Spontaneous Cerebrospinal Fluid Leak at the Clivus: Two Case Reports and Literature Review

Mohammad Samadian1, Seyed Ali Mousavinejad1⁎, Kaveh Ebrahimzadeh1, Guive Sharifi1, Hesameddin Hoseini Tavassol2, Kristen Almagro1, Omidvar Rezaei2 and Hamid Borghei Razavi2

1Professor of Neurosurgery, Loghman Hakim Hospital, Shahid Beheshti University of Medical Sciences, Iran
2Department of Neurosurgery, Pauline Braathen Neurological Center, Cleveland Clinic Florida, USA

Abstract
Spontaneous or non-traumatic cerebrospinal fluid leaks comprise 5%-10% of all CSF rhinorrhea. Generally, CSF rhinorrhea occur at Cribriform plate, sella, sphenoid sinus and ethmoid air. Primary CSF rhinorrhea from clival defect is extremely rare. We herein describe two cases of spontaneous CSF rhinorrhea through the clivus repaired with endoscopic endonasal trans sphenoid approach. Moreover, we collected evidence in the literature regarding potential etiology, symptom and treatment (which occurred in the reported cases).

Introduction
Spontaneous or non-traumatic cerebrospinal fluid leaks comprise 5%-10% of all Cerebrospinal Fluid (CSF) rhinorrhea [1,2]. Generally, CSF rhinorrhea occur at the cribriform plate, sella, sphenoid sinus, or ethmoid air cells [3,4]. However, primary CSF rhinorrhea due to clival defect is extremely rare. The current study describes two cases of spontaneous CSF rhinorrhea through the clivus which were repaired with endoscopic endonasal trans sphenoid approach. Such cases are extremely rare and upon literature review, only 16 cases with clival defect are reported thus far. The peculiar aspect of this case report is related to its rarity. Moreover, evidence was collected from the literature regarding potential etiology, symptom, and treatment (which occurred in the reported cases).

Case 1
A 36-year-old female was admitted for three weeks of clear watery discharge from the right nostril, which was aggravated in prone position. The patient denied any recent trauma. A review of systems was negative except for headaches and nasal discharge. The nasal fluid tested positive for beta-2 transferrin, indicating that the fluid was CSF. Brain MRI revealed that the sphenoid sinus was filled with Cerebrospinal Fluid (CSF) and sagittal T2 weighted MRI revealed a fistula tract from preoptic cistern to sphenoid sinus (Figure 1). There was no evidence of benign intracranial hypertension. Computed tomography cisternography revealed that the contrast material passed from the preoptic cistern into the sphenoid sinus through this bone defect in the clivus (Figure 1). Before surgery, a lumbar puncture was performed to administer 0.25mL of 10% fluorescein with 10mL of Cerebrospinal Fluid (CSF) to help visualize CSF leaks during surgery and to ensure there was no leak after reconstruction of the defect. The patient underwent endoscopic trans nasal trans sphenoidal surgery. The anterior and middle portions of the clivus were exposed between both carotid arteries. During surgery, the defect was defined to the left of the midline in the clivus. The basilar artery was seen through the defect in preoptic cistern (Figure 2). The defect was closed with a multilayer reconstruction consisting of fat, fascia lata, and naso septal flap (Figure 3). There was no recurrence of CSF leak at 2 years follow-up.
Case 2

A 57-year-old man referred for clear watery discharge from the right nostril of no obvious cause. He suffered from intermittent rhinorrhea starting 6 months prior to arrival. He reported recent history of bacterial meningitis one month ago, which was treated successfully at an outside hospital. On admission, he had no focal neurological deficits. Nasal fluid tested positive for beta2 transferrin. Brain MRI revealed that the right sphenoid sinus was filled with CSF (Figure 4). CT cisternography showed that the contrast material passed from the prepontine cistern into the sphenoid sinus through this bone defect in the clivus. (Figure 4). After intrathecal administration of 0.25 mL of 10% fluorescein with 10 mL of cerebrospinal fluid the patient underwent endoscopic trans nasal approach. After stripping the mucosa from posterior wall of sphenoid sinus, CSF leak was observed in the upper region of clivus just below the sella at the midline (Figure 5). The defect was closed by abdominal fat and reinforced by fascia lata and naso septal flap. At the During 30-month follow-up appointment, no signs of recurrence were found. In both of the above reviewed cases, a lumbar drain was not placed pre or postoperatively.

