Cerebrospinal Fluid Rhinorrhea Management

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Definition

Cerebrospinal fluid rhinorrhea (CSF rhinorrhea) is a pathological condition characterized by the leakage of cerebrospinal fluid (CSF) from the nose. This occurs due to a defect in the skull base, which creates an abnormal communication between the subarachnoid space (the space surrounding the brain and spinal cord) and the nasal cavity. The defect typically involves a breach in the arachnoid and dura mater, often accompanied by an osseous (bony) defect. CSF rhinorrhea is a significant clinical condition because it can lead to serious complications such as meningitis, encephalitis, or brain abscess if left untreated. Early diagnosis and management are critical to prevent these life-threatening complications (Arshad et al., 2024).

Normal Physiology of CSF

Cerebrospinal fluid (CSF) is a clear, colorless fluid that surrounds the brain and spinal cord, providing cushioning, nutrient exchange, and waste removal. CSF is produced primarily in the choroid plexus of the lateral, third, and fourth ventricles at a rate of approximately 0.35 ml/min. The total volume of CSF in adults ranges from 90 to 150 ml, and this volume is turned over three to five times per day. CSF flows from the ventricles into the subarachnoid space, where it is absorbed by arachnoid villi along the cerebral convexities. Normal CSF pressure ranges from 5 to 15 cmH_2O when measured in the lateral decubitus position. Neurologic symptoms may occur when CSF pressure exceeds 15–20 cmH_2O, a condition often associated with increased intracranial pressure (ICP). Elevated ICP can result from various conditions, including hydrocephalus, intracranial tumors, or idiopathic intracranial hypertension (IIH) (Saha, Tapuria, & Care, 2024).

History

The understanding of CSF rhinorrhea has evolved significantly over centuries:

- **4th Century BC**: Hippocrates first described CSF leaks as "fluid on the brain," though the underlying mechanisms were not understood at the time.
- **17th Century**: Vesalius and Cotugno advanced the understanding of CSF anatomy and flow through detailed dissections and anatomical studies.
- **1862**: Willis provided the first description of anterior skull base CSF fistulas, linking the nasal cavity to the intracranial space.
- **1926**: Dandy performed the first surgical repair of a CSF leak via frontal craniotomy, marking a significant milestone in the treatment of this condition.

- **1981**: Wigand pioneered the use of endoscopic techniques for repairing CSF leaks, which revolutionized the treatment of this condition by offering a minimally invasive approach with high success rates (Dandy, 1926; Wigand, 1981; Mattox & Kennedy, 1995).

Etiology

CSF rhinorrhea can be classified into **traumatic** and **non-traumatic** causes. Traumatic causes account for 80–90% of cases, while non-traumatic causes include congenital defects, tumors, and spontaneous leaks (Khan et al., 2022).

Traumatic Causes

1. **Head Injury**: Skull base fractures, particularly in the cribriform plate or ethmoid roof, are common causes of CSF leaks. These fractures often result from high-impact trauma, such as motor vehicle accidents, falls, or blunt force trauma to the head. CSF leaks occur in approximately 15–30% of cases involving skull base fractures. The leaks may be immediate (within 48 hours of injury) or delayed, with nearly 95% of delayed leaks manifesting within the first three months of injury. The cribriform plate and ethmoid roof are particularly vulnerable due to the thin bone and tightly adherent dura in these regions (Qazi et al., 2022).
2. **Iatrogenic Causes**: CSF leaks can occur as a complication of surgical procedures, such as endoscopic sinus surgery (ESS), transsphenoidal pituitary surgery, or craniofacial resection. (Aref et al.,2022) The risk of CSF leak after ESS is approximately 0.5%, with the lateral cribriform lamella being the most common site of injury. Other common sites include the posterior fovea ethmoidalis, sphenoid sinus, and frontal recess. Iatrogenic leaks are often identified intraoperatively or in the immediate postoperative period (Ramli, Mohamad, & Shukri, 2022).

