intracranial hypotension requires a high index of suspicion because of potentially normal diagnostic test results and refractory symptoms.

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Spontaneous intracranial hypotension (SIH) is a secondary headache etiology attributed to a cerebrospinal fluid (CSF) leak or CSF-venous fistula involving the nerve root sheath. Symptoms may mimic a post-dural puncture headache, but presentation and prognosis for SIH can be quite variable. Commonly underdiagnosed, SIH has an estimated incidence of 5 per 100,000.[1] Although we believe there is a female predominance and an average age of onset at 40 to 45 years, SIH can be seen at any age.[2,3] Awareness of this diagnosis has been increasing, but because of atypical symptoms, often normal initial findings, and refractory symptoms, SIH diagnosis is often missed or delayed.[4]

Pathophysiology

There are 2 proposed mechanisms for SIH. Dating back 2 centuries, the Monro-Kellie doctrine applied the understanding of physics to the skull, stating that the following volumes must remain constant or intracranial pressure will change: brain, CSF, and intracranial blood.[5] Therefore, when CSF is lost, as seen in SIH, a resultant decrease in intracranial pressure causes intracranial venous structures to dilate. The second proposed mechanism is the hydrostatic indifference point, which highlights the change in lumbar compliance in the presence of SIH.[5] According to the hydrostatic indifference point mechanism, there is a zero-pressure point, usually located in the upper cervical spine, where CSF pressure changes from positive to negative relative to the atmospheric pressure.[6,7] Therefore, if CSF pressure is measured at this point, it will be the same in the upright and supine positions. In people with SIH, the zero-pressure point moves downward leading to negative intracranial pressure relative to the lower spine. This change in the hydrostatic indifference point leads to increased CSF expulsion in the upright position with possible venous dilation causing orthostatic headache. The pressure difference equalizes in the supine position with less CSF leak and headache. Owing to the hydrostatic indifference point, cranial CSF leaks, unlike spinal leaks, may be associated with headache, rhinorrhea, otorrhea, and even recurrent meningitis. Cranial CSF leaks, however, are not associated with orthostatic headache of SIH.[8]

Etiologies

Etiology of CSF leaks is variable. Although a CSF leak may be spontaneous, as the name suggests, it can also be traumatic, masquerading as a posttraumatic headache and leading to misdiagnosis.[9] Potential causes of CSF leak were classified in a study of 568 cases (Figure 1).[10] Type 1 are caused by a dural tear, often from a calcified ventral osteophyte leading to an extradural CSF collection (26.6%). Type 2 are from leaking nerve root diverticula with extradural fluid collection (42.3%). Type 3 are direct CSF-venous fistulae without extradural fluid collection (2.5% reported in the literature,[10] but may be as high as 25%[7]), and indeterminate cause (28.7%) with extradural fluid in over half.[10] The most common region for a CSF leak is the lower cervical to upper thoracic spine. Fistulas, however, tend to be found in the lower thoracic spine, usually originating from nerve root sleeve diverticula.[11,12] Perineural cysts are a common finding and do not necessarily indicate a CSF leak.[13]

Risk Factors

The term intracranial hypotension may be a misnomer. In a review of 106 cases of SIH, only 34% with confirmed spinal CSF leaks were found to have a CSF pressure of ≤6 cm H_2O.[4] A normal CSF pressure appears to be associated with increased abdominal circumference, longer duration of disease, and normal brain MRI.[4] Cases of SIH have even been described in the setting of CSF pressure >20 cm H_2O.[4] Given this variability in pressure, it has been argued that low CSF volume may instead be one of the key factors in SIH.[8]

Risk factors include a history of connective tissue disease and bariatric surgery.[14] It is felt that connective tissue diseases

