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Distinct Pattern of Membrane Formation With Spinal Cerebrospinal Fluid Leaks in Spontaneous Intracranial Hypotension

Levin Häni, MD ^{*,**}, Christian Fung, MD^{*,*}, Amir El Rahal, MD^{*,§}, Florian Volz, MD^{*,}, Luisa Mona Kraus, MD^{*,}, Oliver Schnell, MD^{*,}, Roberto Ferrarese, PhD^{*,}, Daniel Erny, MD^{||}, Marius Schwabenland, MD^{||}, Horst Urbach, MD^{||}, Niklas Lützen, MD^{||}, Jürgen Beck, MD^{*,}

^{*}Department of Neurosurgery, Medical Center—University of Freiburg, Freiburg im Breisgau, Germany; [§]Faculty of Medicine of Geneva, Geneva, Switzerland; ^{||}Institute of Neuropathology, Medical Center—University of Freiburg, Freiburg im Breisgau, Germany; [†]Department of Neuroradiology, Medical Center—University of Freiburg, Freiburg im Breisgau, Germany

*Levin Häni and Christian Fung contributed equally to this work.

Correspondence: Jürgen Beck, MD, Department of Neurosurgery, Medical Center—University of Freiburg, Breisacher Strasse 64, 79106 Freiburg im Breisgau, Germany. Email: j.beck@uniklinik-freiburg.de

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BACKGROUND AND OBJECTIVES: To systematically describe pertinent, intraoperative anatomic findings encountered when approaching spinal cerebrospinal fluid (CSF) leaks and CSF-venous fistulas in spontaneous intracranial hypotension (SIH).

METHODS: In a retrospective study, we included surgically treated patients suffering from SIH at our institution from April 2018 to March 2022. Anatomic, intraoperative data were extracted from operative notes and supplemented with data from surgical videos and images. Prominent anatomic features were compared among different types of CSF leaks.

RESULTS: The study cohort consists of 120 patients with a mean age of 45.2 years. We found four distinct patterns of spinal membranes specifically associated with different types of CSF leaks: (i) thick, dorsal membranes, which were hypervascular and may mimic the dura (pseudodura); (ii) thin, lateral membranes encapsulating a ventral epidural CSF compartment (confining the spinal longitudinal extradural CSF collection); (iii) ventral membranes constituting a transdural funnel-like CSF channel; and (iv) lateral membranes forming spinal cysts/meningeal diverticulae associated with lateral CSF leaks. The latter three types resemble a layer of arachnoid herniated through the dural defect.

CONCLUSION: We describe four distinct spinal (neo-)membranes in association with spinal CSF leaks. Formation of these membranes, or emergence by herniation of arachnoid through a dural defect, constitutes a specific pathoanatomic feature of patients with SIH and CSF leaks. Recognition of these membranes is of paramount importance for diagnosis and treatment of patients with spinal CSF leaks.

KEY WORDS: Spontaneous intracranial hypotension, Spinal cerebrospinal fluid leak, Orthostatic headache

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Spontaneous intracranial hypotension (SIH) is an important cause of incapacitating headache. SIH is usually caused by a spinal cerebrospinal fluid (CSF) leak.^{1–4} Schievink et al³ described three types of CSF leaks in SIH: dural tears, usually ventrally located (type 1); meningeal diverticula, usually laterally located (type 2); and CSF-venous fistulas (type 3).

In refractory cases of SIH in patients with a precisely localized CSF leak, surgical treatment is effective and safe.^{4–6} However, the anatomic configuration of spinal CSF leaks can be complex and challenging to understand intraoperatively. Previous reports concerning the surgical anatomy are scarce. Various configurations of dural defects were described including extensive lateral, axillary, or posterior nerve root arachnoid diverticulae and a nude nerve root configuration.⁷ Beck et al⁴ found discogenic microspurs to be a major cause of ventral CSF leaks. Only recently, CSF-venous fistulas have been recognized by Schievink et al and demonstrated intraoperatively.^{8–12}

Over the past decade, the authors gained extensive experience with the surgical management of patients with SIH and became

ABBREVIATIONS: CVF, CSF-venous fistulas; SIH, Spontaneous intracranial hypotension.

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aware of unique surgical findings.^{4-6,13} In particular, we frequently came across different types of membranes unique to patients with spinal CSF leaks. These membranes may explain imaging findings, pathophysiology, treatment response, or failure of treatment. They can easily disorient the surgeon, sometimes mimic the dura and hinder efficient surgery or percutaneous treatment approaches.

