Review paper

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Spontaneous intracranial hypotension: a case series and literature review

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Abstract

Spontaneous intracranial hypotension (SIH) is a condition of negative intracranial pressure resulting from cerebrospinal fluid (CSF) leakage from the dural sac and is a well-known cause of orthostatic headache. Diagnosis and management can be difficult, often requiring coordination between multiple disciplines. Low CSF pressure and diffuse meningeal enhancement on brain MRI are the major instrumental features of the classic syndrome. Neuroimaging plays a key role in diagnosing SIH, particularly in atypical clinical presentations, by recognizing the specific findings of brain sagging on MRI and detecting the level of CSF leak on spinal imaging, thus guiding therapy accordingly. Since SIH could present with such a heterogeneous clinical picture, careful history taking and increased awareness of atypical presentations are of utmost importance. We review the existing SIH literature, illustrate management, clinical and neuroimaging findings of four consecutive patients with atypical SIH, who were recently referred to our hospital for evaluation to simplify and streamline the management of SIH.

Key words: *orthostatic headache, spontaneous intracranial hypotension, low CSF pressure.*

Introduction

Spontaneous intracranial hypotension (SIH) is a condition of negative intracranial pressure resulting from cerebrospinal fluid (CSF) leakage from the dural sac and is a well-known cause of orthostatic headache. Low CSF pressure and diffuse meningeal enhancement on brain magnetic resonance imaging (MRI) are the major instrumental features of the classic syndrome. The estimated annual incidence of SIH is 5 per 100,000, with a peak incidence around the age of 40 and a female to male ratio of 2 : 1 [25,37,40].

Postural headache is traditionally considered the main clinical feature of SIH, however atypical clinical presentations of SIH, even in the absence of postural headache, have been sparsely reported in the scientific literature, mostly in a case report format: obtundation [3], stupor [30], sensorineural deafness [32], short-term memory deficit [15], dementia with frontotemporal features [28,52], parkinsonism and ataxia [17]. Neuroimaging plays a key role in diagnosing SIH, particularly in atypical clinical presentations, by recognizing the specific findings of brain sagging on MRI and detecting the level of CSF leak on spinal imaging, thus guiding therapy accordingly.

Since SIH could present with such a heterogeneous clinical picture, careful history taking and increased awareness of atypical presentations are of utmost importance. We present here clinical and neuroimaging findings of four consecutive patients with atypical SIH, who were recently referred to our hospital for evaluation.

Description of cases

Case 1

A 55-year-old woman was admitted to a local hospital because of right-side muscular weakness and

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seizures. Her past medical history was unremarkable, although she was taking oral contraceptives. Two weeks before hospital admission she began complaining of neck pain and stiffness that she treated with common pain medications. The day of Emergency Room (ER) admission she complained of worsening of the neck pain associated with orthostatic headache and hyposthenia of the right arm. While in the ER she suffered from two episodes of generalized epileptic seizures. Neurological examination showed orthostatic headache, hemiparesis and hypoesthesia of the right upper extremity. The blood pressure was 100/60 mm Hg, the pulse was regular at 100 beats per minute and the ECG was in sinus rhythm. The electroencephalography (EEG) recording showed no irritative abnormalities. An emergent non-contrast head computed tomography (CT) scan showed thickening of the left frontal meningeal space, while a contrast head CT scan and brain MRI showed diffuse bilateral meningeal thickening and enlargement of transverse venous sinuses at skull base (see Fig. 1 for images and further details). An MRI of the cervical spine subsequently done in another institution (images not available) revealed a CSF leak at the C2 level. Bed rest, oral hydration, caffeine intake and a low dose of steroid (dexamethasone 8 mg/day) were applied. Antiepileptic therapy was started for seizure control (levetiracetam 1000 mg/day). A three-month follow-up brain MRI showed complete normalization of the previous findings.