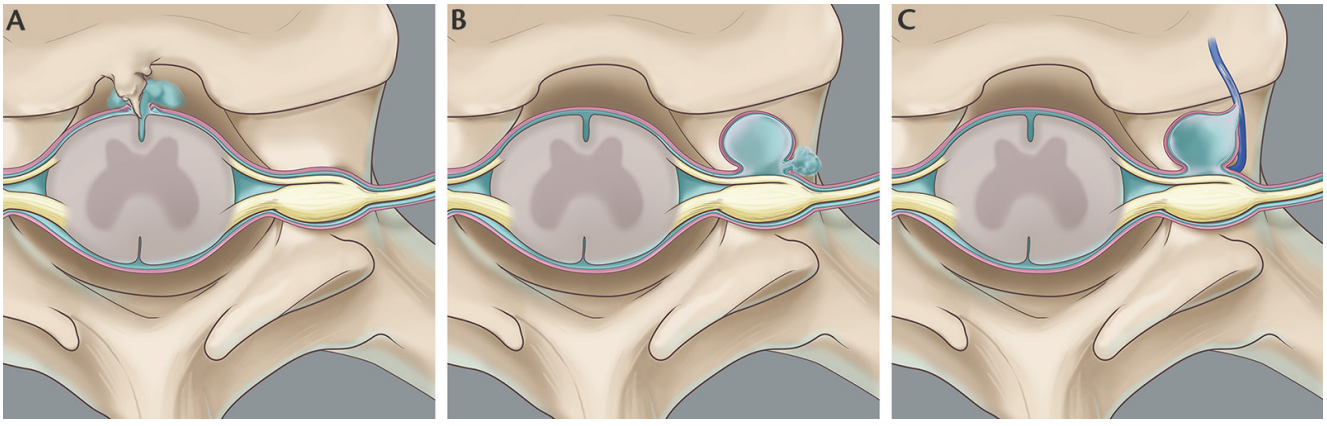

Figure 1. The 3 etiologies of spinal cerebrospinal fluid (CSF) leak are calcified anterior osteophyte causing anterior dural tear (Type 1, A), leaking nerve root diverticulum (Type 2, B) and CSF-venous fistula (Type 3, C). With permission from Barrow Neurological Institute, Phoenix, AZ.

like Marfan syndrome and Ehlers-Danlos syndrome are more common in those with CSF leak; however, this supposition is not unanimously agreed upon in the literature.[15,16] Iatrogenic risk factors include lumbar puncture, epidural or spinal anesthesia, spine surgery, and chiropractic manipulation.[17] It has been postulated that in some without an identified CSF leak, abnormal elasticity and compliance of the dural sac may be a risk factor or even an isolated cause of SIH.[18]

Clinical Presentation

The classic presentation of SIH is an abrupt onset daily persistent orthostatic headache that improves in the supine position. Patients oftentimes recall the exact date, time, and place of onset. The location of pain is often bifrontal/occipital or upper cervical, but can be holocephalic. Orthostatic features may decrease over time, but in a study of 90 cases, 23% did not have an orthostatic headache.[19] Other headache presentations include thunderclap, exertional, or Valsalva induced; chronic nonorthostatic; paradoxical orthostatic (improves when upright); and neck or interscapular pain.[17] Other associated symptoms include tinnitus, muffled hearing, photophobia, phonophobia, nausea, vomiting, and dizziness.[8] Reported atypical presentations include cranial nerve palsies; coma; movement disorders; and neurocognitive changes including frontotemporal dementia, myelopathy, peripheral neuropathy, hyperprolactinemia, seizures, superficial siderosis, and stroke/venous sinus thrombosis.[17,20] Atypical cases are more likely to occur in older indivduals with a more chronic disease course.[20]

Diagnosis and Differential Diagnosis

Two sets of diagnostic criteria exist (Table),[21,22] and the differential diagnoses to consider with orthostatic headache include postural orthostatic tachycardia syndrome (POTS), diagnosed by a 30-bpm heart rate increase on tilt table testing within 10 minutes.[23] Migraine, POTS, and Ehlers-Danlos syndrome can coexist and complicate the clinical picture. Hypermobility should be assessed because of increased risk with connective tissue disorders. Screening for hypermobility is with the Beighton score, and Ehlers-Danlos syndrome is diagnosed based on a recent set of diagnostic criteria.[24]

Other differential diagnoses to consider in the setting of orthostatic headache include cervicogenic headache and craniocervical instability.[8] Migraine is often worsened with activity and may improve when supine simply from resting in a dark quiet room rather than position. Skull-based CSF leaks do not cause orthostatic headache but may cause recurrent meningitis or be associated with idiopathic intracranial hypertension.[8] As described above, the skull is above the zero-pressure point, so orthostatic symptoms are not seen with a cranial CSF leak.[8]

