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LEADING TOPIC

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Spontaneous rhinorrhea and idiopathic intracranial hypertension: a complex and challenging association

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ABSTRACT

Introduction. Spontaneous CSF leak is a known complication of idiopathic intracranial hypertension (IIH). Patients with CSF rhinorrhea present a unique challenge within the IIH population, as the occurrence of a leak can mask the typical IIH symptoms and signs, complicating the diagnosis. Treatment of leaks in this population can also be challenging, with the risk of rhinorrhea recurrence if intracranial hypertension is not adequately treated.

Objective. The aim of this narrative review was to examine current literature on the association between spontaneous CSF rhinorrhea leaks and IIH, focusing on key clinical features, diagnostic approaches, management strategies, and outcomes.

Material and methods. A literature search was executed using the PubMed and Scopus databases. The search was confined to articles published between January 1985 and August 2023; extracted data was then analysed to form the foundation of the narrative review.

Results. This search yielded 26 articles, comprising 943 patients. Average age was 46.8 ± 6.5 years, and average body mass index was 35.8 ± 4.8. Most of the patients were female (74.33%). Presenting symptoms were rhinorrhea, headaches and meningitis. The most common imaging findings were empty sella and encephalocele. The standard treatment approach was endoscopic endonasal approach for correction of CSF rhinorrhea leak, and shunt placement was also performed in 128 (13%) patients. Recurrences were observed in 10% of cases.

Conclusions. The complex relationship between spontaneous CSF leaks and IIH is a challenge that benefits from multidisciplinary evaluation and management for successful treatment. Treatments such as endoscopic repair, acetazolamide, and VP/LP shunts reduce complications and recurrence. Personalised plans addressing elevated intracranial pressure are crucial for successful outcomes.

Keywords: cerebrospinal fluid rhinorrhea, spontaneous rhinorrhea, pseudotumour cerebri, neurosurgery shunt

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Introduction

Nontraumatic cerebrospinal fluid (CSF) rhinorrhea, also known as spontaneous CSF rhinorrhea (SCSFR), occurs without an apparent cause and is often associated with increased intracranial pressure, congenital anomalies, or idiopathic factors [1, 2]. While most CSF rhinorrhea leaks are attributable to traumatic causes such as head injuries or surgical procedures, a small percentage, up to 5%, are associated with other factors such as hydrocephalus, structural anomalies, cerebral venous thrombosis, or

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unknown causes [1, 2]. Primary spontaneous CSF leaks represent a unique subset of this condition, characterised by specific features including its target demographic and a high recurrence rate, of 2.9-46% after repair, compared to other types of CSF leak [3, 4].

Although not all patients with SCSFR have idiopathic intracranial hypertension (IIH), the connection between them was first proposed in 1994 by Clark et al., who identified female gender and obesity as significant risk factors due to their potential to increase intraabdominal pressure, thereby impairing venous return and elevating intracranial pressure (ICP) [6]. Subsequent research has suggested a link between chronic elevated ICP and secondary skull base bony erosion leading to leakage [1, 3, 7]. Recognising and understanding this relationship is crucial for improving treatment outcomes. However, patients with CSF rhinorrhea leaks present a unique challenge within the IIH population. The leak can act as a 'pressure release valve' potentially masking typical IIH symptoms and signs, and even reducing lumbar puncture opening pressure [1, 3, 8]. This can complicate diagnosis under the modified Dandy's criteria, which include papilloedema, absence of structural findings (hydrocephalus, masses and lesions) in neuroimaging, normal CSF composition, elevated ICP (≥ 25 cmH2O), and MRI stigmata of intracranial hypertension such as empty sella and venous sinus stenosis [9].

The aim of this review was to examine the most recent literature on the association between SCSFR leaks and IIH, focusing on key clinical features, diagnostic approaches, management strategies, and outcomes.

