The Use of DuraMatrix-Onlay™ for Dural Reconstruction following Craniotomy for Tumor Resection: Results from 100 Consecutive Patients

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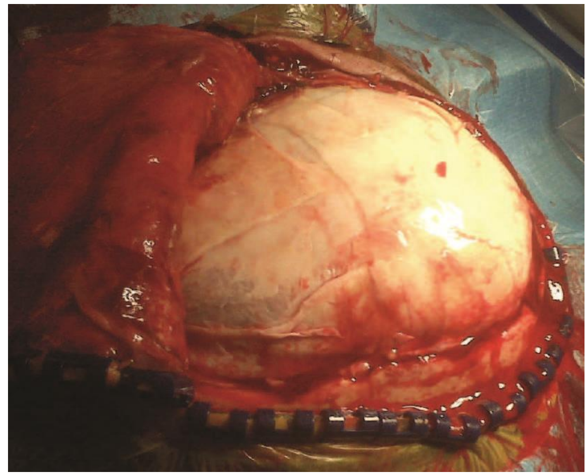
Abstract

Objective: Complications from craniotomy in brain tumor patients lead to worse clinical outcomes either from infection, reoperation, or delays in adjuvant therapies. We tested the hypothesis that DuraMatrix-Onlay™ Collagen Dura Substitute Membrane potentially could reduce operative complications, and we report the unique characteristics of this onlay product in comparison to primary dural closure and other onlay products.

Methods: We reviewed the demographic and surgical data with special attention addressed to postoperative complications in primary or metastatic brain tumor patients undergoing craniotomy. We excluded patients with a posterior fossa craniotomy requiring watertight dural closure, those with secondary exploration for post-operative CSF leaks, or who underwent transsphenoidal resection of pituitary lesions.

Results: A total of 100 patients underwent craniotomy were treated with the DuraMatrix-Onlay™ product. A significant number of patients were at risk for wound healing complications due to either: postoperative radiation (61%), prior craniotomy (26%), or previous brain irradiation (19%). Deep wound infections requiring surgical re-exploration and intravenous antibiotics were encountered in six patients (6%), and three patients (3%) had superficial infections which resolved with oral antibiotics. Pseudomeningoceles were seen in three patients (3%), and five patients (5%) had cerebrospinal fluid leaks including one who developed meningitis. Delayed complications were not encountered in any patient, and there were no complications that could be attributed to the use of the dural substitute.

Conclusion: We have demonstrated that the use of DuraMatrix-Onlay™ for dural reconstruction is safe and efficient. This product is a cost effective and beneficial alternative for those patients not amenable to primary dural closure.



Introduction

Primary watertight dural closure following craniotomy is not possible in every situation. This may be secondary to dural injury or laceration during exposure, dural shrinkage throughout the procedure, when the dura must remain open to accommodate brain swelling, or resection of the dura for dural-based lesions [1-3]. Numerous options for secondary closure include the use of suturable materials such as pericranium and galea or synthetic substances such as gortex and allograft or synthetic collagen-based products [4-6]. In many instances, watertight dural closure is not necessary, and the use of onlay products may be sufficient to recreate a barrier for the intracranial compartment while avoiding the time demands required for dural suturing.

Several materials have been approved by the FDA as onlay products for dural reconstruction, however, data regarding their efficacy and utility is lacking. The premarket approval process requires significant animal and preclinical data regarding product integration and safety while minimal post-market research evaluating the use of these agents in clinical context exists. Approved by the FDA in 2006, DuraMatrix-Onlay ™ Collagen Dura Substitute Membrane (Collagen Matrix Inc., Oakland, NJ) is indicated as a dura substitute for the repair of the dura mater [7].

In an attempt to fill this void and determine the efficacy and complication rates associated with the use of such materials, we conducted a retrospective study evaluating the clinical outcome in a series of 100 consecutive patients using the single onlay product DuraMatrix-Onlay^{TM} for dural reconstruction.

Methods

Following appropriate IRB approval, a list of product usage was obtained from hospital records, and a database was generated. Charts were reviewed for demographic and surgical data with specific attention to evidence of postoperative complications. Patients who underwent surgery by neurosurgeons other than the primary surgeon (TWV) or for non-cranial indications were excluded. In addition, patients with a posterior fossa craniotomy requiring watertight dural closure and those with secondary exploration for post-operative CSF leaks or transsphenoidal resection of pituitary lesions were also excluded.

Dural Closure Rationale

Dural closure in the posterior fossa was always performed with watertight dural grafting, and these patients are not included in this analysis. Primary dural closure was always considered the method of choice for supratentorial procedures, however, if it was determined by the primary surgeon not to be possible then one of several treatment algorithms was utilized. For patients with high-risk procedures (pterional location, ventricular entry, or implantation of carmustine wafers [Gliadel®]), dural grafting with a synthetic suturable material was always considered the treatment of choice. However, if primary closure was not felt to be plausible or if the patient was considered lower risk for a cerebrospinal fluid leak then secondary closure with an onlay product was performed. Dural leafs were loosely approximated with neuralon suture followed by covering of the defect with the dural on-lay product. The bone flap was plated back into place, and excess product was trimmed. The wound was irrigated with bacitracin irrigation and closed in layers with dermabond on the skin. Hemovac drains were placed in the epidural and/or subgaleal space as indicated at the discretion of the surgeon.

