Efficacy and safety of a collagen matrix for cranial and spinal dural reconstruction using different fixation techniques

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Object. The use of dural grafts is frequently unavoidable when tension-free dural closure cannot be achieved following neurosurgical procedures or trauma. Biodegradable collagen matrices serve as a scaffold for the regrowth of natural tissue and require no suturing. The aim of this study was to investigate the efficacy and safety of dural repair with a collagen matrix using different fixation techniques.

Methods. A total of 221 patients (98 male and 123 female; mean age 55.6 ± 17.8 years) undergoing cranial (86.4%) or spinal (13.6%) procedures with the use of a collagen matrix dural graft were included in this retrospective study. The indications for use, fixation techniques, and associated complications were recorded.

Results. There were no complications of the dural graft in spinal use. Five (2.6%) of 191 patients undergoing cranial procedures developed infections, 3 of which (1.6%) were deep infections requiring surgical revision. There was no statistically significant relationship between the operative field status before surgery and the occurrence of a postoperative wound infection (p = 0.684). In the 191 patients undergoing a cranial procedure, cerebrospinal fluid (CSF) collection occurred in 5 patients (2.6%) and a CSF fistula in 5 (2.6%), 3 of whom (1.6%) required surgical revision. No patient who underwent an operation with preexisting CSF leakage had postoperative CSF leakage. Postoperative infection significantly increased the risk for postoperative CSF leakage. The collagen matrix was used without additional fixation in 124 patients (56.1%), with single fixation in 55 (24.9%), and with multiple fixations in 42 (19%). There were no systemic allergic reactions or local skin changes. Follow-up imaging in 112 patients (50.7%) revealed no evidence of any adverse reaction to the collagen graft.

Conclusions. The collagen matrix is an effective and safe cranial and spinal dural substitute that can be used even in cases of an existing local infection. Postoperative deep infection increases the risk for CSF leakage. (DOI: 10.3171/JNS/2008/109/8/0215)

Key Words: cerebrospinal fluid leak • collagen matrix • craniotomy • dural substitute • tumor resection • wound infection

Abbreviation used in this paper: CSF = cerebrospinal fluid.
Methods

In this retrospective study we included consecutive patients who underwent a cranial or spinal neurosurgical procedure with dural closure using the DuraGen collagen matrix at our department between 2003 and 2006. In each case the decision to use the collagen matrix instead of an autograft was made by the surgeon according to his or her preferences and the individual intraoperative situation. It was also the surgeon’s decision regarding the mode of fixation for the collagen matrix: simple onlay without fixation, or additional fixation using stay sutures, fibrin glue, or a collagen sponge.

Data Collection

The following data were collected and analyzed for all patients: age, sex, diagnosis, operative site, Glasgow Coma Scale score on admission, indication for duraplasty, neurosurgical procedures within the preceding 3 months, scheduled or emergency neurosurgical procedures, length of procedure, presence of diabetes mellitus, previous chemotherapy, operative field status before surgery (clean, contaminated, or infected), presence of external CSF drainage, fixation technique, and size of the collagen matrix used.

For the postoperative period, the following events were recorded: repeat surgery, CSF leakage (including subcutaneous CSF collection and CSF fistula); every kind of CSF collection independent of size or duration was regarded as a complication), and postoperative surgical site infection. The postoperative surgical site infections were classified as: 1) superficial infection; 2) bone flap osteitis (either a surgical diagnosis of osteitis, fever with local signs and discharge and a positive blood culture, or a suggestive CT scan); 3) meningitis and/or ventriculitis (either Gram stain and/or CSF culture demonstrating a microorganism or CSF leukocytosis with increased protein concentration and decreased glucose concentration, associated with fever and nuchal rigidity, and antibiotic treatment prescribed by the attending clinician); or 4) brain abscess or empyema (either a microorganism isolated from brain tissue or subdural space, surgical diagnosis of brain abscess, or fever with altered mental status, and/or focal neurological deficit and suggestive CT scan, with antibiotic treatment prescribed by the attending clinician), allergic reactions, and laboratory abnormalities.

The fixation techniques used were analyzed for their relationship to the occurrence of complications. All patients received a single intravenous infusion of 2 grams of cefotiam or 2 grams of cefazolin beginning 30 minutes before surgery and lasting 15 minutes.

