Review Article

Pathophysiology and management of Spontaneous Intracranial Hypotension — A Review

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Abstract

Spontaneous Intracranial Hypotension is a syndrome involving reduced intracranial pressure secondary to a dural tear which occurs mostly due to connective tissue disorders such as Marfans Syndrome, and Ehler Danlos Syndrome. Patients with dural ectasias leading to CSF leakage into the subdural or epidural space classically present with orthostatic headaches and cranial nerve deficits mostly seen in cranial nerves V-VIII. Diagnosis of SIH is confirmed with the aid of neuroimaging modalities of which Cranial MR imaging is most widely used. SIH can be treated conservatively or with epidural blood patches which are now widely being used to repair dural tears, and their effectiveness is being recognized. Recently epidural injection of fibrin glue has also been used which has been found to be effective in certain patients.

Keywords: Intracranial hypotension, Marfans syndrome, Dural tears, Orthostatic headache, Cranial MR imaging.

Introduction

Spontaneous Intracranial Hypotension (SIH) was first described by Schaltenbrand[1] in 1938 as a potential cause of postural headache, and 'spontaneous aliquorrhea' was the term coined by him. This was followed by a classification of Intracranial Hypotension syndromes by Bell and colleagues,[2] according to etiology: primary or spontaneous; postlumbar puncture; following head injury; or craniotomy; due to severe volume depletion.

Since Schaltenbrand's description much has been learnt about SIH, particularly in the 1990s, but an initial misdiagnosis still remains a norm. "Recent evidence suggests that SIH should be considered as an important cause of new daily persistent headaches, particularly among young and middle aged individuals". Only a handful of studies have been reported in Asia and no study has yet been done in Pakistan. Recent studies have shown the statistics to be around 5 per 100,000 with a female preponderance in a ratio of 2:1 and a higher incidence at around 40 years of age.[3,4]

Pathophysiology:

The syndrome of spontaneous intracranial hypotension is caused by a reduced cerebrospinal fluid (CSF) volume leading to decreased CSF pressure. This reduction in CSF pressure is thought to be caused due to a rupture of the arachnoid membrane resulting in the leakage of CSF into the subdural or epidural space.[5] Spontaneous CSF leakage has been reported mostly as occurring at the cervicothoracic and thoracolumbar junction of the spine.[6]

Dural weakness, which maybe due to generalized connective tissue disorders such as Marfan's Syndrome, Ehler Danlos' Syndrome Type-II, autosomal dominant polycystic disease, predispose to the formation of dural defects which allow CSF leakage into the epidural or subdural space.[7-9] These dural tears or defects are easily observed during surgery, ranging from simple dural holes to complex fragile meningeal diverticula (seen in Marfan's Syndrome Patients) or even complete absence of the dura that normally covers the spinal nerve root.[10] The volume of CSF leaking from a dural defect varies considerably. Dural Ectasia is a well established characteristic of patients suffering from generalized connective tissue disorders. Since its first reporting, a number of studies have been done which have shown the relationship between connective tissue disorders and the presence of dural ectasias leading to SIH.[8,10,11] It has been studied that these patients do not carry a mutation in the Marfan syndrome gene FBN1 encoding fibrillin 1, but instead a defect of microfibrils which are important components of the extracellular matrix associated with fibrillin.[12] This has been speculated to be associated with the dural ectasias seen in SIH patients and is thought to relate to alterations in the elastin component of the dura resulting in the dilation of the dural sac due to CSF pulsation.[13] Some patients have also shown to have a personal or family history of early age spontaneous retinal detachment which suggests the presence of a connective tissue disorder affecting both, the dura and the retina. Orthostatic headache is a classical presenting symptom of SIH patients. Two main theories have been put forward to explain the underlying pathology of orthostatic headaches in an SIH patient.

Under normal conditions the brain is supported by the buoyancy provided by the CSF, such that the 1500 gm weight of the brain amounts to only 48 gm within the cranial cavity. The remaining weight is supported by suspensions formed by several pain sensitive structures. These include the meninges,

cerebral and cerebellar veins as well as the 5th, 9th and 10th cranial nerves (CN) and the superior three cervical nerves.[14] Traction on these structures is responsible for some of the other clinical symptoms in SIH. Reduction in CSF volume causes a reduction in the buoyant force allowing the brain to sag downwards which results in headache which is exaggerated by an upright posture. This explains the orthostatic nature of the headache in SIH or ICH. Evidence to support this theory has been reported in a study where postural hypotension in healthy patients was induced by draining CSF. The fact that orthostatic headache in SIH or ICH rarely occurs in older patients as their brain mass has decreased, further supports this theory.[15]

