Spontaneous intracranial hypotension syndrome: a novel speculative physiopathological hypothesis and a novel patch method in a series of 28 consecutive patients

Clinical article

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Object. Spontaneous intracranial hypotension (SIH) is a potentially serious pathological syndrome consisting of specific symptoms and neuroradiological signs that can sometimes be used to assess the efficacy of the treatment. In this paper the authors report a series of 28 patients with this syndrome who were all treated with an epidural blood patch at the authors' institution. The authors propose a novel physiopathological theory of SIH based on some anatomical considerations about the spinal venous drainage system.

Methods. Between January 1993 and January 2007, the authors treated 28 patients in whom SIH had been diagnosed. Twenty-seven of the 28 patients presented with the typical findings of SIH on brain MR imaging (dural enhancement and thickening subdural collections, caudal displacement of cerebellar tonsils, and reduction in height of suprachiasmatic cisterns). The sites of the patients' neuroradiologically suspected CSF leakage were different, but the blood patch procedure was performed at the lumbar level in all patients. The patients were then assessed at 3-month and 1- and 3-year follow-up visits. At the last visit (although only available for 11 patients) 83.3% of patients were completely free from clinical symptoms and 8.3% complained of sporadic orthostatic headache.

Results. The authors think that in the so-called SIH syndrome, the dural leak, even in those cases in which it can be clearly identified on neuroradiological examinations, is not the cause of the disease but the effect of the epidural hypotension maintained by the inferior cava vein outflow to the heart. The goal of their blood patch procedure (a sort of epidural block obtained using autologous blood and fibrin glue at the L1-2 level) is not to seal CSF leaks, but instead to help in reversing the CSF-blood gradient within the epidural space along the entire cord.

Conclusions. The authors' procedure seems to lead to good and long-lasting clinical results. (*DOI: 10.3171/2009.6.JNS09415*)

Key Words • orthostatic headache • spontaneous intracranial hypotension • blood patch

The spontaneous or idiopathic CSF hypotension (also known as SIH) syndrome is characterized by specific symptoms and specific neuroradiological patterns. The most common symptom is orthostatic headache (which is relieved when the individual lies down), and is often associated with nausea, vomiting, dizziness, diplopia, photophobia, hearing impairment, neck stiffness, and blurred vision.⁸ Brain MR imaging findings include intracranial pachymeningeal thickening and postcontrast enhancement, subdural fluid collections, and hematomas (possibly leading to severe neurologi-

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cal impairment with a decreased level of consciousness and acute deterioration)² and downward displacement of the cerebellar tonsils or "sagging" of the brain.^{7,8,11} Another 2 MR imaging patterns that were recently noted in such patients are the increased mean diffusivity (on MR imaging diffusion studies), associated with swelling, in the diencephalic-mesencephalic structures draining into the cerebral deep venous system, and the decrease of the angle formed by the vein of Galen and straight sinus.¹³

In most patients a true CSF leak between the subarachnoid and subdural spaces occurring at 1 or more spinal levels through dural tears is demonstrated by spinal MR imaging, myelo-MR imaging, myelo-CT scanning, and/or radioisotope myelocysternography.⁸

Abbreviation used in this paper: SIH = spontaneous idiopathic hypotension.

Many patients with idiopathic CSF hypotension actually improve spontaneously without any treatment,⁸ and others require a blood patch.^{3,18} The current treatment for patients who do not exhibit any CSF leakage (and thus addressed as being affected by spontaneous CSF hypotension syndrome) consists of an introduction of 10–30 ml of homologous blood (blood patch) along the spinal subdural space through an epidural lumbar puncture. Such a procedure can also be applied directly at the site of the myelo-MR imaging–demonstrated leak.^{3,18} For the latter cases, surgical closure of fistulas through laminectomy has been proposed in patients in which a blood patch was unsuccessful.¹⁶

The aim of this report is to introduce a new hypothesis concerning the origin and physiopathology of the so-called spontaneous CSF hypotension. This hypothesis is based on anatomical and physiopathological considerations about the venous drainage system of the spinal cord. Taking into account these observations, a novel blood patch method is proposed, and a consecutive series of 28 treated patients are reported.

