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# Relationship Between Benign Intracranial Tumor Location and the Side of Spontaneous Cerebrospinal Fluid Leak

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## ABSTRACT

**AIM:** To present cases of spontaneous cerebrospinal fluid (CSF) rhinorrhea and otorrhea, and to conduct a systematic literature review examining the relationship between benign tumor location and the leak side.

**MATERIAL and METHODS:** A PRISMA-based systematic review was conducted to evaluate studies on spontaneous CSF leaks caused by benign intracranial tumors, alongside three newly reported cases.

**RESULTS:** All three cases exhibited CSF leaks ipsilateral to the tumor: Case 1 involved a pituitary ACTH-secreting macroadenoma with rhinorrhea; Case 2, a pineocytoma with hydrocephalus and nasal encephalocele; and Case 3, a petromastoid meningioma with otorrhea.

In the systematic literature review, 28 of 125 studies met the inclusion criteria. The median patient age was 42 years, with a male-to-female ratio of 16:12. Macroprolactinoma was the most frequent tumor (25%), primarily located in the sella (46.4%). Tumors were located at the midline (39.3%), right side (35.7%), or left side (25%). The sphenoid sinus was the most common site of CSF leak (39.3%). The leak occurred through the right nostril (39.3%), left nostril (39.3%), both nostrils (10.7%), right ear (7.1%), and both the nostril and ear (3.5%). Hydrocephalus was present in 25% of cases.

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**CONCLUSION:** Although our cases demonstrated ipsilateral leaks, the literature review revealed equal rates of left-sided rhinorrhea, even with midline or right-sided tumors, suggesting skull base bone destruction alone does not explain CSF leaks, particularly in benign intracranial tumors outside mastoid involvement. Careful patient history regarding the side of rhinorrhea, comprehensive preoperative imaging, and hydrocephalus evaluation are essential for identifying the leak site and preventing complications, such as recurrent meningitis.

**KEYWORDS:** Benign intracranial tumors, Hydrocephalus, Otorrhea, Rhinorrhea, Spontaneous cerebrospinal fluid leak

**ABBREVIATIONS:** CSF: Cerebrospinal fluid, CT: Computerized tomography, HRCT: High-resolution computed tomography, ICP: Intracranial pressure, MRI: Magnetic resonance imaging, PF: Posterior fossa, VP: Ventriculoperitoneal

## ■ INTRODUCTION

Cranial cerebrospinal fluid (CSF) leaks occur when an abnormal connection forms between the intracranial subarachnoid space and the nasal sinuses (CSF rhinorrhea) or the middle ear, often accompanied by a perforated tympanic membrane (CSF otorrhea) (2,49,53). Head trauma, particularly skull base fractures, accounts for 80%–90% of the cranial CSF leak cases, while leaks following intracranial surgery represent about 10% (2). Spontaneous CSF leaks are rare and may result from congenital skull defects, meningoencephaloceles, paranasal sinus abnormalities, or other skull base lesions, including tumors (2,3,17,25,49,54). Miller first described the term “spontaneous” CSF fistula in 1826, in a child with hydrocephalus (46). As spontaneous CSF leaks are uncommon, their initial insidious onset is often mistaken for rhinitis. Accurate diagnosis requires a high index of suspicion, including a detailed history, endoscopic examination, and appropriate investigations, particularly if the discharge is watery, salty, unilateral, position dependent, or refractory to medical management (3,26). While spontaneous cases previously accounted for only 3%–5% of CSF leaks, they are now recognized in 14%–46% of cases, aided by advances in early and accurate diagnosis (12,29,68,70). The duration of spontaneous rhinorrhea ranges from days to years, with persistent leaks (>7 days) carrying an incremental risk of bacterial meningitis (2,18), exceeding 85% if the leak persists for up to a decade, and corresponding to a mortality rate of 4.1% (21,34). Therefore, accurate preoperative localization of the CSF leak is essential for successful surgical repair (2,3).

In this study, we present three cases of benign intracranial tumors associated with spontaneous CSF leaks that underwent surgical treatment. Additionally, we conducted a systematic literature review focusing on the correlation between tumor location and the side of the spontaneous CSF leak. To our knowledge, this study is the first in the English literature to systematically investigate this relationship.

