Intracranial hypotension is not an uncommon diagnosis after lumbar puncture or neurosurgery. However, spontaneous intracranial hypotension (SIH) is a poorly understood entity that can present with a wide variety of symptoms/signs ranging from headache to coma. SIH may result from an occult spinal cerebrospinal fluid (CSF) leak. Alternatively, because a CSF leak is not always found, some posit that SIH is caused by venous hypotension that results in increased CSF absorption. The true incidence of SIH is unknown and the diagnosis is frequently missed given the wide range of presenting symptoms and imaging findings that are mistaken for other diagnoses (ie, subdural hematomas, Chiari malformation). Here, based on a comprehensive literature review, we describe the epidemiology, presentation, diagnostic workup and treatment of SIH.

KEY WORDS: Coma, Epidural blood patch, Spontaneous intracranial hypotension


In 1825, Magendie described vertigo and unsteadiness in a patient after removal of cerebrospinal fluid (CSF), and the turn of the 20th century witnessed reports of patients with headaches from intracranial hypotension after a lumbar puncture (LP). Schaltenbrand introduced “aliqoorhea” in 1938 to describe a patient with spontaneous intracranial hypotension. Despite multiple reports since, intracranial hypotension syndrome is a poorly defined entity that now commonly describes patients with symmetrically low CSF pressure with a spectrum of symptoms and imaging findings. Low CSF pressure is hypothesized to result in decreased buoyancy and resultant brain “sag,” leading to traction on leptomeninges and neural structures. This traction is believed to be the cause of headaches and other neurological symptoms. Alternatively, others posit that headaches from intracranial hypotension result from dural venous engorgement.

Although intracranial hypotension is commonly reported after LPs, the true incidence of spontaneous intracranial hypotension (SIH) is unknown. A community-based study estimated a prevalence of 1 in 50,000 adults. Headache is the most common symptom, although severe symptoms have also been reported including nausea/vomiting, cranial neuropathies, radiculopathies, parkinsonism, quadriplegia, and coma. However, because of the nonspecific nature of symptoms, this diagnosis is often missed. Moreover, these patients are often treated surgically for their subdural fluid collections or tonsillar herniation instead of the underlying cause of their intracranial hypotension. We present a patient who was successfully treated for SIH, and review the literature in the context of approaches to the treatment of this disorder.

METHODS

The medical records and imaging of a patient successfully treated for SIH was reviewed. For the literature review, the English literature from 1900 to 2009 was searched using PubMed and the Cochrane Database with the following search terms: intracranial hypotension, intracranial hypotension imaging, intracranial hypotension and MRI, coma and intracranial hypotension, cerebellar pons, Chiari, and intracranial hypotension. In addition, any relevant references from the evaluated literature were included in the review.
RESULTS

Case Illustration

A 57-year-old female presented with nausea, vomiting, and headache worsening over several days. A similar episode several months previously required hospitalization. During that hospitalization she was found to have a chronic subdural hematoma on the right side that was treated nonoperatively. She now denied any recent trauma or falls. She was neurologically normal on physical examination, and her cranial magnetic resonance image (MRI) from the outside hospital revealed resolution of her right-sided fluid collection and a new left chronic subdural hematoma (Figure 1). The patient was admitted to the intensive care unit for observation. She subsequently became unresponsive. She was taken emergently to the operating room for a left craniectomy and evacuation of subdural hematoma. The patient did not improve postoperatively. Review of the patient’s head MRI revealed pachymeningeal enhancement and brain sag (Figure 2). The patient was treated emergently with an epidural blood patch, and she improved back to her normal neurological baseline within hours. She was still asymptomatic at her 3-month follow-up.

DISCUSSION

Intracranial hypotension secondary to trauma, LP, or surgery has been widely recognized since the early 1900s. Reports of headache, vertigo, nausea, convulsions, stupor, and death from “cerebral hypotension” were documented by Leriche and Wertheimer. SIH, however, has been poorly recognized. In the first documented case of this disorder, Puech wrote about a patient in 1942 who presented with coma from presumed SIH who transiently improved with injection of air and serum into the ventricle, and eventually died.