Non-Traumatic Causes

1. **Spontaneous Leaks**: These are further divided into:
    - **High-Pressure Leaks**: Associated with elevated intracranial pressure (ICP), often due to conditions such as benign intracranial hypertension (BIH) or empty sella syndrome(Abd-elrazek et al.,2023).Elevated ICP leads to thinning and erosion of the skull base, resulting in CSF leaks. Patients with spontaneous leaks often have radiographic evidence of skull base thinning or defects. The cribriform plate, craniopharyngeal canal, and sella turcica are common sites of predilection for these leaks (Georgalas et al., 2021; Rao et al., 2023).
    - **Normal-Pressure Leaks**: Occur without elevated ICP, possibly due to transient pressure fluctuations or congenital skull base defects. These leaks are thought to result from physiological alterations in CSF pressure that lead to point erosions in the skull base (Zahedi et al., 2022).
2. **Congenital Defects**: Congenital causes of CSF rhinorrhea include meningoencephaloceles and persistent lateral craniopharyngeal canals (Sternberg canal). These defects result from incomplete fusion of the skull base during embryonic development. Meningoencephaloceles typically present in childhood as an intranasal or extranasal mass that transilluminates and expands with crying (Furstenberg sign) (Alromaih & Surgery, 2021).
3. **Tumors**: Benign or malignant tumors can erode the skull base, leading to CSF leaks. Tumors may arise intranasally, intracranially, or as metastatic lesions from other primary sites. Treatment of these tumors (surgery, radiation, or

chemotherapy) may also contribute to the development of leaks. For example, invasive prolactinomas can cause multiple defects in the sphenoid sinus, leading to CSF rhinorrhea (Chadha, 2021).

Diagnosis

Clinical Presentation

Patients with CSF rhinorrhea typically present with clear, watery nasal discharge that is often positional (worsens with leaning forward). Other symptoms may include headaches, meningitis, or pneumocephalus. The discharge is usually unilateral and may be intermittent, making diagnosis challenging in some cases. Patients may also report a salty or metallic taste due to the high sodium content of CSF. In cases of traumatic CSF leaks, there may be a history of recent head injury or surgery. Spontaneous leaks are often associated with symptoms of elevated ICP(Abdelhameid et al.,2024), such as chronic headaches, visual disturbances, or papilledema (Xie et al., 2022).

Confirmation of CSF Leak

1. **Beta-2-Transferrin**: A highly specific marker for CSF, detected in nasal discharge. This test is considered the gold standard for confirming CSF leaks. Beta-2-transferrin is a neuraminidase-induced isoform of transferrin that is highly specific to CSF, perilymph, and aqueous humor. The test is highly sensitive and specific, although false-positive results may occur in patients with chronic liver disease or genetic variants of transferrin (Shao et al., 2021).
2. **Beta-Trace Protein**: Another CSF-specific protein, though less widely available than beta-2-transferrin. Beta-trace protein is prostaglandin-D synthase, the second most abundant protein in CSF after albumin. It is produced primarily in the meninges and choroid plexus and can also be detected in other body fluids, such as urine and amniotic fluid (Almela et al., 2023).
3. **Glucose Testing**: CSF has a high glucose concentration (>30 mg/dl), but this test is less specific and can yield false-positive results in the presence of nasal secretions or blood. Glucose estimation is most popular and readily available, but it is not recommended as a confirmatory test due to its lack of specificity and sensitivity (Kinoshita et al., 2022).

Imaging

1. **High-Resolution CT (HRCT)**: Detects skull base defects and fractures with a sensitivity of 88–93%. HRCT is particularly useful for identifying bony abnormalities and planning surgical repair. Coronal CT images are especially valuable for visualizing defects in the cribriform plate and ethmoid roof. HRCT can also demonstrate pneumocephalus or focal fluid accumulation in the paranasal sinuses (Ghosh et al., 2020).
2. **MRI Cisternography**: Provides high soft-tissue resolution and is useful for detecting meningoencephaloceles or tumors. (Shaker et al. 2024). MRI is particularly valuable for evaluating spontaneous leaks associated with elevated ICP. Heavily T2-weighted sequences can visualize CSF flow and identify the site of leakage (Geregele et al., 2019).
3. **CT Cisternography**: Involves intrathecal contrast injection to localize active CSF leaks. This technique is highly sensitive for detecting active leaks but is less useful for intermittent or low-flow leaks. CT cisternography is particularly valuable for identifying leaks in the sphenoid sinus or lateral recess (Foust et al., 2018).