The aim of this study was to systematically describe pertinent, intraoperative anatomic findings encountered when approaching spinal CSF leaks and fistulas in SIH.

METHODS

Standard Protocol Approvals, Registrations, and Patient Consents

We conducted a retrospective, observational cohort study. We obtained approval from the local ethics committee for this study (22-1263-S1-retro). Informed consent was waived owing to the retrospective nature of the study.

Patient Population

We included consecutive patients undergoing surgical treatment of SIH at our institution from April 2018 to March 2022. SIH was diagnosed according to the third International Classification of Headache Disorders.¹⁴ Surgery was indicated after multidisciplinary team discussion at our SIH board.

A standardized diagnostic workup was performed as described previously.¹⁵⁻²¹

Microsurgery

Surgery was performed under general anesthesia in the prone position using a dorsal open approach¹³ or a minimally invasive approach with tubular retractors.⁶ Type 1 leaks (ventral leaks) were disconnected and sealed by a transdural approach.⁶ By contrast, type 2 leaks (lateral leaks) were approached by either an extrathecal technique or a transdural approach. The surgical technique for disconnection and/or clipping of direct CSF-venous fistulas (CVF, type 3 leak) was mostly extrathecal.¹²

Data Analysis

Demographic and clinical data were extracted from the institutional electronic patient data management system. Imaging data were reviewed in the hospital's picture archiving system. Surgical data were extracted from operative notes in the institutional electronic patient management system and supplemented with data from surgical videos and images. Surgical videos and images were reviewed by three board-certified neurosurgeons with experience in the surgical treatment of SIH (L.H., C.F., J.B.). Individual pathoanatomic features were considered based on agreement of the raters. Disagreement was solved by discussion with the senior author. CSF leaks were grouped according to the conventional classification into type 1 (ventral leaks), type 2 (lateral leaks), and type 3 (CVF).^{3,22} Pertinent anatomic features of individual findings were grouped into clusters.

Statistics

Statistical analysis was performed using the statistical software SPSS (IBM, Version 28). Descriptive statistics included calculation of the mean and SD for normally distributed data and the median and IQR for skewed data. Normal distribution was assessed graphically using boxplots and analytically using the Shapiro–Wilk test.

Comparison between groups for nominal variables were made using a χ^2 test. If a significant association was found between a categorical variable and a nonbinary categorical variable in an initially performed χ^2 test, we used a post hoc test to identify the most influential category. Based on these results, we grouped individual features into clusters.

We addressed missing values first by reanalyzing the source data or, if no value was retrievable, by pairwise deletion. For all analyses, *P*-values of ≤ 0.05 were considered significant.

Data Availability

The study data are available and shared at reasonable request of other investigators.

RESULTS

Patient Population

We included 120 patients undergoing surgical repair for a spinal CSF leak between April 2018 and March 2022. The mean age of the study population was 45.2 years (± 12.2). Seventy-six patients (63.3%) were female. The most common chief complaint was orthostatic headache in 80%. The mean duration of symptoms was 16.6 months (± 29.1). A surgical video was available for review in 92 (76.7%) patients.

Surgical Findings

Most commonly, we found type 1 leaks in 84 patients (70%). By contrast, we found type 2 leaks in 26 patients (26.7%). In the remaining 10 patients, we found a type 3 leak in six patients (5%) and a cyst on the lateral nerve root in one patient (0.8%) and could not determine the type in three patients (2.5%).

We found epidural membranes associated with these spinal CSF leaks. These membranes showed a distinct pattern among different leak types. We clustered these membranes in four specific groups (Figures 1, 2, 3A-3F, 4, 5, 6A-6C).

1. Dorsal membranes: They occur mostly posterior to the thecal sac. Because of their hypervascularity, they can be the source of torrential bleeding (Figures 1 and 2, Figure 3A and 3B). They can reach a thickness similar to the dura and mostly look very much like and can be confused with the actual dura (neodura or pseudodura [personal communication with W. Schievink]). These dorsal membranes appear predominantly with ventral CSF leaks (type 1) and less frequently with lateral CSF leaks (type 2).
2. Lateral membranes: They occur lateral to the thecal sac. These membranes appear white-blueish, sometimes translucent and are free of large vessels (Figure 3C and 3D). They are very thin and can easily be overlooked. Visually, they resemble arachnoid that is herniated through the ventral CSF leak and extends laterally. Importantly, these lateral membranes encapsulate an epidural compartment (ie, a neospace, Figure 4) that impresses as the spinal longitudinal extradural CSF collection (SLEC) on imaging. They appear predominantly with ventral CSF leaks (type 1).

