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Fat graft in cerebrospinal fluid leak repair after sellar and parasellar lesion surgery of 2000 patients; a multicenter study



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| ARTICLE INFO | A B S T R A C T |
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| Keywords: CSF Endoscopic Sella Pituitary Adenoma | Introduction: This study investigates the outcome of cerebrospinal fluid leakage repair after endoscopic trans- sphenoidal surgery (ETSS) sellar and parasellar lesions with fat graft. Method and materials: This is a cross-sectional study designed to evaluate the results of sellar and parasellar repair with simplified method of using only fat graft as the primary choice in patients undergoing ETSS surgery at three referral hospitals between 2011 and 2021. Results: In 2000 sellar and parasellar transphenoidal surgeries, 860 patients had intraoperative CSF leak and were repaired to stop CSF leak mostly with fat graft only. 58 patients came back with delayed cerebrospinal fluid leak. Of these, 21 patients did not have intraoperative leak with no primary surgical repair but came back with a delayed CSF leak. Repair method for 37 're-leak' cases was fat in 29 patients, fat with fascia and/or nasoseptal flap for the rest of them. The success rate was 96.3% for intraoperative leaks that were primarily managed with fat graft alone. Conclusion: Our study suggests that fat graft can be considered a reliable material for sellar reconstruction which is easy to harvest and use, regardless of the type of leak flow (high vs low). Using other materials or more complex multilayer methods such as facial grafts or pedicled vascularized flaps are advisable choices for unusual and very large defects or secondary postoperative CSF leaks. |

1. Introduction

Sellar and parasellar lesions are a diverse group including pituitary adenomas, intrasellar or parasellar arachnoid cysts, chordomas, and many other neoplasms [1–3]. Endoscopic approaches through the sphenoid sinus to the sellar area have been widely applied in recent years [4–6]. Compared to microscopic procedures, this method provides a better panoramic view of the surgical field and has a lower incidence of postoperative cerebrospinal fluid (CSF) leakage [7,8]. This method requires resection of an irregular, variable sized portion of the base of the skull with extensive dura and arachnoid dissection, which can result in large CSF leakage during the operation [9].

CSF leakage is one of the most common complications of transsphenoidal surgery with incidence rates ranging from 2% to 64% in heterogeneous cohort studies [5,8,10]. The incidence of intraoperative CSF leakage is much higher than that of postoperative leakage (14.2–61% vs 1.2–16.7%, respectively). Many patients who experience postoperative leakage also had a prior leakage during the surgery [10–17]. CSF leakage increases the likelihood of other complications such as meningitis and leads to longer hospital stays, higher rates of readmission, and increased costs [18,19].

Numerous reports on endoscopic treatment of CSF leakage have provided encouraging results. Although in specific cases, nonendoscopic surgical techniques may still be of interest to many surgeons, non-endoscopic approaches have not received wide acceptance because of their inherent complications [20–23]. The earliest studies of endoscopic treatment of CSF leakage used overlaid free tissue grafts to repair these complications, and thereafter several different methods were developed that yielded successful results [24]. Over the past few decades, sellar repair after trans-sphenoidal surgery has been performed using different autologous, heterologous or synthetic materials including fascia lata, fat tissue, bovine or equine pericardium, collagen

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sponges, silicon sheets, and/or titanium mesh as well as biological, semisynthetic, or synthetic glues [25–29]. These materials can be used individually or in combination, depending on the techniques employed by the surgeon. Proper use of these substances with a promising approach dramatically reduced the rate of CSF leakage after ETSS to 1% during sellar lesions operation [26,28].

Studies have generally used different materials for repair depending on the extent of postoperative cerebrospinal fluid leakage and the extent of dura, arachnoid membrane, and bony defects [30]. Therefore, according to the different opinions regarding the efficacy of sellar repair, this study aimed to investigate the results of our simplified approach in skull base reconstruction using periumblical fat graft and prevalence of CSF leakage.

2. Method and materials

This is a retrospective cohort study designed to evaluate the results of repair of the sellar floor in patients with sellar and parasellar lesions who underwent endoscopic transsphenoid surgery (ETSS). The target population consisted of patients with sellar and parasellar lesions who were candidates for endoscopic transsphenoidal resection referred to Loghman Hakim, Erfan, and Erfan Niayesh hospitals of Tehran between 2011 and 2021. All surgeries were performed by a same surgical team. No record was excluded unless the clinical and surgical information were not available. This study has been approved by the ethics committee of Shahid Beheshti University of Medical Sciences. Since the study was conducted on patient records, need for consent was waived. In all stages of the study the principle of confidentiality with regard to patient information was sought by all persons involved.

