

Management of cerebrospinal fluid leak after surgical removal of pituitary adenomas

Arimantas Tamašauskas, Kęstutis Šinkūnas¹, Wolfgang Draf², Vytenis Deltuva, Algimantas Matukevičius¹, Daiva Rastenytė³, Saulius Vaitkus⁴

Institute for Biomedical Research, ¹Department of Neurosurgery, Kaunas University of Medicine, ²Department of Ear, Nose and Throat Diseases, Head and Neck Surgery, International Neuroscience Institute at the University of Magdeburg, Germany, ³Department of Neurology, ⁴Department of Otorhinolaryngology, Kaunas University of Medicine, Lithuania

Key words: cerebrospinal fluid leak; pituitary adenoma; sella closure; transsphenoidal surgery.

Summary. Objectives. The aim of the study was to evaluate the frequency and the causes of the intra- and postoperative cerebrospinal fluid (CSF) leaks and to discuss the sella closure methods.

Methods. During the period from 1995 to 2005, 313 patients underwent 356 transsphenoidal operations for pituitary adenoma. Microadenoma was found in 80 (22.5%) cases, and in 276 (77.5%) cases, macroadenoma was removed. Two different methods to close the sella were used. The first one consisted packing the sella turcica and sphenoidal sinus with autologous fat and restoring the defect of sella turcica with autologous bone. In more recent practice, the regenerated oxidized cellulose (Surgicel[®]) and collagen sponge with human fibrin (TachoSil[®]) were used to cover the sella membrane defect, followed by packing the sella with autologous fat and covering the dural defect with Surgicel[®] and TachoSil[®].

Results. Adenoma was totally removed in 198 (55.6%) cases out of 356. Microadenoma was totally removed in 91.3% and macroadenoma in 45.3% of cases, respectively. Postoperative complications were noted in 40 (11.2%) patients. Two (0.6%) patients died after surgery. Intraoperative CSF leakage was observed in 58 (16.3%) cases. Postoperative CSF leakages were observed in 3 cases, when the method of packing the sella with just autologous fat was used, whereas in 29 cases when the sella fat packing was used together with Surgicel[®] and TachoSil[®] to cover the sella membrane and dural defects, no postoperative CSF leakages were observed.

Conclusions. The technique of covering the sella membrane and dural defects with Surgicel[®] and TachoSil[®] in the presence of intraoperative CSF leakage appeared to be the most reliable one, as no postoperative CSF leakage applying this technique has been observed.

Introduction

Transsphenoidal approach has been a major technique for surgical treatment of sellar pathology since the 1960s. With the development of technical possibilities and increase in surgeons' expertise, mortality and morbidity after such interventions have decreased. Postoperative cerebrospinal fluid (CSF) leakage, however, remains the most serious and life-threatening complication. Its rate has been reported to vary from 1 to 6% (1–8). Frequent occurrence of intraoperative CSF leakage also poses an important problem, being reported in 15 to 30% of cases (4, 8). Various techniques for packing the sella turcica and closing the CSF leakage have been advocated by different authors. Although in the past decades transsphenoidal

approach has remained the major method in pituitary surgery, neither the risks of intraoperative and postoperative CSF leakage nor its closure techniques have been discussed appropriately. No unanimous agreement has been reached so far as to the techniques of closing the CSF fistula and the sella turcica. The aim of the present study was to present the frequency and the causes of intra- and postoperative CSF leaks as well as to discuss various sella closure methods and to introduce a new multilayer technique for the sella closure.

