

Traumatic Cerebrospinal Fluid Leak: Diagnosis and Management

Ji-Woong Oh, So-Hyun Kim, and Kum Whang

Department of Neurosurgery, Wonju Severance Christian Hospital, Yonsei University, Wonju, Korea

Cerebrospinal fluid (CSF) leaks are one of the common complications after traumatic brain injuries (TBI). The risks of CSF leaks can be detrimental to the outcomes of the patients. Early diagnosis and proper management is imperative for it is strongly associated with a better long-term prognosis of the patients. Diagnostic tools for CSF leaks are still under debate. Nevertheless, many reports of successful treatments for CSF leaks have been published with introduction of various repair techniques for leakage sites even though it is surgically challenging. Hereby, we review about the pathophysiology, manifestations as well as the update of the clinical diagnosis and current management of CSF leaks.

(Korean J Neurotrauma 2017;13(2):63-67)

KEY WORDS: Brain injuries · Cerebrospinal fluid leak · Meningitis.

Introduction

Cerebrospinal fluid (CSF) is a physiologic fluid for protecting brain and maintaining intracranial pressure (ICP). It is produced at choroid plexus and a total volume of 140 mL are actively circulating and turned over daily. After severe craniomaxillofacial trauma, the destruction of the meningeal structure may lead to the CSF leak from the subarachnoid space. Post-traumatic CSF leaks are seen 1% to 3% of all closed traumatic brain injuries (TBI) in adults and 80% to 90% of all the causes of CSF leaks in adult patients are due to head injuries.^{22,28)} The risk of meningitis from the traumatic CSF leak can present with high morbidity and even mortality depending on the cause and site of CSF leak. Except the cases with spontaneous diseases, traumatic CSF leak can be potentially detrimental with various complications such as bacterial meningitis if not self-

resolved.¹²⁾ The traditional treatment involves intravenous antibiotics treatment as well as primary repair of dural defect if the definite injury is suspected. Thus, early detection of CSF leaks is important as it determines the outcome of the patient. The decision of whether to observe or to surgically intervene is most likely to be dependent on the cause, site of leak, and timing of the leak.^{4,11)}

Clinical Pathophysiology of Traumatic CSF Leak

Traumatic CSF leak is reported to be approximately 10% to 30% of the skull base fractures in adults.²⁸⁾ More than half of these CSF leak is presented within 48 hours of the trauma while almost all CSF leaks occur within 3 months in delayed manner. The most common fracture sites leading to CSF leaks following TBI are the frontal sinus (30.8%), sphenoid sinus (11.4–30.8%), ethmoid (15.4–19.1%), cribriform plate (7.7%), frontoethmoid (7.7%) and sphenothmoid (7.7%).^{3,20)}

Blunt injury of anterior fossa

Fractures of anterior cranial fossa were more common than temporal bone fractures. And dura of these sites, was very adherent to the anterior cranial fossa. Therefore, the CSF rhinorrhea caused by anterior cranial fossa fractures, was more common than caused by temporal bone fractures.

Received: September 4, 2017 / **Revised:** September 29, 2017

Accepted: October 8, 2017

Address for correspondence: Kum Whang
Department of Neurosurgery, Wonju Severance Christian Hospital,
Yonsei University, 20 Ilsan-ro, Wonju 26426, Korea
Tel: +82-33-741-0593, Fax: +82-33-746-2287
E-mail: whangkum@yonsei.ac.kr

© This is an Open Access article distributed under the terms of Creative Attributions Non-Commercial License (<http://creativecommons.org/licenses/by-nc/4.0/>) which permits unrestricted noncommercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

And fractures of ethmoidal bone and junction between cribriform and ethmoid were most common cause of CSF rhinorrhea.²⁾ Especially because the ethmoidal artery penetrates the lateral part of the cribriform, it is the most vulnerable part of the trauma. In the situation of anterior cranial fossa fractures caused by head trauma, bony defect size and degree of dural disruption, arachnoid tearing and ICP were influenced the development of CSF rhinorrhea.