Epidemiology and Risk Factors

The true incidence of SIH is unknown. Females are more likely than males to receive this diagnosis (2:1), and peak incidence is at approximately 40 years of age. SIH may result from an occult spinal CSF leak, and is therefore often misdiagnosed if not suspected. Dural “weakness” or abnormalities increase the risk for a spontaneous CSF leak, thereby increasing the risk in patients with connective tissue disorders. Marfan syndrome, Ehlers-Danlos syndrome, and autosomal dominant polycystic kidney disease increase the risk for spontaneous CSF leaks and intracranial hypotension. Other disorders such as a Tarlov cyst, disc herniation/spinal bony abnormalities, or just absence of dural covering a spinal root have also been reported.

Presentation

The International Classification of Headache Disorders has developed diagnostic criteria for SIH (Table). The headaches associated with SIH are often orthostatic in nature, reaching maximal intensity in several minutes to hours. If the CSF leak remains untreated, the headaches may take the form of chronic, daily headaches. Neck stiffness or a description of “pulling sensation from the head down to the neck” may also be associated with SIH. Patients rarely may have sudden onset of headache similar to the thunderclap headache associated with subarachnoid hemorrhage.

Nevertheless, these diagnostic criteria may exclude or not identify patients with early symptoms (without dramatic imaging findings) or late symptoms (eg, mental status changes or coma). Other symptoms can be associated with SIH. Nausea, vomiting, photophobia, or phonophobia may be present and an indication of meningeal irritation. Hearing changes such as tinnitus or “echoing” may be described by these patients. These symptoms can be explained by downward displacement of the brain and stretching of nerves. This mechanism also explains the potential for cranial neuropathies and visual symptoms such as blurring or visual field defects. Less common manifestations include galactorrhea, radiculopathy, parkinsonism, and quadriplegia.

Coma and encephalopathy have also been reported in patients with SIH. Given the general perception that intracranial hypotension is a benign condition, this literature often describes
patients who were initially treated for something else, before a diagnosis of SIH was reached.\(^\text{18,19,21,23,25}\) For example, one patient underwent a nondiagnostic meningeal biopsy before being treated with an epidural blood patch.\(^\text{21}\) The patient became alert within 15 minutes of treatment.

**Pathogenesis**

SIH is traditionally attributed to occult CSF leak. By the Monroe-Kellie hypothesis, decreased CSF volume/pressure results in brain sag and venous engorgement. Treatment with an epidural blood patch is thought to “plug” the leak(s) and resolve symptoms. This theory is especially relevant for patients in whom a site of CSF leak can be determined. Schievink et al emphasize that relatively low CSF volume can be present and symptomatic without low CSF pressure on LP.\(^\text{49}\)

Conversely, some investigators have proposed that the pathogenesis of SIH involves negative pressure within the inferior vena cava (IVC), resulting in more CSF absorption.\(^\text{50}\) Because venous blood flow is controlled only by a pressure gradient, a negative pressure gradient can be produced in the IVC from the heart actively aspirating blood out of the IVC combined with lower-limb musculature driving blood up toward the heart. The negative pressure can result in overdrainage of venous blood from the epidural spinal network and then CSF, thereby changing the CSF-blood gradient. This change causes aspiration of CSF into the epidural space and veins, sometimes even causing a CSF leak.

**TABLE. International Classification of Headache Disorders SIH Criteria\(^\text{ab}\)**

<table>
<thead>
<tr>
<th>A. At Least One of the Following</th>
<th>B. At Least One of the Following</th>
<th>C. Must Be Fulfilled</th>
<th>D. Must Be Fulfilled</th>
</tr>
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<tbody>
<tr>
<td>Neck stiffness</td>
<td>Evidence of low CSF pressure on MRI (eg, pachymeningeal enhancement)</td>
<td>No history of dural puncture or other cause of CSF fistula</td>
<td>Headache resolves within 72 h after epidural blood patch</td>
</tr>
<tr>
<td>Tinnitus</td>
<td>Evidence of CSF leakage on conventional myelography, CT myelography, or cisternography</td>
<td></td>
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</tr>
<tr>
<td>Hypacusia</td>
<td>CSF opening pressure &lt;60 mm H(_2)O in sitting position</td>
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<tr>
<td>Photophobia</td>
<td></td>
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<td></td>
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<tr>
<td>Nausea</td>
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\(^{ab}\)SIH, spontaneous intracranial hypotension.

