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Technical notes & surgical techniques

Evaluation and treatment of spontaneous intracranial hypotension☆

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ABSTRACT

Background and purpose: Spontaneous intracranial hypotension (SIH) is a significant, treatable cause of postural headache, although the best diagnostic approach to diagnosing cerebrospinal fluid (CSF) leaks remains uncertain. The aim of this study is to evaluate the most common techniques used to diagnose leaks, the most frequent leak sites, and epidural patch treatment characteristics.
Materials and methods: We retrospectively reviewed the electronic medical records and radiographic findings of 30 patients clinically treated for SIH at a single university hospital between January 2015 and December 2016. Clinical symptoms, imaging findings and epidural patch details including dates, injection location, and amount of blood/fibrin injected were recorded.
Results: Of 30 SIH patients identified, 11/30 (37%) had a localized leak and 14/30 (47%) had a non-localized leak. The first modality to identify the leak was most commonly CT myelogram (17/25, 68%), followed by MRI spine (6/25, 24%) and MRI myelogram (2/25, 8%). The most frequent leak sites were C7–T1, C5–C6, and T10–T11 in decreasing order. All patients underwent CT-guided epidural patch, averaging 2.3 procedure sessions, 3.4 injection sites, and 7.8 mL of injectate per site.
Conclusion: Spinal CSF leak remains a challenging diagnosis, with CT myelography most frequently confirming the diagnosis, supplemented by spine MRI and MRI myelography. Patients frequently require multiple injections at multiple sites, and physicians and patients should be aware of the possible need for repeat treatments. Given the most common sites of leak, empiric blood patch at the cervicothoracic or thoracolumbar junction should be considered if no definitive leak is identified.

1. Introduction

Spontaneous intracranial hypotension (SIH) caused by cerebrospinal fluid (CSF) leak is a treatable cause of persistent postural headaches [1]. According to the International Classification of Headaches Disorders, headache often occurs immediately upon taking an upright position and improves quickly with horizontal positioning [2]. However, SIH has varied clinical manifestations, and due to its relative infrequency the diagnosis is rarely made on the first physician encounter and can be misdiagnosed [3,4]. Many methods have been proposed to evaluate potential causes of low pressure, but there is currently no universal consensus on the best method to diagnose SIH.

Both brain and spine imaging are currently used for the diagnosis and treatment of SIH [4]. Computed tomography (CT) and magnetic resonance imaging (MRI) of the brain frequently show findings of low pressure such as brain sagging and venous distension, although these findings are not consistently present in all patients [5]. Spine imaging, including MRI, CT or MRI myelography, or cisternography is performed to investigate the source of the suspected leak. Despite the range of diagnostic imaging studies available, visualizing the CSF leak and determining the anatomic leak site remain challenging. Many factors, such as the etiology of the leak, rate of leakage, and imaging modality account for variable radiologic appearances [3].

Once diagnosed with intracranial hypotension, the most common treatment is an epidural patch, in which the patient's own blood and/or a fibrin glue product is injected into the epidural space [6]. This can be performed either based on only anatomical landmarks or with imaging guidance. If the site of the leak can be precisely identified, the procedure is performed as close as possible to the suspected leak. If no definitive leak is seen, attempts at treatment may begin by performing an

Abbreviations: CSF, cerebrospinal fluid; SIH, spontaneous intracranial hypotension
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empiric lumbar patch [7]. If unsuccessful, further attempts may be performed at sites with suspicious imaging features, such as large disk protrusions, osteophytes, or perineural cysts. Many patients respond to blood patch, particularly if the site of the leak is localized, while others will go on to require multiple treatments [8–10]. The most refractory patients may ultimately require surgical treatment [5,11]. There is no clear understanding of which patients will respond to treatment and which will require multiple therapies.

This study retrospectively reviews the diagnosis and treatment of SIH in a series of consecutive patients. First, we will determine the most common modalities used to identify leak sites and the most frequent spine levels of CSF leaks. Second, we will assess typical features of SIH treatment with epidural patch and whether they correlate with patient outcome. We use the resulting information to propose a standardized diagnostic work-up for SIH that may help physicians diagnose and treat this relatively rare but debilitating condition.

