Porcine small intestine submucosal graft for endoscopic skull base reconstruction

Elisa Illing, MD[1], Mohamad R. Chaaban, MD[1], Kristen O. Riley, MD[2] and Bradford A. Woodworth, MD[1]

Background: **Skull base defects and encephaloceles of the sinus and nasal cavities are routinely repaired endoscopically using a variety of materials including bone, cartilage, fascia, acellular dermal allografts, and xenografts, with high success rates. However, there is a paucity of data regarding the use of porcine small intestine submucosal (SIS) grafts for endoscopic dural repair. The purpose of the current study was to review outcomes using SIS grafts in the endoscopic reconstruction of skull base defects.**

Methods: **Review of prospectively collected data regarding skull base defect repair using SIS was performed. Demographics, location, and size of skull base defect, method of repair, successful closure, and complications were recorded.**

Results: **Over 4.5 years, 155 patients (mean age 49 years) underwent 170 primary skull base repairs using porcine SIS. Etiologies included tumor (76), spontaneous (51), trauma (37), and congenital (5). The majority of repairs were in combination with a nasoseptal flap (n = 113). Average defect size (length vs width) was 13 x 10.5 mm. Success rate on first attempt was 94.7% (161/170), and all defects were effectively sealed on subsequent endoscopic revision. The average follow-up was 77 weeks. Major postoperative complications, including recurrent cerebrospinal fluid (CSF) leak (9), meningitis (1), periorbital cellulitis (1), and invasive fungal sinusitis (1), occurred in 6.4% of individuals with no long-term sequelae.**

Conclusion: **Use of porcine SIS dural graft was associated with excellent outcomes in this study and evidence presented here supports its routine use in the endoscopic closure of skull base defects.** © 2013 ARS-AAOA, LLC.

Key Words:
acetazolamide; encephalocele; CSF rhinorrhea; cerebrospinal fluid leak; intracranial hypertension; spontaneous; endoscopic sinus surgery; skull base defect; CSF leak repair; pseudotumor cerebri; empty sella

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Cerebrospinal fluid (CSF) leaks are rare but serious problems that may arise from traumatic, neoplastic, or congenital defects, but they may also occur spontaneously. Components of a CSF leak require a defect in the arachnoid or dura mater, an osseous disruption, as well as intracranial pressure that exceeds the strength of the interrupted tissue.[1]

[1]*Department of Surgery, Division of Otolaryngology–Head and Neck Surgery, University of Alabama at Birmingham, Birmingham, AL;* [2]*Division of Neurosurgery, University of Alabama at Birmingham, Birmingham, AL*

Correspondence to: Bradford A. Woodworth, MD, BDB 563, 1720 2nd Ave South, Birmingham, AL 35294; e-mail: bwoodwo@hotmail.com

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Due to increasing improvements in technology and expertise, endoscopic repair of skull base defects is now a routine treatment for CSF leaks that is less morbid than traditional open craniotomies. Advancements have included enhancements in endoscopes, powered instrumentation, hemostatic agents, and biomaterials.[2]

The use of biomaterials, in particular, have become widespread, and offer the advantages of achieving complete and long-lasting repairs of skull base defects without a second surgical site of harvest. Biodesign® (Cook Biomedical, West Lafayette, IN) is an acellular, resorbable biomaterial material derived from the extracellular matrix of porcine small intestinal submucosa (SIS). Applications for use have been described for repairs of abdominal hernias and congenital diaphragmatic hernias, and for gynecologic and urologic procedures; however, there is a paucity of literature available concerning its application to repair of skull base defects during endoscopic sinus surgery despite widespread

U.S. Food and Drug Administration (FDA)-approved use for dural reconstruction.[3–5]

The objective of the current study was to review outcomes of endoscopic skull base reconstruction using SIS grafts.

Patients and Methods

Patients

Review of a prospectively collected database regarding patients undergoing CSF leak repair was approved by the University of Alabama at Birmingham's institutional review board. Only patients with SIS used in their reconstruction were included in the study. Patient demographics were collected, including age, sex, location of skull base defect, etiology of defect, size of defect, reconstructive technique, and complications. Etiologies of skull base defects were classified as congenital, traumatic (including iatrogenic), spontaneous, or neoplastic.

Surgical technique

Endoscopic management of defects varied according to size and location of the defect, but generally followed standard techniques described.[6–11] Lumbar drains were utilized to instill fluorescein as described[12] in patients with suspected elevated intracranial pressure (spontaneous CSF leaks), questionable defect site (some trauma), or for some large cranial base resections. Fluorescein was used intrathecally according to previous protocols for identification of leak site(s), and to inspect for watertight closure at the end of the case. Fluorescein is not FDA-approved for this use, due to reports of neurotoxicity and seizure when injected at higher quantities and more rapid infusions, and all patients were counseled on these facts to obtain informed written consent. At the investigating institution, 0.1 mL of 10% fluorescein diluted in 10 mL of the patient's CSF was slowly injected over 10 to 15 minutes.