## ■ MATERIAL and METHODS

A systematic review was conducted in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (55). We searched PubMed, Embase, Scopus, Web of Science, and the Cochrane Database of Systematic Reviews for English language articles re-

porting spontaneous CSF leaks. The search strategy included the following terms: (spontaneous rhinorrhea OR spontaneous otorrhea OR spontaneous cerebrospinal fluid leak) AND (meningioma OR skull base tumor OR anterior fossa tumor OR middle fossa tumor OR posterior fossa tumor OR anterior fossa meningioma OR middle fossa meningioma OR posterior fossa meningioma OR pituitary tumor OR intracranial tumor OR pineal tumor OR benign intracranial tumor). Following this search, an additional search was conducted to assess study eligibility based on tumor location and laterality. We also performed a supplementary web search using Google Scholar and Google, incorporating relevant keywords found within the articles. All original English language articles describing spontaneous CSF leaks due to benign intracranial tumors, characterized by at least one benign intracranial tumor and imaging-confirmed spontaneous CSF leak, were included. Studies that did not report the tumor or leak side, as well as laboratory, cadaver, or animal studies, were excluded. Furthermore, cases with a history of head trauma or intracranial surgery, or those medically treated with dopamine agonists for pituitary adenomas, were excluded. Articles published between 1961 and December 31, 2024, were included (Figure 1).

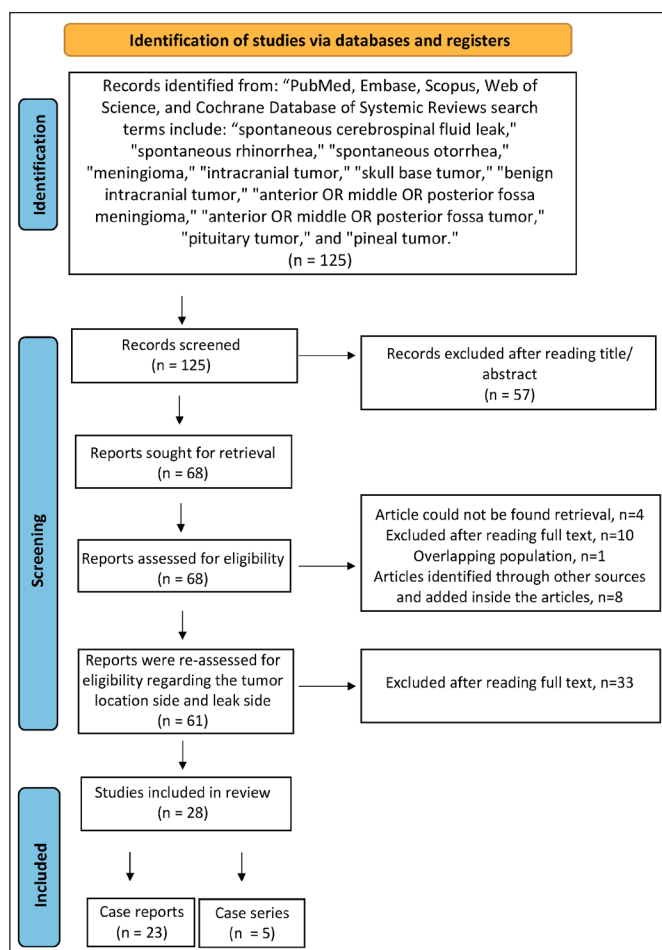
Two reviewers (NK and AT) independently screened titles and abstracts, extracted data, and assessed the risk of bias. Key clinical information was collected from the published records, including age, sex, pathology, primary tumor location and side, CSF leak site and side, CSF leak type (rhinorrhea, otorrhea, or both), and the presence of associated hydrocephalus (Table I).

Disagreements were resolved through discussion, and if consensus was not reached, a third author (MM) conducted an independent review. Two researchers (NG and MM) independently reviewed the search. A clinical chart review was performed to report cases of spontaneous CSF leaks managed at the authors' centers. All cases were reviewed by experienced neurosurgeons to assess clinical presentation, treatment strategy, and outcomes.

## ■ RESULTS

### Literature Review

We identified 125 English language studies reporting preoperative spontaneous CSF leaks, with the earliest included publication dating to 1961. Of these, 28 articles



**Figure 1:** Illustration of the PRISMA flow diagram for this study.

met the inclusion criteria and were analyzed (Table I). Data on tumor location and CSF leak site were extracted from 28 articles reporting spontaneous CSF leaks (1,4,6,9,10,14,15,17,19,20,23,24,27,28,31,34,35,43-45,48,51,52,57,60-62,66). Although 14 cases were presented in the article's case series, the leak side and tumor location were reported for only one case in each study (4,15,24,31,61).

### Demographics

The 28 patients had a median age of 42 years, with a mean of  $43.46 \pm 16.31$  years (range, 20–80 years). Of these, 16 (57.1%) were male and 12 (42.9%) were female.

### Tumor Type and Location

The most common tumor pathology was macro prolactinoma (25%,  $n=7$ ), followed by meningioma (17.8%,  $n=5$ ) and other WHO low-grade tumors, such as choroid plexus papilloma (10.7%,  $n=3$ ) and acoustic neuroma (3.6%,  $n=1$ ).