2. Methods

We retrospectively identified 126 consecutive patients treated with an epidural blood patch at a single university hospital between January 2015 and December 2016. From this group, we excluded patients believed to have iatrogenic or non-spontaneous cause of low pressure, such as intracranial shunt, history of craniotomy or recent spinal procedure (e.g. lumbar puncture or epidural injection). Patients were then included in the study if they met clinical criteria for SIH based on the ICHD-3 diagnostic criteria [2]. This study was approved by the institutional review board.

Available brain imaging, including CT and MRI, for each subject was reviewed for signs of intracranial hypotension such as subdural collection, enlarged pituitary, brainstem sag or decreased pontomamillary distance, prominent or convex-appearing dural venous sinuses, and low-lying cerebellar tonsils [12].

Spine imaging for each subject including available CT, MRI, CT myelography, and MRI myelography was reviewed for the presence of potential spinal CSF leak. No standardized algorithm for spine imaging was followed in these patients, with imaging studies performed according to the preference of the referring provider and neuroradiologist. The first study to denote the possible presence of a leak was recorded. Each spinal exam was categorized as a "localized leak", "non-localized leak", or "no leak" according to the imaging characteristics. A study was classified as a localized leak when there were signs of CSF leak which could be attributed to a single focal anatomic site. For example, a leak was termed localized if contrast from a CT myelogram was visualized in the epidural space and extending along a nerve root sleeve (Fig. 1a). A study was classified as a non-localized leak when there were findings suggestive for CSF leak from visualization of contrast in the extrathecal compartment without identification of a definite single site. This included cases in which epidural extrathecal contrast was visualized over multiple vertebral segments or the entire spine but a precise leak site could not be pinpointed (Fig. 1b). Cases with multiple Tarlov cysts were included in this category. A study was categorized as no leak when there was no imaging evidence of contrast leak. For each localized and non-localized leak study, the most likely spinal site of leak was recorded as follows. For non-localized abnormalities, the region of maximal extrathecal contrast was noted as the possible location. If multiple possible sites were present, they were noted individually. Other findings such as osteophytes which may correlate with the CSF leak were also noted. For myelographic procedures, opening pressure was recorded.

Patients were treated for SIH with CT-guided epidural patch. Access to the epidural space was obtained under intermittent CT guidance via either an interlaminar or transforaminal approach. The use of blood or fibrin glue (TISSEEL) was based on the preference of the performing neuroradiologist. When blood was injected, volume was chosen by injecting until the patient began to experience symptoms or there was significant mass effect (> 50% decrease in thecal sac diameter) on the thecal sac on CT. Fibrin injection volumes were chosen based on manufacturer packaging volumes (either 2 or 4 mL). For each procedure session, treatment date, injection location(s), and blood and fibrin injection volumes were recorded.

Post-treatment outcomes were then categorized based on review of subsequent clinical notes. Patients with > 75% improvement in symptoms (based on a numerical scale from 0, no symptoms, to 10, worst possible symptoms) and no additional procedures for at least 6 months were labeled as complete/near-complete response. Patients with > 25% improvement in symptoms and no additional procedure within 2 weeks were categorized as partial response. Patients who had < 25% improvement in symptoms or required an additional procedure within 2 weeks were labeled as no significant/minimal response. Patients with no-subsequent follow-up were recorded as such and excluded from this portion of the study.

For statistical analysis, group means were compared using unpaired two-tailed *t*-tests. Proportional data was compared using chi-square testing. All testing used a statistical significance level of $p = 0.05$. Linear regression was performed to determine significance of predictors for response to treatment.