Secondary Investigations

- **Radionuclide Cisternography**: Uses radioactive isotopes to detect CSF leaks. This technique involves the injection of a radionuclide into the subarachnoid

space, followed by serial scanning or scintiphotography. Nasal pledgets can also be used to collect the tracer for analysis. The sensitivity for CSF leaks is 50–100%, and the specificity is almost 100% (Hegde & Vamanshankar, 2020).

- **Intrathecal Fluorescein**: Injected into the subarachnoid space to visualize CSF leaks during endoscopy. This technique is highly sensitive but carries a risk of complications such as seizures or allergic reactions. The use of intrathecal fluorescein is controversial and is not approved by the U.S. Food and Drug Administration (FDA) for this purpose (Yadav et al., 2016).

Management

Conservative Treatment

- **Bed Rest and Head Elevation**: Reduces ICP and promotes healing. Patients are advised to avoid activities that increase ICP, such as straining, coughing, or sneezing.
- **Acetazolamide**: Decreases CSF production by inhibiting carbonic anhydrase. This medication is particularly useful in cases of elevated ICP.
- **Lumbar Drainage**: Temporarily reduces ICP but is controversial due to risks like pneumocephalus, meningitis, or cerebral herniation. Lumbar drains are typically used as an adjunct to surgical repair in cases of high-flow leaks or elevated ICP (Deora et al., 2020; Altınel et al., 2021).

Surgical Treatment

1. **Endoscopic Repair**: The gold standard for most CSF leaks, with success rates of 87–100% after the first attempt. Techniques include(Abdelmaksoud et al.,2021):
    - **Overlay Technique**: Graft placed over the defect.
    - **Underlay Technique**: Graft placed beneath the dura.
    - **Bath Plug Technique**: Fat graft used to occlude the defect.
    - **Sinus Obliteration**: Used for frontal or sphenoid sinus leaks (Wigand, 1981; Makary et al., 2020).
2. **Intracranial Approach**: Reserved for complex cases, with higher morbidity and longer recovery. This approach involves a craniotomy to access the skull base defect and is typically used for large defects or leaks associated with intracranial pathology (Vyskocil et al., 2023).
3. **Graft Materials**: Autografts (e.g., nasal mucosa, fascia lata), allografts, and xenografts are used. Vascularized flaps like the nasoseptal flap are preferred for large defects. The choice of graft material depends on the size and location of the defect, as well as the surgeon's preference (Snyderman et al., 2020).

Complications

- **Meningitis**: The most serious complication, with a risk of 10–40% in untreated cases. Meningitis can result from the introduction of bacteria into the intracranial space through the skull base defect (Perez-Vega et al., 2020).
- **Pneumocephalus**: Air entering the intracranial space, often due to lumbar drainage or Valsalva maneuvers. Pneumocephalus can cause headaches, confusion, or neurological deficits (Livingston et al., 2020).
- **Recurrence**: Higher in patients with elevated ICP, lateral sphenoid leaks, or extensive skull base defects. Recurrence rates are up to 50% in spontaneous leaks with high ICP (Hentati et al., 2023; Tai et al., 2022).

References :