Physiopathological Hypothesis

The etiology of SIH is still poorly understood, and the mechanisms that provoke a spontaneous dural leak and/or CSF hypovolemia are still speculative. The postulated hypothesis is based on the current knowledge of the anatomy and physiology of the epidural veins as well as the observations made in a consistent series of patients with SIH described in this report.

Venous drainage of the spinal epidural space is served by 2 main anatomical complexes. The upper thoracic plexiform venous network drains into the superior vena cava system via the radicular veins. Below L-2, the lumbar epidural venous network drains into the inferior vena cava system via a network of large radicular veins. These 2 systems communicate at the thoracolumbar junction.

Antireflux venous valves protect the spinal cord from the high-pressure venous waves of the vena cava system. A continuously modified equilibrium is established between forces that generate venous return to the heart and those that oppose it. The most constant factor opposing venous return is hydrostatic pressure related to gravity. Inversely, certain other forces, such as erect posture or the pumping of the heart during diastole tend to aspirate venous blood. Overall, venous blood flow varies according to the various phases of breathing and posture.

Movement of venous blood tends to obey a single law: the pressure gradient law. This pressure gradient can change at any time based on the diameter of the vessel, the position of the limbs, the phase of respiratory cycle, and posture. At rest, in the middle phase of respiration, blood flow is at its greatest in the deep venous network. Blood is aspirated from smaller veins toward the deep venous network, and venous valves are opened. Venous blood flow decreases during a respiratory pause. Depending on the posture and the presence of an effort with even slight apnea, this pressure gradient is reduced or reversed and the valves close.

The inferior vena cava system is much more affected

by these dynamic modifications than the superior vena cava system due to the strong muscle pump of inferior limbs, which tends to displace a large amount of blood toward the heart during standing and walking. The venous pressure within the inferior cava vena system becomes negative due to the heart aspiration and inferior limb muscles pumping during walking and orthostatic posture.

Negative pressure within the inferior cava vein will then result in overdrainage of venous blood from the epidural spinal vein network via large lumbar collectors through 1-way valves. A decrease in spinal epidural pressure and a decrease in volume of the epidural veins result in modification of the epidural gradient between epidural space pressure (negative) and CSF pressure (positive in orthostatic conduction). This modification results in aspiration of CSF into the epidural space and veins. Existing arachnoid diverticula at the origin of spinal roots from the spinal dural sac may facilitate the generation of actual CSF leakage between the CSF compartment and the epidural venous network. The CSF aspiration may be more common when radicular cysts are present. The suggested mechanism may also explain the developing of CSF hypotension syndrome without neuroradiological evidence of visible CSF leaks; in fact, the aspiration mechanism may act diffusely on the dural surface and at the origin of spinal roots with a considerable outflow of CSF from the subarachnoid compartment to the radicular veins.

When an individual lies down the reduced CSF volume fills the ventricles and the spinal sac appears empty while the epidural veins appear enlarged to balance the loss of content of the spinal cavity. This hypothesis suggests that the origin of CSF hypotension is due to the lowering of venous pressure within the inferior vena cava system, which in turn causes epidural hypotension and outflow of CSF along the entire spinal cavity. Moreover, the low venous pressure within the inferior vena cava system is amplified by the muscles pumping blood from the periphery to the major venous trunks during standing and walking. The high venous flow within the vena cava vein may provoke blood aspiration from the smaller tributary veins. This mechanism may be responsible for a further blood outflow from the lumbar epidural veins during walking and standing and, thus, for worsening of epidural hypotension (Fig. 1). These considerations led us to introduce a novel method to treat thoracic and cervical spontaneous CSF loss in patients with severe signs of CSF hypotension.

Our procedure is aimed to lead to a stable rise in epidural pressure and to disconnect the low-pressure epidural lumbar venous network supplied by the inferior vena cava vein from the epidural thoracic and cervical venous network supplied by the superior cava vein. In other words, our technique is designed to provoke a marked rise in epidural pressure to reverse the CSF-hematic gradient, thus removing the main etiopathogenetic factor that is, in our opinion, the epidural hypotension maintained by the epidural venous drainage through the inferior vena cava system.