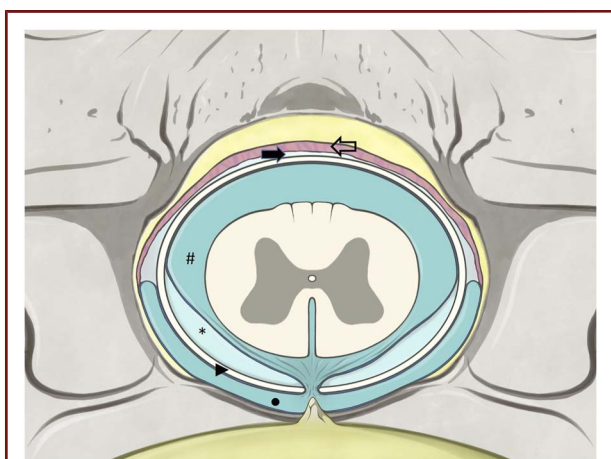


FIGURE 1. Ventral CSF leak (type 1). Drawing illustrating the anatomic overview of a ventral CSF leak (type 1). The dura (►) surrounds the subarachnoid space (#). Intradurally, an arachnoid lift-off creates a subdural compartment (*). Dorsal to the dura, thick dorsal membranes are illustrated (⇔). These encapsulate a dorsal extradural compartment (■). Ventral to the dura, a ventral extradural compartment (neospace) exists (●), which is bordered laterally by lateral membranes. We speculate that the latter represent a layer of herniated arachnoid, which is continuous with ventral transdural funnel-like membranes through the dural defect. CSF, cerebrospinal fluid.

3. Funnel-like membranes forming a transdural channel: They can be visualized during transdural inspection and resemble spinal arachnoid herniated through the ventral dural defect (Figure 3E and 3F).
4. Thin, lateral membranes forming spinal cysts/meningeal diverticulae: They are found laterally to the thecal sac usually originating in the axilla of or around the exiting nerve root. Visually, they also resemble spinal arachnoid and most likely represent a layer of herniating arachnoid through a lateral dural defect (Figures 5 and 6).

We found significantly more dorsal membranes ($P < .001$) and lateral membranes ($P = .006$) in patients with ventral CSF leaks (type 1), compared with other types of CSF leaks (**Supplementary Appendix Table 1**, <http://links.lww.com/ONS/A965>). Macroscopically, dorsal membranes were found to be hypervascular in 53.2% of cases, whereas normal appearance (ie, thin arachnoid-like) was noted in 34.0% and no information was available in 12.8%. In addition, we found significantly less frequent dorsal and lateral membranes in patients with CVF (type 3) ($P < .001$).

Although spinal CSF leaks cause egress of CSF, CSF is often not encountered on opening of the spinal canal or even after flavectomy. According to the type of the leak, extradural CSF could be found at various surgical stages for stepwise progress of the approach and only after opening of different types of membranes. Importantly, all patients had egress of CSF through the dura by the dural defect. However, extradural CSF was confined by the epidural membranes.