Case 2

A 54-year-old female with no previous health issues, arrived at the hospital reporting a two-week history of persistent neck pain and new-onset diplopia that urged her to be examined. Neck pain had postural characteristics and common analgesics were ineffective. Neurological examination was normal except for a mild left

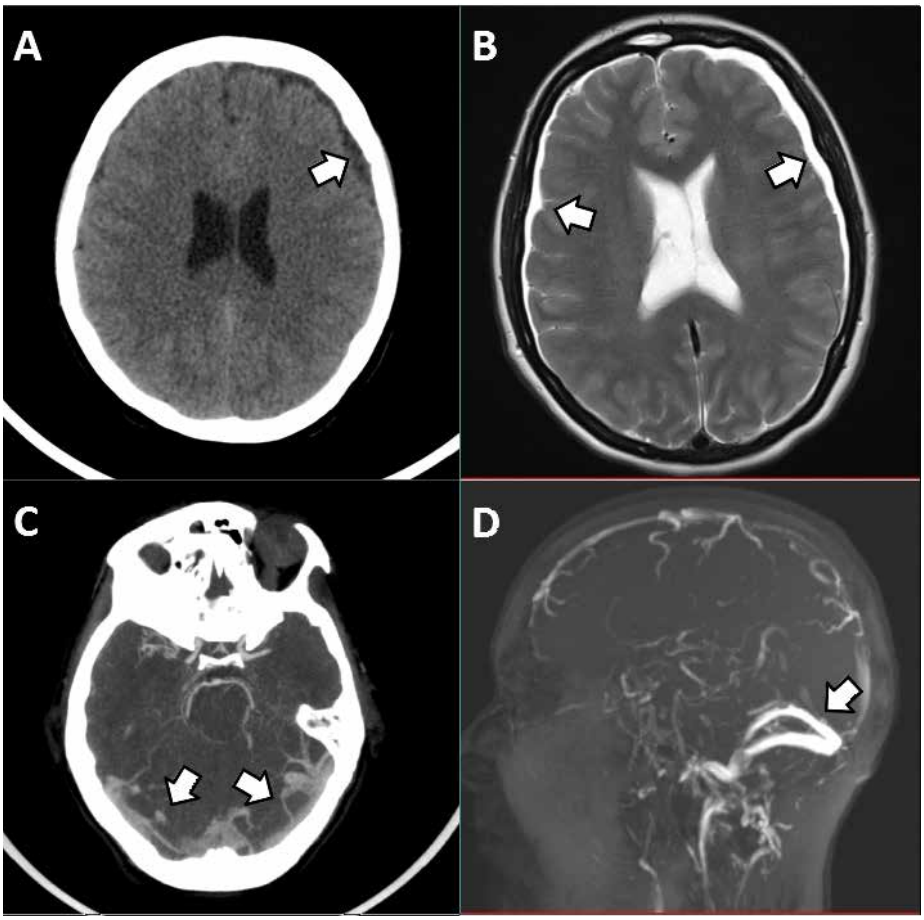

Fig. 1. A) CT scan at admission shows initial thickening of the frontal meningeal space (arrow). **B)** MRI T2 weighted image shows diffuse bilateral meningeal thickening (arrows). **C, D)** CT C+ and MRI venous TOF angiogram show enlargement of venous transverse sinuses at the skull base (arrows).

abducens nerve palsy. Extensive laboratory work-up including haematology, biochemistry and immunology was unrevealing. Brain MRI showed pachymeningeal gadolinium enhancement (Fig. 2).

Conservative treatment with hydration, bed rest, caffeine intake and a low dose of steroid (dexamethasone 8 mg/day) was administrated with resolution of the headache in 3 weeks and improvement of the brain MRI findings in a follow-up MRI scan.

Case 3

A 65-year-old female was admitted to the hospital to be evaluated for a severe headache, localized in the occipital region that started abruptly after sneezing 1 month before and that was not responding to common analgesic drugs. The headache worsened upon standing and resolved in the supine position. Neurological examination was normal, and routine blood tests and immunology was in the normal range. CT scan at admission showed thickening of left transverse and sagittal sinuses while brain MRI displayed bilateral subdural hygromas, a subdural hematoma at the clivus (Fig. 3A) and enlargement of the pituitary gland when compared to a previous MRI scan (Fig. 3B). Conservative treatment with hydration, bed rest, caffeine intake and a low dose of steroid (dexamethasone 8 mg/day) was started with headache resolution in 3 weeks and improvement of brain MRI findings in a follow-up scan 8 months later.

Case 4

A 59-year-old man with unremarkable previous medical history, was admitted to the hospital for a hypoactive–hypoalert state, characterized by apathy, persistent drowsiness, impaired attention and stereotyped motor activity with mood impairment. He also complained of brief episodes of paraesthesia of the limbs, while headache was absent.

