Acellular Dermal Allograft for Sellar Repair after Transsphenoidal Approach to Pituitary Adenomas

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Abstract

Keywords

- ▶ pituitary adenoma
- ▶ acellular dermal matrix
- ▶ AlloDerm
- ▶ fat autograft
- ▶ cerebrospinal fluid leak
- ▶ transsphenoidal surgery

Objectives Our practice has transitioned from using fat autograft to acellular dermal matrix (AlloDerm, LifeCell Corp, Woodlands, Texas, USA). We present the largest series to our knowledge of AlloDerm for sellar floor repair after transsphenoidal approach to pituitary adenoma and compare rates of postoperative cerebrospinal fluid (CSF) leak with an earlier cohort of patients whose CSF leaks were repaired with fat autograft.

Design This is a retrospective cohort study comparing sellar repair with fat autograft versus inlay AlloDerm between the years 2003 and 2012. The primary end point was postoperative CSF leak.

Results A total of 429 patients (368 primary; 83 revision operations) without intraoperative lumbar drainage were included. A total of 18 postoperative CSF leaks were observed (3.9%). Intraoperative CSF leak occurred in 160 cases (35.5%). Among this subset of patients with intraoperative CSF leak, 95 underwent repair with AlloDerm and 46 underwent repair with fat autograft, with postoperative CSF leak rates of 8.4% and 15.2%, respectively ($p = 0.34$, chi-square test); 19 patients underwent repair with other techniques or no repair at all, with postoperative leak rate of 0%.

Conclusions AlloDerm is an effective alternative to fat autograft in cases of low-flow CSF leak following transsphenoidal resection of pituitary adenoma.

Introduction

The ability to effectively manage intraoperative cerebrospinal fluid leak (CSF) is essential to successful transsphenoidal surgery (TSS). In cases without a breach in the diaphragma sellae, the likelihood of developing a postoperative leak is very low and sellar reconstruction is probably unnecessary, though some surgeons advocate repair in selected cases with patulous arachnoid or other factors predictive of postoperative CSF leak.^{1,2} Intraoperative CSF leak is a common occurrence, with a reported incidence of 11 to 54%^{3–8}; however, postoperative CSF leak is only reported to occur in 0.1 to 9% of

cases.^{6,8,9} A wide variety of materials have been used to restore the barrier between CSF and the sphenoid sinus, including fat, bone, cartilage, fascia lata, gelatin foam, polyester-silicone, polyethylene glycol, Vicryl patch (Ethicon, Somerville, New Jersey, USA), lyophilized dura, fibrin glue, cement, collagen fleece, muscle, cellulose, acellular dermal matrix, and mucosal flaps.^{8,10–18} No prospective clinical trials comparing these materials exist; however, fat autograft remains as a gold standard to which new materials must be compared. The present series seeks to compare the use of fat graft sella repair and obliteration of the sphenoid sinus, with pie-crust closure using AlloDerm (LifeCell Corp, Woodlands,

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Texas, USA) for the prevention of CSF rhinorrhea after low-flow CSF leaks.

Although effective and readily available, fat graft harvesting is not without drawbacks. Complications of fat harvesting such as wound dehiscence, infection, scarring, pain, and hematoma may occur. Kaptain et al reported fat autograft complications of ~4% in their series of 257 transsphenoidal operations, including a case of optic nerve compression by fat requiring emergent reoperation.³ The ideal alternative to fat graft should be effective at preventing CSF leak, technically simple to handle, and inexpensive, and it should not contribute to morbidity.