Material and methods

A literature search was executed on 9 August, 2023 to identify relevant articles on spontaneous CSF leak and IIH using the PubMed and Scopus databases. The search strategy incorporated the terms: 'idiopathic intracranial hypertension' OR 'pseudotumour cerebri' AND 'CSF leak'. The search was confined to articles published between January 1985 and August 2023, resulting in a total of 118 manuscripts after the removal of duplicates.

The selection of pertinent studies for inclusion in the systematic review was conducted through a two-stage screening process. Initially, titles and abstracts were independently reviewed by two authors to ascertain their relevance to the research topic. The inclusion criteria at this stage were articles discussing spontaneous CSF leak in the context of IIH and reporting on patients with rhinorrhea as a primary symptom. This initial screening resulted in the selection of 48 full-text articles for further evaluation. Articles that did not meet the inclusion criteria, such as those focusing on spinal leaks, articles not related to spontaneous CSF leak, articles exclusively discussing otorrhea as the presenting sign, and articles not directly relating CSF rhinorrhea leak to IIH (secondary intracranial hypertension), were excluded from further consideration.

As the second stage of screening, the selected full-text articles were meticulously reviewed by two of the authors to assess their eligibility for inclusion in the review. Any disagreements in the selection process were resolved through discussion and consensus among the authors. After reviewing the exclusion criteria, we removed three articles primarily focusing on spinal CSF leaks, four articles that did not pertain to spontaneous CSF leaks, one article exclusively discussing otorrhea without relevance to rhinorrhea, two articles discussing SCSFR but not related to IIH, and 10 articles that there were not criteria for IIH. Consequently, 26 articles [1–6, 10–13, 15, 17, 21–31, 34–36] were included in our review.

Data from the selected articles was extracted and organised into themes, including clinical presentation and reports of rhinorrhea in IIH, diagnostic approaches, treatment modalities, and outcomes. The extracted data was then synthesised and analysed to form the foundation of the narrative review.

Results

Patient characteristics

This review included 943 patients with suspected or definitive IIH and spontaneous CSF leaks. The cohort had a mean age of 46.8 ± 6.5 years and a mean body mass index (BMI) of 35.8 ± 4.8. In terms of gender, only one article didn't distinguished the patients [35]. Overall, most of the patients were female (74.33%), while only 23.97% were male, 929 in total. The data on age, BMI, and gender distribution was obtained from 26 [1–6, 10-13, 15, 17, 21–31, 34-36], 14 [1–3, 5, 10–12, 17, 28–31, 34, 36], and 25 [1–6, 10–13, 15, 17, 21–31, 34, 36] studies, respectively. The mean follow-up period was 22.5 months, based on data from 16 [1, 2, 4, 5, 10–12, 15, 22–24, 26–28, 30, 36] studies. Table 1 sets out the demographic characteristics of the study population. The papers included used either Dandy's criteria or modified Dandy's criteria to label the patients as either 'definitive' or 'suggestive' cases of IIH. This review identified 99 definitive cases [1, 5, 6, 10, 13, 17, 21–23, 25–27, 29–31, 36] of IIH and 782 suggestive ones [2–5, 11, 12, 15, 24, 28, 34, 35].

Clinical presentation

Our review of 26 articles revealed a wide range of clinical features in patients presenting with IIH and spontaneous CSF leak, from classical characteristics associated with IIH such as headache, visual changes, pulsatile tinnitus, and papilloedema, to symptoms directly resulting from a skull base defect, such as rhinorrhea, sinusitis and meningitis, as well as hormonal dysfunction such as elevated prolactin levels, irregular menstrual cycles, and infertility. Headache was the most common symptom among patients included in the review, reported in 19 of the included papers [1–5, 11–13, 17, 21–29, 36], and it was also the most prevalent symptom at presentation, reported in 192 subjects. Meningitis occurred in 110 patients. Moreover,

Table 1. Demographics of IIH patients with spontaneous CSF leak extracted from narrative review