Patients and methods

In 1995, the Department of Neurosurgery of Kaunas University of Medicine Hospital started a prospec-

tive study of patients who had undergone pituitary adenoma surgery by applying transsphenoidal approach. Surgery for adenoma removal is performed in a neurosurgery operating room by neurosurgeons in close cooperation with ear, nose, and throat doctors. To visualize the tumor bed and to assess the completeness of removal, endoscope is used. By the end of 2005, 313 patients (104 men and 209 women) had undergone 356 transsphenoidal surgeries. The mean age of the patients was 47.8 ± 15.3 years. Two surgeries have been undergone by 33 patients, and 5 patients had been operated on three times. All patients underwent pre- and postoperative endocrinological and ophthalmological examination. Interseptal approach was applied in 240 cases, sublabial approach – in 17 cases, and direct transsphenoidal approach under endoscope control – in 99 cases. A tumor was considered to be totally removed when a descended membrane of sella turcica was visualized. No visual evidence of the remaining tumor mass and no preoperative radiological evidence which would allow us to suspect the infiltration of cavernous sinuses, were found. The size of tumor, duration of the illness, radiological data, removal procedure, and CSF leakage during surgery were registered. Rupture of septal mucosa, postoperative CSF leakage, endocrinal complications, such as hypopituitarism, diabetes insipidus, and infec-

tious complications, such as sinusitis, meningitis, and deterioration of vision acuity were considered as postoperative complications. A follow-up of the patients was performed by an endocrinologist and a neurosurgeon. In the case of intraoperative CSF leakage, the sella was closed using two different methods. The first method consisted of packing the sella and sphenoidal sinus with autologous fat and restoring the bone defect of the sella with autologous bone (9). The second, the most recent one, consisted of placing Surgicel® on the defect of sella membrane and a TachoSil® plate on top of it, then packing the sella with autologous fat, covering autologous fat graft with Surgicel®, placing TachoSil® intradurally, and covering dura mater defect with TachoSil® plate and Surgicel® on top of it (Fig.). A Valsalva maneuver was performed after closure to assess its integrity. Lumbar CSF drainage was applied only in the case of severe intraoperative CSF leakage.

Statistic data analysis was performed by using package of computer software programs STATISTIKA/w 5 and SPSS/w 130. Differences were considered statistically significant when the P values were <0.05 .

Results

A microadenoma was diagnosed in 80 (22.5%) and macroadenoma – in 276 (77.5%) cases. Microade-

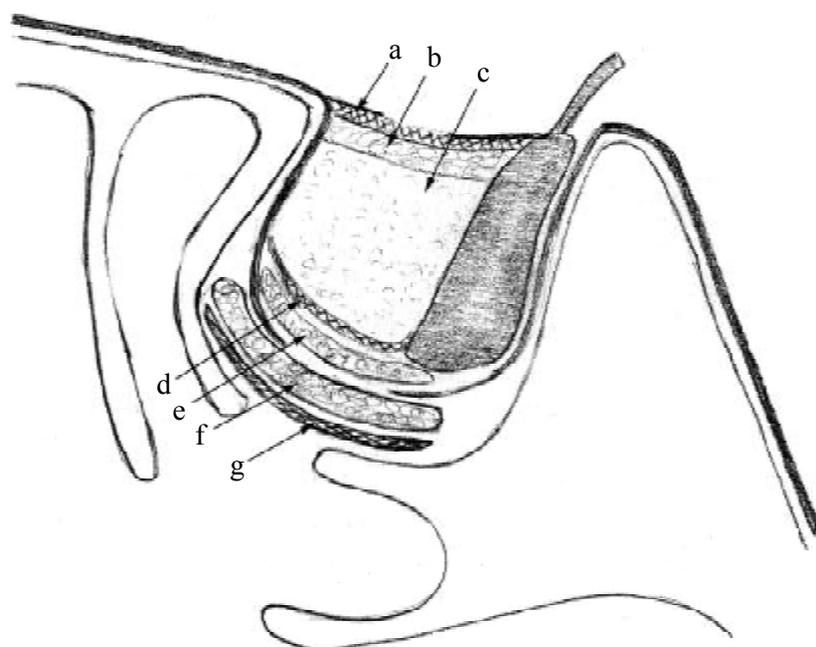


Fig. A new multilayer sella closure method

- a) oxidized cellulose (Surgicel®) is placed on the pituitary membrane; b) Tachosil® layer over Surgicel®;
- c) autologous fat filling the sella; d) Surgicel® layer covers the fat filling the sella intradurally;
- e) Tachosil® is placed over the Surgicel®; f) Tachosil® covers the dura mater defect;
- g) Surgicel® layer covers the Tachosil®.

noma was totally removed in 91.3% and macroadenoma in 45.3% of cases. In 155 (43.5%) cases, it was a nonfunctioning adenoma, in 88 (24.7%) cases – prolactinoma, in 82 (23%) cases – an STH-producing adenoma, in 22 (6.2%) cases – an ACTH-producing adenoma and in 9 (2.5%) – another type of hormonally active adenoma. Postoperative complications were observed in 40 (11.2%) cases. In some cases, more than one complication was observed (Table 1).