Blunt injury of middle and posterior fossa

Fractures that extend from the petrous bone to the middle ear can cause otorrhea if the tympanic membrane is torn. Otorhinorrhea can also occur along the tract of Eustachian tube. Temporal bone fractures are transverse type in 10% to 30% and longitudinal type in 70% to 90%. Frequencies of CSF fistula are constant regardless of each fracture type. And if a fracture extending from the greater wing of the sphenoid to the sphenoid sinus occurs, a rhinorrhea may also occur, even though it is a middle fossa fracture.

Penetrating injury

Although, penetrating injuries are rare, CSF leakage is the common complication of penetrating injuries. When penetrating injury was occurred, Aarabi¹⁾ and Meirowsky et al.¹⁶⁾ reported that at the time of penetrating injury occurred, CSF leakage occurred at a frequency of 8.7% and 8.9% respectively. And in the situation of CSF leakage caused by penetrating injury, infection rate was increased. Aarabi¹⁾ in a study of 379 patients with missile wounds in Iraqi warfare, reported CSF leakage in 33 patients, of whom 12 (36%) had infection.

Time of CSF Leakage

The timing of CSF leak is important that it will affect the long-term prognosis of the patients with other complications such as infection.

Early Onset

The early onset group includes the patients with CSF leak within 48 hours from trauma.^{10,19,21,24)} In most cases of blunt injury, CSF rhinorrhea usually begins within 48 hours, and if it is not large, 60% to 70% is naturally blocked.¹⁷⁾ However, in cases of large bone or dura defect, medical disease such as diabetes mellitus and situation of increased ICP, spontaneous healing of CSF leakage site had a high possibility of fail. They may be required imminent treatment including surgical repair.

Delayed onset or recurrence

The delayed onset group is defined as patients with CSF leak presented at least 1 week after trauma. CSF leakage may be delayed even if there is no CSF leakage at first. Usually they can be healed spontaneous or lumbar drainage may be required for further treatment. Even if the CSF leakage was healed, there were also possibility of delayed CSF leakage. There were two reasons of the delayed onset or recurrence of CSF leakage: 1) blood clot disappears; 2) separation of dura and arachnoid caused by cerebral edema subsides.¹⁵⁾

Very-Late Onset or Infection

CSF leakage may also occur after a considerable period of time, and even before CSF leakage occurs, such as rhinorrhea, infection may occur. The reason for this is that brain shrinkage caused by age may cause CSF leaking site reopening. growth fracture on ethmoidal bone may lead to leakage to fracture site, CSF leaking site has a barrier, which can't work as an infection barrier, could be considered.

Diagnosis and Investigation

Clinical presentation: symptoms and signs

The most common clinical symptom is the leak of clear and watery drainage from the nose and ear with a positional dependency.¹⁴⁾ If the patient is alert, a complaint of the salty postnasal drip is presented. The clear and non-mucoid fluid drainage from nose and ear can be presented with mixed nature of bleeding, however, this can be further tested for a 'double-ring' or 'halo' sign on a filter paper. Furthermore, other otolaryngeal diseases must be differentiated such as allergic rhinitis or vasomotor rhinitis prior to the diagnosis of CSF leak. Patients may experience a salty taste or may have ear fullness or hearing loss. There may also be a 'Reservoir sign' in which the CSF goes out when taking a head up position in the lying position. Most patients of the CSF leakage complained of headache. The headache could be classified as a high pressure type and low pressure type. High-pressure type is a symptom in which headache continues to increase and relieved when CSF was drained out. Early detection of CSF leak will be critical for the patient in order to prevent possible bacterial meningitis and intracranial abscess formation.