The EEG recording showed no epileptic discharges. Both CT and MRI scans showed bilateral meningeal thickening with fluid subdural collections, subdural hematoma and pachymeningeal gadolinium enhancement (Fig. 4). Conservative treatment with hydration, bed rest, caffeine intake and a low dose of steroid (dexamethasone 8 mg/day) was started.

Discussion

The mechanism of production, absorption and flow of CSF plays a key role in the dynamics of intracranial pressure. Alterations in CSF pressure can lead to neurologic symptoms, the most common of which is headache. In the intact craniospinal vault, the brain is supported by the CSF that acts like a supportive cushion in a manner that a brain weight of 1500 g in the air is reduced to only 48 g when surrounded by CSF in the cranial cavity [16]. Therefore, when CSF pressure decreases, a reduction in the buoyancy of the brain occurs. As a result, the brain "sags" in the cranial cavity, causing a traction on the anchoring and supporting structures of the brain [6,15,21,23,50], which causes 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

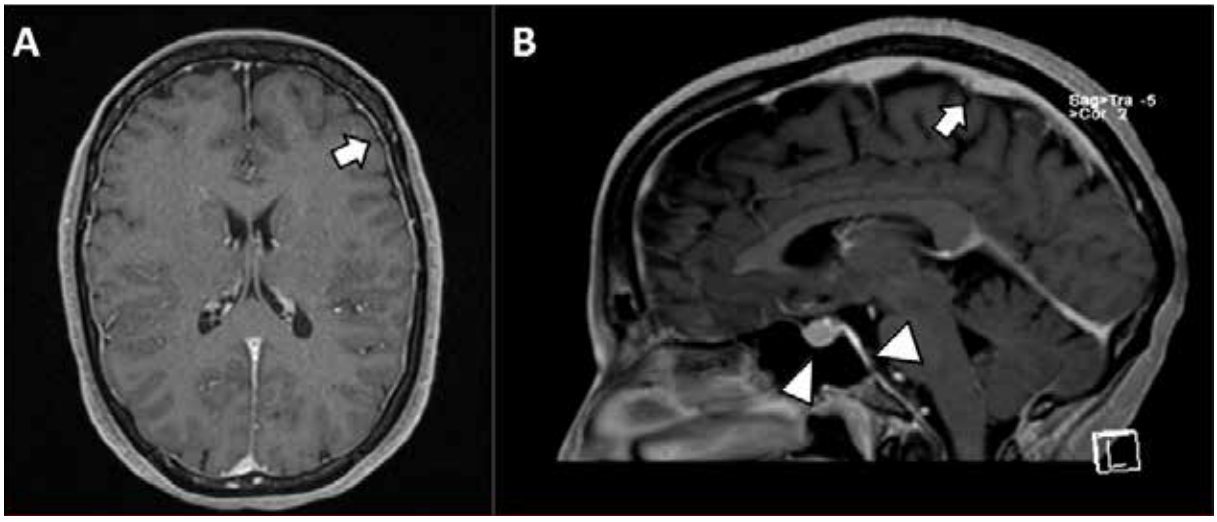

Fig. 2. A, **B**) MRI T1 C+ shows slight diffuse meningeal thickening with contrast enhancement (arrows). Sagittal reconstruction demonstrates slight thickening of the clivus and pituitary gland (arrowheads).

