Spontaneous Intracranial Hypotension: The Syndrome and Its Complications

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Opinion statement

Spontaneous intracranial hypotension (SIH) is a syndrome that was largely unknown until the advent of MRI. The incidence of SIH is estimated at 5 per 100,000, which is half the incidence of subarachnoid hemorrhage. The major feature is a postural headache of acute or subacute onset. This headache is absent or minimal when the patient is lying down and rapidly worsens to great intensity when the patient sits or stands. Other features may include nausea, vomiting, vertigo, tinnitus, and marked exacerbation by Valsalva maneuver. SIH is due to a leak of cerebrospinal fluid from a tear in the dural membrane, which occurs most often at the exit zones where the cervical spinal roots leave the subarachnoid space. Other leak sites may be the vestibular system, the cribriform plate, or the pituitary fossa. If the leak continues, the brain loses buoyancy within the cranial space and sags toward the foramen magnum. This, in turn, may produce subdural hygroma or hematoma, brainstem compression, focal cranial nerve palsies, or cerebellar tonsillar herniation. The initial therapy is generally strict bed rest. If this fails, an epidural blood patch is usually successful in sealing the leak and restoring brain buoyancy. A significant minority of patients require a repeat epidural blood patch. If the blood patch fails, a surgical approach may be needed. Repair of the leak and restoration of brain buoyancy will stop the postural headache and, in most cases, will reverse the complications.

Introduction

Spontaneous intracranial hypotension (SIH) and the associated headache syndrome (SIHH) have received increasing attention in the past 20 years, and the syndrome has emerged as an important area of secondary headache. The entity was first described by Schaltenbrand in 1938 (see Schievink [1••]), but it received little attention, as it was difficult to diagnose and prove. Occasional papers appeared on the subject over the next 40 years, but it was not until the advent of MRI that diagnosis became easier and more certain. Since 1990, interest in SIH, the headache syndrome, and its complications has been growing [1••,2, Class II].

CASE REPORT

The following case illustrates the syndrome: A 39-year-old Asian male laboratory technician noted the onset of headache 10 weeks before being seen in our clinic. The headache had been continuous since onset. The day of onset, the patient awoke with a sensation of giddiness and nausea as well as a feeling like motion sickness but no headache. He attempted to drive, but felt unstable; he returned home and went to bed. That afternoon, he noted onset of headache associated with nausea and vomiting as well as neck pain and stiffness. The headache worsened throughout the remainder of the day, and the next day he went to a local emergency room and was admitted to the hospital. He was seen by a neurologist and treated as a severe migraine. After 1 month, he was again hospitalized and a workup was carried out, including CT and MRI scans of the head, as well as a cerebral angiogram, all of which were reported as within normal limits. A lumbar puncture showed increased white blood cells and red blood cells (values unknown).

While in the hospital for 5 days, he was treated with bed rest, intravenous morphine, promethazine, and cyclobenzaprine. The headache was 8/10 on admission

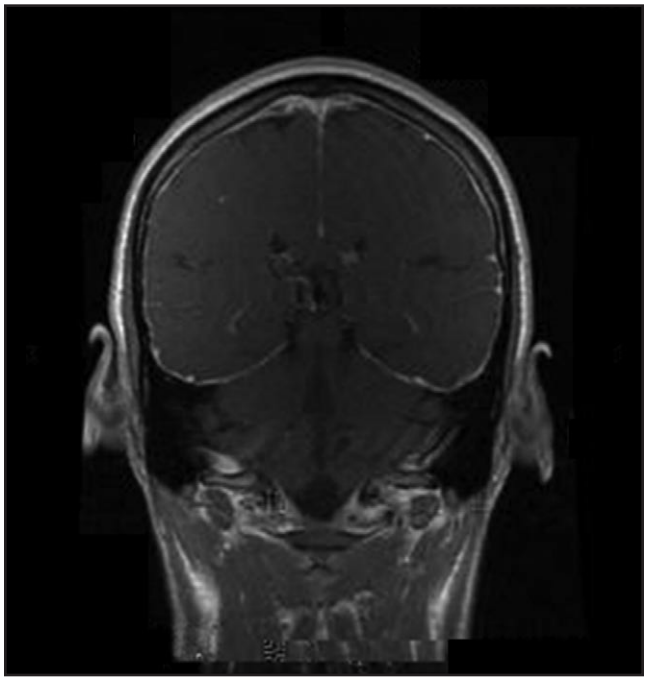

Figure 1. Pachymeningeal contrast uptake seen with a T1-weighted MRI scan taken 4 weeks after onset of spontaneous intracranial hypotension. Note the relatively smooth outlining of the surface of the brain by the contrast uptake in the pachymeninges.