Spontaneous intracranial hypotension treated using a blood patch



Fig. 1. Illustrations. A and B: Depictions of the inferior vena cava system and direction of venous blood flow in our venous aspiration model of the spinal epidural space. C: The site of blood patch procedure is shown in *red* at the right side of the picture. Also note the inversion of direction of blood flow of cervicothoracic segmental epidural veins toward the superior cava system induced by blood patch. *Blue arrows* indicate the direction of the venous blood flow.

Methods

Treatment Technique

In our procedure, 5 ml of fibrin glue is mixed with 5 ml of homologous blood and 3 ml of hydrosoluble contrast medium. The resulting viscous compound is then injected into the epidural space at L1-2 level under fluoroscopic control with the patient lying prone. The epidural needle connected to a syringe filled with saline solution is left in place for a few minutes to balance the epidural pressure with the atmospheric pressure (~ 15-20 ml of saline is usually aspirated spontaneously within the epidural space). Then the compound is injected by applying moderate pressure under fluoroscopic guidance. The syringe is then rapidly removed to maintain the inner pressure above the atmospheric one. After the procedure, CT scanning is performed to confirm the filling of the epidural space at the chosen levels (Figs. 2 and 3). The patient is then allowed to stand and walk freely 24 hours after the procedure, and he or she can be discharged from the hospital (without behavioral limitations) a few days later.

Patient Series

Between January 1993 and January 2007, we treated 28 patients who were admitted with a diagnosis of SIH. There were 18 female and 10 male patients with a mean age of 50 years (range 15–66 years). The typical findings were present on brain MR imaging in 27 of 28 patients. These findings consisted of dural enhancement and thickening (18 patients), subdural collections (15 patients) (Figs. 4–6), caudal displacement of cerebellar tonsils



Fig. 2. A sagittal spinal CT reconstruction showing the presence of hydrosoluble contrast medium (injected together with autologous blood and fibrin glue) in the posterior spinal epidural space, thus confirming a correctly performed segmental blood patch procedure aimed to collapse the epidural veins.

(11 patients), and reduction in height of suprachiasmatic cisterns (4 patients). The sites of neuroradiologically suspected CSF leakage (based on evidence of irregularity or cystic appearance of the sleeves of the radicular roots) were cervical (1 patient), thoracic (5 patients), lumbar (2 patients), sacral (1 patient), cervicothoracic (5 patients), and multilevel ([> 2 levels] 6 patients). In all 28 patients the blood patch procedure was performed at the lumbar level (1 patient had previously undergone a cervical epidural blood patch procedure without any clinical benefit).

Immediate clinical improvement (evident during postprocedural hospital stay) was present in 11 patients at < 72 hours after the procedure and in 17 patients after 72 hours from the procedure. In 3 patients a second blood patch was required because the clinical symptoms recurred; these repeated procedures were all performed at the lumbar level (of these 3 patients, 1 had previously undergone a cervical epidural procedure and 2 had undergone a lumbar procedure).

Of the 28 patients, 27 were available to undergo follow-up at 3 months. Of these 27 patients, 6 (22.2%) complained of sporadic headache, 19 (70.4%) did not show any clinical symptoms, and 2 (7.4%) were clinically unchanged (still complaining of orthostatic headache). Oneyear follow-up was performed in 22 patients. Of these, 18 patients (81.8%) were completely free from clinical symptoms, 2 (9.1%) complained of sporadic orthostatic headache, and 2 (9.1%) were clinically unchanged. Fol-



Fig. 3. An axial spinal CT reconstruction also showing the presence of contrast medium in the epidural space at the lumbar level.

low-up at 3 years was performed in 11 patients; of these, 10 (83.3%) were completely free from clinical symptoms, and 1 (8.3%) complained of sporadic orthostatic head-aches.

All patients underwent serial MR imaging examinations. In 20 of 22 patients with follow-up > 6 months, the MR imaging findings were normal, showing the disappearance of the neuroradiological signs of SIH. Two patients with poor clinical outcome still presented with slight dural enhancement, but in these cases dural enhancement was noticeably less severe than before the blood patch procedure.