3. Results

Thirty patients treated for SIH were identified. 20/30 (66%) patients were female, 21/30 (70%) patients were Caucasian, and 9/30 (30%) patients were African American. Mean age was 54 years old (range, 33–71). The mean opening pressure at lumbar puncture for

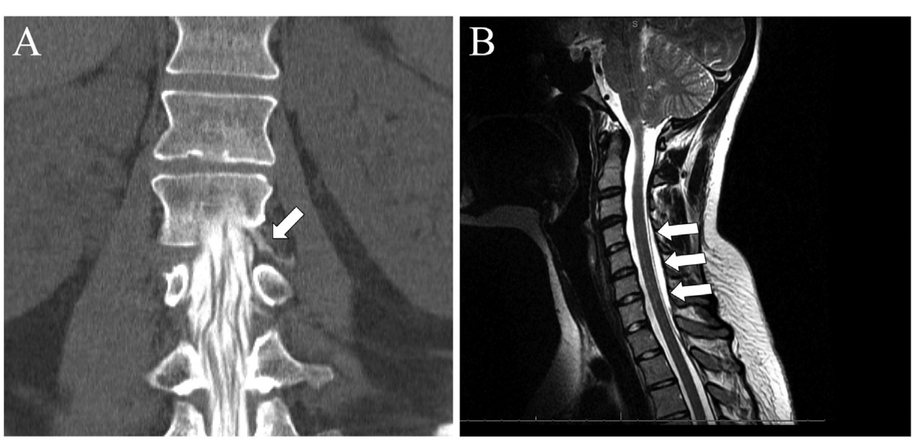

Fig. 1. Coronal images from a CT myelogram showing contrast extravasating along the course of the left L2 nerve root, called a localizing CSF leak. (B) T2-weighted images from a cervical spine MRI myelogram showing a fluid collection in the dorsal spinal canal extending over multiple segments, called a non-localizing CSF leak.

Table 1
Imaging modality first identifying a possible spinal CSF leak.

	Localized Leak (n = 11)	Non-localized Leak (n = 14)
CT myelogram	8 (73%)	9 (64%)
MRI spine	2 (18%)	4 (29%)
MRI myelogram	1 (9%)	1 (7%)

subjects undergoing myelography was 12 cm of H_2O (range, 5–22 cm of water). All patients presented with headaches. In addition, 7 (23%) patients presented with nausea and 2 (7%) patients presented with vomiting.

A localized leak was identified in 11/30 (37%) patients. Of the 11 localized leaks, CT myelogram was the first modality to identify the leak in 8/11 (73%), MRI spine in 2/11 (18%), and MRI myelogram in 1/11 (9%) patients. A non-localized leak was identified in 14/30 (47%) SIH patients. Of the 14 non-localized leaks, CT myelogram was the first modality to identify the leak in 9/14 (64%), MRI spine in 4/14 (29%), and MRI myelogram in 1/14 (7%) patients (Table 1). Five patients had no identified leaks. Among the 5 patients with no identified leaks, CT myelogram and MRI brain were utilized 3 times each, MRI myelogram and MRI spine two times, and CT spine and CT brain were utilized once.

The anatomic distribution of spinal CSF leak sites is summarized by level in Fig. 2. The most common locations of localized and non-localized CSF leak were C7–T1 (n = 7), C5–C6 (n = 4), and T10–T11 (n = 3). Statistically significantly more leaks were seen at C7–T1 ($p = 1 \times 10^{-6}$) and C5–C6 ($p = 0.004$) in comparison to other levels, with a trend towards significance at T10–T11 ($p = 0.09$).

All patients underwent at least one CT-guided epidural patch. 22 patients received blood patches only, 5 patients received fibrin patches only, and 3 patients received both fibrin and blood patches. Among all 30 patients, the average number of treatment procedures was 2.5 sessions. On average, they received injections at 4.3 unique anatomical sites; in other words, patients averaged injection at more than one site per procedure. The mean amount of total injectate was 11.9 mL (range 1–40 mL). Among 25/30 (83%) patients who received epidural blood injections, the average number of treatment procedures was 2.3 sessions and 3.4 injection sites per patient, with 7.8 mL of blood per site. Among eight patients who received fibrin patches, the average number of treatment procedure was 2.0 session at 3.4 injection sites with 3.6 mL of fibrin per site. A larger volume of blood was injected at lumbar spine locations compared to cervical ($p = 0.002$) and thoracic ($p = 0.01$) sites (Fig. 3). A histogram of the total number of treatment sessions required per patient is shown in Fig. 4. Four patients required ≥6 treatment sessions (Fig. 4a) and six patients required ≥6 injection sites (Fig. 4b). The number of procedures and injection sites per patient grouped by leak type is shown in Table 2. Patients with a non-localized leak underwent 38% more injection sites than those with a localized leak ($p = 0.31$).