Discussion

Cerebrospinal Fluid (CSF) leaks most commonly result from nonsurgical trauma (80%-90% of cases), followed by surgical procedures (16%), and nontraumatic or spontaneous causes (4%) [5,6]. first subcategorized spontaneous CSF rhinorrhea in two groups in 1964; primary spontaneous, when there is no cause for skull defect, and secondary spontaneous, when a cause can be found [6,7]. Defects in the roof of the ethmoid sinus or in the floor of the anterior cranial fossa contribute to the most common site of fistula in the patient with traumatic CSF rhinorrhea. However, for primary spontaneous CSF fistulas, a sphenoidal fistula is most common (60%). In these cases, the junction of the floor of the middle cranial fossa to the lateral wall of the sphenoid sinus is the most common site of CSF leak through sphenoid sinus [8], however, primary spontaneous CSF leaks from clival defect are extremely
which can cause discomfort for patients. Additionally, CSF leak cisternography requires intrathecal injection via lumbar puncture date, contrast-enhanced CT cisternography is the standard for CSF tomography (CT) cisternography, radionuclide cisternography, and various imaging studies such as contrast-enhanced computed diagnostic challenge that often involves multiple imaging studies. Radiographic features of increased ICP (empty sella and/or arachnoid pits) were observed only in two cases of four patients [17]. In a case report by Thibaut van Zele in spontaneous clival CSF leak, observed in patients with spontaneous CSF rhinorrhea. However, as empty sella syndrome (80%) and arachnoid pits (63%) are often responsible for CSF leakage was the most important point for successful surgical intervention, since a missed site can lead to improper treatment and recurrence of the leak [25,26]. In a report by Vivek Tandon, sphenoid sinus packing was performed when the exact site of the leak was not identified and the patient presented with recurrent rhinorrhea and meningitis [24]. In a report by Luana Antunes Maranha, the patient underwent anterior skull base repair via bifrontal craniotomy three times since the exact site of leakage was not defined and the patient presented with recurrent CSF leak. Finally, the patient underwent endoscopic transnasal approach for clival defect closure [27]. In some cases, there is more than one defect that should be repaired. For example, in a study by Satiaiwaty Mohindra, a patient had two concomitant defects. In the first surgery, clival defect was missed; the right cribriform plate and right sphenoid sinus defect closures were performed. CSF rhinorrhea recurred after one month and the patient underwent revision surgery. In revision surgery, previous repair site did not show leakage, but a high-pressure leak was observed through posterior wall of sphenoid sinus from clivus [28]. In all of the current study patients, clival defect was the only defect causing CSF leak. To date, various materials such as mucoperichondrium, cartilage, fat, fascia, and fibrin glue have been utilized to seal the fistula with different success rates. Fat and fascia were used for defect closure in all of the patients in the current study, comparable to patients with spontaneous CSF leak or repair of dural defect after adenoma surgery. Similar to Hegazy, we believe that the material used in the closure of the fistula is not important in the success of the intervention. The important key to success is the determination of the bony edge surrounding the defect [29]. Similar to the other authors, we reserved lumbar drainage for patients with elevated intracranial pressure. In both patients, the conservative measures such as bed rest, elevation of the head, and avoidance of straining activities were implemented after surgery [30].
Table 1: Published cases of clival defect leading spontaneous CSF leak.

| Case Reference | Sex | Age | Meningitis | Duration of CDF Rinorrhea | Previous Surgery with no Finding Defect | Surgical Approach for Defect Closure | Recurrent |
|----------------|-----|-----|------------|--------------------------|----------------------------------------|--------------------------------------|-----------|
| Guang Yong Chen [18] | Male | 71  | -          | 3week                    | NO                                     | ETSS                                 | NO        |
| Vivek Tandon [24] | Female | 55  | +          | 3week                    | YES [ETSS]                             | sublabial rhino-septal-trans-sphenoidal | NO        |
| Sheikh Asad [10] | Female | 64  | +          | 2y                       | NO                                     | ETSS                                 | YES       |
| Satiawaty Mohindra [28] | Female | 35  | _          | 2 m                      | YES [ETSS]                             | ETSS                                 | NO        |
| Krzysztof Oleś [25] | Female | 60  | +          | 3y                       | NO                                     | ETSS                                 | NO        |
| Thibaut Van Zele [17] | Female | 37  | -          | 2m                       | NO                                     | ETSS                                 | NO        |
|                       | Female | 61  | -          | 4m                       | NO                                     | ETSS                                 | NO        |
|                       | Female | 78  | -          | 3m                       | NO                                     | ETSS                                 | NO        |
|                       | Female | 42  | -          | 2m                       | NO                                     | ETSS                                 | NO        |
|                       | Female | 48  | -          | 3m                       | NO                                     | ETSS                                 | NO        |
|                       | Male   | 50  | -          | 1m                       | NO                                     | ETSS                                 | NO        |
| Luana Antunes M [27] | Female | 49  | +          | 10y                      | YES [3time]                            | ETSS                                 | NO        |
| Faiz Uddin A [7]     | Male   | 52  | +          | -                        | NO                                     | ETSS                                 | NO        |
|                       | Male   | 56  | -          | 2y                       | NO                                     | sublabial rhinoseptal trans-sphenoidal | NO        |
| Coiteiro [16]        | Female | 53  | +          | 3mo                      | NO                                     | ETSS                                 | NO        |
|                       | Male   | 43  | +          | 1week                    | NO                                     | ETSS                                 | NO        |

Conclusion

Spontaneous CSF rhinorrhea located at the clivus is an extremely rare condition. To date, only 16 cases are reported, and the current study reported a group of two consecutive cases. It seems that a combination of anatomical and functional factors plays a role in the occurrence of this rare phenomenon. To date, endoscopic transnasal approach is the best therapeutic option to repair midline skull base defect such as the current cases. Here, the initial outcome was successful, but long-term follow-up is required.

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