Number of studied patients	943
Mean age	46.8 ± 6.5 years
Mean BMI	35.8 ± 4.8
Gender	
Female	701 (74.33%)
Male	226 (23.97%)
Mean follow-up	22.5 months
Diagnosis of IIH (%)	
Suggestive	782 (82.9%)
Definitive	99 (10.5%)

Table 2. Symptoms at presentation of spontaneous CSF leak and IIH patients

Spontaneous CSF leak (rhinorrhea)	943 (915)
Symptom at presentation	
Headaches (%)	192 (20.36%)
Meningitis (%)	110 (11.66%)
Other (%)	89 (9.43%)
Mean duration of symptoms	11.4 months

89 patients had other diverse symptoms. The average duration of symptoms was 11.4 months. While we presume that all the patients in this study had rhinorrhea as the primary sign, it was explicitly reported in only 915 out of the 943 patients (Tab. 2).

Imaging findings

The radiological data from the studies analysed showed a range of findings related to spontaneous CSF leak and IIH [1, 3–6, 11, 15, 17, 22–31, 34–36]. These imaging findings revealed conditions such as empty sella, optic nerve sheath and Meckel's cave widening, sinus stenosis, bone erosion, meningocele, encephalocele, arachnoid herniation at the olfactory cleft, defects on nasal cavity, sinus stenosis, enlarged ventricles, and others. Meningo/encephalocele was found in 338 cases, while partial/empty sella was reported in 399 cases (Tab. 3). The review also showed different abnormalities in the skull anatomy, such as defects in the anterior fossa, cribriform plate, ethmoid sinus, sphenoid sinus, frontal sinus, and skull base. The most common sites of origin of CSF leaks were the ethmoid and sphenoid sinuses, comprising 446 cases [1–3, 5, 6, 10–13, 15, 17, 21–31, 36]. Other important sites were the anterior fossa, cribriform plate, superior nasal cavity, olfactory cleft, tegmen tympani, skull base, and middle ear. Additionally, some studies indicated high opening pressure in lumbar puncture, with the mean value being 25.52 ± 6.3 cmH2O [1, 3, 5, 6, 10, 11, 13, 17, 21, 22, 26–31, 34, 36], showing the importance of high pressure in relation to CSF leak and its complications.

Table 3. Anatomical and radiological features of patients with spontaneous CSF leak and IIH

Spontaneous CSF leak location (%)	
Cribriform plate	155 (16.4%)
Ethmoid sinus	161 (17%)
Sphenoid sinus	285 (30.2%)
Other	87 (9.2%)
Imaging findings (%)	
Meningo/encephalocele	338 (35.8%)
Partial/empty sella	399 (42.3%)
Optic nerve sheath widening/tortuosity	88 (9.3%)
Flattening of posterior globe	47 (4.9%)
Transverse venous sinus stenosis	25 (2.6%)
Widened Meckel's cave	34 (3.6%)
Others	4 (0.4%)

Management, recurrence and complications

The management of spontaneous CSF leak and IIH in patients was heterogenous among the studies. Obesity was a common factor among patients, and weight loss interventions were often recommended [1–3, 5, 10–13, 15]. Endoscopic endonasal surgery for skull base reconstruction and leak repair was the selected approach to fix skull base defects. Fascia lata graft placement, vascularised nasoseptal flaps, and dura substitutes have been used for the repair of such defects, and the selection of the technique and the tissues for repair vary according to the site, size, previous procedures, and BMI [11, 15]. Leaks of small size and low volume usually can be repaired with the use of dura substitute and/or mucosa graft, while those of larger size and high volume and patients with recurrent leaks, especially those with high BMI and increased intracranial pressure, usually benefit from reconstruction based on vascularised flaps. The most commonly applied vascularised option for reconstruction is the nasoseptal flap, but other options such as lateral wall flap, temporoparietal fascia flap, and pericranial flap are also useful in selected cases.

