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ORIGINAL RESEARCH

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Dural sinus narrowing in patients with spontaneous anterior skull base cerebrospinal fluid leak

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Abstract

Objectives: Current evidence suggests a link between idiopathic intracranial hypertension (IIH) and spontaneous cerebrospinal fluid (sCSF) leak, as well as between IIH and dural venous sinus (DVS) narrowing. However, there are limited data linking DVS narrowing and sCSF leak. This study aims to determine the prevalence of DVS narrowing in patients with sCSF leak.

Methods: A retrospective review of all patients with sCSF leak that presented to a tertiary academic center from 2008 to 2019. Preoperative imaging was independently reviewed by two neuroradiologists to evaluate for DVS narrowing. Available literature was used to estimate the prevalence of DVS narrowing in the general population to allow for comparison. Data were analyzed using Exact binomial test.

Results: Analysis of 25 patients with appropriate imaging revealed the majority were women (21/25, 84%) with a mean age of 51.89 years (SD 13.96). The majority of these patients were found to have narrowing of the DVS (20/25, 80%). In patient with sCSF leaks, there was a significantly higher proportion of patients with DVS narrowing compared with published literature examining this condition in the general population (80% vs. 40%, CI 0.59–0.93, $p < .001$).

Conclusion: The prevalence of DVS narrowing in patients with sCSF leaks is substantial and likely greater than the general population. Moreover, there appears to be narrowing in most patients with sCSF leak. Preoperative radiological evaluation of the DVS using MR venography may be useful in patients with sCSF leaks as DVS stenosis may be an underdiagnosed etiology. Further study is needed to evaluate this.

Level of Evidence: IV.

KEYWORDS

dural venous stenting, idiopathic intracranial hypertension, skull base, spontaneous cerebrospinal fluid leak, venous sinus stenosis

1 | INTRODUCTION

Cerebrospinal fluid (CSF) leaks of the anterior skull base result from a communication between the subarachnoid space and the sinonasal cavity. These may be iatrogenic, posttraumatic, tumor-related, or spontaneous in etiology. Historically, spontaneous cerebrospinal fluid (sCSF) leaks comprised the least common etiology, between 3% and 5% of all CSF leaks.[1,2] More recent literature, however, suggests that 14%–55% of all anterior CSF leaks are spontaneous in nature.[3–6] CSF leaks carry a significant risk of life-threatening intracranial infection. As such, surgical closure, principally via endoscopic approach, is indicated to mitigate this risk.[7,8]

While sCSF leaks are, by definition, devoid of a known etiology, there is a suggested link between Idiopathic Intracranial Hypertension (IIH) and sCSF leaks in the literature. Perez et al. published a full listing of the reports of patients with sCSF leaks and IIH. The authors noted that 72% of patients with beta transferrin-proven CSF rhinorrhea also met criteria for IIH.[9] One proposed mechanism for this suggests that chronic elevation in ICP leads to erosion and thinning of the bone at sites where over-pressurized arachnoid granulations, dura, or dural venous sinuses (DVS) contact the skull base. As such, diligent perioperative ICP management leads to a significant difference in success rates of sCSF leak repairs.[9–14]

Moreover, recent literature indicates a relationship between IIH and DVS narrowing. This typically occurs at the junction of the transverse and sigmoid sinuses. It is unclear if narrowing occurs secondary to increased intracranial pressure (ICP) or if intrinsic DVS stenosis leads to increased ICP. Nonetheless, computed tomography (CT) and magnetic resonance (MR) venographic data from available studies have elicited a 65%–90% prevalence of DVS narrowing in patients with IIH. Further, stenting has been successfully used to treat DVS narrowing and IIH.[15–19]

While DVS narrowing and sCSF leak has each been independently linked to IIH, there is a paucity of data linking DVS narrowing with sCSF leak. Bedarida et al. were the first to report on an association between these two entities. Their retrospective, matched case–control study revealed a 79% rate of DVS narrowing among patients treated endoscopically for sCSF leak versus a 10% rate in the control population.[20] This raises the possibility of finding a correctable underlying cause of sCSF leaks.