Surgical Technique

Suitable patches of the collagen matrix of appropriate size were selected to fit the dural defects. These patches had been cut with scissors to fit the individual form of the dural defect while also considering a sufficient overlap. The onlay patch was then placed over the dural defect, overlapping at the margins and hydrated with physiological saline.

In 2 patients who underwent duraplasty using the collagen matrix and in whom the autologous bone flap was reimplanted in a second intervention, specimens of the collagen matrix were removed for histological examination.

Statistical Analysis

Data are presented as means ± standard deviations. The chi-square and Fisher exact test were used for categorical variables. A multivariate analysis using logistic regression was performed to identify risk factors associated with the occurrence of postoperative wound infection14,18 and postoperative CSF leakage. The probability values were 2-sided and a value < 0.05 was considered statistically significant.

Results

Patient Characteristics

A total of 221 patients (98 male and 123 female; mean age 55.6 ± 17.8 years, range 1–91 years) were included in the retrospective analysis. The patients underwent cranial neurosurgery in 191 cases (86.4%) and spinal procedures in 30 cases (13.6%). Clinical and neurological examinations were performed immediately after the intervention and before discharge. Postoperative MR imaging or CT was performed at discharge and after 3 months in 112 patients (50.7%).

Diagnoses and Indications

Patients with a variety of cerebral and spinal conditions were included in this study (Table 1). The main indications for dural closure with the collagen graft matrix were “tension-free dura closure not feasible,” “dura substitution,” “dura extension,” and “preexisting CSF fistula” (Table 2). The mean collagen matrix size used in the study population was 49.3 ± 51.6 cm² (range 6.3–306.2 cm²).

Complications and Infections

No complications occurred in the 30 patients undergoing spinal procedures. Five of the 191 patients (2.6%) who underwent cranial interventions developed infections. These were superficial infections in 2 cases (1%), bone flap osteitis in 2 cases (1%), and meningitis in 1 case (0.5%). The 2 superficial infections were successfully treated with local wound care and antibiotics,
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<table>
<thead>
<tr>
<th>Indication</th>
<th>Cranial Intervention</th>
<th>Spinal Intervention</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>(191 patients)</td>
<td>(30 patients)</td>
</tr>
<tr>
<td>tension-free dural closure</td>
<td>94 (49.2)</td>
<td>19 (63.3)</td>
</tr>
<tr>
<td>not feasible</td>
<td></td>
<td></td>
</tr>
<tr>
<td>dura substitution</td>
<td>70 (36.6)</td>
<td>9 (30.0)</td>
</tr>
<tr>
<td>dura extension</td>
<td>22 (11.5)</td>
<td>0</td>
</tr>
<tr>
<td>preexisting CSF fistula</td>
<td>5 (2.6)</td>
<td>2 (6.7)</td>
</tr>
</tbody>
</table>
* Values represent numbers of patients (%).

Dura extension 22 (11.5) 0

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whereas surgical revision was necessary in the other 3 cases (1.6%).

No statistically significant association was identified between the operative field status before surgery and the occurrence of postoperative infection (p = 0.684). None of the 5 patients with postoperative infections had a contaminated or infected operative field before surgery. Multivariate analysis including the parameters of age, length of procedure, size of dural graft, indication for use, localization, operative field status before surgery, and preoperative CSF leak could not identify any significant risk factor for postoperative infection (p > 0.05, logistic regression).

Cerebrospinal Fluid Leakage

Postoperative CSF leakage occurred in 10 (5.2%) of the 191 patients following cranial neurosurgery; CSF collection occurred in 5 patients (2.6%) and a CSF fistula in 5 (2.6%). Of these 10 patients, 2 (1%) recovered spontaneously, 1 (0.5%) recovered after repeated local (in the subgaleal CSF collection) puncture, and 4 (2.1%) recovered after lumbar drainage; in 3 cases (1.6%) surgical revision was necessary. In 2 of the patients (1%) who underwent a surgical revision, deep infection (bone flap osteitis and meningitis) was apparent and was the primary cause for revision. The incidence of CSF leakage differed significantly (p < 0.05) among different operative sites: 6 patients (3.1%, or 4.1% of all convexity procedures) experienced CSF leakage after convexity surgery, 4 patients (2.1%, or 15.4% of all posterior fossa procedures) experienced CSF leakage after surgery in the posterior fossa, and 0 patients after surgery in the skull base.