TABLE. DIAGNOSING HEADACHE ASSOCIATED WITH SPONTANEOUS INTRACRANIAL HYPOTENSION

International Classification of Headache Disorders 3rd ed.	
Developed in temporal relation to a low cerebrospinal fluid (CSF) pressure or leak, or led to discovery of low CSF pressure or leak	
OR	Either or both of the following CSF pressure <60 mm CSF Evidence of CSF leak on neuroimaging
AND	Not better accounted for by another ICHD-3 diagnosis
Schievink criteria	
Demonstration of extrathecal CSF on imaging	
OR	Cranial MRI consistent with spontaneous intracranial hypotension show by at least 1 of the following
	Opening pressure <60 mm CSF
	Spinal meningeal diverticulum
	Improvement after epidural blood patch
OR	Orthostatic headache with 2 of the following
	Low opening pressure (<60 mm CSF)
	Spinal meningeal diverticulum
	Improvement after epidural blood patch

Diagnostic Imaging

Classic brain MRI findings (Figure 2) include subdural hematomas, diffuse smooth pachymeningeal enhancement, brain sag (ie, tonsillar ectopia, shortened pontomamillary distance, and elongated anteroposterior midbrain diameter), venous distention, and pituitary engorgement. Although these findings were seen in approximately 90% of 99 SIH cases,[25] brain MRI can be normal in SIH, usually in those with a chronic leak.

The most sensitive imaging sign is diffuse and smooth dural enhancement. Misinterpretation of this imaging finding can lead to an extensive workup and empiric treatment for meningitis. Atraumatic bilateral subdural hematomas should raise the concern for SIH; imaging and history should be reviewed closely before performing evacuation. Low-lying cerebellar tonsils, especially considered in isolation, can lead to misdiagnosis of a Chiari malformation. Importantly, a Chiari malformation generally does not cause an abrupt chronic daily headache or new daily persistent headache, but rather causes a secondary nonprogressive cough headache. Note that SIH can also cause cough headache, but that is usually progressive in nature and can be associated with an underlying daily headache.[26] Low-lying cerebellar tonsils from SIH should maintain the normal tonsillar rounded shape.[27]