The most frequent tumor location was the sellar region (46.4%,  $n=13$ ), followed by the cerebellopontine angle (7.1%,  $n=2$ ) and the temporal bone (7.1%,  $n=2$ ). The majority of tumors arose in midline structures (39.3%,  $n=11$ ), 35.7% ( $n=10$ ) were right-sided, and 25% ( $n=7$ ) were left-sided.

### CSF Leak Site

The most common site of CSF leak was the sphenoid sinus (39.3%,  $n=11$ ), followed by the cribriform plate (17.8%,  $n=5$ ) and the sella turcica (14.3%,  $n=4$ ). Leakage occurred equally from the left (39.3%,  $n=11$ ) and right nostrils (39.3% each,  $n=11$ ), while 10.7% ( $n=3$ ) had bilateral nasal leakage. The right ear was involved in 7.1% ( $n=2$ ) of cases, while one patient (3.6%,  $n=1$ ) exhibited concurrent leakage from the right nostril and ipsilateral ear. Hydrocephalus was present in seven patients (25%). Although the cribriform plate has previously been reported as the most common site for spontaneous CSF rhinorrhea (49), we found the sphenoid sinus to be the most frequently affected site, followed by the cribriform plate. The tumor location may influence this distribution, as midline structures were the most common site of primary tumors (Table I).

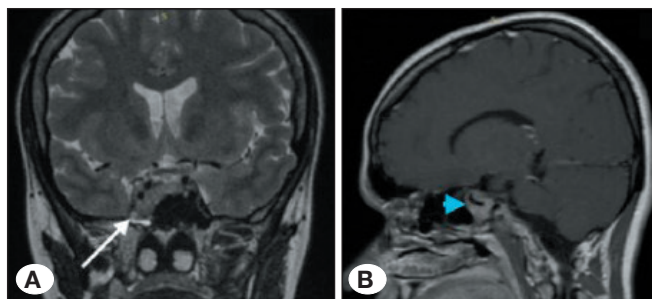
### Level of Evidence

Most included studies were low in the evidence hierarchy, comprising five case series (Level IV) and 23 case reports (Level V), according to the Oxford Centre for Evidence-Based Medicine criteria (Figure 1).

### Case Reports

#### Case 1

A 25-year-old woman presented with clear fluid discharge from her right nasal ostium each morning for the past two years. Analysis of the collective fluid was positive for b2 transferrin, confirming a diagnosis of CSF rhinorrhea. She also reported fatigue, difficulty in getting up, and daytime sleepiness. Medical examination revealed no systemic abnormalities, and her blood pressure, BMI, and neurological examination were all within normal limits. Cranial MRI revealed a 15 x 10 mm pituitary macroadenoma invading the right cavernous sinus (Knosp Grade 3B), with a normal ventricular system and otherwise normal brain structures (Figure 2). Endocrinological evaluation revealed normal pituitary hormone levels except for an elevated ACTH of 62 pg/mL. A 1 mg dexamethasone suppression test (DST) showed a cortisol level of 2.72  $\mu\text{g/dL}$  (not



**Figure 2:** The coronal T2WI preoperative magnetic resonance imaging (MRI) scan shows a pituitary macroadenoma invading the inferior part of the right cavernous sinus (Knosp 3B) and the sellar floor with hyperintensity compatible with CSF in the inferior part of the tumor towards the sphenoid sinus (A). The sagittal T1WI preoperative MRI with contrast demonstrates pituitary adenoma invasion of the cavernous sinus (B).

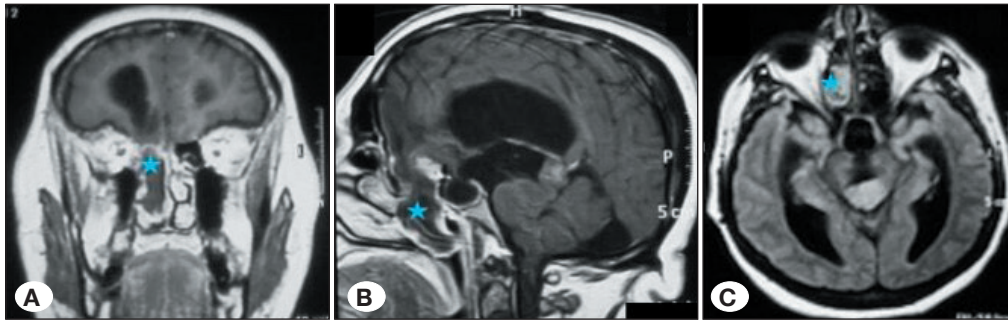
**Table I:** A Literature Review of All Studies on Benign Intracranial Tumors with Spontaneous CSF Leak and their Relationship with Leakage Side