The use of the collagen matrix was found to be 100% reliable in closing preexisting CSF fistulas; none of the 7 patients with preoperative CSF leakage had postoperative CSF leakage. Multivariate analysis identified the site of the intervention (p = 0.009) and postoperative infection (p = 0.002) but not age, length of procedure, size of dural graft, fixation technique, indication for use, operative field status before surgery, and preoperative CSF leakage as risk factors for postoperative CSF leakage.

Association Between Infection and CSF Leakage

A postoperative CSF leak was much more frequent in patients with postoperative infection (2 of 5, 40%) compared with patients without such an infection (8 of 186, 4.3%; p = 0.023, Fisher exact test). These 2 patients with postoperative infections had bone flap osteitis and meningitis. Postoperative deep wound infection increased the risk for postoperative CSF leakage by a factor of 17.4, but no relationship was found between the operative field status before surgery and the occurrence of postoperative CSF leakage (p = 0.868, Fisher exact test).

Allergic Reactions

No systemic allergic or local skin reactions were observed. No rejection or encapsulation of the collagen matrix was identified. No case of aseptic meningitis was observed.

Fixation Technique

According to the design of the study, we did not investigate whether the extent of overlap between the collagen matrix and the remaining dura had any influence on the occurrence of postoperative CSF leakage. The manufacturer of the collagen matrix recommends a minimum overlap of 1 cm. When the overlap was smaller, the surgeon used additional fixation as he or she deemed most appropriate. The collagen matrix was simply placed over the defect in 124 patients (56.1% for the entire group, 58.6% for 112 patients with cranial procedures, and 40% in 12 patients with spinal procedures) or fixed using a single additional procedure (single fixation using fibrin glue, a collagen sponge, or stay sutures) in 55 patients (24.9% for the entire group, 24.6% in 47 patients with cranial procedures, and 26.7% in 8 patients with spinal procedures) and several procedures (multiple fixation) in 42 patients (19.0% for the entire group, 16.8% for 32 patients with cranial procedures, and 33.3% for 10 patients with spinal procedures).

Use of the chi-square test to identify a significant correlation between the fixation technique, postoperative wound infection, and CSF leakage could not be applied because of the low number of events. The number of infections that occurred following cranial procedures with multiple fixation (3 of 32, 9.4%), however, was higher than that compared with no fixation (1 of 112, 0.9%) and single fixation (1 of 47, 2.1%). None of the patients in whom single fixation was used developed postoperative CSF leakage (Table 3).

Discussion

An optimal dural graft must neither cause immunological reactions or neurotoxicity nor act as a vehicle for postoperative infections and bone flap osteitis and meningitis. Postoperative deep wound infection increased the risk for postoperative CSF leakage by a factor of 17.4, but no relationship was found between the operative field status before surgery and the occurrence of postoperative CSF leakage (p = 0.868, Fisher exact test).

<table>
<thead>
<tr>
<th>Complication</th>
<th>None (112 patients)</th>
<th>Single (47 patients)</th>
<th>Multiple (32 patients)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CSF leak</td>
<td>8 (7.1)</td>
<td>0</td>
<td>2 (6.3)</td>
</tr>
<tr>
<td>infection</td>
<td>1 (0.9)</td>
<td>1 (2.1)</td>
<td>3 (9.4)</td>
</tr>
</tbody>
</table>
* Values represent numbers of patients (%).
disease transmission. It should not adhere to surrounding tissue or promote scarring. The material should be soft and pliable, but strong enough to withstand suturing. It should unite with the natural dura and should ideally be degradable and replaced by natural tissue, while providing a sufficient patch until that time.

Many materials have appeared to fulfill these criteria and have therefore been used for dural closure. Autografts bear no immunological risks and eliminate the risk of immunological reactions, but these tissues may be affected by the disease and are therefore not available. Proper incorporation of autografts may be impaired following irradiation, chemotherapy, or surgery. Furthermore, preparation and watertight suturing is time-consuming with autografts. Hypoxia of the graft can induce an inflammatory reaction in the underlying cortex. Moreover, extensive meningocerebral adhesions have been reported to occur after use of autologous grafts. When larger defects have to be covered, it is often necessary to use fascia lata, which involves an additional incision and its attendant complications and stressors for the patient.