1. Abdelhameid, A. K., Fadle, K. N., Hassanin, B. G. Abnormal Migration of Distal End of Ventriculoperitoneal Shunt: A Retrospective Case Series at Sohag University. *SVU-International Journal of Medical Sciences*, 2024; 7(2): 579-593. doi: 10.21608/svuijm.2024.313513.1967
2. Abdelmaksoud, A. A., Gahlan, A. A., Aref, Z., Tayee, U. K. Endoscopicaly assisted microdebrider adenoidectomy versus conventional curettage adenoidectomy. *SVU-International Journal of Medical Sciences*, 2021; 4(2): 212-218. doi: 10.21608/svuijm.2020.48686.1033
3. Abd-elrazek, G. M., Elmalky, I., Saddiq, A. M., Abd-el Wahab, S. M. Diagnostic Value of MRI and MRV in Migraine indicating Intracranial Hypertension. *SVU-International Journal of Medical Sciences*, 2024; 7(1): 345-354. doi: 10.21608/svuijm.2023.227352.1632
4. Almela, M. T., Navarro-Zaragoza, J., Laorden, M. L., Sánchez-Celemín, F., & Almela, P. J. L. I. O. (2023). Cut-off value for β-trace protein (β-TP) as a rapid diagnostic of cerebrospinal fluid (CSF) leak detection. 8(5), 1233-1239 .
5. Altınel, F., Arslantaş, A., & Janus, J. J. C. i. R. (2021). Approaches to Repairing Skull Base Defects for the Prevention of Cerebrospinal Fluid (CSF) Leakage. 177-197.
6. Alromaih, S. R. J. S. J. o. O. H., & Surgery, N. (2021). Pathophysiology of Skull Base Defects and Cerebrospinal Fluid Leak. 23(3), 91-94 .
7. Aref, Z. F., Badawy, B. S., Abdelraheem, A. G., Mohamed, E. A., Taya, U. A Comparative Study between Coblation Adenoidectomy and Conventional Adenoidectomy. *SVU-International Journal of Medical Sciences*, 2022; 5(1): 155-163. doi: 10.21608/svuijm.2020.48334.1028
8. Arshad, M., Faisal, M. J., Ashfaq, A. H., Riaz, N., Maqbool, S. J. I. J. o. O., Head, & Surgery, N. (2024). Trans-Nasal Endoscopic Repair of CSF Rhinorrhea: An Institutional Experience. 76(1), 748-752
9. Chadha, N. K. (2021). Clinical and Surgical Management of Pediatric Diseases of the Nasal Cavity, Paranasal Sinus, and Skull Base. In Pediatric Head and Neck Textbook: Pathology, Surgery and Imaging (pp. 101-123): Springer .
10. Dandy, W. E. J. A. o. S. (1926). Pneumocephalus (intracranial penumatocele or aerocele). 12(5), 949-982 .
11. Deora, H., Sadashiva, N., & Nadeem, M. (2020). Transcranial management of CSF rhinorrhea. In CSF Rhinorrhoea (pp. 73-90): CRC Press.
12. Foust, A. M., Nguyen, X. V., Prevedello, L., Bourekas, E. C., & Boulter, D. J. J. R. C. R. (2018). Dual-energy CT cisternography in the evaluation of CSF leaks: A novel approach. 13(1), 237-240 .
13. Georgalas, C., Oostra, A., Ahmed, S., Castelnuovo, P., Dallan, I., van Furth, W., . . . Locatelli, D. (2021). International consensus statement: spontaneous cerebrospinal fluid rhinorrhea. Paper presented at the International Forum of Allergy & Rhinology .
14. Geregele, L., Baledent, O., Manet, R., Lalou, A., Barszcz, S., Kasprowicz, M., . . . Czosnyka, Z. J. B. o. t. B. (2019). Dynamics of cerebrospinal fluid: From theoretical models to clinical applications. 181-214.
15. Ghosh, S., Maulik, S., Chatterjee, S., Mallick, I., Chakravorty, N., Mukherjee, J. J. C. M., & Biomedicine, P. i. (2020). Prediction of survival outcome based on clinical features and pretreatment 18FDG-PET/CT for HNSCC patients. 195, 105669.