Our surgeons have been using acellular dermal matrix allograft for sellar reconstruction since 2005. AlloDerm is cadaveric dermis that has been processed to remove cellular elements. An early report of AlloDerm use for sellar reconstruction described 1 postoperative CSF leak out of 13 cases (7.6%).¹⁹ Lorenz et al published their experience using AlloDerm in 24 cases for sellar reconstruction after TSS with 2 postoperative leaks (8%).¹⁴ AlloDerm has also been reported to have been used successfully for repair of spontaneous and postsurgical CSF fistulas of the sphenoid sinus in 21 patients.²⁰ AlloDerm use has been described for a variety of pathologies to repair defects of the anterior and middle skull base with a variety of adjuncts including mucosal flaps, fibrin glue, and lumbar drainage.^{14,19–21} AlloDerm alone has yet to be proven as noninferior to fat graft for the management of CSF leaks after TSS. The authors present here the largest historical cohort they are aware of comparing fat graft and AlloDerm for sellar floor repair after TSS for pituitary adenoma.

Patients and Methods

The University of Miami Institutional Review Board approved this retrospective study. A database was reviewed with 766 cases of transsphenoidal pituitary surgery performed between 2003 and 2012. Patients who underwent surgery for pituitary adenoma via the transsphenoidal approach were included in the study. To capture cases with low-flow CSF leak and exclude operations where a more complex repair was indicated, cases with diagnosis other than pituitary adenoma, extended skull base approaches, combined craniotomy, and spontaneous or iatrogenic preoperative CSF leaks were excluded. Forty-six patients with intraoperative placement of lumbar drains were excluded as well, because intraoperative lumbar drainage itself would likely reduce postoperative CSF leak. Cases with biopsy alone or insufficient medical records were also excluded. All available medical records were reviewed for patient age, sex, pathologic diagnosis, previous TSS, occurrence of intraoperative CSF leak, postoperative CSF leak, lumbar drainage, method of closure, and other major complications. Since the presence of intraoperative CSF leak is known to be the most important variable predicting postoperative CSF leak, we focused our analysis of postoperative leak rates on patients with intraoperative CSF leak. A chi-square test was performed to compare the rate of postoperative CSF leak after an intraoperative CSF leak between patients with fat autograft and AlloDerm repair.

Surgical Technique

Surgical Approach

Before 2008, standard TSS using the sublabial approach was performed. Since 2008, we have adopted the endoscopic endonasal approach. Patients included did not receive lumbar drainage unless they experienced a postoperative CSF leak. The operating microscope was used in some endoscopic and all sublabial cases. Either fluoroscopy or frameless stereotactic guidance was used to ensure an accurate trajectory toward the sella.

Sellar Floor Repair

The sellar floor was repaired with autologous fat graft or acellular dermal matrix in most cases with intraoperative CSF leak. In cases where CSF was not seen and the risk of postoperative CSF was judged by the operating surgeon to be low, the defect in the sellar floor was simply covered with a piece of collagen sponge in most cases. AlloDerm or fat graft was also used in cases without intraoperative leak to reinforce a thinned arachnoid according to surgeon preference, using a single layer inlay method. Fat grafts were harvested from the abdomen and used to plug the sellar defect generally buttressed with bone, and the sphenoid sinus was then obliterated with a larger fat plug. Polyvinyl acetal packing (Medtronic Merocel, Jacksonville, Florida, USA) was left in the nasal cavity for 5 to 7 days after fat graft.

AlloDerm should be sized about twice the width of the defect (►Fig. 1A). The first layer of AlloDerm was tucked inside the sella with Gelfoam (Pfizer, New York, New York, USA) used as a wedge to keep it in place (►Fig. 1B). A plug of dry Gelfoam, alone or wrapped with oxidative cellulose (Surgicel; Ethicon), was used to ensure a circumferential seal around the bony sellar defect (►Fig. 1C). This inlay graft is positioned in a manner analogous to a pie's crust so that a thin border of graft is circumferentially draped over the vascularized bone of the sphenoid cavity around the sellar defect (►Fig. 1D). Gelfoam and Surgicel are placed as "pie filling" and compressed with a suction tip over a rayon patty (Cottonoid, Codman, Raynham, Massachusetts, USA) (►Fig. 1E). In cases with intraoperative CSF leak, a second layer of AlloDerm was placed as an onlay graft on the exposed sellar floor and covered with additional Gelfoam. (►Fig. 1F). Polyvinyl acetal packing was left in the sphenoid sinus for 5 to 7 days (►Fig. 1G). Care was taken to overlap the exposed edges of the inlay graft along with surrounded exposed bone in the sphenoid cavity, with no blood or air collection between the grafts and the recipient bony graft site in the sphenoid sinus. Prophylactic antibiotics were used while packing was in place.