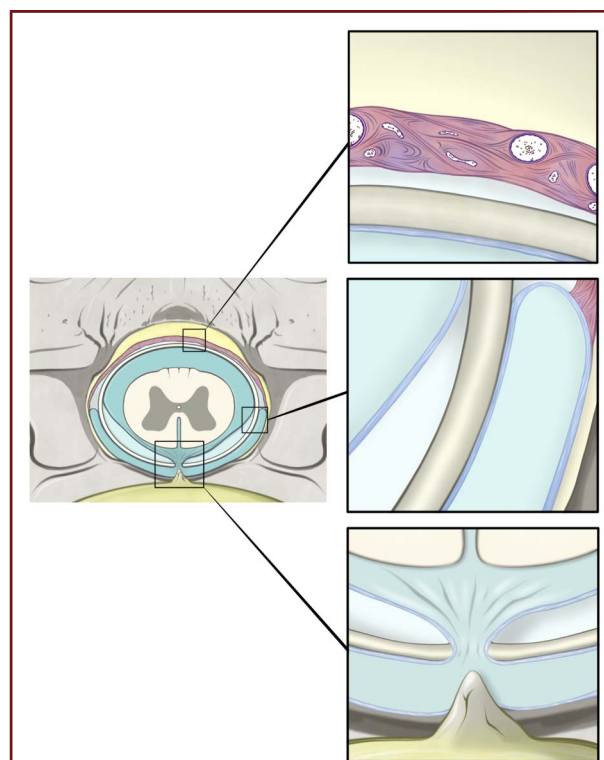


FIGURE 2. Membranes associated with ventral cerebrospinal fluid leak (type 1). Drawing illustrating the simplified anatomic configuration of membranes associated with a ventral CSF leak (type 1). Hypervascular, dorsal membranes are present over the dorsal aspect of the dura (upper right). A ventral extradural compartment (neospace) is formed and bordered laterally by lateral membranes (middle right). Transdural funnel-like membranes, representing a layer of arachnoid herniate through the dural defect—are continuous with the lateral membranes (lower right).

In type 1 leaks, we found less frequently CSF visible directly after removal of the ligamentum flavum ($P < .001$, **Supplementary Appendix Table 2**, <http://links.lww.com/ONS/A966>). In 39.3% of type 1 leaks, extradural CSF was restricted entirely to the ventral extradural compartment bordered by lateral membranes, and therefore, no CSF spillage occurred. In addition, we found egress of CSF only after removal of dorsal or lateral membranes in 27.4% and 21.4% of patients with type 1 leaks, respectively. We found a newly formed ventrolateral spinal compartment, ie, an epidural neospace, in 81% of patients with a type 1 leak, which was more frequent compared with other types of CSF leaks ($P < .001$) (**Supplementary Appendix Table 3**, <http://links.lww.com/ONS/A967>). This neospace represented the SLEC compartment on spinal MRI.²²

In patients with type 2 leaks, free egress of CSF directly after removal of the ligamentum flavum was found more frequently compared with other types of leaks (38.5%, $P < .001$; $\alpha_{\text{corr}} = 0.003$). CSF flow was contained by dorsal membranes in 19.2% of patients with type 2 leaks. A lateral spinal CSF compartment