and 2/10 at discharge. At discharge, he was given 10-mg hydrocodone tablets to take as needed for pain control. After discharge, he observed that lying down diminished the headache intensity to 2/10, but the headache became 8/10 on standing. The headache never remitted completely. Over the next 5 weeks, he saw several physicians and was treated with amitriptyline, valproate, sumatriptan, and ondansetron with little benefit. During this time, he also found that any Valsalva maneuver greatly exacerbated the headache.

When seen in our clinic at week 10 after onset, he reported that the worst headache was bitemporal, retroorbital, throbbing, stabbing, and associated with photophobia, phonophobia, osmophobia, nausea, vomiting, severe kinesiophobia, and severe neck pain. He continued to note that lying down produced significant headache relief but not complete remission; standing made the headache much worse. When the headache was severe, he felt mildly confused and had some difficulty finding words at times. The lesser degrees of headache had similar pain characteristics and distribution but were less intense. He observed some difficulty with cognitive function but attributed it to the headache pain.

The patient denied any personal or family history of significant headache. He did recall playing volleyball 4 weeks before onset of the headache, when he was hit in the left side of the face by a ball that was "spiked" by an opponent. He had a sore jaw the next day but no headache.

General physical and neurologic examinations were within normal limits except for mild unsteadiness on tandem Romberg test. The mental status examination was also within normal limits.

Re-review of the MRI scan done 6 weeks earlier revealed diffuse pachymeningeal uptake of contrast, which had not been noted in the report. There were no other abnormalities and no mass effect or shift (Fig. 1).

A repeat MRI scan of the head again revealed pachymeningeal uptake. In addition, the patient was now noted to have subdural hematomas over the convexity of the hemisphere bilaterally. These were 1 cm thick (slightly larger on the left) and relatively recent in onset, based on appearance of clotted blood (Fig. 2). There was a slight left-right shift of the interventricular septum. The brainstem was sagging against the clivus with compression of the pons, a finding not seen on the earlier MRI scan (Fig. 3).

The patient was hospitalized. Neurologic examination now demonstrated an equivocal extensor plantar response on the right. After neurosurgical consultation, conservative management was suggested. The patient was treated initially with bed rest and stabilized, but the headache continued to be severely exacerbated by standing. A large-volume (20 mL) epidural blood patch (EBP) was carried out on hospital day 3. The patient showed significant improvement but still had some postural headache. A second EBP produced further improvement. He was discharged on bed rest and limited activity. The subdural collections began to diminish in size and completely resolved 3 months later. The patient returned to light duty 4 weeks after discharge and later resumed full activity. One year later, he is doing well, with no recurrence of the headache.

EPIDEMIOLOGY

SIH has an annual incidence of 2 to 5 per 100,000, about half the incidence of subarachnoid hemorrhage [1••]. The onset can be at any age but the peak incidence is in the fourth and fifth decades. The female:male ratio is 2:1 [1••].

ETIOLOGY

The etiology of SIH is related to leakage of cerebrospinal fluid (CSF) from the subarachnoid space due to a tear in the arachnoid membrane [1••,2, Class II]. With advances in imaging, it has become clear that a physical tear or defect in the arachnoid membrane is the most likely cause [1••,2,3, Class II]. The major location of the defect is usually at the root sleeve of the spinal nerve as it exits the arachnoid space [1••,4, Class III]. A diverticulum often develops, which may rupture, most commonly at cervical or thoracic roots [1••,2,3,5, Class III]. CSF leaks may also occur at the cribriform plate (CSF rhinorrhea) or in the cochleovestibular apparatus (CSF otorrhea). At times, the leak may be prolonged or related to a lumbar puncture or epidural anesthesia [1••,2,6••, Class III; 7•].