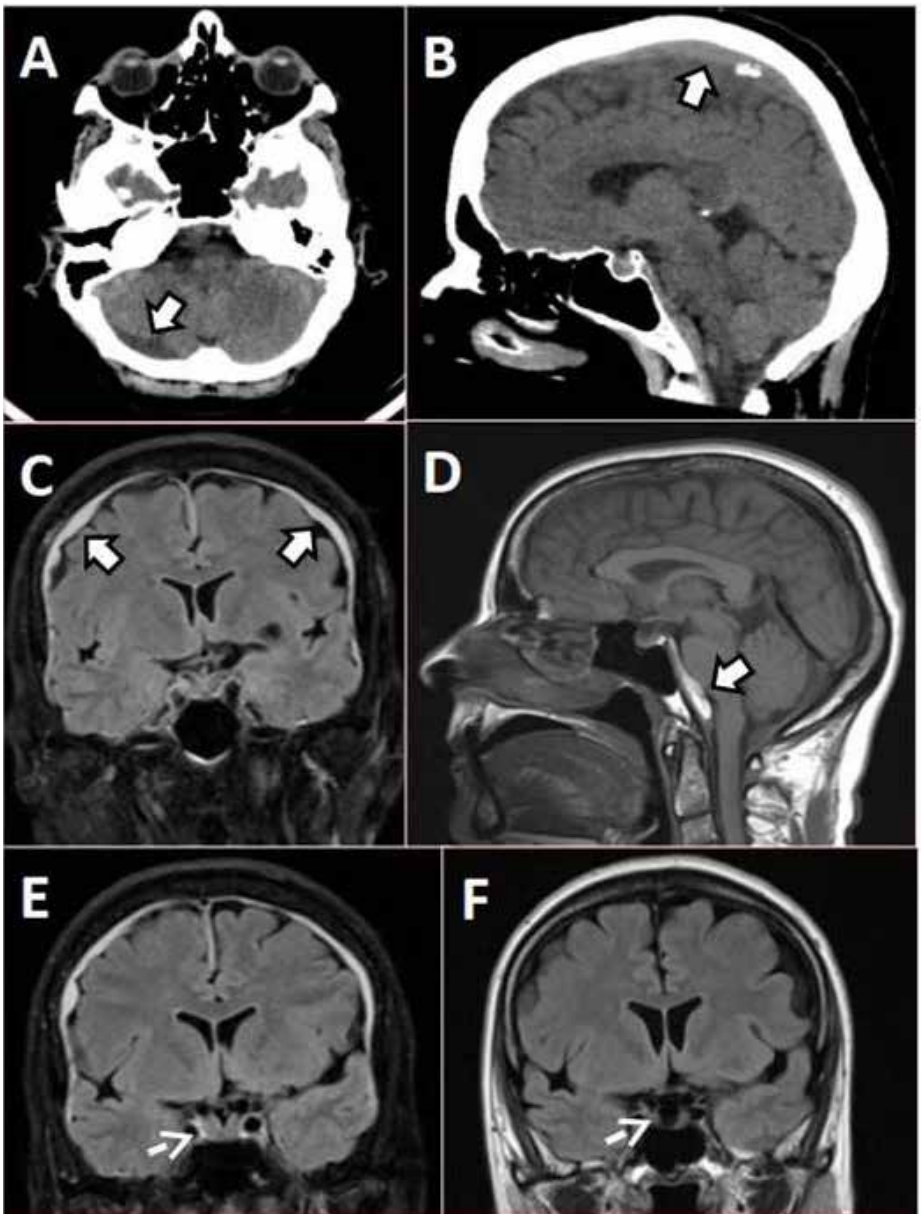

Fig. 3. A, B) CT scan at admission shows thickening of the transversal left sinus and the sagittal sinus (arrows). **C**) MRI FLAIR coronal image shows diffuse bilateral meningeal thickening (arrow). **D**) MRI T1 sagittal image shows hyperintense subdural hematoma at the clivus (arrow). MRI FLAIR coronal reconstructions show enlargement of the pituitary gland during the acute phase (**E**) in comparison with previous examination available (**F**).

other medical conditions have been associated with spontaneous intracranial hypotension [45].

The clinical syndrome of headache attributed to spontaneous intracranial hypotension has been recognized for many years. The syndrome was first proposed in 1938 by Schaltenbrand [33,34], who named 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.

Actually, the prevailing aetiology of SIH is a CSF leakage located in the spine, which may occur in the context of rupture of an arachnoid membrane [19]. An under-