Patient must have diffuse and/or dull headache that worsens within 15 minutes after sitting or standing, and must fulfill criteria C and D.
from the spinal roots into the epidural space. Treatment with an epidural blood patch is thought to increase the pressure and restore a normal CSF-blood gradient. This concept is supported by the fact that many patients have been described to improve with an epidural blood patch even if CSF leak is not sought or found.

**Diagnosis**

Although SIH is often diagnosed based on clinical presentation and imaging findings, many of these patients undergo an LP. The opening pressure is often relatively low or unmeasurable, and the CSF may demonstrate increased white blood cells and protein. However, LP opening pressures can be normal, and SIH is primarily diagnosed by imaging.

**Cranial Imaging**

Abnormalities on cranial MRI are the most commonly reported findings in patients with SIH. Relatively severe intracranial hypotension is characterized by 5 MRI findings described by Schievink: (1) Subdural fluid collections or hygromas, (2) pachymeningeal Enhancement, (3) Engorgement of venous structures, (4) Pituitary hyperemia, and (5) Sagging of the brain. Subdural fluid collections may be seen in 17% to 60% of patients with SIH (Figure 3). This is a late finding of untreated intracranial hypotension. Subdural fluid collections were not seen without pachymeningeal enhancement in a retrospective study of 11 patients with intracranial hypotension.

Risk factors for developing subdural hematoma with SIH include male sex and older age (≥35 years). In a retrospective study, 50% of SIH patients were found to have subdural fluid collections; 60% of these were subdural hygromas and 40% were acute or chronic subdural hematomas. These fluid collections are found over the cerebral convexities and sometimes in the posterior fossa. The hygromas have been hypothesized to develop because of enlargement of the subarachnoid/subdural space from CSF hypovolemia. When these effusions are moderate to large, there can be secondary hemorrhage, possibly because of stretching and rupture of bridging veins. Evacuation of the subdural fluid collections has been reported to result in neurological worsening or no improvement in patients with intracranial hypotension similar to our patient. Successful treatment of the underlying hypotension results in resolution of the subdural fluid collections.

Enhancement of the pachymeninges is the most well recognized imaging finding associated with SIH (Figure 4). Up to 83% of patients demonstrate diffuse enhancement of the meninges on gadolinium-enhanced MRI. Enhancement of spinal dura has also been reported. These changes are a result of fibrocollagenous proliferation in the leptomeninges without inflammation. SIH has been reported without pachymeningeal enhancement; therefore, this diagnosis should not be excluded based solely on the lack of MRI enhancement.

![FIGURE 3. Bilateral subdural fluid collections in patients with intracranial hypotension. A, T2 axial MRI shows bilateral subdural effusions anteriorly with high T2 signal (black arrows) and minimal dependent acute subdural hemorrhage posteriorly with low T2 signal (curved white arrows). B, fluid-attenuated inversion recovery (FLAIR) axial MRI in a different patient with right larger than left effusions.](image-url)
Engorgement of veins has also been described in SIH. Cranial or spinal engorged veins are usually described on MRI in these cases (Figure 5).\textsuperscript{79,80} Some patients underwent cerebral angiography for concern of SAH as a cause of the headache, and prominent venous vasculature was noted.\textsuperscript{81,82} Venous engorgement is often a subtle finding and has been traditionally explained by a CSF leak with compensatory venous engorgement by the Monroe-Kellie hypothesis.