The aim of this study is to further establish the prevalence of DVS narrowing (i.e., stenosis or hypoplasia) in patients with sCSF leaks and to determine whether DVS narrowing is more prevalent in these patients than in the general population.

2 | MATERIALS AND METHODS

A retrospective chart review was performed on all patients with sCSF leak that presented to a tertiary academic center from 2008 to 2019. Patients with CSF rhinorrhea related to antecedent skull base trauma, surgery, tumors, or congenital malformations were excluded from the analysis. Only patients with available three-dimensional imaging of the DVS were included. This included computed tomography angiography (CTA), CT of the sinuses with contrast, cerebral angiography, magnetic resonance venography (MRV), or magnetic resonance imaging (MRI) of the brain with contrast. Those without adequate imaging to evaluate the DVS were excluded. All included patients had beta-2 transferrin-confirmed CSF rhinorrhea. The study was approved by the Institutional Review Board.

Preoperative imaging was retrospectively reviewed by two independent neuroradiologists, each with over 10 years of experience. For cases in which a discrepancy between the two evaluations existed, imaging was reevaluated until a consensus was reached. The DVS was analyzed for stenosis or hypoplasia on the available imaging modality. DVS narrowing was quantified by cross-sectional areas of the narrowest segment of the transverse sinus and the sigmoid sinus such that DVS narrowing $= 100 \times (1-[\text{narrowest segment of transverse sinus}]/\text{sigmoid})$. DVS narrowing was considered significant when this was greater than or equal to 50% and bilateral or unilateral with contralateral DVS hypoplasia with a sinus cross-sectional area < 35 mm^2.[20,21] Imaging was also evaluated for the presence of empty sella, for which the sella was noted to be CSF-filled and further objectified by the height of the pituitary near the infundibulum in a coronal plane.[20,22,23]

To obtain controls representative of the general population, we invoked a study by Durst et al. that evaluated the prevalence of DVS stenosis or hypoplasia in a generalized population of patients. The authors included 355 consecutive patients who underwent CTA of the head for indications other than vision change, headaches, IIH, tinnitus, mass effect, and lumbar puncture with opening pressure greater than 20. All patients had sufficient opacification of the sinuses on CTA (density > 200).[24]

Data were presented as the count and percent of patients with sinus narrowing and analyzed using the exact binomial test comparing the prevalence of DVS narrowing in our sample to that found by Durst et al. Analyses were performed with R software (version 3.5, R Foundation for Statistical Computing) using Rstudio graphical user interface (version 1.1.463, Rstudio Inc.). Due to the small sample size in this study, all *p*-values should be considered descriptive rather than confirmatory. Therefore, a *p*-value less than .05 may suggest areas for further investigation.

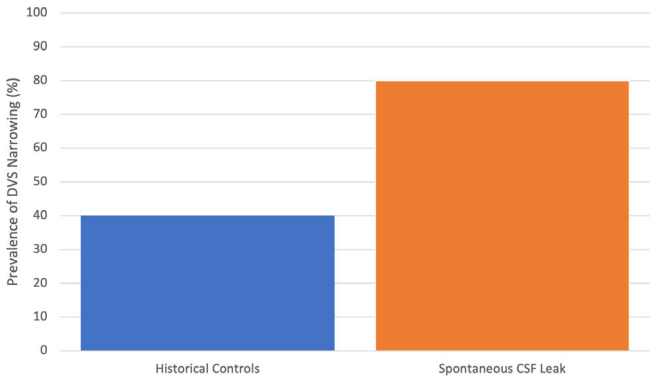

FIGURE 1 Prevalence of DVS narrowing in patients with spontaneous CSF leak versus historical controls.

