Novel hydrogel application in minimally invasive surgical approaches to spontaneous intracranial hypotension

Report of 2 cases

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The authors report 2 cases of orthostatic headaches associated with spontaneous intracranial hypotension (SIH) secondary to CSF leaks that were successfully treated with an alternative dural repair technique in which a tubular retractor system and a hydrogel dorsal sealant were used. The 2 patients, a 63-year-old man and a 45-year-old woman, presented with orthostatic headache associated with SIH secondary to suspected lumbar and lower cervical CSF leaks, respectively, as indicated by bony defects or epidural fluid collection. Epidural blood patch repair failed in both cases, but both were successfully treated with the minimally invasive application of a hydrogel dorsal sealant as a novel adjunct to traditional dorsal repair techniques. Both patients tolerated the procedure well. Moreover, SIH symptoms and MRI signs were completely resolved at 1-month follow-up in both patients.

The minimally invasive dorsal repair procedure with hydrogel dorsal sealant described here offers a viable alternative in patients in whom epidural blood patches have failed, with obscure recalcitrant CSF leaks at the cervical as well as lumbar spinal level. The authors demonstrate that the adjuvant use of sealant is a safe and efficient repair method regardless of dorsal defect location.

KEY WORDS • cerebrospinal fluid leak repair • dural repair • DuraSeal • hydrogel • spontaneous intracranial hypotension • orthostatic headache • surgical technique

Abbreviations used in this paper: EBP = epidural blood patch; SIH = spontaneous intracranial hypotension.

S PONTANEOUS intracranial hypotension (SIH) due to a spinal CSF leak is an uncommon cause of new daily persistent positional headaches. The estimated incidence of SIH is 5 per 100,000.28 Women are primarily affected, with a female/male ratio of approximately 1.5:1 and a peak incidence at the age of approximately 40 years.29,32 However, SIH remains a commonly misdiagnosed disorder.28 Patients with SIH most commonly present with orthostatic headache that improves with recumbency.29 Highly specific findings on MRI include subdural fluid collections, intracranial pachymeningeal enhancement, engorgement of intracranial veins, reduction in height of suprachiasmatic cisterns, and downward displacement of cerebellar tonsils.

Traditionally, SIH is initially managed by a conservative approach consisting of bed rest, oral hydration, generous caffeine intake, corticosteroids, theophylline, and the use of an abdominal binder.30 When symptoms persist, interlaminar epidural blood patches (EBPs) or the injection of autologous blood into the spinal epidural space are the gold standard for SIH, and can be repeated as needed.3,5,21,24,35 Despite being the gold standard, EBPs have a reported failure rate of 23%–44%.4 When the aforementioned treatments fail, approaches such as directed EBP or percutaneous placement of fibrin sealants have been reported to be successful,15,33 but these approaches require that the surgeon know the exact location of the CSF leak, which more often than not is difficult to identify.28,31 Otherwise, except for invasive surgical repairs, limited therapeutic options remain.
We report 2 cases of SIH caused by spinal CSF leaks that were successfully treated with minimally invasive applications of DuraSeal (Covidien, Inc.), a hydrogel widely used as an adjunct to dural repair in incidental durotomy in lumbar spine surgeries. In the first case, DuraSeal was injected into the ventral surface of the spinal cord via a minimally invasive tubular retractor. In the second case, also via a tubular retractor, a small piece of subcutaneous muscle was placed on the suspected origin of the CSF leak, and then DuraSeal was sprayed through the retractor. In both cases, the patients had previously undergone 2 traditional EBPs without improvement of their symptoms, but recovered fully after the minimally invasive procedures with the application of DuraSeal.

Case Reports

Case 1

History. A 63-year-old man presented with a 2-month history of orthostatic headache with decreased hearing on the left side, both with acute onset brought on by a Valsalva maneuver during a colonoscopy procedure. An MRI study of the brain showed features consistent with SIH: subdural fluid collections, vein engorgement, collapse of ventricles (Fig. 1A), pachymeningeal enhancement (Fig. 1B), sagging brain (Fig. 1C), and pituitary hyperemia. Furthermore, an MRI study of the spine revealed a small amount of extradural fluid ventral to the thecal sac from L-2 to L-5, which was suspect for a dural leak (Fig. 2). Based on the MRI criteria, the diagnosis of SIH was made.

Given the severity of symptoms, with no response to conservative therapy of bed rest and hydration, 2 consecutive EBPs were attempted in which 20 ml of autologous blood were infused into the epidural space at L4–5. The patient's hearing improved and positional headache subsided briefly after the first EBP, but returned to initial levels, with radicular pain radiating down the left leg. The EBP was subsequently repeated but provided no additional relief of symptoms. The patient's condition worsened, with more generalized headache, and additional symptoms including dizziness, loss of balance, and sensitivity to light and sound. An MRI study of the brain after the second EBP showed persistent features of SIH seen in the previous study, and a more pronounced right subdural hygroma (Fig. 1A).