| Case No. | Author                              | Study Design | Age (years) | Sex | Rhinorrhea | Otorrhea | Tumor side | CSF leak side | CSF leak site            | Pathology                               | Tumor location                             | HS  |
|----------|-------------------------------------|--------------|-------------|-----|------------|----------|------------|---------------|--------------------------|-----------------------------------------|--------------------------------------------|-----|
| 1        | Abouammo et al., (1)                | Case report  | 44          | M   | Yes        | No       | Left       | Left nostril  | Cribriform plate         | Meningioma en plaque                    | Temporal convexity, sphenoid-orbital ridge | No  |
| 2        | Anderson et al., (4)                | Case series  | 55          | M   | Yes        | No       | Midline    | Left nostril  | Sella Turcica            | Hypophysis adenoma (Non Functioning)    | Hypophysis                                 | No  |
| 3        | Aslan et al., (6)                   | Case report  | 50          | M   | Yes        | No       | Midline    | Both nostrils | Skull base               | Macro prolactinoma                      | Hypophysis                                 | No  |
| 4        | Bhatiwale et al., (9)               | Case report  | 20          | F   | Yes        | No       | Left       | Right nostril | Sphenoid sinus           | Neurofibromatosis, spongiform dysplasia | Occipital squama/Paracondylar area         | No  |
| 5        | Bhayani et al., (10)                | Case report  | 40          | M   | Yes        | No       | Left       | Right nostril | Sella Turcica            | Acoustic neuroma                        | Cerebellopontine angle (CPA)               | Yes |
| 6        | Campbell et al., (14)               | Case report  | 36          | M   | Yes        | No       | Midline    | Both nostrils | Sella Turcica            | Pituicytoma                             | Hypophysis                                 | No  |
| 7        | Candy et al., (15)                  | Case series  | 27          | M   | Yes        | No       | Right      | Right nostril | Ethmoid sinus            | Osteoid osteoma                         | Frontoethmoidal region                     | No  |
| 8        | Chowdhury et al., (17)              | Case report  | 35          | F   | Yes        | No       | Left       | Left nostril  | Cribriform plate         | Meningioma                              | Tentorial base                             | Yes |
| 9        | Deepak et al., (19)                 | Case report  | 37          | F   | Yes        | No       | Midline    | Left nostril  | Cribriform plate         | Colloid cyst                            | Anterior 3rd ventricle                     | Yes |
| 10       | Dias et al., (20)                   | Case report  | 54          | F   | Yes        | No       | Midline    | Right nostril | Sphenoid sinus/ clivus   | Ecchordosis Physaliphora                | Sphenoid sinus/ Superior clivus            | No  |
| 11       | Giovanelli and Perria, (23)         | Case report  | 40          | F   | Yes        | No       | Midline    | Right nostril | Sphenoid sinus           | Macro adenoma (Chromophobe)             | Hypophysis                                 | No  |
| 12       | Grozinsky-Glasberg and Shimon, (24) | Case series  | 55          | M   | Yes        | No       | Right      | Right nostril | Sphenoid sinus           | Macro prolactinoma                      | Hypophysis                                 | No  |
| 13       | Hanel et al., (27)                  | Case report  | 26          | F   | Yes        | No       | Midline    | Right nostril | Sphenoid sinus           | Macro prolactinoma                      | Hypophysis                                 | No  |
| 14       | Harvey et al., (29)                 | Case report  | 70          | M   | No         | Yes      | Right      | Right ear     | Temporal bone/Middle ear | Temporal bone meningioma                | Temporal bone                              | No  |
| 15       | Honegger et al., (31)               | Case series  | 41          | M   | Yes        | No       | Midline    | Left nostril  | Sphenoid sinus           | Macro prolactinoma                      | Hypophysis                                 | No  |

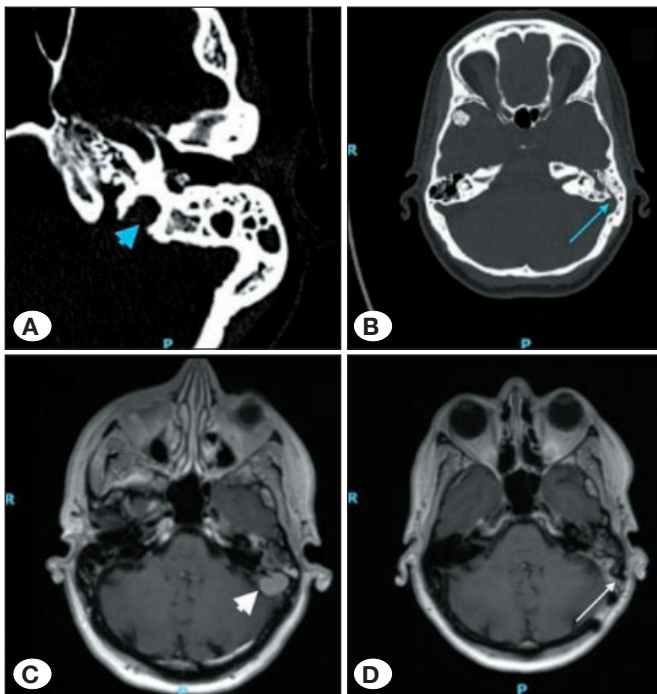
Table I: Cont.

