Case Report

Treatment of pituitary adenoma with spontaneous cerebrospinal rhinorrhea using nasoseptal flap, two case reports

Beom Mo Kang¹, Hyuk-Jin Oh²*, Kwang-Hui Ryu², Jae-Min Ahn¹

Departments of ¹Neurosurgery, ²Otorhinolaryngology, Soonchunhyang University Cheonan Hospital, Cheonan, Republic of Korea.

E-mail: Beom Mo Kang - kaimo0822@naver.com; *Hyuk-Jin Oh - funnylife@schmc.ac.kr; Kwang-Hui Ryu - ghryu@schmc.ac.kr; Jae-Min Ahn - c103028@schmc.ac.kr

INTRODUCTION

The spontaneous cerebrospinal fluid (CSF) rhinorrhea has an extremely rare clinical condition and is difficult to diagnose to the physician. It is usually caused by trauma, but rarely occurs with congenital defects, associated complications after transphenoidal surgery, or pituitary adenoma shrinkage after treatment such as bromocriptine.[19] In most patients, the cause of the rhinorrhea is not readily apparent, so it is often mistaken for allergic rhinitis of chronic sinusitis, leading to delayed diagnosis or improper management. Spontaneous CSF rhinorrhea in treatment-naïve pituitary adenoma reported 16 cases in 13 English literatures.[1,2,4,6,7,9,10,12,18,19,20,21,24] Up to date, CSF fistula was treated using a fat, muscle, fascia, and autologous bone.[22,23] However, no recent treatment using nasoseptal flap (NSF), commonly used for reconstruction of the endoscopic skull base surgery, has been reported.[10,24] Here, we present the case of a pituitary adenoma with spontaneous CSF rhinorrhea using NSF.
CASE PRESENTATION

This study was approved by Institutional Review Board of Soonchunhyang University Cheonan Hospital.

Case 1

A 70-year-old woman presented with a 6-month history of watery rhinorrhea, which was worsened when she lowered her head. She had never had a head trauma or otology-related surgery and had no special medical history other than poorly controlled diabetes. Neurological examinations showed alert consciousness and no visual impairment was observed. Watery rhinorrhea was a clear liquid with no fever or neck stiffness observed. General blood test and CSF biochemical analysis revealed that they were within the normal range without evidence of infection. Osteomeatal unit computed tomography (CT) scan showed fluid collection in sphenoid sinus with bony defects in skull base and pituitary fossa. Magnetic resonance image (MRI) demonstrated large mass of invading pituitary fossa, sphenoid sinus, ethmoid sinus, cavernous sinus, and clivus [Figure 1]. Mass was solid and focal cystic change in the dependent portion. Endoscopic transsphenoidal approach was performed. When the anterior wall of sphenoid sinus was removed, the capsule of the tumor was observed [Figure 2]. When the valsalva maneuver was performed, CSF flowed out between the clivus and the tumor. Tumor was soft and moderate vascularity. Normal pituitary gland was relatively well distinguished, with clear boundaries from mass.

After removal of mass, defect was packed with fat tissue and fibrin glue. The vascularized septal flap using the right nasoseptal mucosa was covered over the entire defect. Lumbar drain for CSF drainage was maintained after surgery and was removed on the 10th postoperative day. There was no CSF rhinorrhea postoperatively. Histopathology was confirmed as a pituitary adenoma. Ki-67 was 1% which demonstrates that invasiveness of pituitary adenoma was low and no other specific findings were observed. No CSF rhinorrhea was observed 18 months after surgery.

Case 2

A 47-year-old woman presented with a huge mass lesion at skull base on a CT performed for a health screening. She had never had a head trauma or otology-related surgery and had a well-controlled hypertension with single medication. She had a little watery rhinorrhea when she lowered her head from 10-month ago, but she thought that it was rhinitis and did not go to hospital. Neurological examinations showed

Figure 1: Preoperative magnetic resonance image in Case 1. (a) Gadolinium-enhanced coronal image was obtained. (b) Gadolinium-enhanced sagittal image was obtained. (c) Vista axial image was obtained. Yellow arrow indicates the thinnest part of the bone and it points to the most likely part as a suspected cerebrospinal fluid leak. (Yellow arrow) (d) Cranial computed tomography axial image showed sphenoid bony defect and fluid collection at the sphenoid sinus (Red arrow).