Proponents of the alternative hypothesis of an abnormal CSF-blood gradient with epidural hypotension explain venous engorgement by enlargement of veins when the patient lies down. Because patients are supine for an MRI, CSF moves toward the ventricles and away from the spinal thecal sac, leading to epidural venous enlargement. This hypothesis is supported by a study demonstrating smaller superior ophthalmic veins in patients with SIH compared with controls.\textsuperscript{83}

However, most studies describe venous engorgement with intracranial hypotension. This finding is also used to explain pituitary hyperemia. The pituitary gland can be larger in patients with intracranial hypotension and become smaller with successful treatment of the underlying disorder.\textsuperscript{84}

Intracranial hypotension is also associated with brain sag (Figure 6). A retrospective study found 48% of patients with intracranial hypotension had descent of the brain.\textsuperscript{85} Patients can have slit ventricles, distortion of the brainstem, and cerebellar tonsillar herniation.\textsuperscript{85,86} These abnormalities can even progress to cause syringomyelia.\textsuperscript{87} These consequences of SIH can be confused with a Chiari malformation,\textsuperscript{88} and are incorrectly treated with posterior fossa decompressions.

The brain sag can result in transtentorial descent of the diencephalon, potentially leading to changes in consciousness,\textsuperscript{85,86} and abnormalities in basal ganglia signal on MRI that can be confused with internal cerebral vein thrombosis.\textsuperscript{85,86}

Quantification of brain sag has been described by measurement of distance of the iter, or opening of the aqueduct of Sylvius on a midsagittal MRI, from a straight line drawn from the tuberculum sellae to the confluence of the straight sinus, internal cerebral vein, and inferior sagittal sinus.\textsuperscript{88} Pannullo et al\textsuperscript{88} found that 5 of the 7 patients with intracranial hypotension had downward displacement of greater than 2 standard deviations from normal (−0.2 mm).

Other intracranial measurements have also been studied in patients with SIH. In a prospective study, Chen et al\textsuperscript{89} found that patients with orthostatic headaches and low LP opening pressures had significantly larger superior ophthalmic veins by color Doppler compared with healthy controls ($P < .001$). In addition, Shankar et al assessed the changes of the angle between the vein of Galen and internal cerebral vein on sagittal MRI, called “venous hinge,” in 17 patients with intracranial hypotension compared with 50 controls.\textsuperscript{92} They found that patients with intracranial hypotension had significantly smaller angles compared with controls, and that with successful treatment, this venous hinge normalized. Setting the upper limit of a normal venous hinge at 79° resulted in a sensitivity of 88% and a specificity of 92% for predicting intracranial hypotension.

Other measurements on MRI that can be useful in SIH include decreased width of the rim of CSF around the optic nerve on coronal short tau inversion recovery images,\textsuperscript{93} decreased mammillopontine distance (Figure 7), and altered alignment of the optic chiasm (Figure 8). These measurements may allow earlier identification of subtle cases of brain sag, although further studies to establish these metrics for SIH are warranted.

**Spinal Imaging**

Once a diagnosis of SIH is considered, CSF leak can be sought with spinal imaging. MRI is not usually helpful in localizing the exact site of an occult CSF leak, because MRI of the spine can be

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positive even if the CSF leak is not active, unlike CT myelography or radionuclide cisternography. However, MRI myelography has been reported to be useful in detecting the site of CSF leak with good outcomes when treated with epidural blood patch or surgery.

Most reports advocate CT myelography or radionuclide cisternography to find a spinal leak. Mokri et al found that the site of CSF leak was determined in 67% of patients evaluated with CT myelography compared with 50% of patients evaluated with MRI and 55% of patients evaluated with radionuclide cisternography. In no cases did radionuclide cisternography reveal the site of the CSF leak when the CT myelogram did not. Similar
to MRI, radionuclide cisternography is limited in demonstrating the exact site of the leak. In SIH, radionuclide cisternography demonstrates early bladder radionuclide activity, no activity over the cerebral convexities, and rapid disappearance from the spine; direct leakage from the CSF leak will rarely be seen.\textsuperscript{55,72,101} In general, most CSF leaks in these patients are found at the cervicothoracic junction.\textsuperscript{102} Small fluid collection between the C1 and C2 lamina have been described as one of the imaging signs of SIH (Figure 9), and may be mistaken for the site of the leak.\textsuperscript{103} Some hypothesize that these fluid collections represent
transudate from dilated epidural veins, or CSF that has leaked into the epidural space from another site and escaped into the soft tissues at C1-2.