Two (0.6%) patients died shortly after surgery: an elderly man due to embolus of the pulmonary artery and a young woman due to postoperative CSF leak and basal meningitis.

Surgery included removing 106 invasive adenomas with intraoperative CSF leakage noted in 11 (10.4%) cases; removing 250 noninvasive adenomas with CSF leakage observed in 47 (18.8%) cases ($P=0.03$). In cases when the descent of the sella turcica membrane was visualized, intraoperative CSF leakage occurred in 53 out of 285 cases (18.6%), whereas CSF leakage was present in 5 of the 71 cases (7%) when membrane descent was not seen ($P=0.004$). Forty-three patients were operated on repeatedly, and during these operations, CSF leakage was observed in 4 cases (9.3%). Single-time operations were made in 313 cases with intraoperative CSF leakage present in 54 (17.3%) patients ($P=0.09$). In the case of intraoperative CSF leakage, postoperative lumbar drainage was applied in 22 (37.9%) cases and was maintained from 2 to 9 days.

Patients with STH-producing adenoma were observed to have an increased incidence of intraoperative

Table 1. Postoperative complications after surgery for transsphenoidal pituitary adenoma (N=356 cases)

| Complication | N | % |
|-------------------------------|----|-----|
| Hypopituitarism | 9 | 2.5 |
| Rupture of septal mucosa | 8 | 2.2 |
| Deterioration of vision | 7 | 2 |
| Sinusitis | 5 | 1.4 |
| Diabetes insipidus | 10 | 2.8 |
| Postoperative CSF rhinorrhea | 4 | 1.1 |
| Meningitis | 2 | 0.6 |
| Transitory diabetes insipidus | 25 | 7 |

CSF – cerebrospinal fluid.

CSF leakage (25.6% compared with 13.5% in patients with other type of adenoma, $P=0.02$).

In 99 cases, we used direct transsphenoidal approach under endoscope control (Table 3).

Usage of the endoscope during adenoma removal and for the purpose of examination of the tumor bed after its removal is important due to higher possibility to achieve total tumor removal and better visualization of slight CSF leakage. We think that this has brought about a statistically significant increase in the number of intraoperative CSF leakage ($P=0.002$).

Intraoperative CSF leakage was observed in 58 (16.3%) cases. For the sella closure in the case of intraoperative CSF leak, two techniques were used: the first one was the sella and sphenoidal sinus packing with autologous fat and the second one – a new

Table 2. Hormonal activity and intraoperative cerebrospinal fluid leakage

| Type of adenoma | Number of operations | Cerebrospinal fluid leakage | % |
|-----------------|----------------------|-----------------------------|------|
| Nonfunctioning | 155 | 24 | 15.5 |
| Prolactinoma | 88 | 9 | 10.2 |
| STH-producing | 82 | 21 | 25.6 |
| AKTH-producing | 22 | 3 | 13.6 |
| Other | 9 | 1 | 11.1 |
| Total | 356 | 58 | 16.3 |

Table 3. Results of operations

| Type of operation | Number of operations | Adenoma totally removed | % | Intraoperative cerebrospinal fluid leakage | % |
|-------------------|----------------------|-------------------------|------|--|------|
| With endoscope | 99 | 64 | 64.6 | 26 | 26.3 |
| Without endoscope | 257 | 134 | 52.1 | 32 | 12.5 |