Identifying of CSF leakage

Target sign: When the CSF is mixed with a blood or nasal discharge, the CSF moves away on the filter paper, and the blood moves closer, so two rings are visible. This is

called a target sign, a double ring sign, or a Halo sign

Handker chief test: When the discharge from the nose is buried in a handkerchief or dry gauze, the CSF is more likely to be clear if it is not sticky. The Handker chief test is a test to determine the nasal discharge, which is unclear and sticky due to mucin secretion from the nose.

Glucose oxidized test: The CSF glucose from nasal or ear secretions has long been a classical method in testing CSF leak. In general, the glucose oxidase strips show positive result when the sample has a concentration over 20 mg/dL. Nasal discharge has a normal concentration of 10 mg of glucose, thus, if the glucose test is negative then it can be ruled out. However, it is only to be used as reference as it has high false positive and negative rates depending on the patients' other medical conditions.⁶⁾ Moreover, the lacrimal secretion can also be tested even if the concentration is less than 5 mg/dL. Meanwhile, a false positive result can be observed in the bloody nasal discharge whereas a false negative results are seen if the meningitis is already progressed in the patients. All these clinical conditions have to be considered before the interpretation and confirmation of the CSF leaks.

β 2 Transferrin: β -1 transferrin is found in serum tears, nasal secretion and saliva ubiquitously while β -2-transferrin is only observed in CSF, perilymph, and vitreous humor. Since the β -2 transferrin is specific in CSF, it is a well-known marker with extremely high sensitivity and specificity. However, it is also present in the vitreous humor, hence, when there is an eyeball rupture, CSF leaks can be false positive in the test. And it is also very expensive and takes longer time for the results to be reported. Therefore, in South Korea, it is not yet a common test to run in the clinical situations

Glucose and Chlorine Concentration: If the serum glucose level is 0.5 to 0.67, then there is a higher possibility that there is a CSF leak. CSF glucose level is undoubtedly affected by the glucose levels in serum, therefore, it is important to consider the two parameters together when confirming the CSF leaks. Furthermore, if the chlorine concentration level is 100 mEq/L, then one must consider the situations with CSF leaks as well.

Identification of CSF leakage site

As the physical examinations are not always reliable, laboratory tests are necessary to supplement the diagnosis. However, the radiologic findings are also important in identification of leaking point and decision making for the treatment. The radiologic evaluation will include plain films of skull and facial bones, high resolution computed tomography (CT), CT cisternography, and magnetic resonance

imaging (MRI) with intrathecal contrast or cisternography.^{18,25,26)}

High resolution CT: This method would give a detailed structural information on the bone details. It is perhaps the best and fast method in viewing the skull base structures. The 3-dimensional structures of anterior and middle cranial fossa in thin sections (usually 1–2 mm) are acquired and provide details on the fractures of those structures. It has a sensitivity of 89% due to high false positivity with artifacts. Nonetheless, it is known to be a good method in deciding treatment plan rapidly. CT cisternography is rather an invasive method as lumbar puncture is required for the study. The sensitivity of finding CSF leak with this method is approximately 60% to 80%.¹³⁾

MRI: MRI can be used to detect the CSF leak in multiple imaging planes. Its accuracy with active CSF rhinorrhea is about 90%.²⁶⁾ While the CT is useful in showing the bone details of fractures, MRI can provide details of the content of the CSF fistula or sacs of CSF content if necessary with contrast information. MRI is a useful tool to differentiate CSF leak and to diagnose arachnoid herniation through bone defect. CSF is observed as a high signal intensity in T2-weighted images while the peri-mucosal discharge is seen in low signal intensity where mucosal diseases also come along with contrast enhancement.

Trace tests

Due to the high risks of anaphylaxis, it is not common to use radionuclide tracers. However, many surgeons use intrathecal fluorescein by using endoscopic skills. Again this is not yet acknowledged by the Food and Drug Administration, in South Korea, thus, it is not used commonly yet. In 2009, Banks et al.³⁾ have reported a research in the use of intrathecal fluorescein in the CSF leakage. The 0.1 mL of 10% fluorescein is mixed in the 10 mL of the patient's CSF and it was injected intrathecally for 5 minutes. Then the endoscopic study was carried out after 1 and 2 hours of injection. One out of 193 patients had a complication of premature ventricular contraction, but the rest of patients showed no neurologic deficits.