The first and original surgery in which lesion is removed is designated here as 'lesion surgery' and the subsequent surgeries for CSF leak repair as 'leak surgery.' Regardless of the size or extent of defect (bone, dura, or arachnoid), fat tissue was the preferred material for repair. Fat graft was harvested form periumblical area and was inserted inside the sellar cavity or plugged into the arachnoid defect. Then, 2 or 3 layers of Gelfoam® were applied over the graft following an antibiotic impregnated gauze to fill the sphenoid cavity. Gauze was removed one week later in an outpatient office-based nasal endoscopy.

Fascia or flaps were used only for patients in whom a method other than transsellar approach was used (for example in transplanum or transclival approach). In patients for whom the sellar approach was used and did not have CSF leakage during lesion surgery, the only material used was fat and/or Gelfoam® inside the sellar cavity or sphenoid sinus. We used a graded method for repairing in patients who came back with CSF leak. We used fat and fascia in patients which were repaired with fat only during lesion surgery and the fascia with nasoseptal flap (NSF) in patients for whom all other previous methods had failed. Although it is suggested to divide the CSF leaks into low flow or high flow, the degree of flow did not influence our reconstruction method or material and we did not stratify for it. NSF was not used in most cases; even in patients with large lesions that third ventricle or other large cisterns were leaking into the sphenoid sinus.

We used counts and proportions for quantitative measures and mean (standard deviation) for continuous ones.. Chi square and Student test were used to compare factors related to the CSF leakage. P values less than 0.05 were regarded significant. SPSS version 24 was used for statistical analysis.

3. Results

In total, 2000 (44.4% male; 55.6% female) transsphenoidal surgeries of sellar and parasellar lesions were detected and their records were assessed. Of these, there were 80.8% pituitary adenomas, 11.2% chordomas, 6.2% craniopharyngiomas, 1.55% intrasellar arachnoid cysts and 0.15% meningioma. The mean age of the study sample was 42.13 (\pm 12.35) years with a range from 13 to 71 years.

Among them, 860 developed intraoperative CSF leakage and 58 delayed postoperative leaks. There were 58 cases of delayed postoperative CSF leakages (at ICU, surgical ward or after discharge). Among them, 37 patients had intraoperative CSF leakage and 21 had no intraoperative leakage but returned with delayed postoperative CSF leaks.

The fat graft alone was utilized for 837 out of 860 (97.3%) intraoperative leaks with no need for fascia and/or NSF with a success rate of 96.3%. Out of 837, 31 returned with delayed 're-leak'; where 23 being managed again with fat alone, 4 with fat and fascia, and 4 others with fat, fascia and NSF. 11 patients out of 23 that were reconstructed with fat returned again with leak which were managed with fascia and/or NSF. In 1140 patients without any leak during operation, 21 developed postop leak that were all managed with fat graft with a success rate of 95.2%. All CSF leakage cases are shown in Fig. 1.

In patients with CSF leaks, 33 cases presented with rhinorrhea, 15 with headache, and 40 with both. 26 had confirmed meningitis at the time of admission. Age (P = 0.457), sex (P = 0.628), tumor type (P = 0.384), adenoma functionality (P = 0.525), and adenoma size (P = 0.446) did not present a statistically significant association with delayed CSF leakage.

4. Discussion

Cerebrospinal fluid leakage remains one of the most important complications and challenges of endoscopic transsphenoidal surgeries as it becomes hard to manage in certain cases and is associated with devastating side effects such as meningitis and increases the duration of hospital stay [5,31]. There is a large number of recent studies which have investigated different materials and introduced multilayer and complex skull base repairs. Availability of many options has led to tendency of surgeons to use more sophisticated methods. Autologous fat graft was the first material used for skull base repair, but in recent decade, it is often used as an adjutant to other materials.

In our operations, the overall incidence of intraoperative and delayed CSF leakage was 43% and 7% respectively, which is comparable with previous studies that suggested a range of 2–64% [5,8,10,11,31–33]. Despite the use of the extended transplanum approach, there was no CSF leakage in patients with craniopharyngiomas. Possibly, using more facial grafts or septal flaps in these patients in comparison with pituitary adenoma or chordoma is a simple explanation for lower rate of CSF leak in craniopharyngiomas.

The onset of postoperative CSF rhinorrhea in most of our patients was within 3 weeks of the operation. History of straining during defecation and early return to exercise and full activity in the postoperative period are some of the major, however, preventable factors for delayed CSF leakage.