Illustrative Cases

Case 1

History and Examination. This 48-year-old woman came to our attention in June 2004. Her family and medical histories were unremarkable. Two months before admission to our institution she started to complain of postural headache occurring ~ 10 minutes after standing upright and disappearing after assuming the clinostatic posture. The pain was localized in the occipitonuchal region, was perceived as constraining, and worsened on physical effort. She did not have a history of previous trauma. General and neurological examinations revealed normal findings.

Brain MR imaging with Gd showed 2 subdural fluid collections at the cerebral convexities, sagging of the brain with midbrain caudal displacement, decreased size in 8 of the perichiasmatic cisterns, and downward tonsillar displacement. The postcontrast examination showed enhancement of the thickened dura along both cerebral convexities, the tentorium, and the clivus. A cervical MR image showed an epidural fluid collection between C-5 and T-1.

Treatment. The patient was treated conservatively with bed rest, hydration, and low doses of steroids (4 mg/



Fig. 4. Axial T2-weighted brain MR images obtained in a patient before *(left)* and after *(right)* the blood patch procedure. Note the disappearance of the subdural collection of both cerebral convexities.

day of dexamethasone for 1 month). After 1 month of bed rest, the headache improved and the patient was able to stand upright with no subsequent clinical disturbances. A brain MR imaging examination obtained at this time showed a volumetric increase in the subdural collection in the left convexity. Further investigations (CT myelography, MR imaging myelography, and radioisotope myelocysternography) demonstrated that the site of the leak was located at the thoracic level between T-1 and T-2. The patient was then treated with a blood patch introduced by 5 ml of fibrin glue, blood, and hydrosoluble iodine contrast medium into the lumbar epidural space between L-1 and L-2. The procedure was well tolerated, and the next day she was discharged from the hospital. She was placed on a regimen of bed rest (\geq 3 weeks), hydration, and no physical activity until the next follow-up visit.

Posttreatment Course. At the next follow-up visit (September 2004), 2 months after the procedure, the patient was completely free from headache. Brain MR imaging studies showed a subtle reduction of the subdural hematoma on the left convexity; the enhancement of dura was still present on the left but markedly reduced on the right. Brain MR imaging performed in December 2004 (her latest clinical follow-up visit) showed complete regression of the convexity's subdural hematomas, the absence of dural enhancement, a normal height of the interpeduncular cistern, and normal positioning of the cerebellar tonsil. The only change on the images was a persistent slight volumetric reduction of the perichiasmatic cisterns. A phone interview performed in December 2006 disclosed that the patient was still free of headache, had returned to her job, and had returned to physical activities.

Case 2

History and Examination. This 55-year-old woman came to our attention in March 2001. Her family and medical histories were unremarkable. One month before admission to our institution, she started complaining of constraining headaches localized in the occipitonuchal region that worsened after physical exertion. Two weeks



Fig. 5. Coronal T1-weighted brain MR images obtained in a patient before *(left)* and after *(right)* the blood patch procedure. Note the disappearance of meningeal thickening and contrast enhancement, which was also present at the falcine level.

after symptom onset she noted that the headache was absent while resting in bed and that it appeared ~ 1 hour after assuming an orthostatic position; she also started complaining of hearing impairment and dizziness. She did not report any previous trauma, and her general and neurological examinations revealed normal findings.

Brain MR imaging showed the presence of subdural fluid collections along both cerebral convexities and the tentorium; other sites of dural detachment were present along cerebellar convexities, the falx, and the clivus. The post-Gd MR imaging study revealed enhancement of the thickened dura.

A spinal myelo-MR imaging study showed an irregularly shaped dural root sleeve at the level of C-7 on the left. The patient was sent home and placed on a regimen of bed rest for ≥ 1 month, hydration, and low doses of steroids for 1 month. After ~ 2 weeks of such treatment, her dizziness and hearing impairment disappeared.

The subsequent neuroradiological evaluation (May 2001) showed only the presence of a slight subdural collection along the left frontoparietal convexity. Two additional cerebral MR imaging examinations (November 2001 and September 2002) revealed normal findings.