Surgical approach varied based upon location of the defect(s); however, most cases involved the transethmoidal approach with skeletonization of the skull base via sphenoidethmoidectomy with additional approaches (eg, transsphenoidal) used as needed (Fig. 1). Using 0-degree, 30-degree, or 70-degree nasal endoscopes for visualization, the defect was identified and a cuff of mucosa was removed surrounding the site. The defect size was determined by endoscopic placement of a ruler intraoperatively, just prior to the repair of the defect. The endoscopic measurement provided details of the defect size and shape, with defect sites consistently measured in the same fashion to remain accurate. If the defect was not a linear crack and large enough for an underlay graft (generally >4 to 5 mm), the dura was lifted gently off of the skull base and an SIS dural graft (with bone graft if possible in cases associated with intracranial hypertension) was placed in an underlay fashion. An SIS overlay graft ± a nasal septal flap (NSF) is then applied to completely cover the location. Evicel® fibrin sealant (Johnson & Johnson, Somerville, NJ) is applied to stick the graft or flap into place, followed by gelfoam to support the graft. A Merocel™ (Medtronic, Jacksonville, FL) cotton spacer placed into a cut finger of a non-latex glove was placed in the ethmoid area for further graft support

Postoperative care

Patients with high intracranial pressure on opening lumbar tap and all individuals with spontaneous CSF leaks had CSF diversion for approximately 48 hours as described.[6,13] Patients were kept on stool softeners, and directed on avoidance of Valsalva maneuvers or strenuous activity for 6 weeks postoperatively. While middle meatal spacers were in place, patients were maintained on an anti-staphylococcal antibiotic or other culture-directed therapy with concomitant infection. Patients were seen for initial follow-up between 8 to 13 days after surgery, at which time the spacers were removed.

Results

Over 4.5 years, 155 patients (average age of 49 years) with a total of 170 skull base defects had skull base repairs treated by a single otolaryngologist. The defects were of various etiologies, including congenital (n = 5), traumatic (n = 37), neoplastic (n = 76), and spontaneous (n = 51). Fifty-five percent of patients were female, with average defect size of 13 (range, 2-48) mm in length by 10.5 (range, 1-35) mm in width. Multiple defects were identified in 15 patients and were counted as distinct defects; however, some single defects involved 2 subsites. The distribution of defect locations is listed in Table 1. For larger skull base resections secondary to tumor resections, the description of anterior cranial fossa (ACF) includes the bilateral cribriform plate, ethmoid roof, and often portions of the frontal sinus posterior table and planum sphenoidale.

SIS was applied in 1 of 3 ways: as an underlay graft (n = 19), an overlay graft (n = 36), or as both underlay and overlay grafts (n = 115). A bone graft was used in 37 cases. NSFs were used in 122 individuals.

The initial success rate for repair was 94.7% (n = 161) with overall success rate of 100% at an average of 77 weeks follow-up. Nine patients required revision surgery due to recurrent CSF leaks. Of these 9 patients, 6 had initial repairs with the use of NSFs; 7 had reconstructions performed with SIS applied in an underlay and overlay fashion (Table 2), and the remaining 2 had SIS used in either an underlay, or overlay fashion, respectively.

Infectious complications occurred in 3 patients: 1 individual with periorbital cellulitis that resolved with administration of intravenous antibiotics, 1 case with acute invasive fungal sinusitis that resolved with intravenous and oral antifungal therapy,[14] and another with meningitis associated