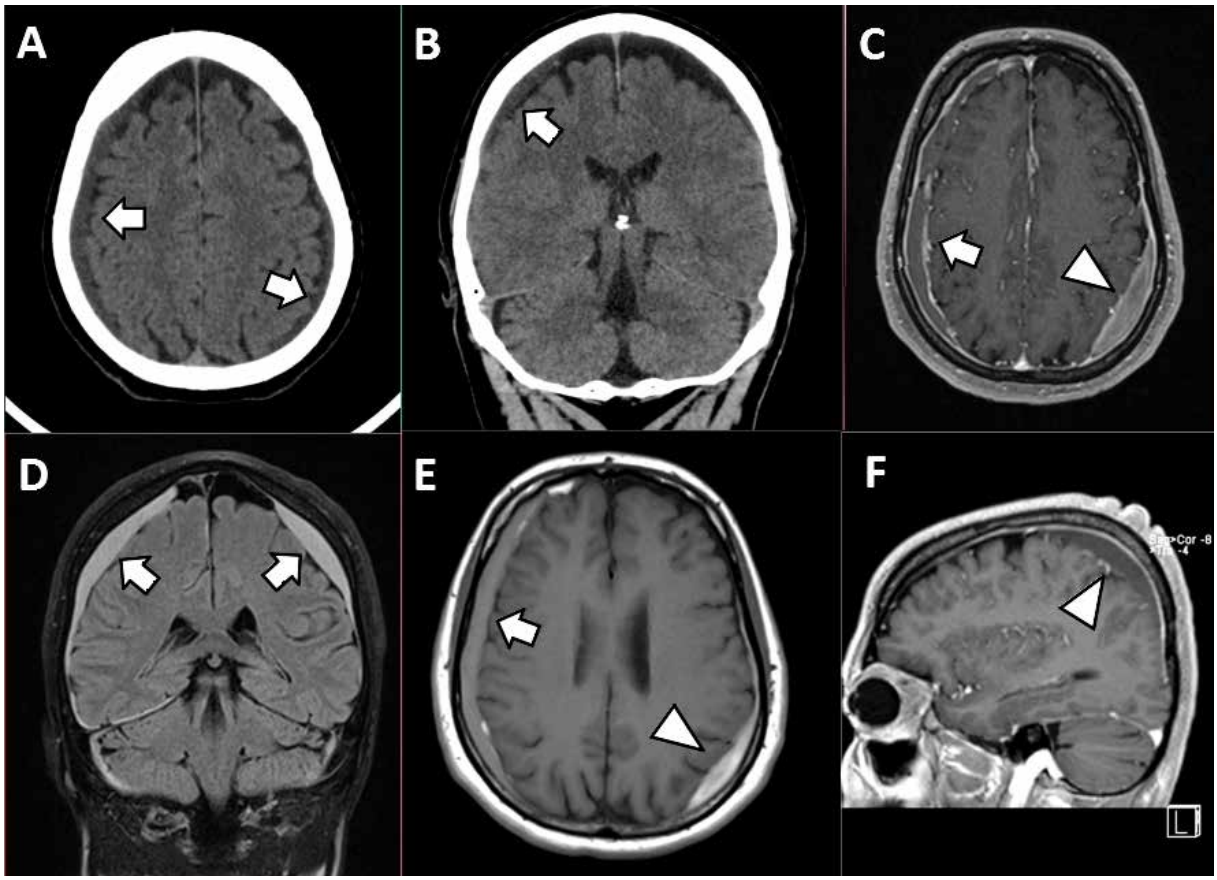

Fig. 4. A, B) CT scan at admission and **C, D**) MRI FLAIR images show bilateral meningeal thickening with fluid subdural collection (arrows). **E, F**) MRI T1 before and after contrast administration show subdural hematoma with hyperdense hematic component (arrowheads) and bilateral meningeal thickening with contrast enhancement.

lying connective tissue disorder may result in dural weakness and play a role in the development of SIH, as suggested by studies reporting abnormal connective tissue abnormalities in patients with spontaneous CSF leaks [11,26] and/or deficient fibrillin, elastin or both in dermal fibroblast cultures from such patients [48]. Meningeal diverticula, often seen in patients with CSF leaks, may be related to this connective tissue problem [13] and meningeal diverticula have been described in patients with Marfan syndrome [11].

A potential contributing factor to the development of spontaneous low CSF pressure are minor traumas or an inciting event, including a fall, a sudden twist or stretch, sexual intercourse or orgasm, a sudden sneeze, sports activity, or "trivial trauma" [20]. These relatively minor events may cause rupture of spinal epidural cysts (formed during foetal development) or perineural (Tarlov) cysts, or may cause a tear in a dural nerve sheath [19] with resultant cryptic CSF leakage. In addition, degenerative disc disease, osseous spurs, and microspurs may lead to spontaneous intracranial hypotension by causing dural tears [2,9,31,52,57]. Another uncommon cause of SIH is the spontaneous development of a spinal CSF venous fistula, which enables CSF to drain from the subarachnoid space directly into adjacent spinal epidural veins in the absence of a dural defect [18,42]. The location of CSF leaks associated with spontaneous intracranial hypotension is almost exclusively spinal; most occur at the thoracic or cervicothoracic junction. Few, if any, cases result from CSF leaks at the skull base. As an example, one series evaluated 273 patients with spontaneous intracranial hypotension, and none had evidence of a cranial CSF leak [46]. In contrast to spinal leaks, some cases of spontaneous CSF leaks at the skull base (i.e. into the petrous or ethmoidal regions, or through the cribriform plate, and typically associated with overt CSF rhinorrhoea or otorrhea) may result from sustained intracranial hypertension as occurs in idiopathic intracranial hypertension [1,29,54].