The current theory is that the CSF leak destroys the hydrodynamics of the CSF space and the ability of the

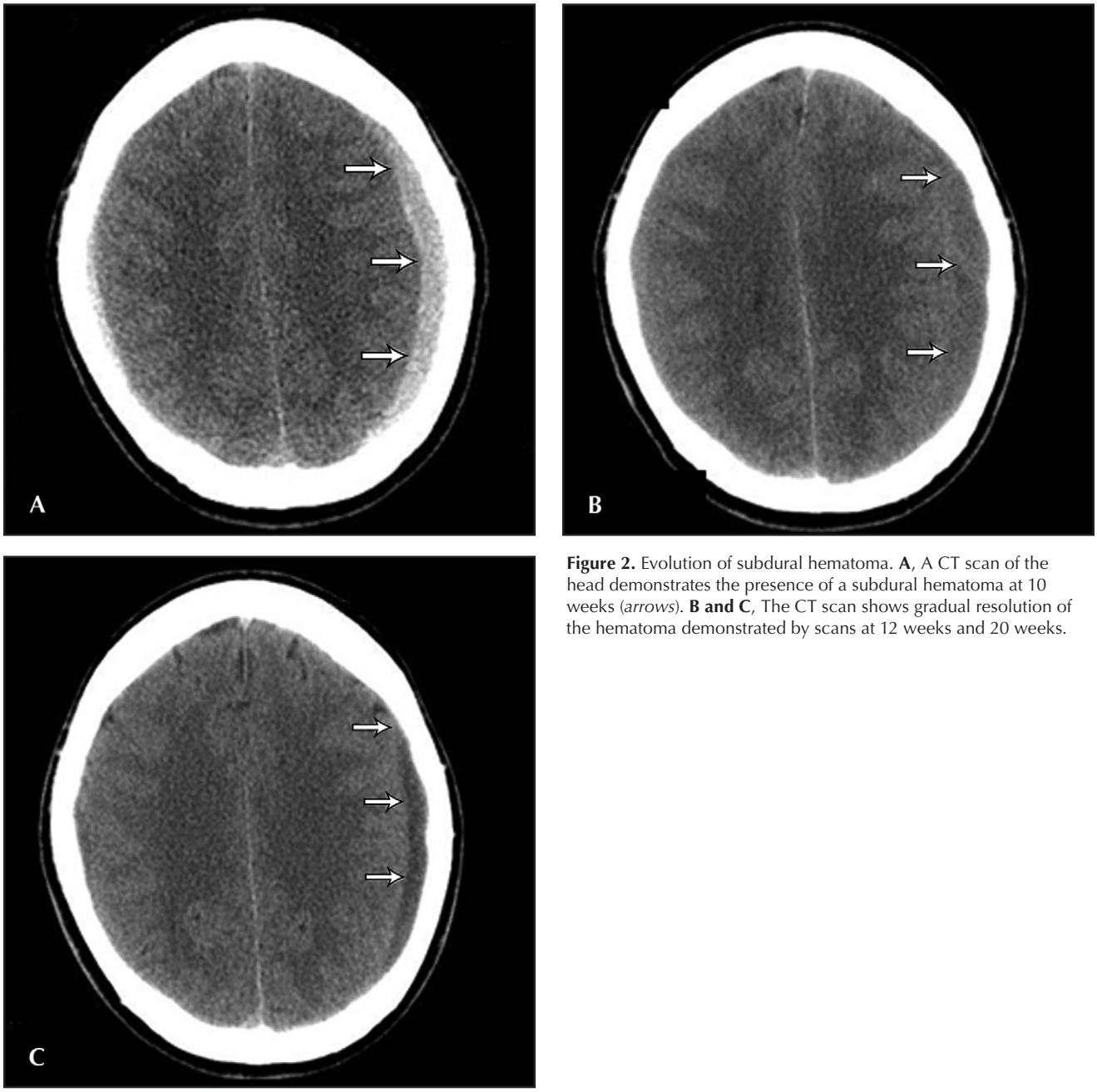

Figure 2. Evolution of subdural hematoma. **A**, A CT scan of the head demonstrates the presence of a subdural hematoma at 10 weeks (*arrows*). **B and C**, The CT scan shows gradual resolution of the hematoma demonstrated by scans at 12 weeks and 20 weeks.