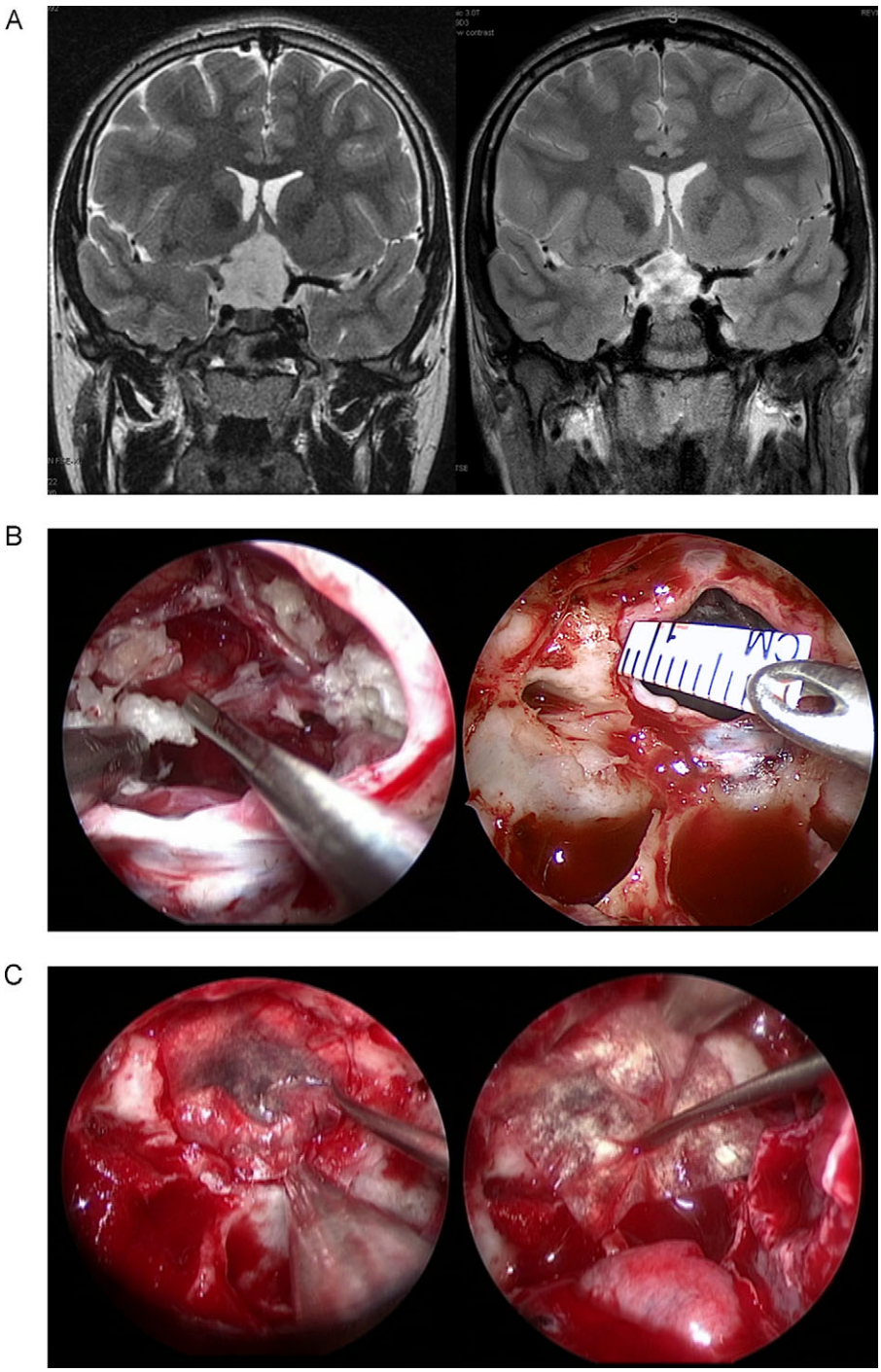

FIGURE 1. (A) A patient with a large suprasellar epidermoid demonstrated on T2-weighted coronal MRI image (left); postresection MRI image at 6 months reveals no residual tumor (right). (B) Transnasal endoscopic view through the defect in the planum sphenoidale during removal of the epidermoid from the optic chiasm (left); measurement of the defect is performed with endoscopic placement of a ruler (right). (C) Reconstruction with porcine small intestine submucosal graft in an underlay (left) and overlay (right) fashion. This patient also had placement of a nasal septal flap. MRI = magnetic resonance imaging.

with CSF leak that resolved with intravenous antibiotic therapy and repair of CSF leak. Two patients required revision frontal sinusotomies for frontal outlet obstruction. Other complications included a small intraparenchymal hemorrhage with no sequelae, and severe respiratory acidosis due to underlying obstructive sleep apnea requiring tracheostomy.

Discussion

The current study demonstrates the safety and effectiveness of SIS grafting for repair of skull base defects from a variety of etiologies. The use of SIS for this purpose has been underreported in the otolaryngology literature to date, although its use has been well-documented as an effective tool in many other surgical specialties. Bejjani et al.[15]

TABLE 1. Location of skull base defects

Location	n	%
Central sphenoid	63	37
FS posterior table	33	19
Cribriform plate	28	17
Ethmoid roof	20	12
LRS	16	9
ACF	8	5
Clivus	2	1
Total	170	100

ACF = anterior cranial fossa (inclusive of bilateral cribriform plate, ethmoid roof, and often portions of the FS posterior table and planum sphenoidale following tumor resection); FS = frontal sinus; LRS = lateral recess of the sphenoid.