| Case No. | Author                    | Study Design | Age (years) | Sex | Rhinorrhea | Otorrhea | Tumor side     | CSF leak side            | CSF leak site                 | Pathology                       | Tumor location                          | HS  |
|----------|---------------------------|--------------|-------------|-----|------------|----------|----------------|--------------------------|-------------------------------|---------------------------------|-----------------------------------------|-----|
| 16       | Kemps et al., (34)        | Case report  | 50          | F   | No         | Yes      | Right          | Right ear                | Petrous bone                  | Intra-osseous meningioma        | Temporal bone                           | No  |
| 17       | Kinoshita et al., (35)    | Case report  | 52          | F   | Yes        | Yes      | Right          | Right nostril+ Right ear | Petrous bone/ clivus          | Choroid plexus papilloma        | Cerebellomedullary cistern              | Yes |
| 18       | Macdonald et al., (43)    | Case report  | 66          | F   | Yes        | No       | Right          | Right nostril            | Sphenoid sinus                | Ecchordosis physaliphora        | Post wall of the sphenoid sinus/ clivus | No  |
| 19       | Makin et al., (44)        | Case report  | 68          | M   | Yes        | No       | Midline        | Right nostril            | Sphenoid sinus                | Pituitary adenoma (GH)          | Hypophysis                              | No  |
| 20       | Mankia et al., (45)       | Case report  | 29          | M   | Yes        | No       | Midline/ Right | Left nostril             | Sphenoid sinus                | Macro prolactinoma              | Hypophysis                              | No  |
| 21       | Mula-Hussain et al., (48) | Case report  | 43          | F   | Yes        | No       | Right          | Left nostril             | Sphenoid sinus/ Ethmoid sinus | Choroid plexus papilloma        | Cerebellopontine angle (CPA)            | Yes |
| 22       | Nutkiewicz et al., (51)   | Case report  | 45          | F   | Yes        | No       | Midline        | Right nostril            | Sphenoid sinus                | Pituitary adenoma (Chromophobe) | Hypophysis                              | No  |
| 23       | Ohtakara et al., (52)     | Case report  | 80          | F   | Yes        | No       | Midline/ Right | Right nostril            | Sphenoid sinus                | Macro prolactinoma              | Hypophysis                              | No  |
| 24       | Patel et al., (57)        | Case report  | 27          | M   | Yes        | No       | Midline/ Left  | Left nostril             | Sella Turcica                 | Macro prolactinoma              | Hypophysis                              | No  |
| 25       | Rothrock et al., (60)     | Case report  | 24          | M   | Yes        | No       | Midline        | Both nostrils            | Sphenoid sinus                | Macro adenoma (Unknown)         | Hypophysis                              | No  |
| 26       | Rovit et al., (61)        | Case series  | 21          | M   | Yes        | No       | Left           | Left nostril             | Cribiform plate               | Meningioma                      | Parieto-occipital region                | Yes |
| 27       | Symss et al., (62)        | Case report  | 61          | M   | Yes        | No       | Midline/ Right | Left nostril             | Cribiform plate               | Choroid plexus papilloma        | 4 <sup>th</sup> ventricle               | Yes |
| 28       | van Manen et al., (66)    | Case report  | 21          | M   | Yes        | No       | Left           | Left nostril             | Ethmoid sinus                 | Osteoma                         | Anterior skull base                     | No  |

HS: Hydrocephalus, M: Male, F: Female



**Figure 3:** The coronal (A), sagittal (B), and axial (C) sections of the preoperative T1WI magnetic resonance imaging with gadolinium show an anterior skull base defect, nasal encephalocele (blue star), hydrocephalus, and pineal tumor.



**Figure 4:** The computed tomography scan illustrating a bloated jugular bulb (A) and dehiscence connecting to the opacified mastoid space (B). Preoperative magnetic resonance imaging reveals a petromastoid meningioma (C), and postoperative imaging of the in-situ tissue graft and adhesive seal the leak after resection of the tumor (D).

suppressed), and a 2-day 2 mg DST showed 3.60 µg/dL (not suppressed), consistent with silent Cushing's disease. The tumor was completely removed via endoscopic transsphenoidal surgery, during which the CSF leak was successfully sealed. The leak was classified as direct, resulting from bony dehiscence caused by tumor invasion through the sellae into the sphenoid sinus. Pathological examination revealed a pituitary adenoma with a Ki-67 index of 10%, showing only weak immunohistochemical staining for ACTH. Dural invasion was confirmed. Postoperatively, the patient experienced a transient sixth nerve palsy, which resolved spontaneously within a month. She remained in remission eight years later, with no recurrence of CSF leakage. At no point did the patient exhibit clinical signs of hydrocephalus.