Spinal imaging is positive in more than half of cases with

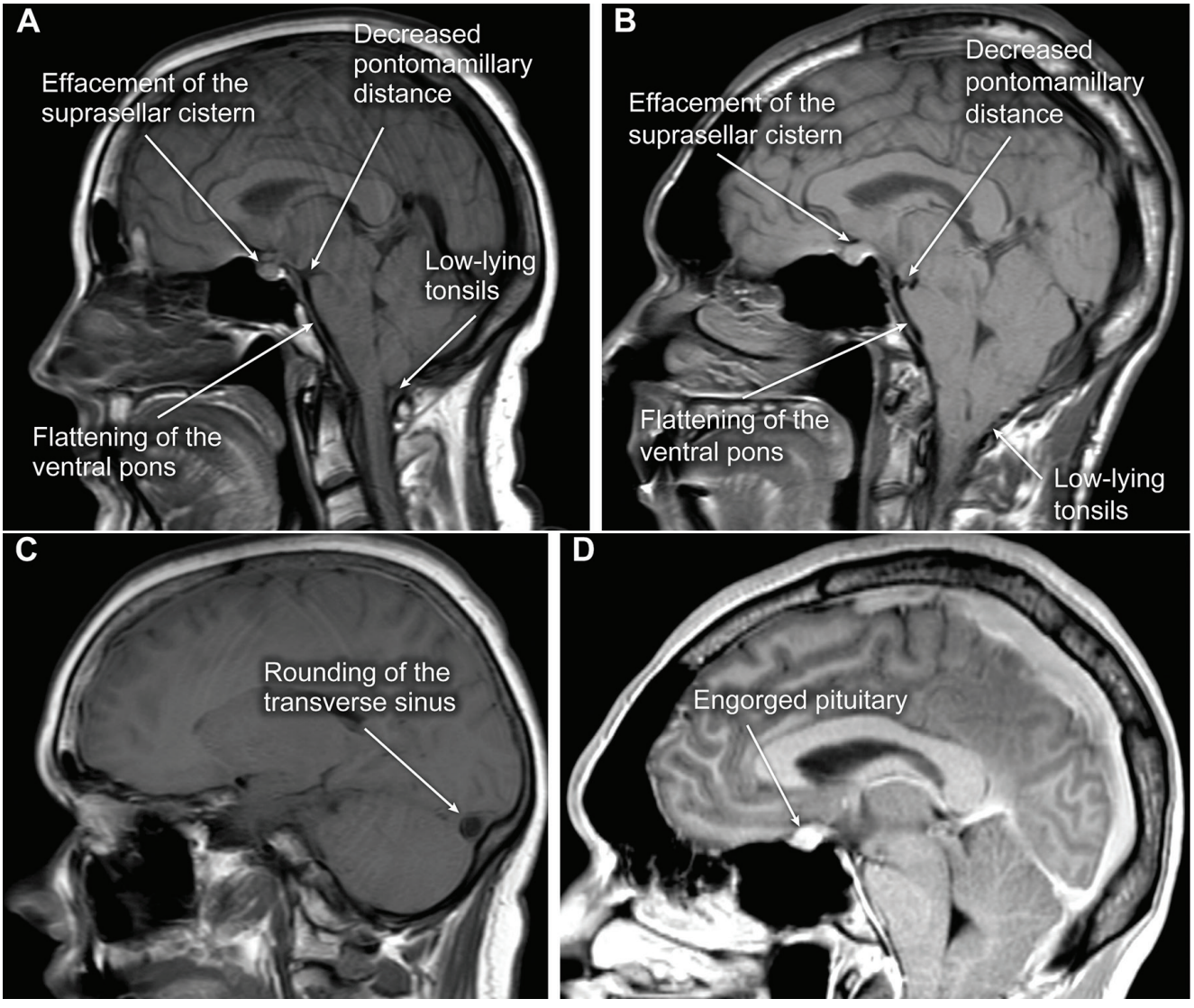

Figure 2. Example of classic MRI brain findings in spontaneous intracranial hypotension (SIH). (A) Sagittal T1-weighted and (B) T2-weighted images demonstrating low-lying tonsils, decreased pontomedullary distance, flattening of the ventral pons, and effacement of the suprasellar cistern; (C) rounding of the transverse sinus; and (D) engorgement of the pituitary. These patients did not have subdural hematomas, which is another common finding, and the classic finding of pachymeningeal enhancement is not well appreciated on these sagittal images. Used with permission from Barrow Neurological Institute, Phoenix, AZ.

findings such as fluid collections, CSF extravasation, spinal pachymeningeal enhancement, dilated nerve root sleeves, and epidural venous plexus engorgement.[28] Spinal meningeal diverticula are common and in isolation do not signify a leak.[29] False localizing signs also exist, including the appearance of a cervicothoracic CSF leak or retrospinal C1-C2 fluid collection on a myelogram or MRI due to dilated epidural veins.[30] Modality preference currently varies between institutions and neuroradiologists but can include the following.[13]

Myelography is a noninvasive study; MR myelogram without gadolinium and with heavily T2-weighted imaging, is recommended. Thin slices improve spatial resolution. Additional coronal cuts are added, and fat-suppressed sequences are recommended. The safety and use of MR myelography with intrathecal gadolinium is controversial. Some centers, however, find this modality to be particularly beneficial for slower CSF leaks even if the CT myelogram is negative.[7] The benefits of CT myelogram include that the entire spine is imaged and sharp osteophytes may be identified. The time from intrathecal injection to CT scanner may be delayed, however, decreasing the yield for high-flow leaks. A dynamic CT myelogram with the patient in prone Trendelenburg positioning can enhance detection of a fast leak.

Digital subtraction myelography can image only a small spine segment at a time, but coverage varies with equipment (our institution can cover 7 vertebrae). Having a suspected site to target is beneficial. After intrathecal contrast injection, conventional myelogram images are obtained dynamically with a high frame rate. General anesthesia and medically induced paralysis are usually used during imaging to prevent motion that would degrade the subtracted images. If a ventral leak is suspected, a prone position is used, whereas with other suspected locations, the lateral decubitus position is used with the side of the suspected leak or CSF-venous fistula facing down.

Nuclear cisternography studies are no longer recommended.

Treatment

The mainstay of treatment for SIH is an epidural blood patch. An untargeted blood patch can be effective but may need to be repeated.[31] The preferred approach is a targeted blood patch where a leak site has been identified.[32] At our institution, we use a large-volume (goal >30 mL) and 2-level untargeted patch as part of our algorithm (Figure 3). The 2 levels most commonly used are T11 through T12 and T12 through L1.[33] Risks with a higher volume include arachnoiditis, tethered cord, or chemical meningitis if blood is injected intrathecally.[33] Targeted patches are often lower volume (<5 mL) and can be unilateral or bilateral. Fibrin glue is sometimes used in addition to blood at the targeted site.[34]