Management of CSF Leak

There are two major ways in treating CSF leak: conservative management or surgical repair. Surgical treatment will be subdivided into three methods: intracranial, extracranial, and transnasal endoscopic method.

Meningitis management

Meningitis is seen in 19% of persistent CSF leakage with 10% of mortality.⁷⁾ The delayed CSF leakage and the longer duration of the leakage with concomitant infection have a higher risk of meningitis. The most common pathogens of meningitis due to CSF leakage are *Streptococcus pneumoniae* and *Hemophilus influenzae*. Meanwhile, there is still a controversy in the use of prophylactic antibiotics with these infections. Brodie⁵⁾ reported that there is a risk of meningitis about 2.5% and 10% with and without prophylactic antibiotics, respectively. Yet, whether it is clinically significant or not, it is still a controversial issue.²⁷⁾ The most common antibiotics used are ceftriaxone and ampicillin/sulfadiazine, but there are no significant difference in the overall incidence rate of meningitis, according to the type of antibiotics.⁹⁾

Conservative management

The indications of conservative management are the patients with linear fractures on facial bones. The patient education is included with head elevation with 30 degrees without blowing nose, coughing or deliberate yawning or staining of stools. Absolute bed resting for at least 3 days of clinical observation will decide whether further treatment is required such as lumbar drainage or immediate surgical repair.⁸⁾ One has to be cautious that the Over-drainage of CSF will result in intracranial aerocoles and brain displacement with herniation followed by comatose mentality. It is usually common to drain the CSF in the rate of 10 to 15 mL per hour with a total drainage volume to be ranged in 150 to 250 mL.⁸⁾

Surgical management

The indications for early surgery is as follows: 1) penetrating injury; 2) intracranial hematoma; 3) meningitis; 4) large intracranial aerocole; 5) herniation of brain tissue from nose and ear; and 6) low probability of natural dural repair. The indications of delayed surgery are as follows: 1) persistent CSF leakage after 10 days of conservative management; 2) recurrence of delayed CSF leakage after 10 days of conservative management; 3) recurrent aerocels after 10 days of conservative management; and 4) the presence of meningitis and abscess formation. Surgical methods are classified into two groups. The first is a classical intracranial approach and the second is extracranial approach. In the past, the transfacial extracranial approach was the main method in extracranial approach. However, nowadays, it is more popular to go for the endonasal repair by endoscopic approach.

Intracranial repair of CSF leakage

The indications of intracranial repair of CSF leakage are as follows: 1) accompanied craniofacial injuries; 2) a large bone defect which cannot be solved by the endoscopic repair method only; and 3) in a situation where the leaking fistula site is not obvious via endoscopic examination. In general, if the leakage site is involved in the anterior fossa, then the anterior fossa craniotomy is carried out via bicoronal incision while the subtemporal craniotomy is considered in the CSF leakage of middle fossa. The advantage of intracranial approach is that the operation field is widely exposed, hence, it is convenient to repair multiple defect of CSF leakage. Another advantage is that it is possible to repair the leakage site even if the ICP is high due to severe brain injury. On the other hand, the disadvantages include anosmia, retraction-related brain injury and longer hospital stay. The open craniotomy procedures should consider the following key points during the repairment: 1) preservation of draining vein and olfactory nerve; 2) knowing the first intradural sign which is an area of adherence of brain and arachnoid to the site of fistula; 3) if no fistula site is found gayer a careful exploration, then a thorough review of radiologic studies is compulsory to look for other possible leakage sites (e.g. middle ear, posterior fossa etc.); 4) a large bone graft is necessary with inner calvaria in the presence of a large bone defect; 5) the temporalis fascia or fascia lata is placed intradurally in the presence of dural tearing; 6) the coverage of the entire anterior fossa floor with fascia is not recommended in the avulsion of intact olfactory nerve; and 7) lumbar drainage shunt is required if there is no other sites of CSF leakage or if there is only a small-sized leakage.