A total of 69 procedure outcomes were recorded within this study.

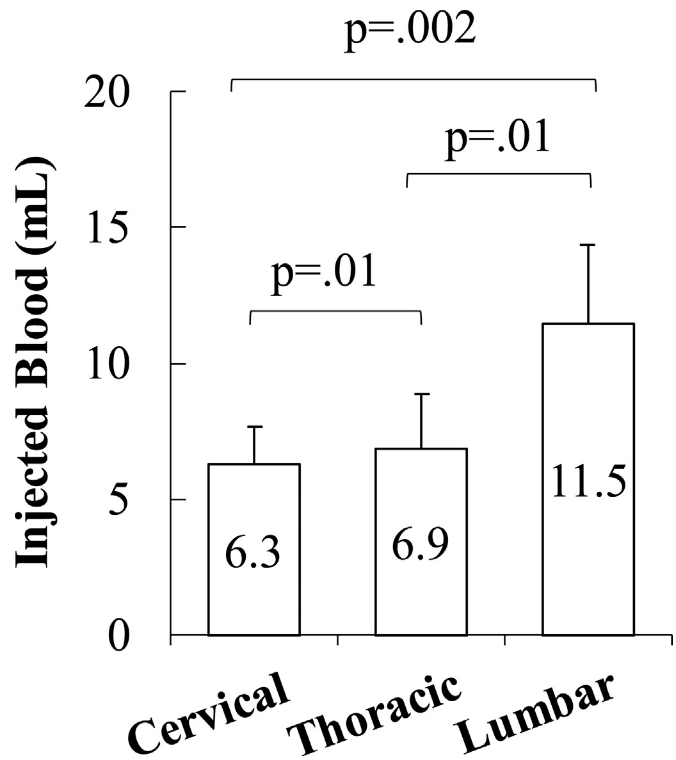

Fig. 3. Histogram showing the average amount of blood used in cervical, thoracic, lumbar blood patches, and the paired *t*-test results.