Insertion of shunting is an important tool in the management of patients with IIH and spontaneous CSF leaks. The decrease in ICP (intracranial pressure) promoted by the presence of a shunt, either ventriculoperitoneal (VPS) or lumboperitoneal (LPS), has been well described as an adjunct in the repair of recurrent spontaneous CSF leaks in this population. In our current review, VPS/LPS placement was performed in 128 (13.57%) patients [3–6, 10, 12, 17, 21–23, 26, 28–31, 34, 36], to manage high intracranial pressure, while acetazolamide was used as an alternative treatment option in 170 [1, 3, 6, 10–12, 17, 21, 25, 28, 29, 31, 34–36] patients. Additionally, several invasive procedures were performed to address the underlying causes of IIH and associated CSF leak, such as perioperative lumbar drains or

Table 4. Treatment of spontaneous CSF leak, management of higher ICP, and surgical complications of spontaneous CSF leak in IIH patients

Treatment — CSF leak	
Patients undergoing surgical repair	792
Remission	713 (90%)
Recurrence	79 (9.97%)
Mean time of recurrence	20.5 ± 13 months
Raised ICP management	
Shunt placement	128 (13.57%)
Acetazolamide	170 (18%)
Long-term surgical complications	
Shunt malfunction/misplacement	14 (1.76%)
Meningitis	5 (0.63%)
Seizures	2 (0.25%)
Other	2 (0.25%)

external ventricular drains, dural venous sinus stent (for those with identified dural stenosis), and lumboperitoneal shunt placement [3, 5, 6, 10–13].

Of a total of 792 patients who underwent surgical repair, 713 were successful within the first surgery and 79 had a recurrence. The average time of recurrence was 20.5 ± 13 months [1, 4, 6, 11, 12, 15, 31], indicating the need for long-term follow-up and effective management strategies (Tab. 4). Long-term surgical complications associated with spontaneous CSF leak and IIH occurred in 23 patients, such as seizures, meningitis, and shunt malfunction/misplacement in a few patients, mainly due to the recurrence of previous symptoms. Some other surgical complications related to surgery were also reported, such as intraparenchymal haematoma, secondary respiratory acidosis, lacrimal dysfunction due to injury of the lacrimal drainage system, injury to the optic nerve, orbital haematoma, and bleeding from the anterior ethmoidal artery [5, 6, 10, 12, 15, 17, 22, 23, 25, 26, 36].

Discussion

Patient characteristics

Spontaneous CSF leak is a known complication of IIH, but its pathogenesis is still not fully understood. Several hypotheses have been put forward to account for how increased CSF pressure could lead to defects in the skull base, dura mater, arachnoid mater, or arachnoid villi [2–5]. However, these factors alone cannot explain why some patients develop a spontaneous CSF leak but others do not. Badia et al. [2] reported nine cases of high ICP and rhinorrhea, six females and three males, with an average age of 50 and an average BMI of 40. They proposed that obesity, especially visceral obesity, could predispose to a spontaneous CSF leak by increasing intra-abdominal pressure, impairing venous drainage, and exacerbating ICP fluctuations. They recommended weight reduction as a preventive measure [2]. Holzmann et al. [14] conducted a comparative study of 61 patients with spontaneous CSF leak of various origins, classified into five groups. They found that the only significant difference among the groups was BMI, which was much higher in the spontaneous CSF leak group, thereby corroborating the role of obesity as a risk factor for leak.