Postoperative Follow-Up

Patients were observed overnight in the intensive care unit before transfer to the neurosurgical floor on the first postoperative day. Charts were reviewed specifically for documentation of CSF rhinorrhea after surgery, lumbar subarachnoid drains with or without reoperation, and the presence of meningitis confirmed by CSF analysis. CSF leaks requiring

Fig. 1A–G (A) Defect after transsphenoidal hypophysectomy for macroadenoma. (B) 1 mm sheet of AlloDerm, twice the size of the defect, is placed. (C) Surgicel wrapped Gelfoam is placed over the first layer of AlloDerm. (D) Edges of the AlloDerm should curl forward as Gelfoam plugs the defect and laid flat over demucosalized bone. (E) Surgicel wrapped gelfoam plugs the defect. A second layer of AlloDerm may be placed. (F) Gelfoam is used to cover the AlloDerm prior to placing packs. (G) Polyvinyl acetyl packing in the sphenoid sinus.

reoperation were repaired using fat graft, AlloDerm, or nasoseptal flap.

Results

Patient Characteristics

A total of 451 cases performed on 429 patients were included in our analysis. The age range of patients was 17 to 85 years (mean age 50.2 years); 173 were male (40.2%) and 257 (59.8%) were female. A total of 83 cases were revision operations (18.3%), and there were 324 surgeries for nonfunctioning pituitary adenomas (71.8%). Apoplexy was the indication for surgery in 44 cases (9.8%). Only 3 of the patients had prior radiosurgery (0.7%).

Surgical Technique

The microscopic sublabial approach was performed in 187 cases (41.4%). Endoscopic endonasal approach was performed in 197 cases (43.6%). A hybrid approach using the microscope with endoscopic assistance was performed in 68 cases (15.1%).

Intraoperative CSF Leak Management

Intraoperative low-flow CSF leak was seen in 160 cases (36%). No intraoperative CSF leak occurred in 291 cases (64%). Sellar floor repair was performed in 259 cases (57.3%) with fat graft ($n = 87$, 19.2%), AlloDerm ($n = 163$, 36.1%), and other

materials ($n = 9$, 2%). The sellar floor was repaired even in some cases without an intraoperative leak; however, the rates were comparable, as 57% ($n = 50$) of fat grafts and 61% ($n = 100$) of AlloDerm repairs occurred in the presence of an intraoperative leak.

Postoperative CSF Leak

CSF leak was observed postoperatively in 18 cases (3.9%). There were 8 postoperative leaks in the AlloDerm group and 7 in the fat graft group amongst patients with intraoperative CSF leak. Of the 291 cases without intraoperative CSF leak, there were 3 (1%) postoperative leaks. Of those 3 patients, 1 had no repair, 1 had fat graft, and 1 had AlloDerm. Repair methods and postoperative leak rates with intraoperative CSF leak were, respectively, AlloDerm ($n = 95$; 8.4%); fat ($n = 46$; 15.2%); fascia lata, nasoseptal flap, other or no repair ($n = 19$; 0%). There was no statistically significant difference in postoperative CSF leak rates between AlloDerm and fat graft in the presence of an intraoperative CSF leak ($p = 0.34$, chi-square test).