Another theory proposes the dilation of intracranial vasculature as the pathophysiological mechanism underlying headaches in SIH or ICH patients.[16] Venous engorgement occurs in patients with SIH both intracranially and in the spine. Application of the Monro-Kellie hypothesis also indicates that upright posture would lead to further dilation of pain sensitive intracranial venous structures, thus explaining the orthostatic headache. Decreased venous return to the heart as occurs during the Valsalva maneuver, jugular venous compression and coughing and therefore increased intracranial venous volume can also precipitate headache in an SIH patient even while positioned supine. This finding provides evidence that vascular dilation plays a role in the pathogenesis of headache in SIH. Such dilation may also cause diapedesis of cells and proteins into the subarachnoid space, explaining the reticulocytes, xanthochromia, mononuclear pleocytosis and increased protein found in CSF from patients with SIH or ICH.[17]

Other Medical Causes:

Thyroid metabolism plays a significant role in the maintenance of normal connective tissue and thyroid dysfunction may be associated with the ligamentous laxity and deposition of the excess mucopolysaccharides in connective tissue disorders. This association is suggestive of the fact that thyroid dysfunction could predispose patients to the rupture of congenital meningeal diverticula or the formation of acquired diverticula which have also been noted in patients with Marfan's syndrome and other connective tissue disorders. Other medical causes of SIH may include: dehydration, diabetic coma, hyperpnoea, uraemia and severe systemic illness.[18]

Clinical Presentation:

Orthostatic headache that improves rapidly in the recumbent position and worsens in the erect position is the classical sign of Spontaneous intracranial hypotension although patients with chronic headaches or even no headaches have been described.[6] This pain may be

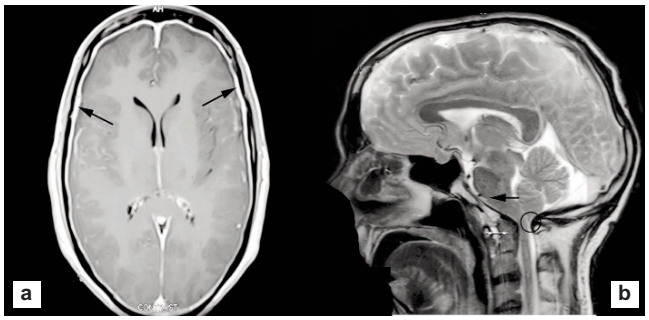

Figure-1: (a): MRI Brain. Axial T1 weighted post contrast image; significant meningeal enhancement (black arrows) suggestive of pachymeningitis is shown. (b): MRI Brain. Sagittal T2 weighted image; showing characteristics of Spontaneous Intracranial Hypotension: flattening of pons (white arrow) and inferior orientation of cerebellar tonsils (encircled). Atlanto-axial subluxation (white double arrow), is also demonstrated.

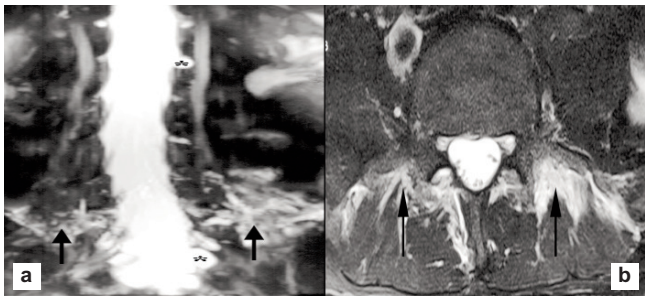

Figure-2: (a): Time of Flight MR Myelogram of Lumbosacral Spine revealing multiple dural out pouchings representing dural ectasias (black asterisks). Also seen is CSF fluid in para-spinal muscles (black arrows). (b): MRI Lumbar spine. T1 weighted post contrast Image, revealing leakage of Cerebrospinal fluid into the adjacent paraspinal musculature (white arrows) from dural ectasias (not shown here).

exacerbated by laughing, coughing, jugular venous compression, Valsalva maneuver, and does not respond to analgesic treatment. Additional clinical manifestations include. Cranial nerves (CN) palsies, radicular upper limb symptoms, vomiting, anorexia, neck pain, dizziness, horizontal diplopia, changes in hearing, facial numbness or weakness, visual burning and visual field cuts, tinnitus, vertigo, cerebellar ataxia and encephalopathy. Some other clinical presentations that are increasingly being recognized include Parkinsonism or frontotemporal dementia, syringomyelia, hypopituitarism, seizures, coma, and death.[19]