CSF to provide buoyancy for the brain and anatomic support for the brain within the cranial cavity. Consequently, the brain may sag toward the posterior fossa and foramen magnum when the patient is erect. This sagging can produce compression of the brainstem as well as descent of the cerebellar tonsils below the foramen magnum [1••,2,5,8,9]. Traction on the bridging veins within the subdural space may produce subdural hematomas over the convexity of the cerebrum or around the tentorium or brainstem [1••,2,5,6••; 10–14, Class III].

About one third of patients report a history of trivial trauma to the neck or a Valsalva maneuver before onset of the SIH, but in most cases the onset appears to be without a predisposing event [1••,2,6••]. Some patients have a history of an occupation that requires heavy lifting or of weight-lifting exercise. Chiropractic manipulation may produce SIH [9]. The onset of the headache may be immediate or may develop insidiously, suggesting that the leak is a dynamic process that may worsen over time. Subdural effusions and hematomas, as well as coma, can result from SIH, as discussed later [10–14].

An underlying weakness of the dural membrane may predispose to the leak [9,15,16, Class III]. Loss of elasticity of the craniospinal unit may be the overriding problem in the pathology and manifestations of the SIH syndrome [1••]. Thinning or even absence of the dural membrane at the nerve root sheath has been noted. Table 1 lists some of the conditions that may be related to the CSF leak.