TABLE 1 Characteristics of patients with sCSF leak and historical controls.[24]

	Dural venous sinus narrowing ($n = 20$)	No sinus narrowing ($n = 5$)	Overall ($n = 25$)	Durst et al. ($n = 325$)
Sex				
Male (%)	1 (5)	2 (40)	3 (12)	183 (52)
Female (%)	19 (95)	3 (60)	22 (88)	172 (48)
Median age (IQR)	49 (43.3–60.5)	56 (46–70)	51 (45–62)	57.4 (±17.6)[a]
Ethnicity				
Caucasian (%)	5 (25)	2 (40)	7 (28)	
African American (%)	5 (25)	2 (40)	7 (28)	
Hispanic (%)	3 (15)	0 (0)	3 (12)	
Asian (%)	2 (1)	0 (0)	2 (8)	
Other (%)	5 (25)	1 (2)	6 (24)	
Past medical history				
Hypertension (%)	12 (60)	3 (60)	15 (60)	
Diabetes mellitus (%)	6 (30)	1 (20)	7 (28)	
Obese (BMI > 30) (%)	15 (75)	4 (80)	19 (76)	
Obstructive sleep apnea (%)	1 (5)	0 (0)	1 (7)	
Imaging modality				
CT (%)	2 (10)	0 (0)	2 (8)	
CTA (%)	7 (35)	0 (0)	7 (28)	
MRI (%)	9 (45)	5 (100)	14 (56)	
MRV (%)	1 (5)	0 (0)	1(4)	
Cerebral angiography (%)	1 (5)	0 (0)	1 (4)	
Meningitis (%)	4 (20)	0 (0)		
Empty/partial empty Sella (%)	14 (70)	1 (20)	15 (60)	

Abbreviations: BMI, body mass index; CT/A, computed tomography/angiography; DVS, dural venous sinus; IQR, interquartile range; MRI/MRV, magnetic resonance imaging/venography.
[a]Age data presented as a mean with standard deviation in Durst et al.

3 | RESULTS

In our patients with sCSF leaks, there was a significantly higher proportion of patients with DVS narrowing compared to that found in the aforementioned literature examining the presence of DVS narrowing in the general population (80% vs. 40%, CI 0.59–0.93, $p < .001$) (Figure 1).

Ninety-one patients presented to our institution with sCSF leaks during the study period. Of these, 66 patients were excluded from the study due to insufficient imaging to evaluate the DVS. The remaining 25 patients were included in the analysis. The characteristics of these patients are summarized in Table 1. The majority of patients were women (21/25, 84%) with a mean age of 51.89 years (SD 13.96). Twenty of these 25 (80%) patients had DVS narrowing. Fifteen of these patients (60%) were also noted to have empty or partially empty sella. Four patients (16%) had a prior history of meningitis. MRI of the brain with contrast was the most common imaging modality used to identify DVS narrowing (56%) (Figure 2), followed by CTA (28%). The ethmoid and sphenoid sinuses were the most common location of sCSF leak (Table 2).

In the study population analyzed by Durst et al., the prevalence of unilateral transverse sinus stenosis or hypoplasia was 33%, the

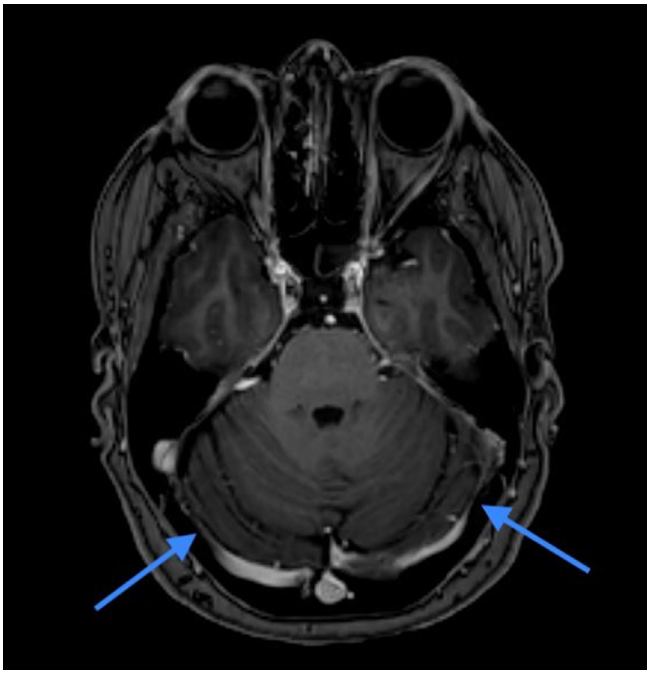

FIGURE 2 Contrast-enhanced T1-weighted MRI demonstrating bilateral transverse sinus narrowing.