Management of CSF Rhinorrhea

CSF Drainage

CSF drains were placed in 12 cases of postoperative CSF leak after an intraoperative leak was seen at surgery. Lumbar subarachnoid catheters were used in 11 cases and a cervical

subarachnoid catheter in 1. The mean duration of drainage was 5.5 days (range 1 to 9 days).

Complications of Subarachnoid Catheters

One patient with a lumbar drain subsequently underwent an early operative repair after the catheter failed to flow after placement. Another patient had a retained sheared catheter that required a return to the operating room for retrieval and replacement via laminotomy. No permanent complications of subarachnoid catheters were observed.

Reoperation for CSF Leak

Four patients required reoperation for CSF rhinorrhea (0.9%). Two patients with initial fat repairs had definitive repair with endoscopic AlloDerm allograft. Patients with AlloDerm repair at their primary surgery were repaired with repeat AlloDerm closure ($n = 1$) or nasoseptal mucosal flap ($n = 1$).

Other Complications

Meningitis was confirmed by CSF culture in 3 of 18 patients with postoperative CSF leak (16.7%). The organisms recovered were methicillin-resistant *Staphylococcus aureus* (MRSA), *Enterobacter aerogenes*, and *Pseudomonas aeruginosa*. In cases without CSF leak, two patients developed meningitis (0.5%).

Significant epistaxis requiring readmission to the hospital occurred in 5 (1.1%) cases. However, there were no complications specific to fat autograft or AlloDerm recognized. There was one sudden postoperative death (0.2%) that occurred 5 days after surgery. The results of a postmortem exam were inconclusive but did not reveal carotid injury.

Discussion

Although infrequent, the complications of TSS can be devastating. Unlike carotid, optic nerve, or endocrine complications, which are generally irreversible, the surgeon has the opportunity to ameliorate the consequences of an intraoperative CSF leak. At times, a thorough tumor resection will unavoidably result in CSF leakage and is acceptable if a secure closure can be achieved. To provide meaningful results, the closure method in a series of TSS should be scrutinized by the rate of CSF rhinorrhea after intraoperative CSF leak.

Preoperative counseling before TSS should quote surgeon-specific complication rates; however, some CSF leaks may be predictable. Previous TSS, macroadenoma, radiotherapy, obesity, and intraoperative leakage have been associated with a higher incidence of postoperative CSF leak.^{12,18,22,23} Mehta and Oldfield have suggested intraoperative removal of CSF via lumbar drain as a strategy to reduce intraoperative leakage. In their series, the rate of postoperative CSF leak was unchanged, but reoperation for CSF leak was reduced.²⁴ We excluded patients with intraoperative lumbar drainage in our study to evaluate the effectiveness of AlloDerm alone.

Another strategy to prevent postoperative CSF leaks is to raise a nasoseptal mucosal flap. Vascularized mucosal flaps are a very effective method of skull base reconstruction, even

in the setting of high-flow CSF leak; however, they may result in increased patient discomfort.²⁵ Anosmia, crusting, and increased procedure time are deterrents to using mucosal flaps routinely on all transsphenoidal patients. In general, these flaps are raised at the beginning of the procedure before it is known if an intraoperative CSF leak will occur, adding unnecessary morbidity in cases without a leak. Techniques to prepare a flap with minimal septum morbidity have been described for cases where a CSF leak is not expected.²⁶

Allograft, though convenient for the surgeon, incurs additional cost. The charge for an 8 cm² sheet of AlloDerm at our institution is approximately \$400. The surgical time saved is negligible given the relative speed with which a fat graft can be obtained. If a statistically significant reduction in postoperative CSF leak was observed, a cost-effectiveness analysis could be warranted for its routine use. For some patients, avoiding a visible surgical incision might be justification on its own for allograft use.

Conclusions

Allograft materials have not been shown to be a panacea for definitive sellar reconstruction. AlloDerm has an adjunctive role in skull base reconstruction and though this data are not powered to prove superiority of AlloDerm over fat graft, our experience suggests it is effective.

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