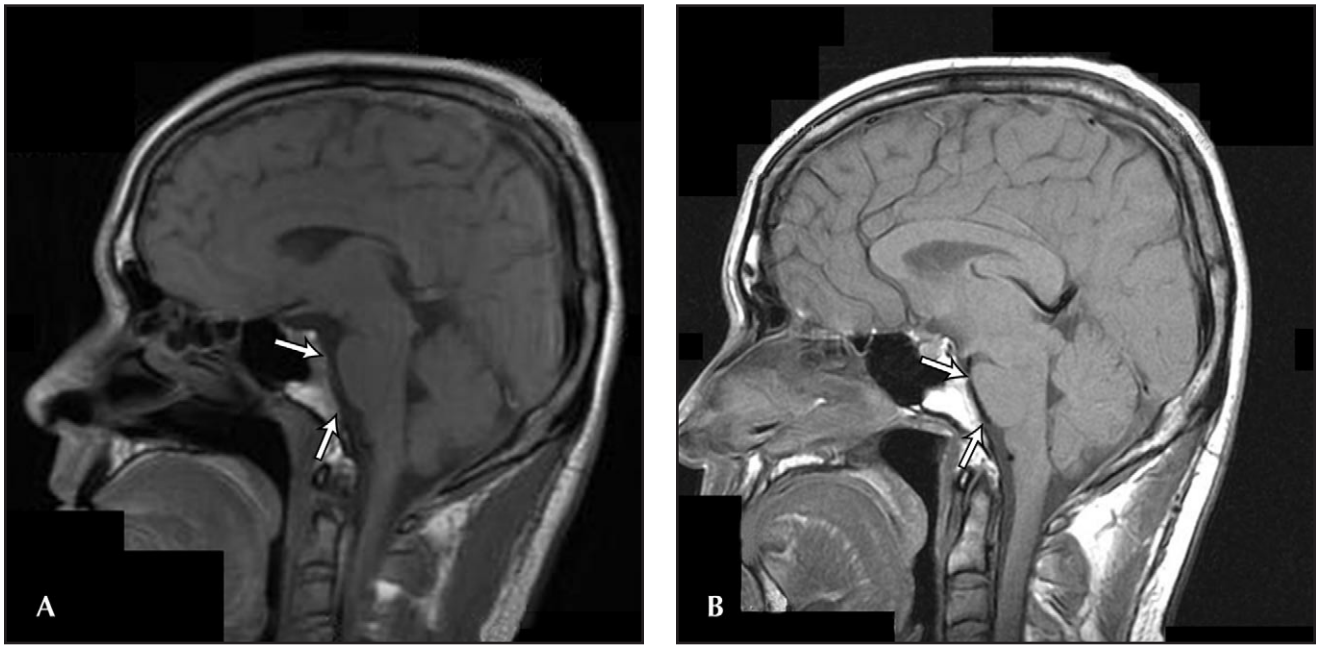

Figure 3. MRI scan showing the sagittal view of the brain at the midline at 4 weeks (**A**) and at 10 weeks (**B**) after onset of symptoms of spontaneous intracranial hypotension. Note the relative flattening of the pons against the clivus by the 10th week as compared with the 4th week (*arrows*).

Table 1. Conditions possibly associated with spontaneous intracranial hypotension

Connective tissue disorders
Marfan syndrome
Isolated features of Marfan syndrome
Ehler-Danlos syndrome, type II
Autosomal dominant polycystic kidney disease
Joint hypermobility, possibly with fascial thinning
Spontaneous retinal detachment
Neurofibromatosis I
Boney disorders
Congenital osseous spur
Acquired degenerative disc disease

(*Adapted from* Schievink [1••].)

The clinical syndrome, in turn, relates to the loss of buoyancy and sagging of the brain in the craniospinal space [17, Class III]. The Monro-Kellie hypothesis states that CSF volume fluctuates with intracranial blood volume to keep intracranial volume constant [1••,17]. Extrapolation of this hypothesis suggests that vascular volume will increase and extravasation of fluid will result if there is a greater deficit of CSF. As noted previously, with a deficit in CSF volume, brain buoyancy will decrease and the brain will sag toward the posterior fossa and foramen magnum. The result may be the development of a subdural hygroma over the cerebral convexity and eventually pressure on the cerebrum. With rupture of bridging veins, the subdural hygroma may be transformed into a subdural hematoma [1••,11,15]. Hygroma has also been reported in the posterior fossa (on the inferior side of the tentorium) and could result in posterior fossa subdural hematoma [11].

A related problem is pressure on the brainstem, especially the basis pontis, as a result of the sagging. Flattening of the basis pontis is a well-described complication of SIH that can lead to problems ranging from isolated cranial nerve palsies to parkinsonism to alteration of consciousness and coma [18–20, Class III]. Moving down the neuraxis, tonsillar herniation at the foramen magnum and cervical radiculopathies also can occur.

The traction and the increased vascularity may produce enlargement of the pituitary gland [21,22, Class III]. This finding may be misinterpreted as a pituitary adenoma if the syndrome of SIH is not considered. This enlargement will reverse with therapy of the dural leak and restoration of intracranial hydrodynamics. Hyperprolactinemia and galactorrhea have been associated with SIH.

Another finding of uncertain significance is hygroma in the retrospinal area in the superior and inferior occipital triangle. Collection of fluid in this space outside the spinal canal has been described [1••,17,23, Class III] and is of uncertain significance. Patients with SIHH often complain of neck pain and stiffness. The collection of fluid here, with reported "boggy" upper cervical muscles in the suboccipital space, may relate to these symptoms. The etiology of the fluid is unclear. Although it may relate directly to the subarachnoid leak, it has also been postulated to be due to extravasation related to increased volume in the suboccipital plexus, which in turn is related

Table 2. ICHD-II diagnostic criteria for spontaneous intracranial hypotension headache

Diffuse and/or dull headache that worsens within 15 min after sitting or standing and with 1 or more of the following:
Neck stiffness
Tinnitus
Hypoacusis
Photophobia
Nausea
At least 1 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 mm water in sitting position
No history of dural puncture or other cause of CSF fistula
Headache resolves within 72 h after epidural blood patching

CSF—cerebrospinal fluid; ICHD-II—The International Classification of Headache Disorders, 2nd edition.
(*Adapted from* Headache Classification Subcommittee of the International Headache Society [26].)

to the increased intracranial vascular volume due to SIH. Cervical radiculopathy has been reported as a complication of hygromas in the craniospinal junction area and the posterior cervical triangle [23].