TABLE 2 Location of sCSF leak in patients with and without DVS narrowing.

	DVS narrowing ($n = 20$)	No DVS narrowing ($n = 5$)
Location		
Cribriform plate	2 (10)	1 (20)
Ethmoid sinuses (%)	9 (45)	2 (40)
Anterior (%)	6 (30)	2 (40)
Posterior (%)	3 (15)	0 (0)
Sphenoid sinuses (%)	8 (40)	2 (40)
Medial (%)	1 (5)	1 (20)
Lateral (%)	7 (35)	1 (20)
Frontal sinuses (%)	3 (15)	0 (0)
Supraorbital (%)	1 (5)	0 (0)
Laterality		
Left (%)	14 (70)	1 (20)
Right (%)	9 (45)	4 (80)

Note: Counts may add up to more than total *n* as some patients had multiple leaks.
Abbreviation: DVS, dural venous sinus.

prevalence of bilateral transverse sinus stenosis was 5%, and the prevalence of unilateral stenosis with contralateral hypoplasia was 1%. This imputes an overall prevalence of DVS narrowing of 40% in this generalized population. Age (mean age of 57.4 years, range of 3–92) and gender (48% women) were reported, however, further demographic data and comorbidities were not included.[24]

4 | DISCUSSION

Our study is the second study, with that by Bedarida et al. being the first, to show a strong association between DVS narrowing and sCSF leak. It also demonstrates that the prevalence of DVS narrowing in patients with sCSF leak may be significantly higher than the prevalence of DVS narrowing in the general population.

Recent literature indicates a relationship between IIH and DVS narrowing, which typically occurs at the junction of the transverse and sigmoid sinuses. It is unclear if narrowing occurs secondary to increased ICP or if intrinsic stenosis results in an elevation in ICP.[15] Nonetheless, there is suggested to be a high prevalence of DVS narrowing in patients with IIH. Higgins et al. reported a 65% incidence of bilateral DVS narrowing on magnetic resonance venography (MRV) in patients with IIH versus 0% in their control population.[16] Farb et al. suggested a 90% incidence of narrowing of the distal transverse sinuses on MRV in patients with IIH.[17] Computed tomography venography (CTV) has also been used to demonstrate a 90% incidence of DVS narrowing in patients with presumed IIH.[18] Notably, stenting of the DVS has been successfully used as treatment for IIH.[19]

Moreover, there is a suggested link between IIH and sCSF leak.[9,11,14] Perez et al. published a full listing of reports of patients with sCSF leak and IIH, revealing that 72% of patients with beta-2 transferrin-proven sCSF leak also met criteria for IIH. The authors summarize that the association has been based on several factors. These include demographic similarities between classic IIH patients and patients with sCSF leak (mostly obese women of childbearing age), development of CSF leak in some patients with elevated ICP of known cause, elevated ICP in some patients following repair of spontaneous CSF leak, and higher recurrence rate of CSF leak in patients with elevated ICP after repair.[9,14] One proposed mechanism for this suggests that chronic elevation in ICP leads to erosion and thinning of the bone at sites where over-pressurized arachnoid granulations, dura, or DVS contact the skull base. Attenuation of the bone eventually leads to development of dehiscent communications.[13,14] As such, diligent postoperative ICP evaluation and management leads to a significant difference in success rates of sCSF leak repairs.[10,12]

Given that DVS narrowing and sCSF leak have each been independently linked to IIH, current investigations are exploring the relationship between DVS narrowing and sCSF leak. Bedarida et al. were the first to report an association between these two entities. Their retrospective, matched, case–control study of 29 patients treated endoscopically for sCSF leak revealed a 79% rate of DVS narrowing among patients vs. a 10% rate in the age- and sex-adjusted control population. These controls had undergone MRV or 3D-enhanced T1-weighted imaging with contrast for indications other than IIH, mass effect, hydrocephalus, venous thrombosis, or CSF leak.[20] Our results are consistent with those published by Bedarida et al., as 80% of our patients with sCSF leak were found to have DVS narrowing.