Endoscopic endonasal approach

As there has been an advancement in the endoscopic techniques, the endoscopic method is chosen as the first choice of repairing CSF leakage. However, it is important to have a good knowledge of the leakage site of fistula prior to the repair operation during the endoscopic endonasal approach. The major advantages of endoscopic endonasal repair are a low risk of retraction injury of brain cortex and anosmia and a relatively convenient approach to the sphenoid parasellar and posterior ethmoid region. Banks et al.³⁾ reported the overall success rate of 98% in the treatment of 193 patients with CSF rhinorrhea. And complications of endoscopic surgery are reported to be very low. According to the report by Senior et al.²³⁾ in 2001 with the compilation of 522 cases with retrospective questionnaires, the complication rate was 2.5% meanwhile the overall success rate was 90%

in the first attempt of endoscopic approach in a single institutional analysis.

Conclusion

Post-traumatic CSF leaks are uncommon and usually are combined with spontaneous healing. However, there are refractory cases with high morbidity and mortality, henceforth, these cases are required for further surgical management. The successful management of CSF diversion is critical for the prognosis of patients. Therefore, it is important to be aware of various diagnostic options and management plans including surgical methods in order to optimally treat the patients with the complications of CSF leaks.

■ The authors have no financial conflicts of interest.

REFERENCES

- 1) Aarabi B. Causes of infections in penetrating head wounds in the Iran-Iraq War. *Neurosurgery* 25:923-926, 1989
- 2) Abuabara A. Cerebrospinal fluid rhinorrhoea: diagnosis and management. *Med Oral Patol Oral Cir Bucal* 12:E397-E400, 2007
- 3) Banks CA, Palmer JN, Chiu AG, O'Malley BW Jr, Woodworth BA, Kennedy DW. Endoscopic closure of CSF rhinorrhea: 193 cases over 21 years. *Otolaryngol Head Neck Surg* 140:826-833, 2009
- 4) Bell RB, Dierks EJ, Homer L, Potter BE. Management of cerebrospinal fluid leak associated with craniomaxillofacial trauma. *J Oral Maxillofac Surg* 62:676-684, 2004
- 5) Brodie HA. Prophylactic antibiotics for posttraumatic cerebrospinal fluid fistulae. A meta-analysis. *Arch Otolaryngol Head Neck Surg* 123:749-752, 1997
- 6) Chan DT, Poon WS, Ip CP, Chiu PW, goh KY. How useful is glucose detection in diagnosing cerebrospinal fluid leak? The rational use of CT and Beta-2 transferrin assay in detection of cerebrospinal fluid fistula. *Asian J Surg* 27:39-42, 2004
- 7) Choi D, Spann R. Traumatic cerebrospinal fluid leakage: risk factors and the use of prophylactic antibiotics. *Br J Neurosurg* 10:571-575, 1996
- 8) Dalgic A, Okay HO, Gezici AR, Daglioglu E, Akdag R, Ergungor MF. An effective and less invasive treatment of post-traumatic cerebrospinal fluid fistula: closed lumbar drainage system. *Minim Invasive Neurosurg* 51:154-157, 2008
- 9) Demetriades D, Charalambides D, Lakhoo M, Pantanowitz D. Role of prophylactic antibiotics in open and basilar fractures of the skull: a randomized study. *Injury* 23:377-380, 1992