Treatment

The goals of treatment of SIH include restoration of CSF pressure and relief of symptoms and/or neurological deficits. Treatment options include conservative medical therapy, epidural or intrathecal injections, and/or surgery. Medical therapy is most appropriate for patients with only headaches or mild symptoms, and involves bed rest, oral hydration, caffeine, and/or steroids. Epidural infusion of saline has also been used for temporary relief. These measures are low risk with limited efficacy. Epidural infusions aim to increase CSF volume. Caffeine produces its effects primarily by vasoconstriction, possibly lending support to the theory of venous hypotension as a cause of SIH.

The most commonly reported treatment for intracranial hypotension is an epidural blood patch—injecting autologous blood into the spinal epidural space. The lumbar cisterns are usually accessed for the injection, although thoracic injections have been reported in patients with refractory symptoms. Ten to 35 mL are usually injected for the first treatment, and larger volumes of up to 100 mL are injected if this is unsuccessful. Patients are usually placed in Trendelenburg for 30 to 60 minutes after injection. In patients with SIH symptomatic with headaches, with or without identifying a CSF leak, approximately 30% to 70% improve after the first epidural blood patch, and 30% to 50% of the remainder improve after repeat blood patches. Patients typically have almost immediate relief with the epidural blood patch, even when presenting with severe symptoms, such as the patient in our case presentation. Similar results have been reported with injection of fibrin glue at the site of the CSF leak.

Some advocate the use of the epidural blood patch without identifying a CSF leak. In a recent study, Franzini et al described 28 patients treated with an epidural blood patch for SIH. The patients received an epidural injection of a mix of fibrin glue, homologous blood, and contrast medium at the level of L1-2 while lying prone. At 1 year, 18 of 22 patients had no clinical symptoms. Ten of the 11 patients with 3-year follow-up were symptom free. Another study found that, despite clinical improvement in the majority of patients treated with an epidural blood patch (13/15), 4 of the 15 had persistent imaging abnormalities on follow-up. Possible side effects and complications include back pain, radiculopathy, meningitis, and rebound intracranial hypertension.

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CONCLUSION

Spontaneous intracranial hypotension is a treatable cause of headache and more severe neurological symptoms such as encephalopathy. Timely diagnosis requires a high index of suspicion, and is important to avoid unnecessary procedures resulting in increasing morbidity for patients. Further studies, including animal physiology studies, will be necessary to elucidate the pathophysiology of this disease process. Moreover, randomized prospective trials are necessary to further evaluate the efficacy of different treatment modalities of intracranial hypotension.

Disclosure

The authors have no personal financial or institutional interest in any of the drugs, materials, or devices described in this article.
REFERENCES
Intracranial hypotension is an important complication after lumbar puncture or neurosurgical procedures that include durotomy and may come to clinical attention through a broad variety of symptoms that reflect the loss of intracranial cerebrospinal fluid (CSF) including orthostatic headaches, nausea, vertigo, radiculopathy, cranial nerve affection, visual impairment, or even tetraplegia and coma with a possibly fatal outcome. Rahman et al, in this issue of Neurosurgery, present an excellent review of the current state of knowledge on spontaneous intracranial hypotension (SIH), its possible pathogenesis, and approaches for successful treatment. In SIH, a specific site of leakage of CSF is often not identified even though symptoms and imaging findings strongly support the diagnosis of intracranial hypotension. The hypothesis that intravenous hypotension may be the pathogenetic mechanism for development of SIH is of particular importance: according to this theory, the loss of intravasal pressure in the venous system leads to an increased suction pressure on the CSF through a gradient of CSF pressure compared with venous pressure. The result of this pressure gradient may be the disruption of the dura mater at not only one, but more likely several sites with subsequent leakage of CSF. This theory may explain the success of treatment via unselective epidural blood patches producing a gelatinous tamponade within the epidural space, thus compressing the leakage sites. Treatment of another consequence of SIH, subdural hematoma (SDHs), is another matter of debate? Do we observe chronicification or resolution of SDHs? Do they need additional treatment? This review draws the reader’s attention to this important disease entity that needs further clarification and validation of treatment approaches.

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