To obtain control representatives of the general population, we invoked a study by Durst et al. that evaluated the prevalence of DVS narrowing in a generalized population of 355 patients. They noted the prevalence to be 40%.[24] Subjects included in the Durst publication had fewer women and a wider age range than in the current study. Per our analysis, the prevalence of DVS narrowing in patients with sCSF leaks is significantly greater than that of the general population. Thus, we affirm that there is an association between sCSF leak and DVS narrowing.

Historically, patients with elevated ICP after CSF leak repair have often required long-term therapy, such as acetazolamide or CSF diversion, to reduce ICP. Long-term acetazolamide use carries risks including paresthesias, dysgeusia, fatigue, and metabolic derangements.[25] CSF diversion carries the risks of shunt migration, infection, acquired Chiari malformation and intracranial hemorrhage.[19] However, knowledge of the association between DVS narrowing and sCSF leak raises the possibility of finding a correctable underlying cause for sCSF leaks and foregoing these long-term measures. In fact, DVS stenting as a stand-alone treatment for sCSF leak with comorbid DVS narrowing has been reported.[26,27] More recently, Labeyrie et al. published a retrospective case–control study evaluating the use of DVS stenting after repair of sCSF leak in patients with confirmed DVS narrowing. They found that DVS stenting resulted in significantly less recurrence of CSF leaks and trended toward less adjunctive treatment.[28] Notably, their study does not describe the long-term efficacy of stenting for lowering intracranial pressure in the absence of other interventions.

Further, the risks of stenting, including intracranial hemorrhage, stroke, and risks of postprocedural dual antiplatelet therapy must be considered.[19] While the literature exploring the relationship between sCSF leak and DVS narrowing is promising, it remains in its infancy, and further study is needed.

This study is not without limitations. Given the retrospective nature of the study, the preoperative imaging modality was not standardized. This resulted in the majority of our sCSF leak population being excluded from the study due to lack of adequate imaging to evaluate the DVS. This greatly impacted the power of the study. Further, lack of standardized imaging resulted in inconsistency among the imaging modalities used to evaluate the DVS for the included patients. This inconsistency may have led to over- or underestimation of the prevalence of DVS narrowing in our cohort. The lack of standardized imaging was partially mitigated by the imaging studies being evaluated solely by board-certified Neuroradiologists. Finally, use of external controls precluded matching based on sex and age. In addition, the control population did not have its detailed demographic data published to allow for confirmation that this population was similar to our cohort. Further, the control population uniformly underwent CTA to evaluate the DVS while the imaging of our population was heterogeneous.

5 | CONCLUSION

The prevalence of DVS narrowing in patients with sCSF leaks is substantial and likely greater than the general population. Moreover, there appears to be narrowing in the vast majority of patients with sCSF leaks. Preoperative radiological evaluation of the DVS using MR venography may be useful in patients with sCSF leaks as DVS narrowing may be an underdiagnosed, and potentially correctable, etiology. Further study is needed to evaluate this.

CONFLICT OF INTEREST STATEMENT

William C. Yao serves as a consultant for Aerin Medical and on the speaker's bureau for Optinose Inc. Martin J. Citardi: Consultant: Acclarent, Intersect/Medtronic, LynxMD, MicroGenDx, Polyganics, Povinez. Amber U. Luong: Consultant: Acclarent, Lyra Therapeutics, Maxwell Bioscience, Stryker ENT, Medtronic, ENTvantage and Sanofi; Advisory boards: AstraZeneca and GlaxoSmithKline Grant support: Sanofi; Speaker honorarium: GSK and Aerin Medical. Karim W. Asi, Brian H. Cameron, Elliot R. Friedman, and Jeffrey P. Radabaugh: No financial disclosures.

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