Because of compensatory changes with chronic CSF leak, the benefits of an epidural blood patch for orthostatic headache may take days or even weeks to be seen.[8] Success from the first patch is seen in 30% to 70% of cases.[8] Surgical treatment is used when a CSF leak or fistula is identified, especially if there is no response to epidural blood patch. Surgery can include ligation of diverticula; placing an absorbable gelatin compressed sponge, fat, or muscle within the site of the leak; aneurysm clipping of the fistula; or electrocautery to ligate the fistula.[35]

Treatment has been found to be complicated by rebound intracranial hypertension in more than one-quarter of 46 cases studied, often within 24 hours.[36] The rebound intracranial hypertension headache is more likely to be frontal or periorbital and worsen with recumbency.[36]

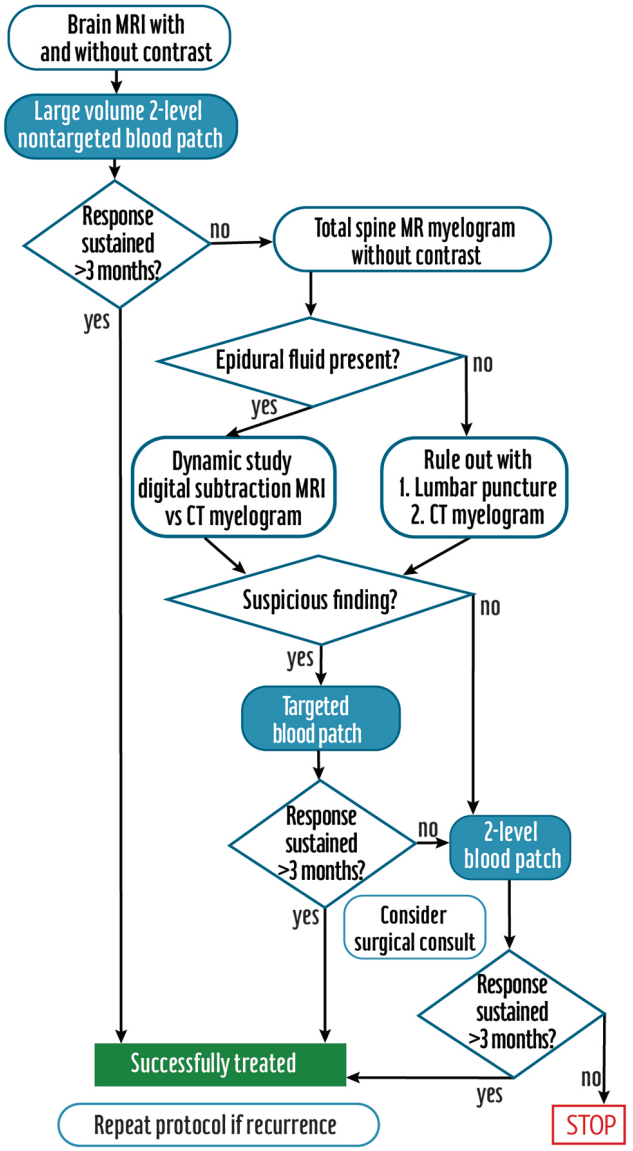

Figure 3. Spontaneous intracranial hypotension treatment algorithm.

Papilledema can be present or absent.[8] One study suggests venous sinus stenosis may be a predictor.[36] Rebound high intracranial hypertension can be transient or last several months. This is treated with acetazolamide, topiramate, or a similar diuretic with lumbar puncture if necessary to evaluate and lower CSF pressure.[36]

Summary

An underdiagnosed cause of abrupt-onset orthostatic refractory headache, SIH does not respond to medical treatment and over time becomes a chronic daily headache with significant disability. The 3 types of spinal CSF leak that cause SIH are dural tear, meningeal diverticula, and CSF-venous fistula, but approximately one-quarter have indeterminate causes.

The classic presentation is a new daily persistent headache that improves when supine and worsens when upright, although many presentations exist. A high level of suspicion is needed to avoid misdiagnosis and to initiate appropriate treatment. Workup is not standardized, however, and results of initial investigations can be normal. Brain MRI and myelography aid diagnosis.

Although there are no universal management guidelines, initial treatment is an untargeted or targeted large-volume epidural blood patch, sometimes with fibrin glue. This treatment may be complicated by rebound intracranial hypertension. Refractory cases may require surgery. ■

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