Figure 2: Intraoperative endoscope image and follow-up sinus endoscopy image in Case 1. (a) After exposing sphenoid sinus, cerebrospinal fluid leak point was identified on posterior wall of sphenoid sinus and clivus. (Yellow arrow and Yellow circle) (b) After subtotal removal of the tumor, defect was packed with fat tissue, fibrin glue, and tensor fascia lata. And the cavity was entirely covered by vascularized nasoseptal flap. (c) Nasoseptal flap was stably observed on postoperative T1-weighted sagittal magnetic resonance image. (Red arrow). (d) Sinus endoscopy image was obtained after 8 months after surgery. No defect was identified.
alert consciousness and no visual impairment was observed. Watery rhinorrhea was a clear liquid with no fever or neck stiffness observed. General blood test and CSF biochemical analysis revealed that they were within the normal range without evidence of infection. Brain CT showed large mass in the mid-cranial fossa, sella, and suprasellar region with bony destructions. Sella MRI demonstrated large mass of invading middle cranial fossa, pituitary fossa, sphenoid sinus, ethmoid sinus, cavernous sinus, and clivus [Figure 3]. Endoscopic transsphenoidal approach was performed. Clivus was destroyed due to tumor invasion. When right side ethmoid bone, upper tuberculum sellae was removed, the capsule of the tumor was observed [Figure 4]. Tumor was soft and highly vascularity. Normal pituitary gland was relatively well distinguished, with clear boundaries from mass.

After removal of mass, defect was packed with fat tissue and fibrin glue. The vascularized septal flap using the nasoseptal mucosa was covered over the entire defect. Histopathology was confirmed as a pituitary adenoma and ki-67 was 1% and no other specific findings were observed. Lumbar drain for CSF drainage was maintained after surgery. Lumbar drain for CSF drainage was maintained after surgery and was removed on the ninth postoperative. There was no CSF rhinorrhea postoperatively and no CSF rhinorrhea was observed 18 months after surgery.

**DISCUSSION**

The spontaneous CSF is usually caused by trauma, complications after transsphenoidal surgery, or pituitary adenoma shrinkage after during treatment such as bromocriptine. Spontaneous rhinorrhea without a history of trauma, nasal disease, and surgery is rare clinical case, making it difficult for doctors to diagnose. The spontaneous CSF rhinorrhea in pituitary adenoma without treatment reported 16 cases in 13 English literatures. Including our cases, description of clinical features of these cases is listed in Table 1. In the literature reported so far, the CSF leak was resolved using fat, tensor fascia lata, etc. We solved the CSF leak using NSF for the first time, so far there have been no particular problems.

Although the pathophysiology of spontaneous CSF rhinorrhea in pituitary adenoma without treatment is unknown, there are three possible mechanisms. First, direct erosion of the skull base by tumor can lead to spontaneous CSF rhinorrhea. Nutkiewicz et al. assumed that a strong and competent diaphragm sellae could possibly be combined with the folding of the evaginated arachnoid space membrane, allowing the pituitary tumor to expand downward and...
promote CSF leakage into the sphenoid sinus.\[18\] Second, spontaneous necrosis or regression of tumor can lead to CSF rhinorrhea. Tumors may regress spontaneously due to hemorrhage or infarction, leading to unblocking of CSF flow through the defect.\[6,10,20,24\] Third, CSF flow and pulsation through the defect can cause spontaneous CSF rhinorrhea. Tumors cause intracranial hypertension. Therefore, the flow and pulsation of CSF tend to pass through the anatomically weak area of the skull base, which can cause spontaneous CSF rhinorrhea.\[6,10,19\]

The spontaneous CSF rhinorrhea is often mistaken for allergic rhinitis of chronic sinusitis, resulting in delayed diagnosis or inappropriate management. Duration of spontaneous CSF rhinorrhea in these cases is long. Therefore, spontaneous CSF rhinorrhea may be high risk factor of meningitis. Among 16 cases, six got meningitis.\[18-20,24\] Thus, adequate evaluation including neurologic examination, spinal tapping, laboratory, and brain imaging study should be performed urgently. Furthermore, surgery aimed at exploring CSF leak points and covering fistulas or defects is recommended.

At present, endoscopic transphenoidal surgery appears to be the treatment of choices for CSF rhinorrhea because success rate reported is close to 95%.\[24\] Among 16 cases, 12 cases underwent endoscopic transphenoidal approach. In most cases, CSF fistula was treated using a fat, muscle, fascia, and autologous bone.\[18-20,24\] Many surgeons tried to use vascularized flaps harvested from the nasal cavity. Septal flap and middle turbinate flaps were used for endonasal repair of CSF leak.\[3,13,16\] However, these flaps had many disadvantages. For example, these flaps were rotation flaps with a random blood supply so these flaps often migrated from the CSF leak defect resulting persistent CSF leakage. The flaps were often necrosis due to the random bloody supply and movement of the flap.\[3,16\] NSF is a pedicled local flap supplied with the posterior septal branches of the sphenopalatine artery.\[11\] Compared to other previous described flaps, NSF is highly vascularized flap because the posterior nasoseptal arteries supply the entire septum.\[5,8,15\] This highly vascularized flap prevents CSF leak superior to the previously mentioned flaps by increasing adhesion to