To localize the site of the spinal CSF leak, a CT myelogram of the cervical, thoracic, and lumbar spine with intrathecal contrast was performed, but results showed no evidence suggestive of a CSF leak except for a filling defect at the L5–S1 level and a small amount of extradural fluid ventral to the thecal sac from L-2 to L-5. The decision was made to proceed with a minimally invasive dural sealing closure, ventral to the spinal cord.

Operative Technique. Tubular retractors were used to dock on the right L-5 lamina: a high-speed matchstick drill was then used to perform the laminotomy at the L-5 level, and Kerrison punches were used to remove the ligamentum flavum, with subsequent exposure of the dura mater. On exposure and inspection of the meningeal layer no obvious CSF leak was evident, but there was extensive scarring on the exiting nerve root, presumably from previous blood patches and epiduals. Despite completion of a Valsalva maneuver with tilting in the reverse Trendelenburg position, an active intraoperative spinal CSF leak was not identified. At this point, 5 ml of dural sealant (DuraSeal) were advanced into the ventral epidural space by using a bent Tuohy spinal needle for better access into the narrow ventral epidural corridor (Fig. 3A). An EBP in which the patient’s blood was used was then placed; approximately 20 ml of blood patch was applied directly onto the theca in the epidural space via the tubular retractor (Fig. 3B and C).

Postoperative Course. Five days after surgery, the

Fig. 1. Case 1. Magnetic resonance images obtained before (left) and after (right) treatment; characteristic MRI findings of SIH. A: Subdural fluid collection. Axial T1-weighted Gd-enhanced fat-saturated images revealing a right subdural hygroma (arrow), engorgement of superior sagittal sinus (arrowheads), and collapse of ventricles (ovals). B: Pachymeningeal enhancement. Axial T1-weighted Gd-enhanced fat-saturated images revealing thickening and enhancement of pachymeninges (arrowheads). C: Sagging brain. Sagittal T1-weighted images showing obliteration of preopticine cistern (arrows) and flattening of pons (arrowheads).
patient reported being almost completely relieved from headache but complained of right hip pain, radiating down the posterior aspect of the leg, with mild weakness. Despite the pain he was ambulating well, with sufficient pain control under Percocet. In a follow-up visit at 2 weeks postsurgery, the right hip pain persisted but was significantly improved; it was now associated with slight numbness. Ambulating with a cane for added support and taking Lyrica for pain relief, the patient only reported mild occasional headaches. An MRI study of the brain obtained 1 month after the procedure showed near complete resolution of previous right subdural hygroma, complete resolution or improvements of pachymeningeal enhancements at various regions, and restoration of the ventricle size (Fig. 1). Six weeks after surgery, the patient reported being headache free, with no other symptoms and almost complete alleviation of radiculopathy symptoms.

Case 2

History. A 45-year-old woman presented with a 1-month history of orthostatic headache associated with nausea, vomiting, dizziness, left-side hearing loss, and tinnitus, which were relieved by lying down but not by hydration or metoclopramide injection. The MRI findings of the brain and spine such as dural enhancement of the posterior fossa as well as epidural enhancement in the ventral cervical spine and dorsal thoracic spine were consistent with intracranial hypotension due to a CSF leak.

The patient had undergone 2 EBPs with no relief of symptoms. To better investigate the location of the leak, fluoroscopy-guided lumbar puncture and CT myelography of the cervical, thoracic, and lumbar spine with intrathecal contrast were performed (Fig. 4A and B). Findings from the CT myelogram revealed a long extraarachnoid collection of contrast anterior to the spinal cord, spanning from C-3 through T-3, that was compatible with a CSF leak (Fig. 4C), but there was no defined channel to localize the exact site of contrast leakage. However, 2 identified osteophytes at the T1–2 and C7–T1 levels were considered potential leakage sites.
Hydrogel dural repair for spontaneous intracranial hypotension

Operative Technique. A decision was made to proceed with a right C6–7, C7–T1 minimally invasive posterior laminotomy and repair of the CSF leak. A 3-cm incision was made, and a tubular retractor was docked on the right C6–7 and C7–T1 facet joints. The high-speed drill was used to perform a laminotomy and foraminotomy at C6–7 and C7–T1. Particular attention was paid to preserving the facet joints and ensuring stability. Ligamentum flavum was removed with Kerrison punches. The C-7 and C-8 nerve roots were exposed following foraminotomy. Although no punctate hole was visualized on exposure of the dura mater, visualization of clear fluid following a Valsalva maneuver was suspect for a CSF leak, with thinned areas of dura representing potential breach sites and subsequent CSF leak. Small pieces of muscle harvested from the subcutaneous trapezius were placed as dural grafts onto these areas of thin meningeal lining, and dural sealant was sprayed to cover all aspects of the C-7 and C-8 nerve roots and the exposed dura to prevent any further postoperative CSF leak (Fig. 5).