As mentioned above, clinical symptoms could be atypical. A clinical syndrome that mimics frontotemporal dementia, with cognitive and behavioural dysfunction, the latter including impulsivity, perseveration, and disinhibition, has been recorded [22]. Sometimes, the behaviour of those affected can be termed "hypoactive–hypoalert" and is characterized by decreased initiative, persistent somnolence, impaired attention, and stereotyped motor activity: lesions in the brainstem, basal ganglia, and frontal lobes caused by brain sagging can underlie such behaviour [53]. Moreover, a reversible dorsal midbrain syndrome with postural headache, episodic stupor, and vertical gaze palsy owing to the displacement of the brain as the result of the leakage of CSF, has been described, with improving of signs and symptoms when treated [51]. Such deformities of the brain can also cause damage to the hypothalamus, which results in a deficiency of growth hormone [10] or cranial nerve palsies, especially of the sixth cranial nerve and, more rarely, of the third one [10]. It has been found that the presence of diplopia and the absence of limb numbness strongly suggest the existence of leaks of CSF in patients suspected to have intracranial hypotension [24].

Table I. Typical and atypical manifestations of spontaneous intracranial hypotension (SIH)

Common
Headache (orthostatic, non-positional and reverse orthostatic)
Vestibulocochlear symptoms (dizziness, vertigo, tinnitus, hypoacusis)
Nausea and emesis
Disequilibrium
Posterior neck pain
Cognitive impairment
Fatigue
Facial numbness, paraesthesia
Phonophobia or photophobia
Least common
Interscapular pain
Dysgeusia
Low back pain
Behavioural-variant frontotemporal dementia
Diplopia with abducens nerve palsy
Coma
Hemifacial spasm
Cerebral venous thrombosis
Spinal cord herniation
Syringomyelia

Spontaneous intracranial hypotension is deemed a risk factor for cerebral venous thrombosis, but it has been seen only in about 2 per cent of patients. This may occur because of venous engorgement and slowing of the blood flow, sagging of the brain and distortion of the blood vessels, or by impaired absorption of CSF into the cerebral venous sinuses resulting in an increased blood viscosity in the venous compartments [5]. A change in the pattern of the headache is not a reliable predictor of such a complication.

Affected patients are also predisposed to subdural haemorrhage after minor trauma because of stretching of the dural veins [38].

This latter description is a rare presentation of SIH. Several reports have noted the development of superficial siderosis, characterized by hemosiderin deposition in the leptomeninges and subpial layer, often years after the onset of spontaneous intracranial hypotension [39,43,47,56]. The proposed mechanism is recurrent haemorrhage from friable vessels at the site of the CSF spinal leak or from cerebellar bridging veins that are stretched due to brain sagging [44].

Diagnosis

The cardinal symptom of spontaneous intracranial hypotension is a headache that worsens with standing and subsides with lying down (orthostatic headache) but there may be atypical clinical manifestations (Table I) [7]. It is useful to ask patients how they feel on awakening, before getting out of bed, and whether the headache occurs soon after rising up. The interval between standing and the onset of the headache is typically a minute or several minutes, but the headache can develop instantaneously, after a number of hours, or after a delay that extends into the afternoon.

The orthostatic feature of the headache may lessen over time [14]. A few patients have a non-positional or even reverse orthostatic headache (worse when the patient is recumbent). The headache is usually holocephalic or bilaterally suboccipital but may be unilateral and occasionally has a throbbing component that simulates migraine. Valsalva manoeuvre–induced worsening of the headache has been reported to be common in patients with CSF–venous fistulas [8]. Other neurologic manifestations can accompany or overshadow the headache and may become apparent only days or weeks after the onset of headache or even after the headache has resolved. Common aural symptoms are muffled hearing, pulsatile tinnitus, and hearing loss.

Other symptoms that occur variably across patients are posterior neck pain or stiffness, nausea, vomiting, photophobia, and phonophobia, leading to a diagnosis of meningitis or migraine.