Orthostatic headache in SIH patients is a prototypical manifestation. According to the International classification of Headache Disorders criteria,[20] the headache occurs or worsens within 15 minutes of assuming the upright position. But in some patients this period maybe as long as several hours. Improvement of the headache is less variable and improves within 15 to 30 minutes of assuming a recumbent position. The headache may vary in its localization. It may be diffused or localized to the frontal, temporal or most commonly the occipital or sub occipital position. The headache is usually

bilateral and is rarely unilateral. It may be throbbing or non-throbbing. The initial onset of headache generally is gradual or sub acute , but it maybe instantaneous. Patients with such patterns of headaches maybe suspected to have a subarachnoid haemorrhage and may undergo invasive testing.[19-21]

As discussed earlier, the brain is supported by pain sensitive structures such as venous sinuses and cranial nerves, so downward displacement of the brain due to decrease CSF volume causes traction on these structures resulting in some of the above mentioned clinical symptoms other than headache. Thus, traction on the cranial nerves results in hyperacusis and dizziness (CN VIII), horizontal diplopia (CN VI) and facial numbness (CN V) or facial weakness (CN VII). Galactorrhea and hyperprolactinemia may occur due to traction on the pituitary stalk or it maybe associated with pituitary hyperaemia resulting in secretory dysfunction.[22] Traction on spinal nerves also explains the neck pain and radicular symptoms occurring in the upper limb. Photophobia and phonophobia is another clinical symptom occurring along with the neck pain or stiffness and may suggest underlying meningeal irritation. Tinnitus, hyperacusis and a disturbed sense of balance may also occur due to a direct transmission of abnormal CSF pressure to the perilymph. It has also been seen that lowering CSF pressure in cats causes a direct reduction in the intralabyrinthine pressure which does not allow certain frequency tones to be transmitted across the cochlear duct. Similarly, optic nerve or optic chiasma damage may cause visual blurring or diplopia.[23]

Imaging Studies for the Diagnosis of SIH:

Advancements in neuroimaging modalities have led to better diagnosis of SIH. In particular, findings on MR imaging studies have allowed physicians to understand and appreciate its true incidence and varied modes of presentation. Some of the methods used in the diagnosis of SIH are:

Cranial MR Imaging:

Magnetic Resonance Imaging has revolutionized the understanding of SIH and has played a very important role in arriving at the proper diagnosis without having to resort to invasive procedures such as spinal puncture or intracranial pressure monitoring. The five characteristic imaging features of SIH visible on MRI are: (1) Subdural fluid collection and presence of extrathecal CSF (2) Enhancement of the pachymeninges (3) Engorgement of venous structures (4) Pituitary hyperaemia and (5) Sagging of brain or downward displacement of brain. (Mnemonic: SEEPS). In addition to these characteristic features, other findings may include: spinal meningeal diverticula, collapsed superior ophthalmic vein, reduction in the angle of vein of Galen and internal cerebral vein (the venous hinge sign).[19-24]

Evidence suggests that these abnormalities occur as a result of vascular dilation which in itself is a compensatory mechanism for reduced CSF volume as per the Monro-Kellie hypothesis which states that: 'the sum of the volumes of intracranial blood, CSF and brain tissue must remain constant in an intact cranium.' The compensation stated above occurs through dilation of the venous side of the circulation due to its greater capacitance and compliance. Thus, venous sinus engorgement, abnormal pachymeningeal enhancement (with gadolinium), subdural effusions and enlargement of the pituitary gland occurring in ICH may represent a tetrad of compensations occurring in the face of reduced intracranial pressure.[25]

Enhancement of the meninges has become the most well known imaging characteristic of SIH. The enhancement is thick, linear and without nodules and usually involves both the infra- and supratentorial compartments, without evidence of the involvement of the leptomeninges. The absence of leptomeningeal involvement is important in differentiating SIH from meningitis and meningeosis. Another noticeable finding on MR imaging is meningeal fibrosis and these findings provide a basis for the hypothesis that meningeal enhancement may be attributable to meningeal inflammation.[26]

Evidence suggests that about 20% of patients never exhibit enhancement or other abnormalities on MRI. Mokri et al[14] documented patients who showed resolution of enhancement while they were still symptomatic, a patient without enhancement on initial studies and patients whose MR imaging never revealed any enhancement.[14-26] Thus, it can be concluded that Gadolinium enhancement may vary according to the course of a patient's illness.[16-26]

Subdural effusions and presence of extrathecal CSF occur in almost 50% of patients. Subdural effusions are typically thin, crescentic and located either below or between enhancing membranes. They maybe bilateral and may not show any appreciable mass effect. Thus subdural effusions may represent a more severe CSF volume loss resulting in greater compensatory venous dilation then mere meningeal enhancement.[27,28]

Pituitary hyperaemia another characteristic abnormality of SIH on MR imaging is mostly seen during the symptomatic phase of SIH compared with after recovery and also presumably reflects compensatory venous dilation. It may acquire a striking size and mimic a pituitary tumor or hyperplasia.