Clinical presentation

The diagnosis of IIH remains a complex task for clinicians, despite the existence of well-defined diagnostic criteria and a characteristic patient profile (i.e. female and obese). As most patients in our review had presumed or suspected IIH, not all of them fully fitted the criteria for IIH. Hong et al. [3] analysed 716 patients with a spontaneous CSF leak who were suspected of having IIH. They found that their mean age was older than that of newly diagnosed IIH patients, suggesting a slow progression of IIH in these cases, with the leak potentially serving as a 'pressure release valve' that alleviated the symptoms of elevated ICP and postponed the diagnosis. Similarly, other researchers have reported that the leak obscures the main manifestations of IIH such as headaches, papilloedema and even CSF opening pressure, leading to a delayed diagnosis, failure to meet the criteria, and the assumption that most patients with spontaneous CSF leak have underlying IIH and only developed rhinorrhea later. In a study by Bidot et al. [5], only 20% of 36 patients fulfilled the Dandy's criteria, while the rest had presumed or suggested IIH.

Ophthalmological evaluations serve as a crucial component in the diagnostic and follow up process, aiding in the comprehensive assessment of spontaneous CSF leak patients [8, 10, 22, 29]. Notably, the absence of papilloedema, a hallmark of traditional IIH, is frequently observed in spontaneous CSF leak patients. However, postoperative emergence of papilloedema following leak repair has been documented in certain cases, underlining the importance of thorough postoperative follow-up [42]. Proper postoperative management, including the administration of acetazolamide or shunting, is crucial in selected cases, reducing the risk of postoperative complications, and promoting favourable outcomes [20, 30, 34, 35].

Although lumbar puncture (LP) is routinely recommended for preoperative intracranial pressure assessment, the existence of the leak itself complicates the interpretation of preoperative ICP values, as it acts as a natural treatment for elevated ICP, hiding the typical symptoms of those with high ICP — headache or visual disturbance — often leading to underestimation [10]. Thus, careful monitoring of immediate and short-term postoperative ICP values is vital to evaluate the efficacy of the surgical intervention [40]. In a study by Aaron et al. [10], CSF opening pressure (CSF-OP) was measured in 16 patients who underwent surgical repair for spontaneous CSF leak. The mean CSF-OP before surgery was 27.4 cmH2O, which increased to 36 cmH2O at six hours after clamping and at 48 hours after repair, indicating a significant rise of CSF-OP following the

intervention. These patients were compared to a control group of 16 patients who had a previous diagnosis of IIH with papilloedema and no leak, and had a mean CSF-OP of 36.2 cmH2O.

The results suggest that both groups had the same underlying condition and that the spontaneous CSF leak acted as a 'treatment' for the high ICP symptoms such as papilloedema in the first group, as the CSF-OP increased to the level of the second group after the repair.

Imaging findings

The diagnosis and management of IIH and spontaneous CSF leak benefits from a multidisciplinary approach that employs a variety of diagnostic tools. Volumetric CT scans with thin cuts are crucial for accurate assessment of the bone anatomy and identification of the site of the leak, thereby facilitating precise surgical planning [4, 15, 21]. Furthermore, MRI plays a pivotal role in identifying the leak and associated intracranial pathologies, such as meningocele and encephalocele, providing a more comprehensive understanding of the condition [1–3, 5, 6, 10–32, 36, 37, 39–41]. Additionally, MR venography (MRV) is useful in evaluating the presence of venous sinus stenosis, guiding potential future management strategies [23]

The MRI features of IIH were recently investigated in a cohort of 117 patients by Rupa et al. [4]. The most prevalent finding was empty sella, observed in 62.4% of cases, followed by optic nerve sheath widening in 53%. Posterior globe flattening and widening Meckel's cave were less frequent, occurring in 27.1% and 23.1% of the patients, respectively. Only 12 patients had no MRI abnormalities, while 68 patients had at least one of the high specificity signs (i.e. empty sella, posterior globe flattening, or widened Meckel's cave). Notably, empty sella was present in all patients with these signs, and all patients with papilloedema (n = 11) had at least one MRI feature of IIH. These results suggest that the inclusion of MRI criteria in the Dandy's diagnostic framework could increase the accuracy and confidence of IIH diagnosis.