| Author              | Year | Age/ Sex | Tumor | Tumor size | Duration of CSF rhinorrhea | Meningitis | Treatment | Defect reconstruction | Follow-up |
|---------------------|------|----------|-------|------------|---------------------------|------------|-----------|----------------------|-----------|
| Giovanelli and Perria | 1967 | 40/F     | NF    | ND (micro) | 8 months                  | +          | Craniotomy | Muscle               | 6 months  |
| Nutkiewicz et al.   | 1980 | 45/F     | NF    | Macro      | 3 years                   | -          | Craniotomy | Muscle, fascia       | 22 months |
| Cole and Keene      | 1980 | 41/M     | P     | Macro      | 6 months                  | -          | TS        | ND                   | 12 months |
|                     |      | 28/F     | P     | Macro      | 3 months                  | -          | TS        | Muscle, fascia       | ND        |
|                     |      | 38/M     | NF    | Macro      | 17 months                 | +          | TS        | Muscle, fat, fascia  | 18 months |
| Rothrock et al.     | 1982 | 24/M     | NF    | Macro      | 10 years                  | +          | TS        | Muscle, bone fragment| ND        |
| Bilo et al.         | 1984 | 42/M     | P     | Micro      | 2 years                   | +          | TS        | Mucosal flap fat, bone fragment | 6 months  |
| Obana et al.        | 1990 | 63/M     | P     | Macro      | 1 year                    | -          | Craniotomy, LD | 2 years  |
|                     |      | 36/F     | P     | Macro      | 2 months                  | -          | TS        | TS                    | 7 years   |
| Bell                | 1991 | 40/M     | NF    | Macro      | 6 weeks                   | -          | TS        | Fat, bony fragment  | ND        |
| Carroll et al.      | 1991 | 23/M     | ACTH  | Macro      | 8 weeks                   | -          | TS        | ND                   | ND        |
| Ohtakara et al.     | 2000 | 80/F     | P     | Macro      | 3 months                  | -          | TS, LD    | Fat, fascia          | 14 months |
| Hanel et al.        | 2001 | 26/F     | P     | Macro      | 1 year                    | +          | TS, LD    | Fascia               | 4 years   |
| Telera et al.       | 2007 | 36/M     | P     | Macro      | 2 years                   | +          | TS, LD    | Muscle, fat          | 20 months |
| Goyal et al.        | 2012 | 35/M     | NF    | Macro      | 6 months                  | -          | TS        | Fat, fascia          | 10 months |
| Chu et al.          | 2019 | 66/F     | P     | Micro      | 1 week                    | -          | TS        | Fat, fascia          | 6 months   |
| Present cases       | 2020 | 70/F     | NF    | Macro      | 6 months                  | -          | TS        | Fat, Nasoseptal flap | 18 months |
|                     | 2020 | 47/F     | NF    | Macro      | 10 months                 | -          | TS        | Fat, Nasoseptal flap | 18 months |

F: Female, M: Male, NF: Nonfunctional pituitary adenoma, ACTH: Adreno-cortico-tropic-hormone, ND: No data, TS: Transsphenoidal endoscopic surgery, CSF: Cerebrospinal fluid
surrounding tissue, restricting movement, and providing superior defect coverage. The previous studies have shown that CSF leak treatment using NSF is more effective than other methods.\cite{14,17,23}

We underwent endoscopic transsphenoidal repair using NSF in both cases, commonly used for reconstruction of the endoscopic skull base surgery. To the best of our knowledge, this is the first reported of pituitary adenoma with spontaneous CSF rhinorrhea using NSF.\cite{6,24} The postoperative clinical course of cases was uneventful and CSF rhinorrhea disappeared completely.

**CONCLUSION**

We present two cases of a pituitary adenoma with spontaneous CSF rhinorrhea using NSF. Pituitary adenoma should be suspected if there is a CSF rhinorrhea that occurs without a history of trauma or nasal disease. In addition, effective treatment can be performed using NSF, a technique for endoscopic skull base reconstruction.

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**Author contributions**

Data curation: Beom-Mo Kang, Hyuk-Jin Oh, and Kwang-Hui Ryu, Resources: Hyuk-Jin Oh, Writing – original draft: Beom-Mo Kang, Hyuk-Jin Oh, and Jae-Min Ahn Writing – review and editing: Hyuk-Jin Oh.

**Declaration of patient consent**

The authors certify that they have obtained all appropriate patient consent.

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Nil.

**Conflicts of interest**

There are no conflicts of interest.

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