Intracranial Hypotension Causing Reversible Frontotemporal Dementia and Coma

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Spontaneous Intracranial Hypotension (SIH) was first described over 60 years ago by Schaltenbrand and termed "aliquorrhea"[1]. In 1997, this syndrome was defined by a classical triad of postural headaches, low cerebral spinal fluid (CSF) pressure and imaging abnormalities[2]. More recent evidence has redefined this concept and our understanding of the pathological mechanism, as well as the variable clinical presentations and alternative treatment approaches in this condition.

In many SIH cases, identification of the CSF leak may be a challenge[2,3]. Cerebral spinal fluid pressures less than 60 mm H_20 may not be present; in fact, normal CSF pressures have been reported in 18-46% of cases[4-6]. Current understanding suggests that the etiology of SIH is CSF volume loss through a dural CSF leak, and that the clinical features, imaging abnormalities and CSF pressures depend on the extent of this CSF volume loss[7]. As such, alternative names of "CSF hypovolemia syndrome" and "spontaneous spinal CSF leak" have been proposed[4-9]. However, not all cases are "spontaneous", and underlying culprit lesions such as subarachnoid (Tarlov) cysts, other anatomical defects[3,5,10-13], or dural micro tears from minor trauma, neck manipulation and violent coughing[3,14,15] can lead to CSF leaks. Identifying the CSF leak site and interventional or surgical correction of the underlying defect is therefore necessary to permanently abate persisting symptoms.

Various symptoms and neurological findings have been reported with this condition. Nausea, vomiting, dizziness and posterior neck pain are all common. Neurological manifestations include visual symptoms such as diplopia, visual blurring, field defects, or photophobia[16], hearing abnormalities including tinnitus, distortions and sensory neural hearing loss[15,16], various cranial nerve palsies, and even peripheral manifestations of interscapular pain or radicular symptoms[2,5,12,14]. Unusual clinical manifestations have been described in case reports and include parkinsonism, gait abnormalities, cerebellar ataxia[17], bipolar disorder[18], encephalopathy, cognitive changes (including one case of frontotemporal dementia [FTD])[19], obtundation and coma[11,20-23]. Only one case of death related to SIH has been published to date[24].

We describe the first case of frontotemporal dementia syndrome and coma caused by SIH that was successfully reversed with intrathecal saline infusion and an epidural blood patch targeted at a culprit C2 dural tear with consequent CSF leak. An Medline search from 1966 to present was conducted, and a review of the literature with emphasis on related cases is provided.

Case Presentation

A 58-year-old right-handed financial advisor was referred to the Neurology service at the Vancouver General Hospital for assessment of cognitive dysfunction in the setting of bilateral subdural collections. He had a motor vehicle accident five years prior causing whiplash and chronic cervical neck pain, but was otherwise previously healthy. Over the recent few months, his behaviour had become odd: he would ask inappropriate questions to strangers on the street, use neologisms in conversation, and respond to questions with confabulatory, bizarre responses. Over time his speech became perseverative and echolalic, especially in the evenings. He became neglectful of personal appearance and hygiene. Simultaneous to the more recent cognitive deterioration, he had developed an intense, postural headache with nausea and vomiting.

Cognitive examination revealed that he had become disorientated to time and place. He lacked insight into both his behavioural changes and the cause of his hospitalization. His affect was inappropriate and blunted, and his thought process was disorganized and tangential. He had perseverative speech, with poor initiation, word finding difficulties and circumlocution. Short and long-term memory was impaired; spontaneous recall of words was 0/3, and little improvement was noted with cueing (1/3). He could not recall the events of "9/11" or who the Prime Minister was. Clock drawing was abnormal and artistically enhanced (see Figure 2A), however language comprehension, calculations and visuospatial skills were remarkably normal. The presenting behaviour and cognitive syndrome was consistent with a rapidly progressive frontotemporal dementia syndrome. Neurological exam otherwise revealed bilateral grasp and snout responses, mild dysarthria, and markedly ataxic gait.