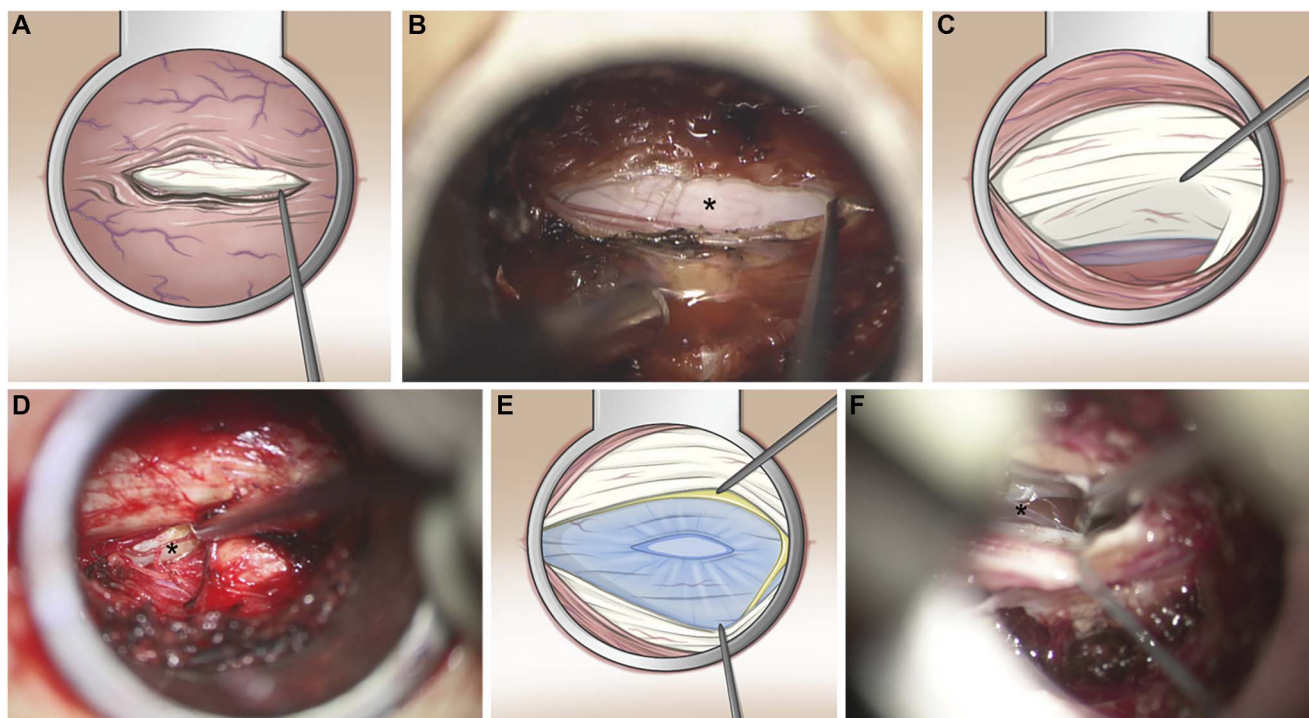


FIGURE 3. Membranes associated with ventral CSF leaks. **A and B,** View through a tubular retractor during a dorsal approach to a ventral CSF leak. The image displays the anatomy after complete removal of the ligamentum flavum. Under the ligamentum flavum, the surgeon can encounter a hypervascular, dorsal membrane. This membrane can be thick and therefore mistaken for the dura. Only after opening of the membrane, the surgeon can clearly identify the dura (*). **C and D,** The images display the dura in the upper half of the exposure. Ventrolateral to the dura, the avascular, lateral membrane is indicated with a dissector (*). **E and F,** The images display the ventral CSF leak after dorsal durotomy. At the leak site, transdural funnel-like membranes can be identified (*). Visually, these represent herniated arachnoid. In the authors' view, disconnection of these membranes is a key step in the surgical treatment of spontaneous intracranial hypotension. CSF, cerebrospinal fluid.

was found more frequently in patients with type 2 leaks with a dural tear compared with other leak types (34.6%, $P = .002$).

In patients with type 3 leaks, we found no egress of CSF at all in most cases (66.7%). While no information was available in one patient (16.7%), egress of CSF after removal of a dorsal membrane was noted in only one patient (16.7%). In addition, no CSF compartment formation was found intraoperatively among patients with type 3 leaks (Figure 7).

In patients with a ventral dural leak (type 1), a causative discogenic microspur was found intraoperatively in 64 patients (76.2%). On intradural inspection of type 1 leaks, transdural funnel-like membranes resembling herniating arachnoid at the site of the dural defect were found in 75 cases (94.9%). The funnels connect the intradural subarachnoid space with the extradural ventrolateral neospace like a connecting tube.

DISCUSSION

We could identify four distinct patterns of (neo-)membranes in patients with a spinal CSF leak. The pattern of membrane formation, their distinct anatomic features, and their configuration

were specifically related to three types of spinal CSF leaks as described by Schievink.³ Recognition of these membranes is of paramount importance for deciphering pathophysiology and efficient surgical or percutaneous treatment of spinal CSF leaks. Importantly, our study was not meant to propose a new classification of CSF leaks, but rather describe surgical features associated with different types of CSF leaks.

Pathoanatomic Implications

Extradural membranes were abundant in patients with spinal CSF leaks. CSF egress was encountered only after opening of these membranes. The dorsal membranes are often hypervascular and thick yet fragile on manipulation and can easily be mistaken for the dura. By contrast, at the lateral aspect of the dura, we encountered a very thin, sometimes translucent lateral membrane. This membrane borders the ventrally located neospace and was often the last membrane that enclosed extrathecal CSF. According to our understanding, this neospace corresponds to the SLEC space on spinal imaging. Most often, they insert laterally at the level of the nerve root sleeve running laterally to the bony confinement of the spinal canal.