There are various opinions about the importance of sellar repair, in particular that sellar repair is not necessary in patients who have no CSF leakage during operation [34]. In our study, most patients had no CSF leakage during lesion surgery, but a small portion of them came back with CSF leakage later. All these patients had at least 1 cm bone and dura defects during lesion surgery and Gelfoam® was the only material used to fill the sellar cavity. Therefore, it is advisable to use a material other than Gelfoam® in patients without CSF leak and large bone/dural defect. It is advisable to use a multilayer method in cases with recurrent CSF leaks in which fat was the only material used for primary repair.

Based on our sample and experience, we developed an approach to sellar repair in pituitary adenomas. For microadenomas with no intraoperative leak, Gelfoam® only can be inserted into the defect with no need for any further reconstruction. But in microadenomas that present with intraoperative leak, a fat graft to fill the intrasellar space and bone borders is advised, especially for cases with Cushing's disorder. For intraoperative leak of macroadenomas where a larger bone defect is created, we recommend using an intrasellar fat graft plus Gelfoam® and compression with a mesh material. For macroadenomas without leakage



Fig. 1. The flowchart of patients and leak surgeries.

a fat graft to fill the defect is advisable. In latter cases with presence of arachnoid pushout, coagulation of the arachnoid before fat insertion is recommended. For large defects created in transplanum approach of giant suprasellar masses (e.g., prolactinomas), we developed a special fat graft shaped like a mushroom. This graft should be inserted into the defect in a way that its head goes inside the defect and the trunk to stick inside the bone defect. Then a mesh compression of clival area is carried out to seal the defect.

We did not use lumbar drains in our patients. The indications for postoperative lumbar drains are not clearly defined in the literature. Most of the time, a lumbar drain is used depending on the surgeon's preference or hospital policy. Many studies attempted to assess the necessity of lumbar drains after repair of CSF leaks. Casiano and Jassir [35] studied 33 patients with CSF rhinorrhea, whether iatrogenic surgical or spontaneous, who underwent endoscopic repair and reported a 97% success rate without any lumbar drain. The study concluded that in smaller defects, which normally occur with the endoscopic approach to sellar and parasellar lesions, endoscopic repair of CSF leakage can be safely operated without placement of a lumbar drain. A review by Kirtane et al, which evaluated the outcome of endoscopic repair in 267 patients with CSF rhinorrhea of mixed etiology, supported this conclusion, reporting an overall success rate of 96% [36]. On the other hand, some authors use lumbar drainage more routinely and generously [37–39]. While many surgeons [38,39] have used postoperative lumbar drainage in selected patients, others use them in all endoscopic surgeries while its role has not been proved [40]. In the Caballero et al. study [41] of 105 patients who underwent endoscopic CSF leak repair, the recurrence rate in patients with and without a lumbar drain was 22% vs. 14%, respectively. They concluded that there was no association between lumbar drain placement and CSF leak recurrence rates after endoscopic repair. Therefore, in our study, due to the uncertainty of its utility, we decided not to use the lumbar drainage.

There are several limitations that need to be mentioned. Recent studies have identified body mass index (BMI) as a risk factor for postoperative but not intraoperative CSF leakage [11,15,16,32]. Unfortunately, in this study, this correlation was not investigated. Moreover, we were not able to adjust for confounders such as operation length and size of lesion and defect is another drawback of current work. On the other hand, being operated in a single center and single team and being followed make our sample a homogenous group of skull base surgeries.

5. Conclusion

Fat graft is a reliable and easily harvested material for primary sellar and parasellar repairs with high success rate. It also suggests that the use of multi-layered or vascularized flaps is not necessary for repair of many of skull base defects. They can be used as an adjunctive method in secondary or complicated postoperative CSF leak repairs. While being a readily available graft, fat alone is not a reliable choice for delayed postoperative CSF leaks and it is advisable to use multilayer methods in

G. Sharifi et al.

these patients. Also, it is advisable to use a reconstruction material other than Gelfoam® to fill the sellar cavity for patients who do not have CSF leakage during lesion surgery. This is especially advisable in cases with dura or bony defects exceeding 1 cm, a matter that needs to be further investigated.

Author contributions

GS and NAD developed the theory and performed the surgeries. EM and AB collected the data, analyzed them, and prepared the manuscript. NAD supervised the study and is the corresponding author.

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Availability of data

Data used in this work can be accessed after official inquiry sent to the corresponding author.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Interdisciplinary Neurosurgery: Advanced Techniques and Case Management 30 (2022) 101643

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G. Sharifi et al.

Interdisciplinary Neurosurgery: Advanced Techniques and Case Management 30 (2022) 101643

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