Postoperative Course. At 1-week follow-up, the patient’s symptoms improved considerably but had not resolved completely. She reported decreased tinnitus in both ears, with decreased occasional pressure-like headaches that were exacerbated by bending over, and required Tylenol for relief. Otherwise, no headaches were noted in the upright position and normal ambulation was duly noted on examination. At 1-month follow-up, the patient’s symptoms were greatly improved. She reported feeling very well, and denied headaches other than the occasional pressure-like sensation noticed over a period of a few seconds, with subsequent complete dissipation.

Discussion

Delivery mode and access route to the exact CSF leak site are of particular importance in achieving a successful repair with the EBP technique. Despite being the gold standard in the treatment of SIH secondary to spinal CSF leaks, EBPs have a reported failure rate of 23%–44%. For patients in whom the traditional EBP attempt fails, a few minimally invasive options remain, such as directed EBP, intrathecal fluid infusion, and fibrin glue injection, which have been reported to be successful. However, these approaches require the exact location of the CSF leak, which in some cases such as the 2 described here, cannot be precisely identified despite advanced imaging studies. For instance, preoperative spinal MRI studies may yield false localizing signs such as fluid collections in the cervical region preventing...
adequate management or delaying diagnosis, with subsequent rapid neurological decline. Thus, some authors advocate for an early intervention, with the diagnosis solely based on the classic constellation of symptoms. Also, CT myelogram studies are often used preoperatively to localize the leakage site and identify associated bony defects, but as in our cases, although these findings may provide clues on suspected sites of leakage, they lack specificity.

Even with successful localization of leak sites and the use of intraoperative 3D CT myelography, the targeted delivery of EBP or alternative sealing materials such as DuraSeal and fibrin glues to the site of a dural defect may remain a challenge. Although some case reports describe the efficiency of fibrin glue in repair procedures of the spinal dura, the viscous nature of the fluid makes delivery difficult, requiring the use of a catheter rather than a spinal needle. The higher flexibility of the catheter allows closer access to the leak site; in cases with obscure ventral leaks, such as the first case described, the spinal needle can be advanced more easily through the narrow corridor obtained through a foraminotomy and/or laminotomy and with minimal risk, offering a safer and more efficient delivery method than the catheter. For EBP, even with successful localization of leak sites, repetitive directed EBPs might be required to achieve complete symptom alleviation due to multilevel or recurrent CSF leaks.

On the other hand, in the 2 reported cases, we show that a precise delivery site is not required for optimal outcome when using DuraSeal as an adjunct to EBP via a tubular retractor. Regardless of the different hypotheses on the pathophysiological mechanisms of SIH and the etiological role of spinal CSF leaks, sealing the dural defect remains the necessary component in the management of this syndrome. Beyond just the simple prevention of CSF egress through a tamponading effect, the EBP most likely acts through local irritation and induction of dural fibrosis, thus placing additional pressure on the CSF system and producing a shift of the CSF from the spinal to the cranial compartment. Most frequently injected at the lumbar level, the autologous blood will spread over multiple levels of the spine, allegedly acting through this dual effect. The resulting blood clot will plug and seal the meningeal breach, but through this spread along the length of the spinal dura along with the volume reduction due to inherent clotting, the pressure effect will eventually dissipate, with no effective changes in intracranial pressure.

Moreover, because structural defects are seldom identified on preoperative imaging studies, sealing the breach most often implies coverage of a rather large dural surface. The epidural blood can extend up to 9 spinal segments from the site of injection; 6 segments in a cephalad direction and only 3 segments caudally. This necessitates the injection of autologous blood at the lumbar level to plug all potential defects along the spinal cord meningeal lining. Thus, to effectively restore CSF and intracranial pressure to baseline levels, we used a sealant along with the traditional blood patch, to place additional pressure on the epidural space. Although there is no direct evidence that the sealant was the effective agent in closing the leak, because both autologous blood and sealant were applied in the first case described here, additional mechanisms may come into play to restore CSF dynamics.