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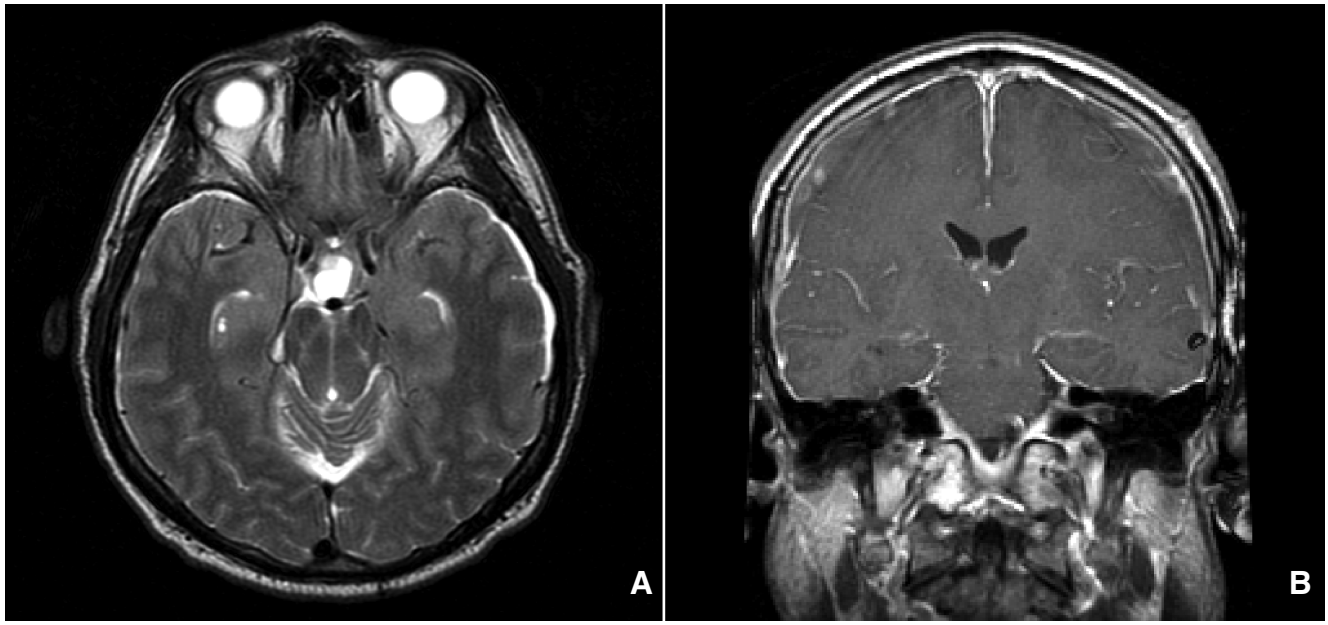

Figure 1: *Selected images from MRI brain performed prior to CSF leak identification. (A) T2-weighted axial image demonstrating crowding of the perimesencephalic cisterns by medial temporal lobe tissue herniating through the tentorial hiatus bilaterally. Additional prominence of the chiasmatic portion of the third ventricle. (B) Post-gadolinium enhanced coronal T1 scan demonstrating bilateral subdural collections with thin and diffuse pachymeningeal enhancement intracranially.*

Brain MRI showed bilateral subdural fluid hygromas, diffuse smooth pachymeningeal enhancement and sagging of the brain in the posterior fossa, findings consistent with the radiographic features of SIH (see Figure 1). Further investigations, including a posterior fossa cisternogram and spine MRI with gadolinium did not reveal a CSF leak. Over the next few days in hospital, his level of consciousness rapidly deteriorated, and he became comatose with no response to noxious or verbal stimuli. An intrathecal saline infusion (ITSI) was initiated via lumbar catheter and based on published reports[11], although 25cc bolus and 10 cc/hr infusion rate was used. One hour after initiation of the infusion he became alert and responsive.

Previously unrevealing diagnostic investigations were repeated with the ITSI running in an attempt to identify a CSF leak site[11,21]. Radionuclide cisternography demonstrated early tracer uptake in the kidneys and bladder, but failed to identify the leak location. Both repeat CT and MR Myelography, as well as gadolinium enhanced cervical spine MRI succeeded in identifying a large CSF leak posterior to the arch of C2 (see Figure 3A-B). A therapeutic CT guided, large volume epidural blood patch of the C2 leak was performed (Figure 3C), followed two hours later by discontinuation of the ITSI.

By the next day, the patient's headache resolved and he remained awake, alert and fully oriented. He was more appropriate, and his memory and language were significantly improved. In follow-up both three months and one year later, he no longer suffered from headaches, and both his gait and mental status normalized. He was well groomed, displayed normal social graces, executive functioning, language and memory were normal, and he had returned to part-time employment. His MMSE score was 30/30, and his clock drawing had normalized