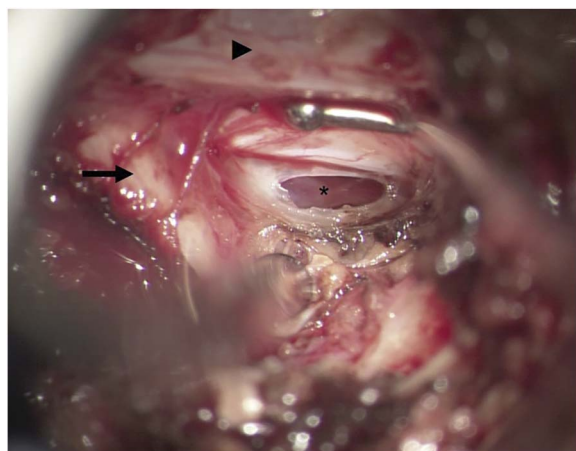


FIGURE 4. Intraoperative view of ventral extradural compartment (neospace). View through a tubular retractor during a dorsal approach to a ventral CSF leak. The image displays the dura in the upper half of the exposure (arrow head) and the exiting nerve root to the left (arrow). The lateral membrane anterolateral to the dura is opened. After opening of the lateral neomembrane, the surgeon has a view into the ventral extradural compartment (*) with a direct communication to the intradural space through the ventral leak (not visible). In this instant, egress of CSF occurs from the ventral compartment. CSF, cerebrospinal fluid.

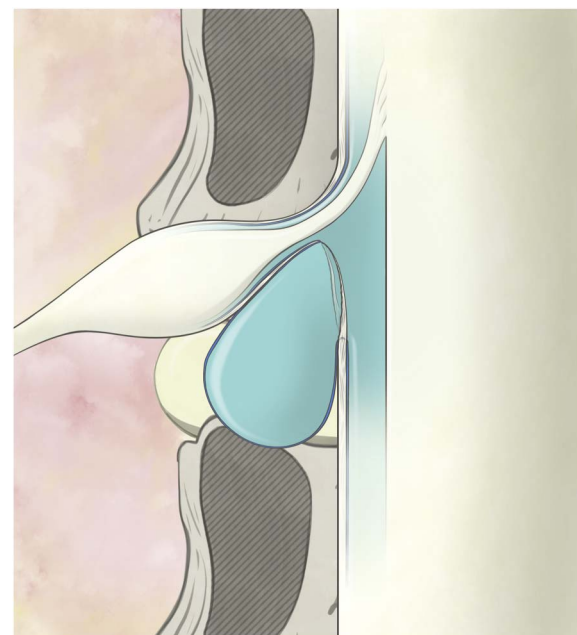


FIGURE 5. Lateral CSF leak (type 2). Drawing illustrating the simplified anatomic configuration of a lateral CSF leak (type 2). Lateral CSF leaks originate mostly in the axilla of the nerve root on the stem of the thecal sac. A thin lateral membrane forming spinal cysts/meningeal diverticulae is recognized, which represents a layer of herniated arachnoid. CSF, cerebrospinal fluid.

We can only speculate about the pathophysiological processes underlying membrane formation. We hypothesize that dorsal membranes form reactively, whereas lateral membranes originally represent an arachnoid layer prolapsed through the dural defect, but the lateral membranes may also form reactively. Interestingly, patients with long-lasting symptoms seemed to have more prominent, thicker membranes compared with patients with a short symptom duration (Figure 5). Currently, we have no objective way of measuring this. Based on our surgical findings, we speculate that membrane formation is a progressive process and might explain why symptoms and CSF dynamics change over time in patients with SIH.²³

During intradural inspection in type 1 leaks, we found funnel-like membranes representing transdurally herniating arachnoid at the site of the ventral dural defect in almost all cases. From the visual appearance of transdural funnels and the lateral membranes, we speculate that these two types of membranes are identical. They might represent a layer of herniated arachnoid through the dural defect that extends laterally. We speculate that this channel from the inside to outside of the dura needs to be disconnected surgically and only then the dural defect may heal and CSF loss stops.

In type 2 leaks, we found a lateral membrane originating from the inside of the dura and protruding in the axilla of the nerve root on the stem of the thecal sac, which formed a spinal cysts/meningeal diverticulae.²⁴ This pouch also probably represented herniated arachnoid although it might be attenuated dura in cases without a clear dural tear. Nevertheless, this intraoperative finding is likely to correspond to the imaging finding of a spinal meningeal diverticula or cyst.⁴

In type 3 leaks, the surgeon does not encounter egress of CSF and encounter only rarely membranes or compartment formation during the approach, maybe because there is no free CSF egress and no dural tear. According to our current findings, it looks like the vein immediately drains the CSF—a direct CSF-venous connection. This concept of configuration was recently corroborated by our group using intraoperative, intrathecal fluorescein injection at a distant site, allowing us to visualize the direct egress of contrasted CSF from the intradural space into a vein.¹²

The cause of the different types of CSF leaks remains speculative. While osteodiscogenic microspurs are clearly associated with ventral leaks and probably their cause, no microspurs are found in lateral leaks. By contrast, we speculate that the axilla of the nerve root represents a locus minoris resistentiae for a dural breach. Even without a CSF leak, the axillary dura frequently appears thin and fragile. The cause of CVF remains obscure.