Overall, DuraSeal appears to be an effective adjunct in the treatment of spontaneous spinal CSF leaks, by expanding through hydration and placing constant pressure while concomitantly extending along the length of the cord through this same hydration effect. In the second case described here, the sealant alone was injected in the vicinity of the leak site, as identified by preoperative imaging studies, and potentially had an additional plugging effect. Further studies are required to answer important questions; specifically, if the effect of the dural sealant is additive to or independent of that of EBPs, and if the dural sealant can and should be used as an alternative to EBPs.

The most common complications after EBP are transient low-back pain, but rare adverse events include radicular pain, cauda equina syndrome, hematomata, and arachnoiditis. In the first case, the patient experienced left radicular pain after the first attempted EBP of 20 ml of blood, and then delayed right radicular pain after the DuraSeal procedure. All signs of radiculopathy had resolved almost completely without further intervention by 6 weeks. Similar adverse events have been reported in patients who received high-volume EBPs without DuraSeal, including an obstetric patient receiving 58 ml of blood and a nonobstetric patient who received 40 ml of blood within 24 hours. Both patients achieved complete resolution of radicular pain in 1 month without surgical intervention.

Although the causal relationship between EBP and radiculopathy is still unclear, mechanisms of radiculopathy after high-volume EBP have been speculated to be either an inflammatory response to autologous blood or mechanical compression on the nerve roots or cauda equina. In our Case 1, the initial episode of left radicular pain prior to the application of DuraSeal could be attributed to the inflammatory response to or the mechanical compression of blood. The second episode of delayed right radicular pain might raise concern about DuraSeal’s added mechanical compression as a contributing factor to radiculopathy; however, there is no direct evidence of DuraSeal’s role in this adverse event, and the symptoms could still have been caused by the sheer inflammatory response to the blood or the mechanical compression of the repeated EBPs, independent of DuraSeal. Moreover, in the second case reported here DuraSeal was applied without EBP, with no reported adverse events.

The DuraSeal dural sealant system, a polyethylene glycol hydrogel, was approved in 2005 by the US FDA as an adjunct to sutured dural repair to provide watertight closure in cranial surgery. It is now approved by the FDA as a spine sealant system that can be applied over sutures to prevent CSF leaks. When its 2 solutions, polyethylene glycol (blue solution) and trilysine amine (clear solution), are combined, they form a blue gel that can be sprayed or layered onto the site of dural repair. The hydrogel sealant remains in place for 4–8 weeks before being resorbed by the body without residue. The DuraSeal manufacturer’s insert includes a warning against applying the hydrogel in confined body spaces with neural structures in proximity, due to the hydrogel’s swelling tendency, which may create subsequent neural encroachment and compression.
The safety and efficacy of DuraSeal have been demonstrated in animal studies, a clinical study after posterior fossa craniotomy, and a clinical study in lumbar spine surgery. Nevertheless, compression of neuronal architecture caused by volume expansion of DuraSeal has been described. DuraSeal expansion is reported to have caused postoperative quadripareisis\(^5\)\(^-\)\(^8\) and postoperative cauda equina syndrome,\(^2\)\(^3\)\(^5\)\(^-\)\(^8\) in which the volume of hydrogel allegedly expanded from 3 ml to 10 ml over the course of 10 days. In a canine study, DuraSeal's volume expansion was reported to peak between Day 3 and 2 weeks after implantation.\(^9\) In this report we show the safety of DuraSeal in both ventral and dorsal spinal dural repair when injected at both the lumbar and cervical levels.

Treatment outcome may be assessed either based on symptom resolution or in conjunction with MRI assessment of persisting SIH signs.\(^4\)\(^1\) Although most patients undergoing targeted EBP placement describe almost instantaneous and complete resolution of symptoms,\(^4\)\(^1\) the durability of this symptom-free interval is of particular concern due to frequently reported recurrences.\(^4\)\(^2\) In the 2 reported cases, we observed complete resolution of symptoms and MRI signs of SIH at the last follow-up visits at 1 month and 6 weeks after the procedure.

Conclusions

Spontaneous intracranial hypotension secondary to spinal CSF leaks is a difficult-to-treat pathological entity due to inconsistent visualization of the dural defect on preoperative imaging studies. The traditional EBP most often requires exact site localization for optimal outcomes. Even so, the success rates of EBP are rather low due to certain limiting pathophysiological mechanisms. In the subset of patients with no response despite repeated EBP, closure with a tubular retractor and DuraSeal may provide a viable and safe treatment alternative.

Disclosure

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

Author contributions to the study and manuscript preparation include the following. Conception and design: Chai. Acquisition of data: Boockvar, Cobb, Mehta, Heier. Analysis and interpretation of data: Chai, Banu, Heier. Drafting the article: Chai, Banu. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Administrative/technical/material support: Boockvar, Chai. Study supervision: Boockvar.

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