Sagging or downward displacement of the brain is another notorious feature of SIH. It may be accompanied by ventricular collapse and may include: Descent of Cerebellar tonsils, which maybe mistaken for an Arnold-Chiari malformation Type I, prepontine cistern effacement, an

inferiorly displaced optic chiasma, obliteration or effacement of the prechaismatic cistern, and reduction of the subarachnoid cisterna. This sagging of the brain occurs mainly due to the loss of buoyancy provided by the CSF owing to the reduced CSF volume. Additional features can be collapsed superior ophthalmic vein, reduction in the angle of vein of Galen and internal cerebral vein (the venous hinge sign).[29]

Computerized tomography Myelography: Computerized Tomography myelography has been shown to be the study of choice to accurately define the location and extent of CSF leak. Mokri et al[28] have demonstrated in a study that the detection of CSF leaks with CT myelography was 67% as compared to 50 and 55% with spinal MR imaging and RC, respectively. Meningeal diverticula, a potential cause of SIH maybe demonstrated but they are found frequently below the range of myelography. Frequently multiple CSF leaks are uncovered at the cervicothoracic junction.[30]

Spinal MR Imaging has gained considerable importance due to the fact that unlike RC and CT myelography, MR imaging of the spine does not require active CSF leakage to yield positive results, and can also be used to demonstrate CSF accumulation in paraspinal musculature.[23,30]

Doppler Flow Imaging: Chen et al[26] have successfully demonstrated that the engorgement of the intracranial venous sinuses can be determined by measuring the diameter and maximum flow velocity of the superior ophthalmic vein, a tributary of the cavernous sinus, using Doppler Flow imaging. Statistical analysis indicates a very high sensitivity and specificity, demonstrating a 100% increase in the parameters in all patients. In addition, the parameters return to normal after treatment, paralleling resolution of symptoms.[30]

Treatment and Outcome:

Although clinical data is lacking and no randomized clinical trials have been done to assess the standing of different treatment outcomes, conservative management has been a mainstay for treating SIH patients. A purely conservative approach includes bed rest, oral hydration, acetaminophen, generous caffeine intake, and use of an abdominal binder.[17,19] This regime is effective in most patients but in patients with debilitating illness, administration of steroids, intravenous caffeine or theophylline all have been proposed as treatments of SIH but their effectiveness is limited. It is believed that supine position reduces CSF pressure at the site of leakage and therefore allows healing of the underlying meningeal defects. It has also been proposed that methylxanthines produce arterial constriction through the blockade of adenosine receptors resulting in decreased intracranial blood flow and reducing venous engorgement .Other strategies used to treat SIH involve the fluid restoration to increase CSF or eliminating the leakage site. Strategies to increase CSF volume include intravenous or oral hydration, increased salt intake, carbon dioxide inhalation and steroid therapy.[31]

However, the persistence of postural headache or occurrence of neurological disorders, calls for definitive therapy. If conservative management fails, epidural blood patches are considered to be the safest and most efficacious in treating leakage sites causing SIH.[16,19] It involves injection of autologous blood into the epidural space. Lasting results are achieved with the first patch with its efficacy ranging from 85 to 90 % and a repeat patch may improve the efficacy to 98%.[24] It has also been observed that the procedure is most successful if performed at or within one interspace of the leak.[32]

Instantaneous relief of symptoms occurs, which also serves as diagnostic criteria. Alternatively, epidural infusion of saline has also shown immediate relief for patients with SIH but it is not as efficacious .A new technique now being employed involves the epidural injection of fibrin glue. It has shown encouraging initial results and has been effective in patients in whom blood patches did not show improvement. This therapy requires the location of the exact site of the leakage.[33]

Surgical repair is the last treatment option in patients who do not respond to conservative management and blood patches. Meningeal diverticulae have been completely treated by simple ligature and 100% relief has been achieved. Repair of meningeal tears has shown similar success.[7] In some patients, the repair of CSF leakage is followed by a bout of intracranial hypertension which is typically transient and self limiting.[32,33]

Conclusion

Spontaneous Intracranial Hypotension is a diagnostic dilemma as the patient may or may not present with the classic signs of SIH. Thus, the patient's recent history leading up to the first episode of headache is essential. Correlation of any other presenting symptoms coupled with imaging modalities such as MRI should be employed to arrive at the correct diagnosis. Prompt management is necessary to prevent further complications. Conservative management along with autologous blood patches is an efficacious method to reduce the hypotension and to restore the CSF pressure to normal. The patient should be monitored till the resolution of symptoms and further imaging employed to validate closure of underlying dural defects. If this fails, surgical repair is the last treatment option.

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