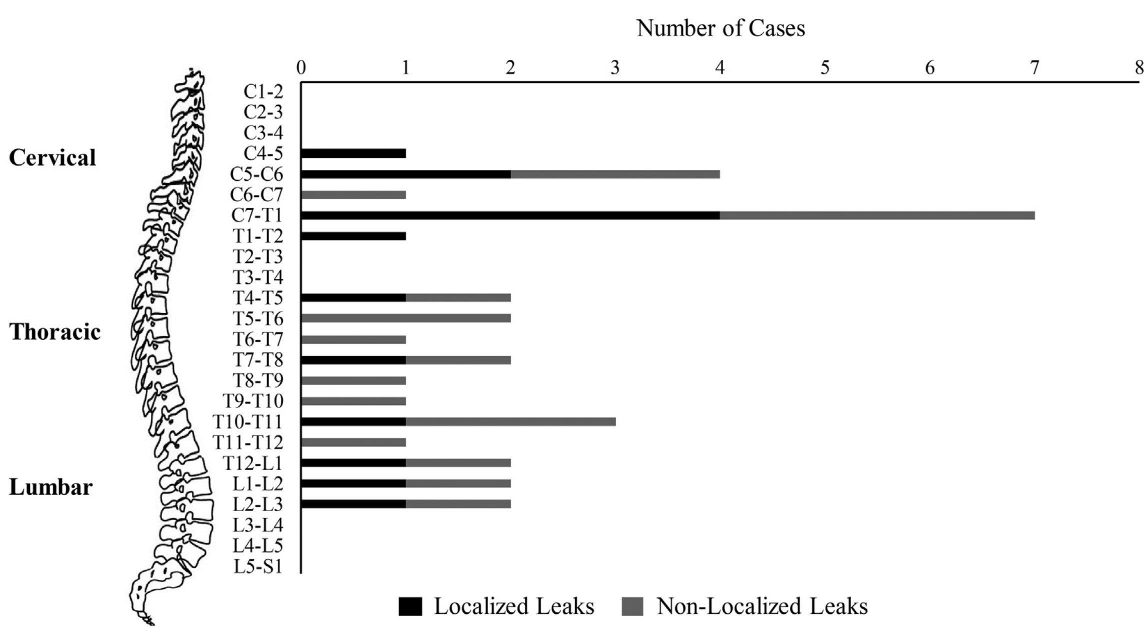

Fig. 2. Histogram showing distribution of definite and suspected leak sites by spinal level.

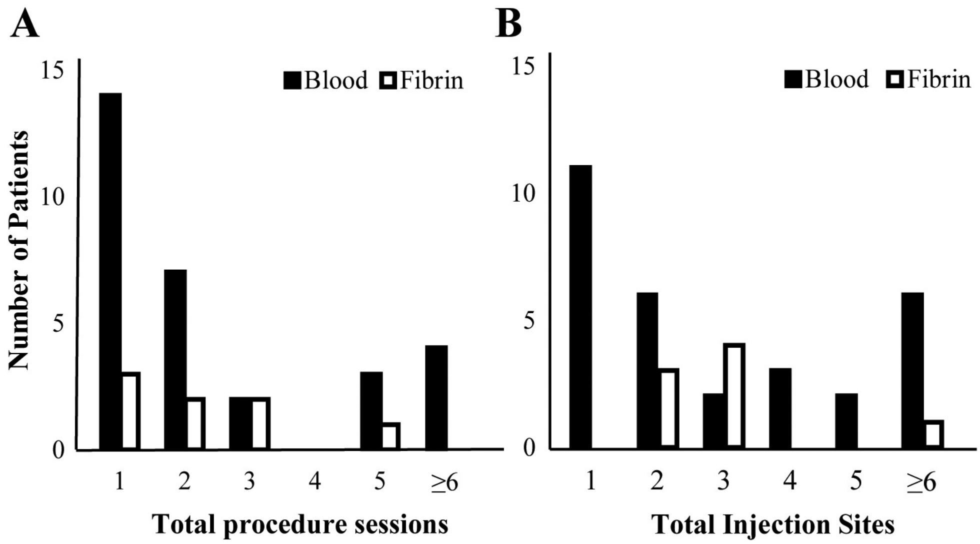

Fig. 4. (A) Histogram showing a count of patients by the number of blood patch procedures and (B) total injection sites per patient.

Table 2
Injection procedures and sites by leak type.

	Localized leak (n = 11)	Non-localized leak (n = 14)	No leak (n = 5)
Procedures (mean)	3	2.9	1
Procedures (range)	1 to 9	1 to 5	1 to 1
Injection sites per session (mean)	2.9	4.0	1.2
Injection sites per session (range)	1 to 9	1 to 10	1 to 2

Seventeen procedures (25%) were classified as a complete/near-complete response, 25 (36%) yielded a partial response, 18 (26%) had no significant/minimal response, and 9 (13%) had insufficient follow-up. On linear regression analysis using independent predictors of leak type, leak location, injection sites, amount of injectate, blood/fibrin injection, and history of prior treatment, there was no significant predictor of patient response.

4. Discussion

In the last 15 years, the diagnosis of SIH has been estimated to affect 1–25 cases per 50,000 people [13]. Diagnosis of SIH is based on a combination of clinical symptoms (postural headache) and typical features on brain imaging, including low-lying cerebellar tonsils, venous distension, subdural fluid collections, and dural enhancement [5,12,14–16]. Despite diverse modalities available to diagnose SIH, the diagnosis and clinical management of SIH remain a challenge, primarily due to difficulty in localizing the exact site of spinal CSF leaks. Whether CSF leaks are readily localized depends on several factors such as the rate of CSF leak, the time between contrast introduction and imaging, and chronicity of the leak [3].