Clinical Implications

These results have implications for management of SIH. With our current findings, we add (neo-) membranes to our understanding of patients with spontaneous intracranial hypotension. Specifically, four distinct patterns of membranes are peculiar to the microanatomic phenotype of spinal CSF leaks: (i) dorsal membranes, which are thick and often look exactly like and might

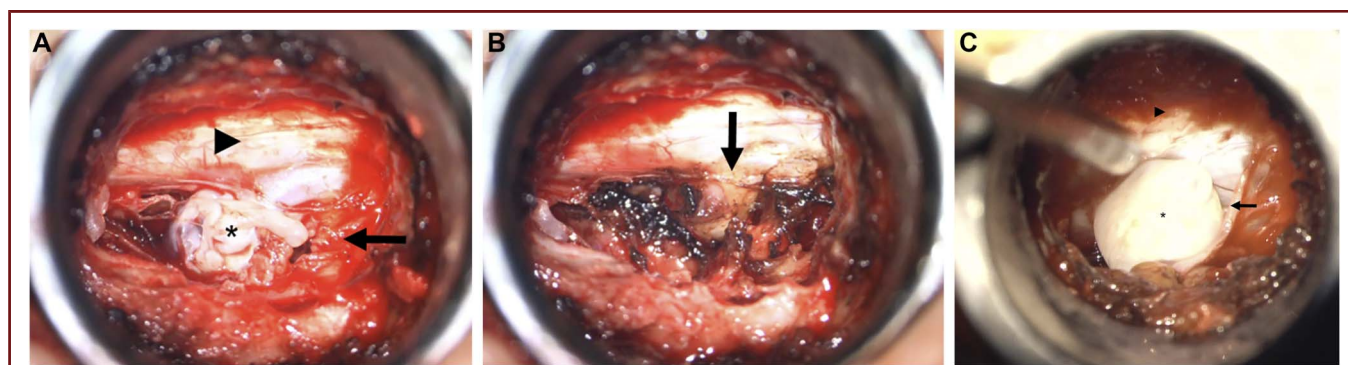


FIGURE 6. Intraoperative view of lateral CSF leak (type 2). **A**, View through a tubular retractor during a dorsal approach to a lateral CSF leak. The image displays the anatomy after complete removal of the ligamentum flavum. In the upper part of the exposure, the dura is seen (arrow head). To the right, the exiting nerve root is displayed (arrow). Centrally, the thin membrane representing a layer of herniated arachnoid at the leak site is identified (*). **B**, After coagulation and shrinkage of the membrane, the site of the leak can be identified at the proximal dural stem in the axilla of the nerve root (arrow). **C**, Lateral CSF leak (type 2) with lateral compartment formation in another patient. The image displays the anatomy after complete removal of the ligamentum flavum and opening of a lateral compartment (arrow). The nerve root is to the right. In the upper part of the exposure, the dura is seen (arrow head). Only after opening of a membrane, the surgeon has a view into a lateral spinal compartment encompassing the CSF leak. At the site of the leak, a thin membrane representing prolapsing arachnoid through the dural defect is seen and forms a spinal cysts/meningeal diverticulae (*). CSF, cerebrospinal fluid.

be mistaken for the dura (neodura); (ii) lateral membranes; (iii) ventral, transdural funnel-like membranes forming a transdural channel; and (iv) initially thin, lateral membranes forming spinal cysts/meningeal diverticulae.^{3,22}

We believe that knowledge about these anatomic features facilitates efficient surgery. CSF leaks might even be missed without

a proper understanding of the complex anatomy. Moreover, the presence of these membranes might lower the success rate of epidural blood patching, in particular, with ventral leaks. Easily, the surgeon can misinterpret the dorsal epidural membrane as the dura, which prevents effective surgical treatment of SIH. Cohen-Gadol described significant regional attenuation of the dura, which prevented primary closure in 62% of patients.⁷ In addition, we have encountered many patients referred to us after surgical procedures at other institutions with reports about a thin and fragile dura prone to bleeding and not amenable to suturing. In all these patients, we then identified a prominent dorsal epidural membrane (type 1) imitating the dura. In all cases, the proper dura was identified, unremarkable on inspection, good to handle, and readily suturable.