## Case 2

A 50-year-old woman presented to the emergency service with severe headache, vomiting, and neck stiffness. Her medical history revealed that two years earlier, she was diagnosed with triventricular hydrocephalus secondary to a pineal tumor and underwent VP shunting at another institution. She was obese and hypertensive, and was found to have right-sided CSF rhinorrhea and meningitis. High-resolution computed tomography (HRCT) and brain magnetic resonance imaging (MRI) scans revealed a bone defect on the right side of the cribriform plate, along with a small nasal encephalocele (Figure 3). Her VP shunt was removed, and an external ventricular drain was placed. Following broad-spectrum antibiotic treatment, a two-step surgical intervention was performed. First, the encephalocele was excised, and the anterior skull base defect was repaired microsurgically. Subsequently, a neuroendoscopic third ventriculostomy with a biopsy of the pineal tumor was performed, confirming the diagnosis of pineocytoma. Postoperative follow-up over five years showed no tumor progression or evidence of persistently elevated intracranial pressure (ICP).

## Case 3

A 56-year-old woman presented to an ear-nose-throat (ENT) specialist with left ear fullness and CSF otorrhea. Otoscopic examination revealed a gray, bulging tympanic membrane due to fluid accumulation in the middle ear. A grommet was inserted in the left eardrum to allow fluid drainage. Nine months later, the ENT surgeon became concerned about the excessive volume of fluid emerging from the middle ear, and b2 transferrin analysis confirmed that the fluid was CSF. The grommet was removed; however, a minor leak persisted through the perforated tympanum. Subsequent MRI of the head revealed multiple intracranial abnormalities, including several meningiomas, prompting referral to the neurosurgical unit for further evaluation. On the left side, a small petromastoid meningioma adjacent to the left sigmoid sinus was associated with bone destruction of the mastoid air cells. Fluid was detected within the mastoid air cells and the middle ear. HRCT demonstrated partially opacified mastoid cells and thinning of the bone underlying the left petromastoid meningioma (Figure 4), which was suspected to be the source of the CSF leak. The tumor was surgically resected, and the bony defect was repaired. The CSF leak resolved, with no recurrence noted during follow-up.

## Imaging Methods

In our two illustrative cases, preoperative HRCT was used to determine the path of CSF fistulas. However, despite a meticulous preoperative diagnostic work-up, the exact CSF leak location was ultimately identified intraoperatively in one case (Case 1).

The identified leak pathways were located in the sphenoid sinus, cribriform plate, and mastoid air cells, each associated with corresponding bony defects.

## DISCUSSION

Spontaneous CSF leaks are rare in untreated brain tumor patients, and their pathophysiology depends on whether the leak is direct (resulting from tumor invasion) or indirect (caused by elevated ICP due to hydrocephalus) (2,3,8,17,25,29,35,40,42). Ommaya classified spontaneous CSF rhinorrhea as normal-pressure leaks (direct-type) and high-pressure leaks (indirect type) (53). Direct-type spontaneous CSF rhinorrhea occurs when the tumor erodes through the meninges and bone, creating a direct passage for CSF leakage. The cribriform plate is the most commonly reported site for hydrocephalus-related (indirect type) spontaneous CSF rhinorrhea (65). Likewise, Locke reported two cases from his series and 12 additional autopsy cases identified through a literature search. All cases involved obstructive hydrocephalus with elevated ICP and CSF egress through the cribriform plate (42).

In most cases, the cisterna basalis communicated with the nasal cavity. However, in three cases, there was direct communication between the frontal horn of a dilated lateral ventricle and the nasal cavity (4,42). Understanding these pathophysiological categories is crucial for preoperative planning and for avoiding complications. Since spontaneous CSF leaks increase the risk of meningitis, timely intervention guided by precise preoperative imaging is crucial.

**Signs and symptoms:** Many tumor patients with spontaneous CSF leaks may present with early symptoms and signs of elevated ICP, including headache, nausea and a clear, salty discharge from the nose or ear (11,13,26,41,54,69). Seizures and meningitis can also occur as initial symptoms in cases of CSF rhinorrhea (36). The presence of a headache should raise suspicion for elevated ICP and underlying intracranial pathology (13). Liang et al. reported that remote tumors causing preoperative rhinorrhea were all benign and provided evidence that rhinorrhea resulting from elevated ICP develops as a chronic process (41).