Most of the CSF leak sites were identified by CT myelogram in our cohort, which identified the majority of both localized and non-localized leaks. Since no standardized workup algorithm was followed by radiologists in our study, the frequent use of CT myelogram in this study likely reflects its broad availability, ease of performance, and low costs compared to MR myelogram. CT myelogram has been a long-standing study of choice for visualization of CSF leaks, which is confirmed in the current study.

Our investigation revealed that cervicothoracic and thoracolumbar junctions were the most common sites of leaks. This likely reflects true increased incidence as contrast would not be likely to pool in these locations in the conventional supine imaging position. This important finding suggests that for patients with no detectable leak but a compelling clinical history for low CSF pressure, an empiric treatment at the cervicothoracic or thoracolumbar junction may be worthwhile as they may be the most likely site of an undetected leak [17]. Our finding corroborates previous study which found similar patterns of CSF leaks at these regions [18]. False localization of a CSF leak to the cervicothoracic region when the CSF leak is elsewhere in the spine (such as the thoracic spine) has been reported, as fluid can track along the epidural space and even along exiting nerve roots [19]. More specific signs of localization such as early filling on dynamic myelography may be useful in differentiating true leaks from pseudolocalization, especially if there is a long segment CSF extravasation at these regions. The use of an empiric patch at the cervicothoracic or thoracolumbar junctions however has not been previously reported in the literature and represents a novel finding from this study. Treating physicians should be aware of potential complications of performing cervical epidural patches, as they may have increased risk of severe complications such as spinal cord injury. However, other reports have described safely performing cervical epidural patches with imaging guidance in patients who did not respond to lumbar patches [20–22]. At our institution, we perform all cervical patches with CT guidance to minimize the risk of spinal cord injury. Based on these results and previous reports in the literature [3,6,23,24], we propose the diagnostic and treatment workflow in Fig. 5.

The optimal amount of blood and fibrin injected for the treatment of SIH has previously been studied. Clinicians are inclined to treat with highest volume possible to allow the best spread of epidural blood to adjacent levels and maximize the chance of success [25], and higher rates of treatment success has been reported with large injection volumes [26]. Our work revealed an average of 6–7 mL of blood injected in cervical and thoracic regions and 11–12 mL of blood in lumbar regions. More blood was used at the lumbar sites, likely due to termination of the spinal cord above these levels, greater potential space in the spinal canal, and fewer patient symptoms on injection. We would propose the use of these injection volumes as reference values in practice and suggest that clinicians performing patches try to achieve these volumes unless limited by patient symptoms or appearance of > 50% spinal canal narrowing by the injection on imaging.

The number of injections patients received during one procedure session predominantly depended on the certainty of the leak sites. Patients with a non-localized leak site underwent the same number of procedure sessions; however, these patients were treated at more injection sites. The higher number of injection sites in this population