Table 4. Postoperative complications (N=58)

| Postoperative complication | Method I* N=29 | Method II** N=29 |
|---------------------------------|-------------------|---------------------|
| Postoperative CSF leakage | 3*** | 0 |
| Hypopituitarism | 1 | 0 |
| Sphenoidal sinusitis | 2 | 0 |
| Transitory diabetes insipidus | 3 | 2 |
| Permanent diabetes insipidus | 2 | 1 |
| Paresis <i>n. oculomotorius</i> | 1 | 0 |
| Intraventricular hemorrhage | 0 | 1 |
| Total | 12 (41.4%) | 4 (13.8%) |

*Packing the sella and sphenoidal sinus with autologous fat and restoring the bone defect of the sella with autologous bone. **Multilayer sella closure using Surgicel® and TachoSil®. ***One patient was reoperated and resolved, two patients – resolved after CSF lumbar drainage.

multilayer sella closure method using Surgicel® and TachoSil® (Table 4).

Using multilayer sella closure method, there were no postoperative CSF leakages, and the number of postoperative complications was significantly smaller compared to the first method (13.8% and 41.4%, respectively; $P=0.02$). Therefore, we consider this method to be sufficiently simple and reliable in the case of intraoperative CSF leakage.

Discussion

Transsphenoidal surgery seems to be a reasonably safe procedure, with a mortality rate of less than 1%, in our study it being 0.6%. Still, a significant number of complications occur. To compare with the study of transsphenoidal surgery complications by Ciric *et al.* (3), the numbers of intra- and postoperative complications in our series are similar. Patients with STH-producing adenoma were observed to have an increased incidence of intraoperative CSF leakage. There was no significant difference in size between STH-producing adenomas and other types of adenomas. It may be assumed, therefore, that CSF leakage risk arises due to changes in the membrane of sella turcica resulting from the excess of somatotrophic hormone. Still this remains to be proved by histological studies. In our opinion, special attention should be given to identification of CSF leakage during surgery for STH-producing adenomas.

According to the American National Survey (3), postoperative sphenoidal sinusitis occurred with an incidence of 8.5%. We had 5 (1.4%) such complications in the first hundred of operations. Nevertheless, we noted that 4 (25%) of the 16 patients after packing

the sphenoidal sinus with autologous fat developed inflammation of the sphenoidal sinus, whereas sphenoiditis developed only in 1 (1.2%) of the 84 patients who did not undergo such packing. Therefore, we evaluated that packing the sphenoidal sinus with fat brings about a higher risk of developing a postoperative sphenoiditis ($P<0.001$), which was the reason why we refused this method.

Although in the past decades transsphenoidal approach has remained the major method in pituitary surgery, neither the risks of intraoperative and postoperative CSF leakage nor its closure techniques have been discussed appropriately. No unanimous agreement has been reached so far as to the techniques of closing the CSF fistula and the sella turcica. In the series of other authors, the rate of postoperative CSF leak has been reported to vary from 1 to 6% (1–8) and intraoperative CSF leakage – from 15 to 30% (4, 8). In our series, it was 1.1% and 16.3%, respectively. There exist numerous opinions and methods regarding the sella closure. Some authors advocate the sella closure only in severe intraoperative CSF leakage (10), others in all occasions (11, 12). There are many materials and techniques used for this – autologous dura and fibrin glue, synthetic dura, synthetic vicryl, silicone plate, alumina ceramic and others (13–18). Two sella closure methods described above were used in our clinic. In the beginning, we were packing the sella turcica with autologous fat and restoring the defect of sella turcica with autologous bone. In our recent practice, we place Surgicel® on the defect of the sella membrane and a TachoSil® plate on top of it, then we pack the sella with autologous fat, cover autologous fat graft with Surgicel® and TachoSil® intradurally, place

TachoSil® on the dura mater defect, and cover TachoSil® plate with Surgicel®. In the case of CSF leakage, the majority of authors emphasize the necessity to restore the defect of sella with autologous bone graft or cartilage (11, 12). As during repeatedly performed surgery we have observed that TachoSil® plate was overgrown by collagen fibers of connective tissue, our opinion is that additional repair of the sella floor is not necessary. According to the data of other authors who applied various methods of sellar defect plastic, postoperative CSF leakage rate ranged from 1% to 6% (1–8), whereas using our multilayer method, in 29 cases of intraoperative CSF leakage we had no postoperative CSF leakage at all. In

our opinion, closing the sella membrane with TachoSil®, packing sella turcica with fat, Surgicel and closing sella with TachoSil® is a technically simple and reliable method. Still, in the case of intense intraoperative CSF leakage, lumbar drainage of CSF is essential.