**Diagnostic test and imaging:** CSF b2 transferrin testing has a sensitivity approaching 100% and a specificity of 95% (3,29,30,34). However, results should be interpreted cautiously in conditions that increase the likelihood of false-positive results, such as concomitant orbital injuries or chronic liver disease (29). HRCT scans have been recommended as the noninvasive radiological investigation of choice (30,59). While MRI is useful for evaluating the soft tissues surrounding the leak and does not expose the patient to ionizing radiation, bony defects are better visualized on CT scans (3,29). However, CT cannot reliably identify concomitant dural defects in

patients with multiple bony abnormalities and cannot distinguish between dehiscent and thin, non-dehiscent bone. Identification of a single defect that correlates with the patient's clinical symptoms may eliminate the need for further imaging (29). Historically, CT cisternography was used for leak localization, but it has largely been replaced by the combined use of HRCT and 3D CISS MRI, which provides a sensitivity exceeding 89% (47, 50).

**Management of spontaneous CSF leaks:** Various treatment options are available. Conservative management for spontaneous high-pressure CSF rhinorrhea includes bed rest and lumbar drainage (2,18). If these measures are unsuccessful, surgical repair of the CSF leak becomes necessary. Tumor resection is indicated when the tumor is the primary cause of CSF leakage (3,10). Endoscopic transnasal transsphenoidal repair has reported a success rate of approximately 95% for most types of CSF rhinorrhea (3,18,32). However, in our experience, to maximize the likelihood of a satisfactory long-term outcome, both direct and indirect mechanisms of the CSF leak should be identified and addressed in patients with benign tumors.

Our first case exemplifies a direct-type leak. Here, a pituitary macroadenoma invaded the right sphenoidal sinus, resulting in right-sided rhinorrhea. Spontaneous CSF rhinorrhea in patients with pituitary adenomas following medical therapy (e.g., dopamine agonists) or radiation has been well-documented (38). However, spontaneous CSF rhinorrhea in untreated pituitary adenomas is rare, with only 16 cases reported in the English literature between 1967 and 2019 (18,38). As in Case 1, none of the pituitary cases in our review were associated with hydrocephalus, suggesting that pituitary tumors rarely cause indirect spontaneous CSF leaks. The pathogenesis of spontaneous CSF rhinorrhea in untreated pituitary adenoma patients remains uncertain. Potential contributing factors include direct erosion of the sellar floor by the expanding tumor, spontaneous tumor necrosis or regression (due to hemorrhage or decreased estrogen levels at menopause in female patients), and CSF flow dynamics and pulsation through the defect (2,18,27).

Indirect leaks arise from chronic hydrocephalus, which increases ICP and causes CSF leakage through anatomically weak areas of the skull base, such as congenital dysplasia in the olfactory nerve region (50,52,60). Numerous case reports in the literature have documented indirect spontaneous CSF fistulas (3,5,10,17,19,25,27,33,35,37,39,42,48,50,53,56,61,62,64). Posterior fossa tumors, such as acoustic neuroma, tentorial base meningioma, third ventricle colloid cysts, cerebellomedullary cistern lesions, CPA tumors or fourth ventricle choroid plexus papillomas, typically cause rhinorrhea via an indirect mechanism (10,17,19,35,48,62); rarely, a direct mechanism occurs, such as bone erosion of the posterior wall of the sphenoid sinus/clivus by ecchordosis physaliphora (43). Case 2 illustrates the indirect mechanism, in which the patient's pineocytoma and associated triventricular hydrocephalus contributed to her right-sided rhinorrhea.

Our systematic review also identified seven cases (case 5, 8, 9, 17, 21, 26, and 27) in which the tumor was distant from the

fistula site. All seven cases had hydrocephalus, suggesting a high-pressure, indirect leak. Five cases presented with spontaneous left-sided rhinorrhea, one with right-sided rhinorrhea, and one with right-sided rhinorrhea accompanied by right-sided otorrhea. This case involved a choroid plexus papilloma, a rare condition, as these tumors rarely cause CSF rhinorrhea (35). The cribriform plate is reported to be the most common site for hydrocephalus-related spontaneous CSF rhinorrhoea (65). Consistent with the literature, our second case also had a leak originating from the cribriform plate. Furthermore, in our systematic literature review, four cases had leaks originating from the cribriform plate, and interestingly, the rhinorrhea occurred exclusively from the left nostril (Table I). We, therefore, hypothesized that the left side of the cribriform plate might be thinner than the right, or that congenital skull base defects may be more common on the left side.