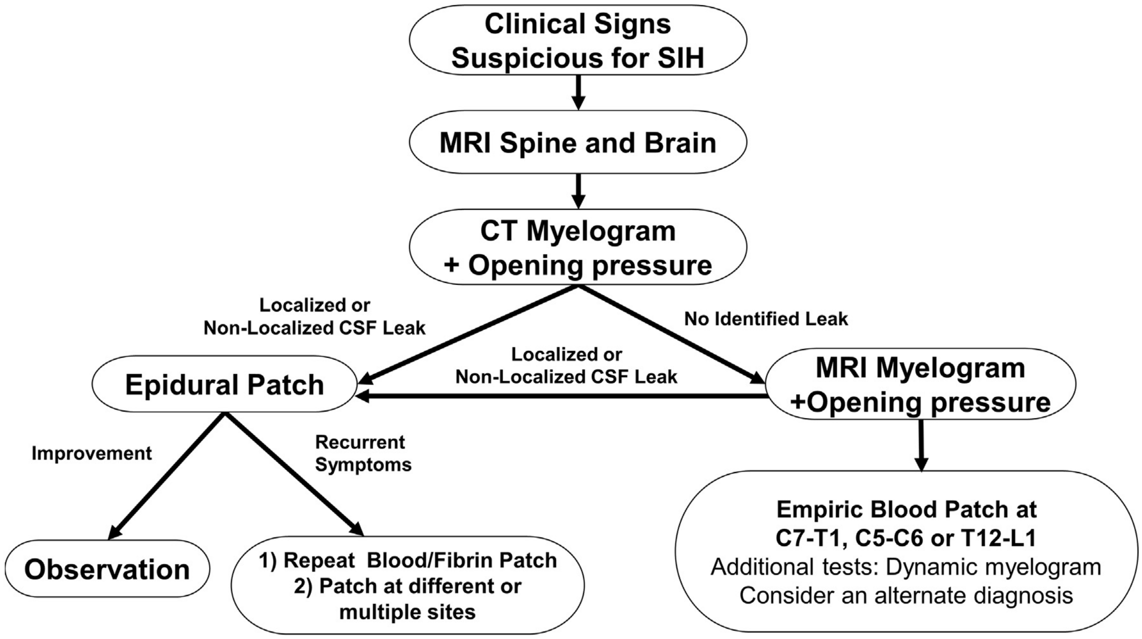

Fig. 5. Proposed algorithm for the work up of SIH.

likely reflects greater uncertainty about the leak site and a desire to maximize the chance of success. Most patients received more than one treatment, averaging 3 procedure sessions, with a subset of the group receiving as many as 6 treatments. These results corroborate evidence in the literature suggesting need for multiple treatments [27,28]. Furthermore, failure to respond to prior treatment attempts was not associated with failure of subsequent treatment attempts. Therefore, physicians should be aware of the potential need for repeat treatments for SIH and counsel patients accordingly, as persistence may be needed to achieve complete response.

Despite a strong clinical history and exhaustive imaging investigations, CSF leak sites often cannot be identified. Those patients with no imaging signs of spinal leak identified received one procedure on average. If these patients did not have a response to an initial patch, typically no additional procedures were pursued, and alternate diagnoses were considered. However, if there is a continued strong clinical suspicion of leak, we suggest that aggressive attempts to identify a leak are warranted. If a patient has not undergone MRI of the spine, it can be performed with routine sequences or preferably with dedicated thin-slice heavily fluid-weighted sequences, or virtual myelogram, to further identify leak sites [29]. In our study, MRI myelogram with intrathecal gadolinium identified leaks in a smaller subset of patients. This finding likely reflects its use as a troubleshooting tool, as prior reports have suggested MRI myelography may be more sensitive than CT myelograms for slow leaks [30,31]. Previous studies have also reported the use of digital subtraction myelography as an ancillary tool to visualize direct CSF-venous fistulae in patients with refractory SIH [32,33], although this technique was not used by neuroradiologists in our study.

There are several limitations to this study. First, this was a retrospective study where no single diagnostic algorithm was followed to diagnose spinal leaks. In addition, a significant number of these patients were referred to our institution after a partial workup elsewhere. As patients did not receive the entire range of available tests, no conclusion can be made about the sensitivity of different test methods. However, results are useful in determining effectiveness of imaging and treatment in a real-world practice environment. When leaks were identified, they were categorized as localized or non-localized, without further attempts to pinpoint the leak. Studies have suggested that dynamic CT myelography is a potentially useful tool which could further localize leaks in a subset of patients, but its use may not be widespread [34]. Choice of treatment site and type, such as use of blood or fibrin, was chosen based on practitioner preference. Overall, there were no significant predictors of response, including leak type, leak location, injection sites, amount of injectate, blood/fibrin injection, or history of prior treatment, possibly due to the small size of the cohort. Prospective randomized trials in larger numbers of patients could potentially be used to explore these relationships further and better guide treatment.

5. Conclusion

In patients suspected of a diagnosis of SIH, CT myelography detects the majority of leaks and is the recommended first tool for evaluating SIH, which can be supplemented with MRI and MRI myelography. Cervicothoracic and the thoracolumbar junctions were the most common leak sites, suggesting a role for empiric therapy in symptomatic patients whose leaks cannot be visualized. Multiple treatment sites and procedure sessions may be needed before symptom resolution, reinforcing the need for conservative expectations about outcome.

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