- 10) Friedman JA, Ebersold MJ, Quast LM. Post-traumatic cerebrospinal fluid leakage. *World J Surg* 25:1062-1066, 2001
- 11) Jones NS, Becker DG. Advances in the management of CSF leaks. *BMJ* 322:122-123, 2001
- 12) Kaufman BA, Tunkel AR, Pryor JC, Dacey RG Jr. Meningitis in the neurosurgical patient. *Infect Dis Clin North Am* 4:677-701, 1990
- 13) La Fata V, McLean N, Wise SK, DelGaudio JM, Hudgins PA. CSF leaks: correlation of high-resolution CT and multiplanar reformations with intraoperative endoscopic findings. *AJNR Am J Neuroradiol* 29:536-541, 2008
- 14) Mantur M, Łukaszewicz-Zajac M, Mroczko B, Kulakowska A, Ganslandt O, Kemona H, et al. Cerebrospinal fluid leakage--reliable diagnostic methods. *Clin Chim Acta* 412:837-840, 2011
- 15) McCormack B, Cooper PR, Persky M, Rothstein S. Extracranial repair of cerebrospinal fluid fistulas: technique and results in 37 patients. *Neurosurgery* 27:412-417, 1990
- 16) Meirowsky AM, Caveness WF, Dillon JD, Rish BL, Mohr JP, Kistler JP, et al. Cerebrospinal fluid fistulas complicating missile wounds of the brain. *J Neurosurg* 54:44-48, 1981
- 17) Mincy JE. Posttraumatic cerebrospinal fluid fistula of the frontal fossa. *J Trauma* 6:618-622, 1966
- 18) Oakley GM, Alt JA, Schlosser RJ, Harvey RJ, Orlandi RR. Diagnosis of cerebrospinal fluid rhinorrhea: an evidence-based review with recommendations. *Int Forum Allergy Rhinol* 6:8-16, 2016
- 19) Oakley GM, Orlandi RR, Woodworth BA, Batra PS, Alt JA. Management of cerebrospinal fluid rhinorrhea: an evidence-based review with recommendations. *Int Forum Allergy Rhinol* 6:17-24, 2016
- 20) Reilly PL, Wormald PJ, Marshall LF. Traumatic cerebrospinal fluid fistulas in Winn HR (ed): Youmans and Winn neurological surgery. ed 7th. Philadelphia, PA: Saunders, pp2980-2987, 2016
- 21) Safavi A, Safavi AA, Jafari R. An empirical approach to the diagnosis and treatment of cerebrospinal fluid rhinorrhoea: an optimised method for developing countries. *Malays J Med Sci* 21:37-43, 2014
- 22) Schlosser RJ, Bolger WE. Nasal cerebrospinal fluid leaks: critical review and surgical considerations. *Laryngoscope* 114:255-265, 2004
- 23) Senior BA, Jafri K, Benninger M. Safety and efficacy of endoscopic repair of CSF leaks and encephaloceles: a survey of the members of the American Rhinologic Society. *Am J Rhinol* 15:21-25, 2001
- 24) Shorter CD, Connor DE Jr, Thakur JD, Gardner G, Nanda A, Guthikonda B. Repair of middle fossa cerebrospinal fluid leaks using a novel combination of materials: technical note. *Neurosurg Focus* 32:E8, 2012
- 25) Stone JA, Castillo M, Neelon B, Mukherji SK. Evaluation of CSF leaks: high-resolution CT compared with contrast-enhanced CT and radionuclide cisternography. *AJNR Am J Neuroradiol* 20:706-712, 1999
- 26) Tuntiyatorn L, Laothammatas J. Evaluation of MR cisternography in diagnosis of cerebrospinal fluid fistula. *J Med Assoc Thai* 87:1471-1476, 2004
- 27) Villalobos T, Arango C, Kubilis P, Rathore M. Antibiotic prophylaxis after basilar skull fractures: a meta-analysis. *Clin Infect Dis* 27:364-369, 1998
- 28) Yilmazlar S, Arslan E, Kocaeli H, Dogan S, Aksoy K, Korfali E, et al. Cerebrospinal fluid leakage complicating skull base fractures: analysis of 81 cases. *Neurosurg Rev* 29:64-71, 2006