THE CLINICAL SYNDROME OF SIH

The features of the clinical syndrome are well described in the literature [1••,2,5,6••,7•,23–25, Class III] and are illustrated by the case presented. Table 2 presents the criteria for diagnosis of SIHH from the International Classification of Headache Disorders [26]. The most typical feature is the postural headache. The patient will usually note that headache begins shortly after assuming a position with the head above the heart, whether sitting or standing. The headache usually develops more rapidly if standing. The headache is almost always bilateral and has a sensation of the head being pulled downward, or the "brain sinking into the body." The pain intensity may be mild at onset but steadily and rapidly worsens to become quite severe. The patient may also complain of dizziness, giddiness, or even true vertigo. Nausea and occasionally vomiting may be seen, as well as photophobia and phonophobia. The patient almost always notes marked relief with lying down, although the relief may take 5 to 15 minutes to occur. At times, headache of SIH may be difficult to differentiate from migraine, but the relief with lying down is almost complete with SIHH, whereas with migraine, the relief is usually moderate at best. As in the case reported, however, the patient may have a residual mild headache even when lying down.

Instead of headache, initial symptoms in patients with SIH may include tinnitus, hypoacusis, or strange sensations in the head [1••,2,3,6••,24]. In the case presented, vestibular symptoms and sensations of feeling unwell were the initial manifestations; the headache developed later. If the SIHH remains untreated, symptoms often progress [1••,2,5,6••,7•].

In most cases, the patient notes a rapid onset of the symptoms of postural headache. The change in symptoms in going from lying to standing is usually very dramatic. Typically, any Valsalva maneuver also will cause marked exacerbation of the headache. These two factors are usually very powerful in helping to make the diagnosis [1••,5,7•].

Other symptoms and neurologic signs usually depend upon the amount of brain displacement or "sagging." There may be isolated or multiple cranial nerve palsies. Involvement of nerves III, IV, V, VI, VII (motor and chorda tympani), VIII, and IX has been reported. Visual field losses from involvement of the second cranial nerve or optic chiasm also have been noted. Stupor and coma from pressure on the brainstem or from herniation at the tentorium due to expanding subdural hematoma have been reported [1••,5,7•,20]. Reversible parkinsonism related to SIH also has been reported, presumably due to pressure on the midbrain from SIH-related brain sagging and herniation at the tentorium [18].

DIAGNOSIS

The major components of the diagnosis are the history and physical examination. The physical and neurologic examinations should be within normal limits. As noted previously, neurologic signs and symptoms may result when the intracranial hypotension leads to brain sagging, subdural fluid or hematoma, or posterior fossa subdural hematoma. Cranial neuropathies also may occur.

The major accessory study is the MRI scan of the head with contrast [1••,2,17]. With SIH, MRI shows smooth, uniform pachymeningeal uptake of contrast (Fig. 1), including the supratentorial as well as infratentorial meninges. This uptake must be differentiated from the meningeal uptake of carcinomatous meningitis, which is often uneven and "lumpy." Also to be ruled out are septic or aseptic meningitis. Other features on

the MRI include subdural fluid collections (hygroma or hematoma); engorgement of venous structures (related to the Monro-Kellie hypothesis); pituitary hyperemia; sagging of the brain with flattening of the basis pontis; and tonsillar descent at the foramen magnum, tentorial herniation, or both.

There have been occasional reports of SIH without pachymeningeal uptake of contrast on the MRI head scan [27–29, Class III]. Schievink et al. [27] reported a series of 33 subjects, seven (22%) of whom did not show pachymeningeal contrast enhancement. This finding was associated with a more prolonged course and a poorer response to therapeutic attempts to seal the CSF leak.

Although pachymeningeal contrast uptake is a key finding in the SIH syndrome, other findings can suggest the diagnosis. These include the presence of a tight posterior fossa with flattening of the pons (Fig. 3) and mild descent of the cerebellar tonsils, or the presence of bilateral supratentorial subdural hematomas in the absence of other causative factors [28,29].

A lumbar puncture is usually necessary. CSF pressure is usually less than 60 mm of water; finding this pressure in a patient in the sitting position is one of the diagnostic criteria for SIH [26]. In the lateral decubitus position, the CSF pressure may be at the lower end of the normal range.