Conclusions

The recent multilayer technique of using Surgicel® and TachoSil® that we use to close the sella turcica in the presence of intraoperative cerebrospinal fluid leakage is reliable as no postoperative cerebrospinal fluid leakage has been observed when applying this technique.

Smegenų skysčio tekėjimo, atsiradusio po hipofizės adenomų chirurginio pašalinimo, gydymas

Arimantas Tamašauskas, Kęstutis Šinkūnas¹, Wolfgang Draf², Vytenis Deltuva, Algimantas Matukevičius¹, Daiva Rastenytė³, Saulius Vaitkus⁴

Kauno medicinos universiteto Biomedicininų tyrimų institutas, ¹Neurochirurgijos klinika,

²Tarptautinio neuromokslų instituto prie Magdeburgo universiteto

Ausu, nosies ir gerklės ligų, galvos ir kaklo chirurgijos klinika, Vokietija,

³Kauno medicinos universiteto Neurologijos klinika, ⁴Ausu, nosies ir gerklės ligų klinika

Raktažodžiai: smegenų skysčio tekėjimas, hipofizės adenoma, turkiabalnio uždarymas, transsfenoidinė chirurgija.

Santrauka. *Tyrimo tikslas.* Įvertinti operacijos metu ir pooperaciniu laikotarpiu atsirandančio smegenų skysčio tekėjimo dažnį bei priežastis, aptarti turkiabalnio uždarymo būdus.

Metodai. Išnagrinėtos 1995–2005 m. 313 ligonių atliktos 356 transsfenoidinės hipofizės adenomos pašalinimo operacijos. 80 (22,5 proc.) ligonių rasta mikroadenoma, 276 (77,5 proc.) ligoniams – makroadenoma. Turkiabalnį buvo uždarymas dviem būdais. Pirmasis būdas – tai turkiabalnio ir pleištakaulio ančio užpildymas autologiniu riebaliniu audiniu ir turkiabalnio kaulo defekto rekonstravimas autologiniu kaulu. Uždarydami turkiabalnį antruoju būdu, kurį taikėme naujausioje savo praktikoje, turkiabalnio membranos defektą mes dengėme regeneruota oksiduota celiulioze (Surgicel®) ir kolageno kempine su žmogaus fibrinu (TachoSil®), po to užpildėme turkiabalnį autologiniu riebaliniu audiniu, o kietojo dangalo defektą dengėme Surgicel® ir TachoSil®.

Rezultatai. Atlikus 356 operacijas, visiškai pašalinti adenomą pavyko 198 (55,6 proc.) ligoniams. Mikroadenoma visiškai pašalinta 91,3 proc. atvejų, makroadenoma – 45,3 proc. Pooperacinių komplikacijų atsirado 40 (11,2 proc.) ligonių. Du ligoniai (0,6 proc.) po operacijos mirė. Operacijos metu smegenų skysčio tekėjimas nustatytas 58 (16,3 proc.) ligoniams. Turkiabalnį užpildžius tik autologiniu riebaliniu audiniu, pooperacinis smegenų skysčio tekėjimas nustatytas trims ligoniams, taikant antrąjį turkiabalnio uždarymo būdą (turkiabalnį užpildžius autologiniu riebaliniu audiniu ir turkiabalnio membranos bei kietojo dangalo defektus padengus Surgicel® ir TachoSil®), 29 ligoniams pooperacinio smegenų skysčio tekėjimo nepastebėta.

Išvada. Turkiabalnio uždarymo būdas, kai turkiabalnio membranos ir kietojo dangalo defektai buvo padengiami Surgicel® ir TachoSil®, pasirodė besąs patikimiausias, nes nenustatyta nė vieno pooperacinio smegenų skysčio tekėjimo atvejo.

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