The role played by imaging studies in the diagnosis of spontaneous CSF leak associated with IIH is crucial, as they can reveal the location and nature of the leak, as well as signs of increased intracranial pressure, such as skull base erosion, arachnoid pits, enlarged foramen, and optic nerve sheath dilatation. Quatre et al. [15] reported a series of 65 patients with spontaneous CSF leak, of whom 15 (eight women and seven men), with a mean age of 50 and only three of them obese (BMI ≥ 30), had isolated rhinorrhea without any other symptom. MRI showed that eight of these patients had a dura defect, six had encephalo/meningocele, six had empty sella, and six had optic nerve sheath dilatation. These findings suggest that imaging studies can provide diagnostic clues even in patients who do not fit the typical profile or criteria for IIH.

Management, recurrence and complications

In terms of therapeutic interventions, conservative approaches including antibiotic therapy, weight management, and rest, have been widely discussed, although the efficacy of these measures remains the subject of debate [1–3, 5, 6, 10–12, 16, 17, 22, 23, 25, 26, 28, 29, 31, 34, 36]. Notably, weight loss of at least 10% has been suggested as a potential therapeutic target, and reports have highlighted the positive outcomes associated with certain bypass procedures in this context [1–3, 5, 10–15].

Endoscopic repair is a commonly advocated therapeutic approach considering the risks associated with persistent spontaneous CSF leak [19, 20, 32, 33]. Various repair techniques involving different types of grafts and flaps have been employed to address the leak; however, recurrence rates remain a concern [1, 4, 6, 11, 12, 14, 15, 32]. Failure to identify and treat elevated ICP has been identified as a significant factor contributing to higher recurrence rates associated with endoscopic repair in this specific patient population [1, 4, 6, 11, 12, 14, 15, 32]. The use of fluorescein for leak identification has been demonstrated to be useful and safe for successful endoscopic skull base repair [43]. Martinez et al. [11] reported that 35 patients who underwent surgical repair also received acetazolamide as an adjunct therapy for 6-8 months or until the symptoms of high ICP resolved. The recurrence rate was only 2.9%, indicating that acetazolamide may help regulate the ICP, lower the risk of papilloedema, and prevent recurrences. Spontaneous CSF leaks are known to have the highest recurrence rate among different leak aetiologies. Dallan et al. [12] described 18 patients with recurrent spontaneous CSF leak, defined as a new leak in a different site at least three months after the previous repair. Four patients required a ventriculoperitoneal shunt and one patient received acetazolamide for managing elevated ICP. That study suggested that interventions for elevated intracranial pressure increased the success rate of spontaneous CSF leak repair.

Conclusions

The complex relationship between spontaneous CSF leaks and IIH is a challenging issue that benefits from multidisciplinary evaluation and management for successful treatment. Obesity, especially visceral fat, plays a significant role in causing spontaneous CSF leaks by affecting intra-abdominal pressure, hindering venous drainage, and increasing intracranial pressure. This underlines the importance of weight management as a preventive measure. Moreover, endoscopic repair, and additional treatments such as acetazolamide and VP/LP shunts, have been shown to reduce postoperative complications and the recurrence of spontaneous CSF leaks. Managing elevated intracranial pressure is key to successful outcomes, highlighting the need for personalised treatment plans.

Spontaneous CSF leaks can mask IIH symptoms, making it difficult to meet diagnostic criteria. This review also underlines the importance of using multiple diagnostic methods, including CT scans and MRI, to locate the leak and identify related intracranial pathologies. These techniques, along

with careful monitoring of intracranial pressure before and after surgery, are vital for effective treatment and improved patient outcomes.

We conclude by emphasising the need for a comprehensive approach to manage the complex interaction between spontaneous CSF leaks and IIH. This includes timely diagnosis, appropriate intervention, and improved patient outcomes. Future research should focus on understanding the complex mechanisms underlying this relationship in order to improve diagnostic and therapeutic strategies.

Article information

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