The CSF may show significant abnormalities [1••,2,6••,7•]. The cell count is usually mildly elevated (< 50 cells/mm^3), but there may be a lymphocytic pleocytosis up to 200 cells/mm^3. CSF protein may be mildly elevated, but occasional values up to 1000 mg/mL have been reported. Viral or bacterial meningitis, carcinomatous meningitis, sarcoid, or other autoimmune processes must be ruled out. The clinical picture should be very helpful in doing so. CSF cultures and a VDRL test should always be obtained.

Radionuclide cisternography may be helpful [1••,2,5,7•,24]. The most common findings are early appearance of the radionuclide in the bladder and poor progression of the nuclide into the cranial cavity and over the convexity. At times, the radionuclide may show the site of the leak, but this is not always the case.

Myelography with thin-cut CT scanning or MRI myelography with thin cuts may be the best method of localizing the leak and replacing radionuclide studies. With advanced reconstructive techniques, it may be possible to identify one or more diverticulae in the nerve root exit zone [1••,2,5].

DIFFERENTIAL DIAGNOSIS

Table 3 lists the differential diagnosis for SIHH. A careful history remains the best tool for diagnosis of SIH. The presence of a postural headache is the most important clue, and marked exacerbation of the headache with a Valsalva maneuver is an important adjunct. For the most part, the typical clinical syndrome and the postural headache will guide the diagnosis, but it is extremely important to take a careful history and carry out a thorough physical and neurologic examination to be certain of the diagnosis and rule out other causes.

Table 3. Differential diagnosis for spontaneous intracranial hypotension headache (SIHH)

Primary headache
New daily persistent headache unrelated to SIHH
Secondary headache
Subarachnoid hemorrhage
Arterial dissection
Carotid
Vertebral
Intracranial artery
Cerebral venous sinus thrombosis
Cortical venous thrombosis
Meningitis
Pseudotumor cerebri
Post-trauma headache

LONG-TERM OUTCOME

The long-term outlook for SIHH is not well documented. Because it is relatively uncommon, few large series have been reported and there has been no long-term follow-up. Recurrence of SIHH has been reported [1••,2]. If SIH is due to an underlying connective tissue defect, recurrence would not be unexpected. Chung et al. [6••] reported a series of 53 subjects (66% female) with SIH and headache. Of the 53 patients, 81% had EBP and the others were managed conservatively. In the acute period, 96% of patients did well. At 1 year's follow-up of 26 available subjects (49%), 25 had complete relief and one had only partial relief. No recurrence was reported. Schievink et al. [1••,3] have estimated that SIH recurs in approximately 10% of their patients.

Subdural hematoma is one of the major complications of SIH. In a series of 40 subjects, Schievink et al. [14] noted subdural collections in 20; eight of these had subdural hematoma. All of the hygromas and five of the subdural hematomas resolved spontaneously after the CSF leak was stopped and brain buoyancy was restored. Three of the subdural hematomas required surgical drainage. In the series of Chung et al. [6••], no subject required surgical drainage of a subdural collection.

Early diagnosis decreases the number of complications and improves outcome. Schievink et al. [14] noted that subdural hygromas resolved within days, but subdural hematomas took months to resolve. In the case presented, the subdural hematoma was not present at the time of the first MRI scan, approximately 1 month after headache onset, but was present at 10 weeks. The

subdural hematoma resolved spontaneously but took 3 months to do so (Fig. 2). In other reports, mental deterioration, confusion, coma, and parkinsonism have been reported if treatment is delayed [18,20,30,31, Class III]. Schievink et al. [32, Class III] reported segmental constrictions in the cerebral circulation that were reversible with correction of SIH.

A large majority of subjects get good relief from appropriate therapy. As most subjects cannot identify a precipitating event, it is difficult to advise the patient to avoid specific activities. It does seem reasonable to tell the patient to avoid strenuous exertion or heavy lifting for several months after the SIHH is resolved, but this suggestion is empiric. Patients should be told to watch carefully for headache recurrence and return for evaluation if headache reappears.

Overall, SIHH has a very good outcome if it is diagnosed correctly and the treatment is applied appropriately. Delay in diagnosis results in increased morbidity and diminishes the probability of a good outcome.