Another potential fallacy originates in the formation of the ventral or ventrolateral compartment (neospace) in ventral CSF leaks. The ventral compartment, bordered by lateral membranes, encloses the ventral CSF leak. Surgeons might misinterpret the situation because there is no free egress of CSF after exposure of the thecal sack. The surgeon might abort the procedure prematurely because of the lack of extradural CSF. Because extradural CSF is frequently contained within a ventral compartment (neospace) bordered by lateral membranes, spillage of CSF occurs only after opening of these membranes.

While we found a transdurally herniating arachnoid in the form of funnel-like membranes in almost all cases of type 1 leaks, we found an discogenic microspur in only 76.2%. Thus, the presence of these transdural funnel-like membranes—constituting a CSF channel from the inside to the outside of the thecal sack—might be even more relevant for the persistence of an existing leak than the microspur. We believe that disconnection of the transdural funnel-like membrane is a key step in the surgical treatment of SIH to secure healing of the defect.

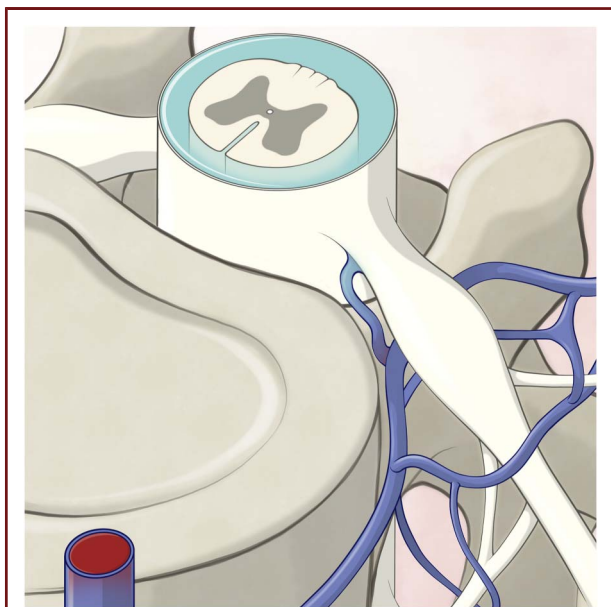


FIGURE 7. CSF-venous fistula (type 3). Typical anatomic configuration of a CSF-venous fistula originating from the caudal aspect of the proximal nerve root sheath. Typically, no membrane or compartment formation occurs. CSF, cerebrospinal fluid.

The existence of such a transdural funnel-like membrane might explain the reduced efficacy of patching procedures in patients with type 1 leaks.

Limitations

Our analysis is subject to several important limitations inherent to single-center, retrospective studies on a limited number of patients. In addition, our results are subjective surgical findings.

CONCLUSION

We surgically describe four distinct patterns of membranes formed in association with CSF leaks. Formation of these membranes seems to be a common and fundamental pathoanatomic feature of spinal CSF leaks, and there seems to be a specific pattern of membrane formation associated with specific types of spinal CSF leaks and fistulas. Their occurrence explains imaging findings like SLEC and spinal diverticulae and gives a clue why some therapeutic measures are more efficient than others. Recognition of these membranes is of paramount importance for effective surgical treatment and for refining treatment of spinal CSF leaks and fistulas.

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Supplemental Digital Content. Supplemental Table 1. Neomembrane formation. Assessment of the presence of dorsal and lateral neomembranes intraoperatively. CVF, CSF-venous fistulas.

Supplemental Digital Content. Supplemental Table 2. Egress of CSF intraoperatively. Egress of CSF intraoperatively depending on the type of leak. Egress of CSF is classified as no egress of CSF, free egress of CSF after removal of the ligamentum flavum, egress of CSF after removal of dorsal membranes, or egress of CSF after removal of lateral membranes. CVF, CSF-venous fistulas.

Supplemental Digital Content. Supplemental Table 3. Formation of spinal compartments. Assessment of the presence of ventral, lateral, or dorsal compartments intraoperatively. CVF, CSF-venous fistulas.