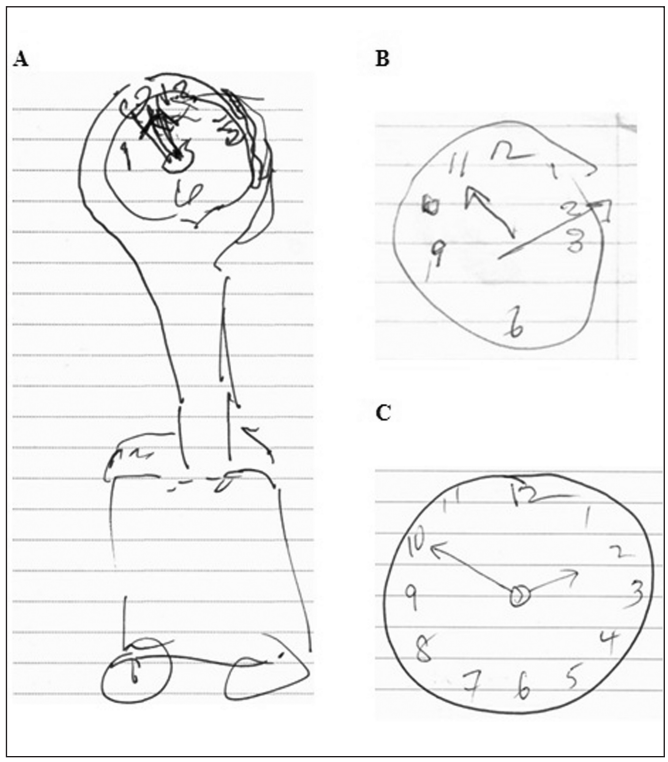

Figure 2: *Clock drawing before and after treatment in the described case. The patient was asked to indicate the time "ten minutes to two". (a) Prior to treatment with FTD syndrome, (b) one day following administration of the ITSI, and (c) at three months post epidural blood patching.*

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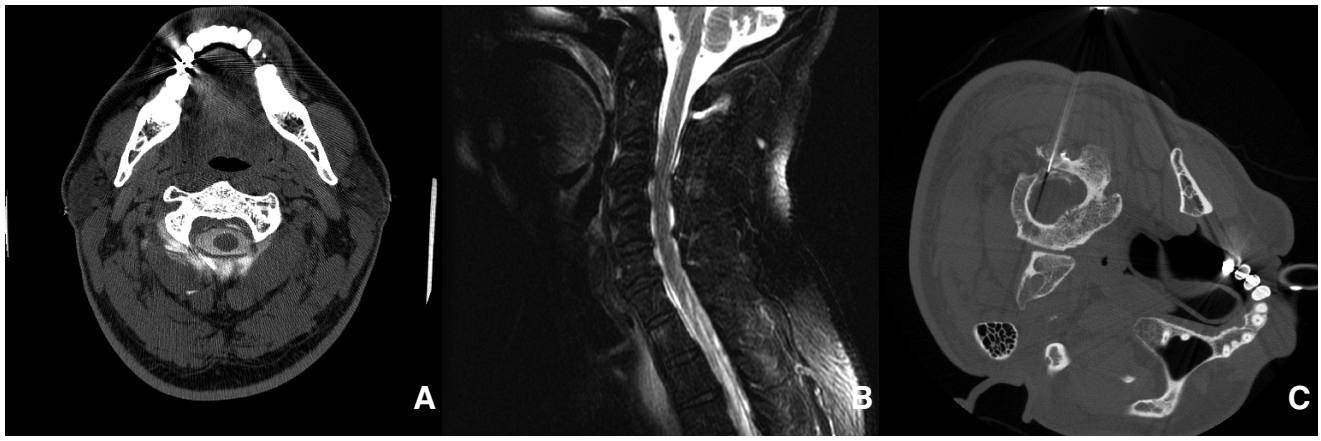

Figure 3: *Selected axial images from CT and MR myelogram. (a) CT Myelogram demonstrates the point of CSF leak, at the C2 level, with the MR myelogram image (b) showing the presence of a spinal subdural CSF collection, opacified by leaking contrast. (C) CT-guided C2 epidural blood patch, performed from a left posterolateral approach.*

(see Figure 2C). A repeat MRI showed an appropriately located epidural blood patch and obliteration of the C2 CSF leak. He had made a complete recovery from his FT syndrome and comatose state (see Figure 4).

Discussion

The pathophysiological mechanism of SIH is based on the Monro-Kellie Doctrine and basic physical principles of buoyancy. In SIH, loss of CSF volume from a CSF leak, results in a compensatory increase in blood volume, namely intracranial venous hyperemia, in order to maintain a constant intracranial pressure (ICP). Once venous compensation is maximized, subdural fluid collections may accumulate to provide further volume for maintaining ICP[4,25,26]. The CSF pressure decreases when the rate of CSF volume loss cannot be further compensated by these mechanisms[7]. Loss of CSF volume also results in decreased buoyant action, which increases the weight burden and traction on brain anchoring vascular structures and neuronal pathways[3-5,7]. Nocioceptive receptors on these dural and intracranial vessels are sensitive to this dilatation and stretch, resulting in the postural nature of headaches seen in SIH[4,7]. Various neurological symptoms can arise as a result of traction on central long tracts, cranial nerves or cervical roots. The downward herniation of the brainstem results in diencephalic compression and reticular activating system dysfunction, which can ultimately lead to coma[11,21].