Treatment

- The objective of therapy is to stop the CSF leak, restore CSF volume, and restore the buoyancy of the brain, thus potentially reversing the effects of sagging of the brain [1••,2,5,6••,7•]. This therapy may allow conservative treatment of subdural hematoma.
- The symptoms of confusion, somnolence, parkinsonism, and cranial neuropathies, which appear to be related to brainstem compression or pressure on cranial nerves, usually respond well to repair of the CSF leak. Restoring buoyancy of the brain will reverse these symptoms if the restoration occurs before significant anatomic damage has been done.

Conservative therapy

- The simplest therapy is bed rest with the objective of diminishing hydrostatic pressure against the defect in the dural membrane and allowing the defect to heal. Although bed rest is often a good strategy for post–spinal-tap headache, it is probably somewhat less successful in SIHH. This difference may be because the dural defect is often larger and more irregular, with a longer duration, or it may relate to underlying structural abnormalities in the dura mater. Nevertheless, conservative therapy with bed rest and hydration is a good initial step in an uncomplicated case.
- Adding caffeine to the regimen is often mentioned, but scientific proof of its efficacy is lacking.

Epidural blood patch

- With complications or failure of conservative treatment with bed rest, a more aggressive approach may be required. Initiation of an EBP from a lumbar site has been the major initial treatment in most series. There are numerous variations on the method for carrying out the EBP. Typically, 10 to 20 mL of autologous blood is infused into the epidural space. This usually will give rapid relief, possibly by producing dural tamponade. The patient should remain lying flat or should be placed in the Trendelenburg position for a time. If the patient does not get immediate relief, then a larger volume of blood—up to 100 mL—may be infused. This volume will produce sustained relief in a large majority of patients.
- The EBP can be repeated in 5 days if the SIH headache recurs or if headache relief is incomplete. In some patients, additional trials of EBP may be needed.

- Complications with EBP are, by and large, the complications of doing a lumbar puncture, including infection, creation of a spinal epidural hematoma, and pain from the paraspinal muscles and ligaments. If the EBP is done by an individual trained in the procedure, complications are relatively rare.
- Berroir et al. [33] took a more aggressive approach in treating 27 patients in whom the diagnosis of SIH seemed readily apparent. They proceeded with an EBP without a diagnostic lumbar puncture or a trial of conservative therapy and reported good results in 77% of their patients. As the lumbar puncture is used to rule out meningitis or meningeal irritation due to nonseptic causes, this approach probably should not be generally recommended.

Other techniques

- Intrathecal saline infusion can be used for acute relief of symptoms [1••,27]. This procedure also may be used to help confirm the diagnosis of SIH.
- Other therapeutic techniques have included injections at high and low lumbar sites and focal injections of autologous blood at thoracic or cervical sites of a presumed leak identified by imaging techniques [1••,34, Class III]. This technique is more difficult to use and requires an individual with specialized training in positioning of the epidural needle under fluoroscopy. Whether focal injections at the identified leak site have an advantage over the standard lumbar epidural injection is unclear. Chung et al. [6••] reported on results at 1 year after EBP therapy for SIH. They compared EBP using lumbar epidural injections with the use of focal injections at the site of the CSF leak by fluoroscopic guidance. No difference in outcome was noted between lumbar-originated "blind" EBP and targeted injections at the site of the leak [7•].
- Injections of fibrin sealant have been reported to be successful when EBP fails [1••].

Surgery

- Large or persistent leaks may require surgical repair. This should be undertaken only by neurosurgeons with skill at this procedure. A muscle pledget, Gelfoam, or fibrin sealant may be used to repair smaller leaks [1••,2]. Suture ligation or clipping may be needed for more complex diverticula.
- Treatment of subdural hematoma follows standard neurosurgical dictum. In many patients, the subdural hematoma or hygroma can be treated with an EBP followed by bed rest and appropriate clinical and imaging follow-up. The hematoma may be reabsorbed physiologically. If there is danger of complications from the fluid collection, however, surgical removal should be undertaken [1••,2,6••].

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have been highlighted as:
- • Of importance
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