Treatment. In January 2003 the patient began again to complain of postural headache and dizziness; the headache started to limit her daily activities and she had to leave work. She was again admitted to our institution in February 2003, and brain MR imaging was performed, which revealed a recurrence and a worsening of the previously described radiological pattern (presence of subdural collections along both cerebral convexities, the tentorium, and the falx, caudal displacement of brainstem structures, and flattening of the interpeduncular cistern and basal cisterns) together with an enlargement of the epidural spaces along the upper spinal cervical tract. Myelo-MR imaging and myelo-CT scanning studies showed the presence of a radicular cyst at T-9 on the left, suggesting that this was the site of the CSF leak. The patient was treated with a blood patch, which was well tolerated. The day after the procedure she was discharged from the hospital and placed on a regimen of bed rest for 3 weeks, hydration, and no work or physical activity.

Posttreatment Course. At the first follow-up visit (October 2004), 6 months after the procedure, the patient



Fig. 6. Coronal FLAIR brain MR images showing a bilateral subdural fluid collection extending along the subdural falcine space *(left)*. The fluid is no longer present after the blood patch procedure *(right)*.

was completely free from headache, and brain MR imaging showed improvement of the previously described neuroradiological pattern. At the second follow-up visit (December 2006) she was still free of headache and resumed her job and physical activities.

Case 3

History and Examination. This 49-year-old woman first came to our attention in May 2003. One month before admission she started to complain of headache localized in the occipitonuchal region; as with the other cases, it was present when she was standing and was relieved by lying down. Her family and medical histories were unremarkable for any kind of general or neurological pathological condition, and general and neurological examinations revealed normal findings. Brain MR imaging showed dural thickening and enhancement along the cerebral convexities and tentorium. Spinal myelo-MR imaging showed a radicular cyst at the S-2 level on the left and at the T11-12 level on the right. A subsequent radioisotope myelocysternography study confirmed the presence of multiple radicular cysts, the largest one at T-12 on the right.

Treatment. The patient was treated with a blood patch. The procedure was well tolerated, and the next day she was discharged from the hospital. One week after the procedure the patient was free from headache. A brain MR imaging study performed 2 months later revealed a regression of the pathological radiological pattern, except for the persistence of a slight thickening of the dura along the tentorium.

Posttreatment Course. At the last follow-up (November 2006) the patient was completely free from headache, and the last brain MR imaging study performed in January 2005 showed no signs of CSF hypotension.

Discussion

Intracerebral CSF hypotension (either idiopathic or presumably derived from neuroradiologically demonstrable dural cysts, or from real loss of CSF) results from low CSF volume. The postlumbar puncture is the most frequent form and is attributable to leakage of CSF from the hole made in the dura by the needle. Conversely, SIH, first described by Schaltenbrand¹⁴ is rare. Earlier theories about a decreased CSF formation have never been substantiated.⁶ The majority of the spontaneous CSF leaks occur at the level of the spine, particularly at the thoracic level.¹⁰ The exact cause of spontaneous CSF leaks remains unknown, although 2 factors have been proposed as a determinant: trivial trauma and congenital weakness of the dural sac.^{1,4,9,15,17}

The cardinal clinical manifestation of SIH is orthostatic headache due to traction or distortion of various anchoring pain-sensitive cerebral structures caused by the displacement of the brain,⁵ with compensative dilation of cerebral veins and sinuses. Similarly, traction, distortion, or compression of some of the cranial nerves or brainstem and diencephalic structures have been deemed responsible for cranial nerve palsies, visual blurring, visual field cuts, brainstem-related clinical manifestations, and even stupor and coma.

This syndrome usually has a benign course; however, cases in which the patients have a reduced level of consciousness and subsequent stupor and coma (caused by diencephalic compression or by large subdural hematomas) have been reported.¹² Many patients improve spontaneously, whereas others require pharmacological or surgical treatment (if a clear point of CSF leakage is demonstrable). Bed rest has traditionally been advocated as the first-line treatment, together with hydration or overhydration, but the real therapeutic efficacy of such treatments has still not been established. Caffeine and theophylline have been demonstrated to be effective in some studies, but their beneficial effects are often temporary; some patients report a partial improvement with steroids, but a substantial and long-lasting effect is exceptional.⁸

If these therapeutic measures are ineffective and the site of CSF leak is known, an epidural autologous blood patch with fibrin glue or continuous epidural saline infusion can be attempted to stop the CSF leak by plugging the dural gap. The surgical closure of fistulas through laminectomy has been proposed in patients in whom the blood patch is unsuccessful.¹⁶