The mechanism by which SIH causes an FTD syndrome is uncertain. Possible explanations include compression of the frontal and temporal cortices against the skull base by the caudal sagging of the brain, as postulated by Hong et al[27], or alternatively by cortical compression from hemispheric subdural hygromas. Additionally, intraparenchymal venous engorgement

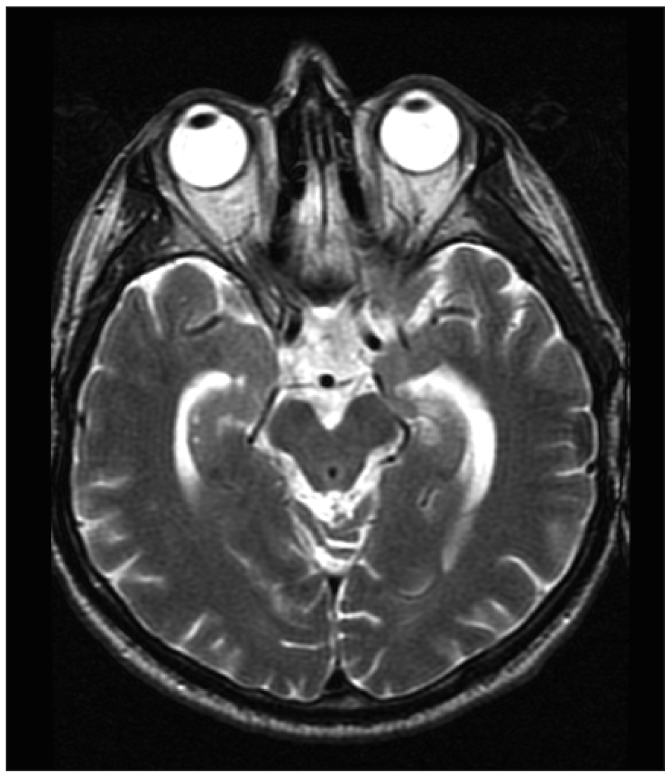

Figure 4: *T2-weighted axial image post-CT-guided C2 epidural blood patch shows resolution of the extra-axial collections, as well as complete resolution of the crowding of the perimesencephalic cisterns due to parenchymal crowding at the level of the tentorial hiatus.*

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Table: Summary of laboratory and radiological findings in Spontaneous Intracranial Hypotension (CSF Hypovolemia) Syndrome

Diagnostic Modality	Reported findings
CSF studies[18,34]	Opening pressure may be decreased, normal or elevated Mildly elevated protein (95%) Elevated erythrocyte count (86%) Pleocytosis (59%) usually 6-50 cells/mm^3, lymphocytic predominance
Brain MRI[2,3,5,9,25,26,28,35]	Subdural fluid collections Diffuse pachymeningeal enhancement secondary to engorgement of dural bridging veins (usually with leptomeningeal sparing) Engorgement of venous sinuses Pituitary gland enlargement or hyperemia Downwards displacement of cerebellar tonsils or brain sagging Narrowed lateral ventricles and cisternal effacement *Severe cases:* brainstem herniation and diencephalic compression
Spine MRI[4,6,9,36]	Dural enhancement Spinal hygromas Meningeal diverticuli Dilation of cervical epidural/ intradural veins Dilation of anterior internal vertebral plexus (T2 band of hypodense dura hyperdense CSF and hypodense extradural collection) CSF fluid extravasation into paravertebral tissues (extra axial gadolinium collection)
CT / MRI Myelogram[2,4]	Epidural extravasation/ collection of contrast at location of CSF leak Abnormal root sleeve anatomy (cysts, spurs, etc).
Radionuclide Cisternography[3,7,28,35]	Decreased radioactivity reaching brain convexities Rapid elimination of isotope from CSF & early appearance in bladder Soft tissue uptake of isotope Leak visualization
Dural / subdural biopsy[37]	Non-inflammatory reactive changes Organized hygromas comprised of fibroblasts, thin-walled blood vessels and amorphous matrix.

and blood stasis may preferentially interrupt frontotemporal circuits resulting in dysfunction. The Table summarizes the laboratory and radiological findings of SIH described in the current literature (See Paldino et al (2003), & Schievink (2006) for a comprehensive review).