Posterior fossa (PF) tumors causing rhinorrhea are even rarer (17,50). Benvenuti et al. reported a total of 14 PF tumor cases presenting with hydrocephalus and rhinorrhea (8). In our case series, no spontaneous CSF rhinorrhea was observed due to PF tumors. However, in our systematic literature review, five studies reported both the PF tumor side and the spontaneous rhinorrhea side (10,17,35,48,62). Of these, three cases had left-sided rhinorrhoeas (17,48,62), one had right-sided rhinorrhea (10), and one had right-sided rhinorrhea with otorrhea (35).

#### *Spontaneous CSF Otorrhea*

CSF leaks through the mastoid space are a well-known post-operative complication of posterolateral skull base approaches that involve exposing the mastoids with the drill (22). CSF otorrhea can also result from dehiscence of the tegmen tympani, which may be revealed by the insertion of a grommet (58). In our study, Case 3 presented with CSF otorrhea caused by direct invasion of the mastoid air cells by a benign petromastoid meningioma, with an undefined pathological mechanism. Bone erosion adjacent to meningiomas is uncommon, in contrast to hyperostosis and intraosseous manifestation (28,34,63,67). Recurrent otorrhea and progressive hearing loss that are resistant to medical treatment are rare manifestations of the slow, insidious growth of a low-grade meningioma within the temporal bone. When clinical and radiographic findings exclude other possible causes, meningioma should be considered in the differential diagnosis (28). Our systematic literature review identified three cases of otorrhea, all of which involved a leak on the right side (Table I). Contrary to the findings of the systematic review, our patient's otorrhea occurred on the left. This represents a unique case of left-sided spontaneous CSF otorrhea secondary to a petromastoid meningioma, contrasting with the right-sided predominance reported in the literature.

No cases of indirect (high-pressure) spontaneous CSF otorrhea were identified in our literature review, suggesting that hydrocephalus is unlikely to play a significant role in the development of secondary CSF otorrhea. However, it may be associated with congenital anomalies and rare entities, such as arachnoid granulations involving the middle ear (65).

Our literature review found that, while spontaneous rhinorrhea can occur on either side regardless of the tumor location, otorrhea cases were consistently ipsilateral. This discrepancy suggests that spontaneous rhinorrhea may involve additional factors, such as congenital skull base defects, variations in skull base thickness, or the presence of Sternberg's canal, which predisposes certain areas to spontaneous leakage. A patent Sternberg canal arises from the incomplete fusion of the different components of the sphenoid bone. This predisposes the formation of CSF leaks into the inferolateral recess of the sphenoid sinus (7,16,30,50). Additionally, although concomitant skull base defects causing spontaneous CSF rhinorrhea are uncommon, these defects can sometimes be multiple (50).

Our findings emphasize that, while skull base destruction is a key mechanism in CSF otorrhea, spontaneous CSF rhinorrhea cases warrant thorough preoperative evaluation for potential coexisting skull base defects to prevent fatal complications, such as recurrent meningitis.

Our study has several limitations. Only studies with available full-text manuscripts were included, introducing a risk of publication bias. No randomized or prospective trials were identified, highlighting the impracticality of conducting a randomized trial in this patient population. Additionally, the analysis was limited by the small number of studies on this topic and the low patient volume in all of the studies, as only case reports and case series were available.

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## ■ CONCLUSION

In both the literature review and our three reported cases, left-sided rhinorrhea occurred nearly as frequently as right-sided rhinorrhea, despite most benign tumors being midline or right-sided. In contrast, cases of otorrhea consistently presented with CSF leaks on the same side as the tumor, likely resulting from direct tumor invasion. Skull base dehiscence may be solitary, but it is not the predominant feature in benign tumors causing spontaneous CSF rhinorrhea. Therefore, a meticulous, preoperative diagnostic work-up, guided by clinical signs and incorporating both HRCT and MRI, is essential. The presence of accompanying hydrocephalus and/or a concomitant congenital defect is crucial for understanding the underlying pathophysiology and mitigating the risk of complications associated with CSF leak.

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**Availability of data and materials:** The datasets generated and/or analyzed during the current study are available from the corresponding author by reasonable request.

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**Ethics approval:** In accordance with institutional policies, formal ethics committee/IRB approval and individual informed consent were not required because all patient data were fully de-identified and no identifying information was disclosed. All procedures were conducted in accordance with applicable institutional and national ethical standards and the principles of the Declaration of Helsinki.

**AUTHORSHIP CONTRIBUTION**

Study conception and design: NK, MM

Data collection: NK, AEA, APE, AsT, ZH

Analysis and interpretation of results: NK, MM, NG

Draft manuscript preparation: NK

Critical revision of the article: NK, MM, NG, APE, AEA, MK, NS, AT, ET, and SM

Other (study supervision, fundings, materials, etc...): MM, NG

All authors (NK, MM, AEA, APE, MK, NS, AT, ET, SM, AsT, ZH, and NG) reviewed the results and approved the final version of the manuscript.

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