Based on our hypothesis, which could be applied even in cases in which there is no neuroradiologically demonstrable clear point of CSF leakage or spinal radicular cysts, this syndrome is derived from CSF aspiration and loss (and not necessarily by a real leakage) from the subarachnoid into the epidural space and then into the venous system (inferior vena cava system), due to the low epidural pressure created by the presence of the large 1-way valve collector veins in constitutionally predisposed individuals such as those with constitutional weakness of dura or those with multiple subarachnoidal microdiverticula. We think that the dural tear, even when clearly identified, is not the cause of the disease but the effect of the epidural hypotension maintained by the inferior cava vein outflow to the heart. Furthermore, the presence of a radicular cyst demonstrated on myelo-MR imaging studies does not necessarily correlate with a definite CSF leak at that level. The goal of our blood patch procedure is not to seal CSF leaks (in fact the epidural blood patch is always placed in the epidural lumbar space, even when the radiologically evident radicular cyst is not at the lumbar level), but in-



Fig. 7. Sagittal *(upper)* and axial *(lower)* spine CT reconstructions showing the presence of air in the spinal lumbar posterior epidural space, as a consequence of air aspiration (following epidural puncture) due to a strong negative epidural pressure.

stead to help in reversing the CSF-blood gradient within the epidural space along the entire cord. Our procedure, an epidural block of sorts obtained with the use of autologous blood and fibrin glue at the L1–2 levels, seems to lead to good and long-lasting clinical results.

A question may arise regarding the long-lasting effect of the described procedure despite the unavoidable phenomenon of resorption of the injected compound over time. To address this topic, one must remember that a certain number of less severe SIH syndromes may recover only with bed rest and hydration. In our opinion, the acute restoration of the physiological gradient between epidural and intrathecal pressures removes the actual cause of CSF outflow, allowing for stable recovery in a similar way as it would happen with conservative measures alone; moreover, the temporary absence of flow through the dural leak or through the dura itself may allow tissue reparation and remodeling. It must be mentioned that in this syndrome the dura mater can show rapid structural modifications as demonstrated by the appearance and disappearance of contrast enhancement on MR imaging (Fig. 5).

Moreover, at the L1–2 levels there is no risk of damaging the spinal cord, and the radicular compression by the injected fibrin glue may be easily avoided if one is aware of the eventual occurrence of radicular pain or numbness during the injection. Regardless, this event did not occur in any case treated with a blood patch at our institution, perhaps because of the fluid consistency of the injected compound during the epidural administration, facilitating its laminar diffusion within the epidural space.

The following remarks reinforce our aforementioned etiological hypothesis: 1) In most of our patients the clinical and brain MR imaging findings of the disease disappeared after the procedure, and postural headache disappeared immediately in 1 case despite a quick return to upright posture. 2) The hydrosoluble iodine contrast-injected CT scans obtained immediately after the procedure confirmed the filling of a considerable portion of the lumbar epidural space by the blood-fibrin glue compound. 3) In our cases a marked negative epidural pressure was measured at the injection site with the patient lying down $(-10 \text{ cm H}_2\text{O})$ and volumes up to 10 ml of air or saline solution were aspirated from the epidural space in 2 and 3 seconds, respectively (the same aspiration mechanisms, we believe, as on the dural surface in the closed system) (Fig. 7).

We are aware that the number of cases is not sufficient to confirm our etiopathogenetic hypothesis about the origin of the so-called spontaneous CSF hypotension syndrome, and we deemed the only procedure that could effectively demonstrate it (that is, invasive measurement of the venous pressure in the vena cava system) not to be ethically correct to perform. Nevertheless, as it is believed to act on the aforementioned actual etiological factors of SIH (and then, independently from the radiologically evident point of an evident CSF leakage), we consider the proposed procedure a safe method that should be considered before attempting a direct surgical procedure or before undertaking the more dangerous epidural puncture at a thoracic or cervical level with the aim to seal topically the CSF fistulas (that is to say, aimed to act on the pathogenetic and not on the etiological moment of the disease).

Conclusions

We believe that the blood patch method leads to good and long-lasting clinical results in patients with SIH.

Disclaimer

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

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