reported in 2007 regarding the use of porcine SIS grafts for dural repair during neurosurgical procedures, achieving repair rates similar to those using fascial grafting, as well as similar complication rates. In the present study, the repair success rate using SIS meets or exceeds previously reported success rates for primary endoscopic closure of skull base defects (>90%), with complications also similar to reported values.[16]

Advantages of SIS grafts over autologous tissues such as fascia lata or temporalis fascia include the lack of donor site morbidity and decreased operative time. Additionally, the neurosurgical literature has shown that SIS is an excellent product for dural repair, and it has FDA approval for this use. In our experience (although not specifically evaluated), SIS is easier to manipulate endoscopically than other allografts or xenografts because it does not swell with hydration or adhere to itself when folded in the presence of blood. Disadvantages inherent to the graft include expense (although counteracted by decreased operative time), the source of the material as a xenograft, and lack of vascularity. As indicated by the data presented in this study, we usually use a vascularized NSF for overlay when possible, but SIS grafts used in multilayer and sometimes single layer (eg, small traumatic linear defect) repairs also demonstrated excellent results.

Multiple layered closure using underlay and overlay type grafting was performed in the majority of patients (115/170), particularly in those with larger defects. The epidural and/or intracranial graft is positioned such that the cerebrum will rest on the graft, securing it in position, while the extradural, or overlay, graft assists with ingrowth of tissue to strengthen the repair and reestablish the sinonasal mucosal lining.[17] Recent in vitro studies of bladder regeneration after repair with SIS suggest presence of bioactive factors present in SIS encourage cell regrowth and angiogenesis resulting in decreased wound healing time.[18] With regard to durability of the graft over time, a study of the tensile strength of SIS was performed by subjecting the material to repetitive loading pressures. The graft was found to retain its strength completely, which supports its use in repair situations when a graft would be exposed to increased pressure (eg, hernia repair or skull base repair during Valsalva maneuver by the patient).[19]

Infectious complications are rare following skull base reconstruction, with cases of meningitis reported as less than 1%.[20] There are varied reports in the literature of acute sinusitis following endoscopic sinus surgery, ranging from 7.5% to 29% in some studies (complicated by the presence of expected postoperative crusting), with preseptal cellulitis infrequently described.[20] The incidence of meningitis (0.6%) and periorbital cellulitis (0.6%) in the present study fall within the expected range of infectious complications. One case of acute invasive fungal sinusitis occurred in an individual treated with prednisone for his allergic fungal sinusitis, but the location of involvement was completely separate from the area of graft placement and it was not thought to be associated with the material.[14] A recent study

TABLE 2. Recurrent CSF leak patients

Age (years)	Sex	Etiology	Defect sites	Length (mm)	Width (mm)	Biodesign	Bone graft	NSF	Complications
45	F	Tumor	Central sphenoid	10	10	Underlay/overlay		Y	CSF leak revision
73	F	Tumor	Central sphenoid	15	15	Underlay/overlay		Y	CSF leak revision
22	F	Congenital	Central sphenoid	18	18	Underlay/overlay		Y	CSF leak revision
56	F	Tumor	ACF	40	25	Underlay/overlay		Y	Pneumocephalus; CSF leak revision
48	F	Spontaneous	Cribriform	9	10	Underlay		Y	CSF leak revision
47	F	Spontaneous	LRS	6	6	Underlay/overlay	Y		CSF leak revision
38	M	Spontaneous	Cribriform	8	8	Overlay		Y	CSF leak revision
41	F	Tumor	Cribriform	7	6	Underlay/overlay			CSF leak revision
6	F	Congenital	Central Sphenoid	10	10	Underlay/overlay			Meningitis; CSF leak revision

ACF = anterior cranial fossa (inclusive of bilateral cribriform plate, ethmoid roof, and often portions of the FS posterior table and planum sphenoidale following tumor resection); CSF = cerebrospinal fluid; FS = frontal sinus; LRS = lateral recess of the sphenoid; NSF = nasal septal flap.

has shown that SIS is more resistant to biofilm formation compared to synthetic grafting materials, though it has not been shown to express overt antimicrobial activity.[21]

CSF diversion via lumbar drains was continued postoperatively only in select cases of intracranial hypertension. No complications were noted in patients due to lumbar drain placement. In this subset of patients, we believe postoperative control of intracranial pressure with acetazolamide or permanent CSF diversion is integral to successful repair, and likely is responsible for our excellent closure rate (94% primary) in a group of patients known for recurrence.[12,22]

Conclusion

The current study reported on the safe and effective use of SIS dural grafting in a large series of patients with prospectively collected data. The material is a useful reconstructive option for endoscopic repair of skull base defects.

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