Allografts using materials such as cadaveric dura mater have been abandoned in most countries because of the high risk of transmitting bovine spongiform encephalopathy (Creutzfeld–Jacob disease). Severe meningocerebral adhesions have been observed in patients with cortical injury who received allografts.

Synthetic dural substitutes—such as polytetrafluoroethylene (Gore-Tex, WL Gore & Associates Inc.) or polyester urethane (Neuropatch, B. Braun, Melsungen AG)—have a fairly rigid structure. The surrounding natural tissue does not form a strong bond with these grafts, which therefore require watertight suturing. These materials are associated with markedly higher complication rates caused by foreign body reactions, scarring, encapsulation, delayed bleeding, infections, and CSF leaks.

Xenografts may consist of processed whole tissues or highly engineered collagen matrices. Processed whole tissue such as pericardium is strong and pliable but requires watertight suturing. Collagen matrices have the advantage of being completely replaced by the patient's own tissue within a few months, which is not the case when whole tissues are used.

Collagen has been identified in animal experiments as an inert and easily handled adhesive material. The collagen fibers serve as a scaffold for the attachment of collagen produced by invading fibroblasts. After rehy-
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The findings of the present study show that the collagen matrix can be safely used even if there is preoperative contamination or infection of the surgical site. Postoperative infection, however, increases the risk of postoperative CSF leakage. This risk was fulfilled in 2 of 3 patients (66.7%) with postoperative deep wound infection or meningitis. On the other hand, in the majority of these patients a revision is required anyway because of the infection. A disadvantage of the revision is the extra cost for the matrix.

The collagen matrix used in this study is an onlay graft that does not need additional fixation if the overlap between graft and dura is sufficient. This concept of sutureless dural repair reduces the time needed for surgery and facilitates application of small patches in anatomically difficult locations. The sutureless procedure was used in > 50% of the patients in the present study. If the overlapping zone between dura and graft is too small, however, additional fixation should be used. The type of fixation technique used appears to influence the complication rate. Cerebrospinal fluid leaks in those cases with-

Fig. 2. Illustrations of the application of the collagen matrix graft. A: This collagen matrix (CM) is an onlay graft that does not need to be fixed with sutures in most cases as long as there is at least 1 cm overlap between the graft and the remaining dura mater (DM). BF = bone flap. B: Additional fixation is recommended if the overlap is smaller. For an overlap of 0.5–1 cm, additional fixation using fibrin glue (FG) is recommended. C: Alternatively, the overlap can be extended along the bone margins, which should also be performed in all cases with < 5 mm overlap. D: The same procedure used for supratentorial defects is recommended in the posterior fossa after an osteoplastic craniotomy. If an osteoplastic craniotomy has been performed, the autologous bone chips (ABCs) can be mixed with fibrin glue and then placed on the collagen matrix over the bone defect. Alternatively, bone substitutes can be used. M = muscle.
out additional fixation are probably caused by insufficient overlap. No CSF leakage was observed when a single fixation method was used. The simultaneous use of multiple fixation methods was associated with a higher rate of infections and CSF leaks (Table 3). These results are based on a retrospective analysis and one has to take into account the fact that the study could therefore not have been specifically designed to answer these questions. Based on these observations, however, the most suitable fixation techniques have been identified for cranial use (Fig. 2). In spinal procedures the bone of the laminae can be used to fix the collagen matrix. In this case, additional fixation using fibrin glue is recommended if the overlap is < 1 cm.

The results suggest that autografts are not necessarily the best option in patients requiring some form of dural graft. Instead, the neurosurgeon should select the most suitable graft on a case-by-case basis after carefully weighing the individual factors involved in each patient.

Conclusions

The collagen matrix is an effective and safe dural substitute that can be used even in cases of an existing local infection. Postoperative deep wound infection or meningitis increases the risk for CSF leakage, however, so it should be used with caution in immunocompromised patients. The collagen matrix dural graft is an invaluable alternative for closure of surgical or traumatic defects of the cranial and spinal dura mater.

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