16. Hegde, J. S., & Vamanshankar, H. (2020). Endoscopic management of CSF rhinorrhea. In CSF Rhinorrhoea (pp. 53-72): CRC Press.
17. Khan, S. A., Ahmad, B., Sajjad, M., Ahmed, M., Khan, A., Ahsan, A., . . . Khan, A. A. J. J. o. A. M. C., Abbottabad: JAMC. (2022). Efficacy Of Conservative Management Of Early Post Traumatic Cerebrospinal Fluid Rhinorrhoea. 34(3), S691-S694 .
18. Kinoshita, K., Nishida, H., Kanegi, R., Nakamoto, Y., Tanaka, T., Shimamura, S., . . . Akiyoshi, H. J. F. i. V. S. (2022). Case Report: Detection of Transferrin in a Dog Suspected of Having Cerebrospinal Fluid Rhinorrhea. 9, 845809 .
19. Livingston, A. J., Laing, B., Zwagerman, N. T., & Harris, M. S. J. A. J. o. O. (2020). Lumbar drains: practical understanding and application for the otolaryngologist. 41(6), 102740 .
20. Makary, C. A., Zalzal, H. G., Ramadan, J., & Ramadan, H. H. J. I. j. o. p. o. (2020). Endoscopic endonasal CSF rhinorrhea repair in children: Systematic review with meta-analysis. 134, 110044 .
21. Mattox, D. E. J. O.-.-H., & Surgery, N. (1995). Endoscopic management of CSF leaks and cephaloceles. 112(5), P106-P106 .
22. Perez-Vega, C., Robles-Lomelin, P., Robles-Lomelin, I., & Garcia Navarro, V. J. N. S. (2020). Spontaneous intracranial hypotension: key features for a frequently misdiagnosed disorder. 41(9), 2433-2441 .
23. • Qazi, R., Rehman, L., Ahmed, T., Qazi, S. A., & Afzal, A. J. P. J. O. N. S. (2022). The Frequency of Early Post Traumatic Cerebrospinal Fluid Rhinorrhea in Patients with Head Trauma. 26(2), 250-257.
24. Ramli, R. R., Mohamad, S., & Shukri, N. M. (2022). Endoscopic Nasal and Paranasal Sinus Surgery. In Head and Neck Surgery: Surgical Landmark and Dissection Guide (pp. 249-274): Springer.
25. Rao, S. M., Grayson, J. W., Woodworth, B. A. J. C. F. R. C. G. t. E., & Management. (2023). Radiologic Findings in Idiopathic Intracranial Hypertension. 131.
26. Saha, D., Tapuria, P. J. P., & Care, P. o. N. (2024). Cerebrospinal Fluid Dynamics. 27-42 .
27. shaker, N. S. A., Elnagar, R. M., Eldeeb, B. S. (2024). 'Magnetic Resonance Imaging pearls in the Diagnosis of Coronavirus associated rhino-orbital-cerebral fungal infection : Retrospective Imaging Analysis of 80 Patients', *SVU-International Journal of Medical Sciences*, 7(1), pp. 402-418. doi: 10.21608/svuijm.2023.180096.1469
28. Shao, W., Shurin, G. V., He, X., Zeng, Z., Shurin, M. R., Star, A. J. A. A. M., & Interfaces. (2021). Cerebrospinal fluid leak detection with a carbon nanotube-based field-effect transistor biosensing platform. 14(1), 1684-1691 .
29. Snyderman, C. H., Wang, E. W., Zenonos, G. A., & Gardner, P. A. J. J. o. n.-o. (2020). Reconstruction after endoscopic surgery for skull base malignancies. 150, 463-468.
30. Tai, Y.-C., Tai, Y.-S., Ou, C.-H., Lui, C.-C., Wang, H.-K., Kuo, H.-C., & Hsu, S.-P. J. B. S. (2022). Treatment, outcome, and relapse of spontaneous and nonspontaneous cerebrospinal fluid leak. 12(3), 340
31. Vyskocil, E., Wormald, P.-J. J. C. F. R. C. G. t. E., & Management. (2023). Categorizing Cerebrospinal Fluid Leaks: A Framework for Understanding. 1 .
32. Wigand, M. J. R. (1981). Transnasal ethmoidectomy under endoscopical control. 19(1), 7-15 .

33. Xie, M., Zhou, K., Kachra, S., McHugh, T., Sommer, D. D. J. A. j. o. r., & allergy. (2022). Diagnosis and localization of cerebrospinal fluid rhinorrhea: a systematic review. 36(3), 397-406.
34. Yadav, Y., Parihar, V., Janakiram, N., Pande, S., Bajaj, J., & Namdev, H. (2016). Endoscopic management of cerebrospinal fluid rhinorrhea. Asian Journal of neurosurgery, 11(03), 183-193.
35. Zahedi, F. D., Subramaniam, S., Kasemsiri, P., Periasamy, C., Abdullah, B. J. I. J. o. E. R., & Health, P. (2022). Management of Traumatic and Non-Traumatic Cerebrospinal Fluid Rhinorrhea—Experience from Three Southeast Asian Countries. 19(21), 13847 .