Less common symptoms include facial pressure or paresthesias, diplopia (usually from sixth-cranial nerve palsies), and tremor. Some patients report fatigue or difficulty with concentration and word finding, but the nonspecific nature of these symptoms makes them difficult to interpret and to attribute to the CSF leak.

In rare cases, coma and cerebral venous thrombosis occur days to months after the onset of spontaneous intracranial hypotension [12,41]. Coma is the result of extreme downward displacement of the midbrain and brain stem (brain sagging). Placing a comatose patient with spontaneous intracranial hypotension in the Trendelenburg position may result in improvement in the level of consciousness [41].

The diagnosis of spontaneous intracranial hypotension 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. Headache caused by low CSF pressure following a lumbar puncture rarely creates a clinical dilemma. Confirmation of the diagnosis requires evidence of low CSF pressure, most often by MRI (e.g., pachymeningeal enhancement) or less often by radioisotope cisternography, and/or evidence of a CSF leak on other neuroimaging studies, mainly CT myelography. The advent of MRI has greatly improved the diagnosis of spontaneous intracranial hypotension. While brain and/or spine MRI is abnormal in most patients, a systematic review estimated that brain MRI remains normal in up to 20 percent of patients with spontaneous intracranial hypotension [36].

The acronym SEEPS (for Subdural fluid collections, Enhancement of the pachymeninges, Engorgement of the venous structures, Pituitary enlargement, and Sagging of the brain) refers to the major features of spontaneous intracranial hypotension on brain MRI [36].

Indeed if SIH is suspected, brain MRI with and without gadolinium contrast enhancement is the initial imaging examination of choice. Brain sag, or the downward displacement of the cerebellar tonsils and brain stem, is a classic finding [35]. Flattening of the ventral pons, effacement of the subarachnoid spaces including the prepontine and perichiasmatic cisterns, and descent of the iter (superior opening of the cerebral aqueduct) below the incisural line are additional manifestations of brain sag. With or without brain sag, many patients' scans will demonstrate diffuse, smooth dural thickening and enhancement [27]. Other possible imaging features include ventricular collapse, dural venous sinus engorgement, atraumatic subdural hematomas or hygromas, and pituitary enlargement.

Due to the effacement of the perichiasmatic cistern and pituitary engorgement, the optic chiasm can appear to be directly draped over the pituitary gland. Note that there is wide variability as to how many signs may or may not be present in a given patient.

Approaches to spinal imaging in patients with suspected SIH vary widely among institutions. Either a spinal MR imaging or CT myelography may be performed to evaluate the presence of extradural fluid collections. A "fast" leak is suspected if such a dynamic CT myelogram or a digital subtraction myelogram to localize the CSF leak [52]. Spine MR imaging may also demonstrate secondary/ supportive findings of SIH such as dural thickening and enhancement or engorgement of the epidural venous plexus [58] or may be helpful both for confirming the diagnosis and for identifying the exact location of the CSF leakage [4,25,49,55].

Understanding the clinical and imaging features of SIH and its mimickers will lead to more prompt and accurate diagnoses. We summarize the conditions that mimic the radiologic (Table II) and clinical (Table III) presentation of SIH, as well as other disorders that CSF leaks can imitate [55]. Nonspecific radiographic findings include bilateral subdural fluid collections or hematomas and conditions with dural thickening. Conditions with some shared imaging features include Chiari type I malformations and diencephalic-mesencephalic junction dysplasia. Nonspecific clinical mimics

Table II. Radiological features of spontaneous intracranial hypotension (SIH) mimic

Radiological aspects	Distinguishing features	SIH
Chiari type I malformation	Cerebellar tonsils inferiorly pointed Midbrain descent absent	Normal cerebellar tonsil shape Midbrain descent present
Subdural collections	Usually unilateral	Usually bilateral Brain sag and focal dural enhancement
Condition with dural thickening (neurosarcoidosis, tuberculosis, autoimmune disease, infection disease)	Focal or diffuse May have leptomeningeal involvement. Skull base prominence, hypertrophic pachymeningitis. Usually systemic symptoms and involvement of other organs	Diffuse, non-nodular dural thickening and enhancement