The treatment of some cases of SIH can prove challenging. A two-month trial of conservative management comprised of bed rest and hydration, analgesics, caffeine and theophylline, in mild cases of postural headaches without disabling neurological symptoms has been recommended by some[5,9,28,29], with a success rate of less than 30% reported[28]. There has only been one previously published case report of a patient with SIH who presented with chronic daily headache and neuropsychiatric features of FTD[27]. Following a four-month course of steroids, some improvements were noted in the patient's personality, cognition and MRI findings. However, the use of steroids in such cases is controversial, improvements are usually limited to resolution of headache and mild neurological symptoms[30]. Given the non-inflammatory etiology of SIH, attributing such improvement to steroids is questionable[3,30]. Further, in the published cases of steroid use in SIH[27,30], insufficient efforts were made to identify a CSF leak site, even after the use of ITSI. It is conceivable that, in rare instances, symptoms may plateau or even resolve spontaneously depending on the size, dynamics and location of the CSF leak. It is unlikely that steroid treatment alone will provide definitive treatment in most severe cases as the one reported here.

Failing conservative medical management, one should consider the use of an epidural blood patch to seal dural CSF leaks[5,9,10,19,28,29,31,32]. The proposed mechanism for the efficacy of blood patching is two fold: an initial displacement of the dura towards the spinal cord moves peri-spinal CSF into cranium, thus immediately increasing intracranial CSF volume, pressure and buoyancy forces; and later, as blood coagulates at the leak site, further CSF loss is prevented. Variation exists in the site of blood patch administration, however targeted patches are theoretically and therapeutically more effective. Cousins et al reported a 57% response rate to blind lumbar epidural blood patches in patients with SIH[10], whereas Chung et al report an 80% success rate of guided epidural blood patch at the site of a single CSF leak[28]. Therefore, a large volume (20 to 60 cc) targeted blood patch of a demonstrated CSF leak is recommended. Recurrence of neurological symptoms is usually a consequence of insufficient volume, failure of formation of a dural plug, incorrect leak site identification, or the presence of multiple leaks.

When a CSF leak site is not identified, an intrathecal saline infusion can be administered to aid in diagnosis. The likelihood of successfully identifying a precise leak is significantly increased with the expanded CSF volume, as witnessed in our case and two previously published cases of encephalopathy, obtundation and/or coma secondary to SIH[11,21]. Similarly, ITSI can be used to provide temporary treatment when neurological symptoms and level of consciousness are deteriorating. The importance of accurate diagnosis and knowledge of the procedural options available to treat SIH can result in a life saving intervention.

Neurosurgical procedures have a specific role in the treatment of a minority of cases of SIH. The surgical evacuation of subdural hygromas is a common treatment; however, since the subdural collections are a compensatory mechanism for the low CSF volume, they invariably recur. Large subdural hygromas causing symptomatic cerebral compression and caudal brain herniation may require urgent surgical decompression in conjunction with epidural blood patching of the CSF leak. Other neurosurgical options such as surgical ligation of a dural tear on a spinal nerve root sleeve, repair of leaking diverticuli or ruptured Tarlov cysts, and removal of causative bony lesions (i.e. bone spurs) deserve consideration in refractory cases[3,5,11-13]. Ong et al also described a leak at the C1-C2 level in a patient with SIH[33]. Lumbar epidural blood patching failed in this patient, necessitating surgical repair of the leak with epidural muscle packing and fibrin glue injection; however, no targeted cervical epidural blood patch (EBP) was attempted. One other case of a targeted EBP for a C1-C2 CSF leak site has been reported to date; however, in this case the patch was introduced at the C4 level, below the leak site, and was repeated twice before the patient achieved symptomatic improvement[32].

Our understanding of the syndrome of "spontaneous intracranial hypotension" has evolved. There is much evidence to support that the clinical presentation and pathophysiological mechanism of this syndrome results from the dynamics of an

existing CSF leak and resultant CSF hypovolemia. Patients may present with postural headaches and a variety of other neurological symptoms depending on the neuronal structures that are disrupted, stretched or compressed. It is important to consider this diagnosis in cases of unexplained rapidly progressing frontotemporal dementia, encephalopathy, obtundation and even coma. When identification of the CSF leak site is difficult or if the patient is rapidly clinically deteriorating, an intrathecal saline infusion can be utilized to increase diagnostic yield and improve clinical symptoms. The definitive treatment of choice in these patients is a targeted large volume epidural blood patch to the site of the CSF leak. With early diagnosis and appropriate treatment, neurological symptoms and imaging abnormalities are reversible and complete recovery can be achieved.

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