Table III. Clinical features of spontaneous intracranial hypotension (SIH) mimic

Clinical aspects	Distinguishing features	SIH
POTS	Increased heart rate with minimal change in blood pressure on standing from a seated or supine position	Stable heart rate with postural changes
Vestibular migraine	Vertigo, unilateral headache, nystagmus, presence of aura, history of migraine	Hearing changes and tinnitus more than vertigo or nystagmus
Orthostatic hypotension	Autonomic failure, medication effect, hypovolemia Fall in systolic (20 mmHg) and/or diastolic (10 mmHg) blood pressure on standing from a seated or supine position	Stable blood pressure with postural charges
Cervicogenic headache	Headache with neck pain that worsens with cervical motion, relieved with medication	Pain is typically centred in the head and not worsened by cervical motion or improved with medications

Table IV. Conditions that occasionally coexist with SIH

Coexisting condition	Pathogenesis
Cerebral venous sinus thrombosis	Compensatory venous engorgement and stasis secondary to decrease in intracranial CSF volume
Frontotemporal dementia	Brain sag, obstruction of venous outflow, and swelling of the diencephalon may precipitate behaviour and personality changes
Pituitary enlargement or apoplexy	Compensatory enlargement and congestion of hypophyseal veins may cause pituitary engorgement and predisposition to apoplexy
POTS	Prolonged supine deconditioning secondary to spinal CSF leak
Superficial siderosis	Venous traction at the skull base may cause microhaemorrhages, or bleeding may occur at the site of the dural defect

CSF – cerebrospinal fluid

include orthostatic headaches, cervicogenic headache, and vestibular migraine. Postural orthostatic tachycardia syndrome (POTS) is an alternative diagnosis with shared symptoms. SIH may present as an alternative clinical entity with the leak ultimately found as the cause for the condition. These secondary conditions include cerebral venous sinus thrombosis, frontotemporal dementia, and superficial siderosis. Other entities that are associated with SIH include pituitary tumours and apoplexy (Table IV).

Treatment and prognosis

For patients with acute, uncomplicated spontaneous intracranial hypotension of mild to moderate severity, we suggest using conservative measures as initial therapy [36]. We preferred a regimen based on bed rest and a generous caffeine intake. When the symptoms do not improve with conservative treatment, several options are available. The mainstay of treatment is an epidural blood patch, which is effective in relieving symptoms in about one-third of patients and can be repeated. Other options include percutaneous placement of fibrin sealant and surgical repair (epidural blood patches – EBP). These treatments require identification of the exact site of the CSF leak.

There is only anecdotal evidence that treatment with epidural fibrin glue is beneficial for spontaneous intracranial hypotension, and larger studies are needed before this technique can be routinely recommended. However, some experts favour the use of epidural fibrin glue in an effort to avoid surgery for patients with a clearly identified site of CSF leak who have failed an adequate trial of repeated EBP. For patients with spontaneous intracranial hypotension who have failed an adequate trial of repeated EBP and have a clearly identified site of CSF leakage, we suggest surgical repair. For patients with spontaneous intracranial hypotension who have failed an adequate trial of repeated EBP and in whom the site of the CSF leak cannot be identified, continuous epidural infusion of saline or dextran may be an option at centres with expertise in this technique.

The estimated recurrence rate of spontaneous spinal CSF leakage is approximately 10% regardless of treatment.

Conclusions

We believe that the cases presented here further point out that: 1. Although SIH is a rare disorder, it could lead to serious complications, thus it is mandatory for clinicians to gain increased awareness of

this entity and to keep it in mind in the differential diagnosis of headaches, even if the symptom "headache", as in our series of cases, could not be conclusive in the diagnosis. 2. SIH could be triggered by lumbar puncture, overdrainage of CSF shunt or minor head/spine trauma, however SIH without a known risk factor is frequent, as in our series of cases, there absence of trauma. 3. Ortostatic feature of headache or an accompanying cranial nerve deficit or other neurological symptoms should trigger the suspicion of SIH and prompt the use of gadolinium-enhanced MR imaging of the brain and spinal cord. 4. A diffuse and continuous dural–arachnoid enhancement is the most common brain MR abnormality and should be accompanied by spinal imaging, to reveal CSF leak (one case alone), dilated vertebral venous plexuses or extradural fluid collection, in particular when evaluating patients for invasive treatment. However, when brain imaging and clinical picture strongly support the diagnosis, brain MR could be sufficient, as in most of our cases. 5. The condition usually clinically resolves with conservative management. Surgery aimed at stopping the leakage is often undertaken when less invasive such as EBP have failed. It is essential to determine the site of the leak by appropriate imaging before surgery is undertaken.

Disclosure

The authors report no conflict of interest.

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