Results

Data for 100 consecutive patients meeting the inclusion criteria between January 2009 and December 2010 was collected. There were 49 men and 51 women. The ages ranged between 24 and 86 years (mean = 57 years). Most patients underwent craniotomy for the treatment of primary or metastatic brain tumors. This group consisted of a significant number of patients at risk for wound healing complications: secondary to the use of postoperative radiation (61%), prior craniotomy (26%), or previous radiation to the brain (19%). In addition, there were risks associated with the use of high-dose steroids which were required at least transiently in most patients.

Deep wound infections requiring surgical re-exploration and intravenous antibiotics were encountered in six patients (6%), and three patients (3%) had superficial infections which resolved with oral antibiotics. Pseudomeningoceles were seen in three patients (3%), and five patients (5%) had cerebrospinal fluid leaks including one who developed meningitis. Seven of these eight patients eventually were determined to have hydrocephalus and were treated with ventriculo-peritoneal shunt insertion. The other patient most likely had hydrocephalus although died during her hospitalization for the treatment of her spinal fluid leak secondary to complications of her surgery and metastatic lung cancer. Delayed complications were not encountered in any patient, and there were no complications that could be attributed to the use of the dural substitute such as delayed subdural fluid collections.

Table 1: Postoperative Incidence of Complications using Dural Onlay Products

Studies in Literature	Number of Patients	Incidence of Complications
Present study 2011	100	Pseudomeningocele: 6% CSF leak: 2% Infection: 6%
Danish et al. (2) 2006	56	DuraGen group: Pseudomeningocele: 9% Infection: 3.6% CSF leak: 1.8% Repeat surgery: 7.1% AlloDerm: Pseudomeningocele: 11% Infection: 2.2% CSF leak: 2.2% Repeat surgery: 4.4%
Litvack et al. (6) 2009	475	CSF leak: 6.7% Infection: 4.2%
Narotam et al. (10) 2007	79	CSF leak: 0% Infection: 3.8%
Parizek et al. (11) 1997	2665	CSF fistula: 2.8% Meningitis: 2.3% Pseudomeningocele: 2% Infection: 0.6%
Stendel et al. (13) 2008	221	CSF collection: 2.6% CSF fistula: 2.6% Infection: 2%.

Discussion

The rationale for dural reconstruction following craniotomy varies significantly from surgeon to surgeon. Strategies from meticulous primary closure to usage of either autologous, allogenic, or synthetic onlay products exist [5, 8]. Typically, the decision on how to close the dura depends more on the surgeon's beliefs based on previous experience, training, or practice demographics rather than on sound scientific principles.

DuraMatrix-Onlay™ Collagen Dura Substitute Membrane is a white, nonfriable, conformable, resorbable, membrane matrix developed from purified type I collagen derived from bovine Achilles tendon. It has a thickness comparable to that of native dura and is flexible allowing it to conform to the contours of the defect site. DuraMatrix-Onlay™ has been designed to not adhere to the brain cortex, native tissue, or bone flap and permits an easy plane of dissection.

Several collagen matrix products are available on the market, including DuraMatrix™ (Collagen Matrix Inc.), DuraGen® Dural Graft Matrix (Integra) DuraGen® Plus Dural Graft Matrix (Integra), and Durepair® Regeneration Matrix (Medtronic). It has been reported that bilayer collagen sponges (suturable DuraGen®) are associated with a decrease in postoperative CSF leak as compared to monolayer collagen sponges (DuraGen® or DuraGen® Plus) [9]. Furthermore, resorbable collagen dural grafts have been shown to be acceptable alternatives to primary dural closure in situations of infected wounds [4].

We have demonstrated that the use of DuraMatrix-Onlay™ for dural reconstruction following craniotomy is safe and effective. Our 6% deep infection rate is similar or better than previous reports in the literature when the high-risk nature of these patients is taken into consideration (Table 1) [3, 9-12]. In addition, 8% of the patients in this study had failure of dural closure (pseudomeningocele, CSF leak) (Table 1), however, this was felt to be attributed more to the development of hydrocephalus rather than a true failure of dural reconstruction. Of the eight patients with failure of dural closure, seven had elevated intracranial pressure with ventriculomegaly and required shunting. In fact, the risk of post-operative CSF leak in untreated hydrocephalus is excessively high, regardless of the process used for dural reconstruction.

The postoperative complications associated with dural substitutes have been presented in the literature [2]. Moskowitz and colleagues conducted a study of dural substitutes in suboccipital craniotomies and determined that the complication rates for most products were comparable except for suturable bovine collagen matrix, with 50% of patients demonstrating hydrodynamic complications including CSF leak, symptomatic pseudomeningocele, aseptic meningitis, and delayed hydrocephalus [2]. In contrast, Parizek et al. reported their 50-year experience with posterior fossa surgery and addressed the issue of hydrodynamic complications [13]. The complication rate was 40% of those who underwent primary closure, 26.9% of those closed with dural reconstruction, and 18.8% when the dura was left open [13]. Furthermore, onlay grafting has shown comparable complication rates to duraplasty with a watertight dural closure while drastically decreasing operative time (92 minutes for the former; 128 minutes for the latter) [10].

Several studies have addressed the use of collagen autograft implants as a dural substitute. Zerris and colleagues studied three collagen dural graft substitutes, including Dura-Guard, DuraGen®, and Durepair. Each of the products was safe and effective and displayed differences in postoperative biological responses based on varying collagen characteristics [14]. The collagen biomatrix TissuDura® consists of a colloidal colalgen from equine Achilles tendon and has been used in dural reconstruction [5]. In a study of 74 patients treated with TissuDura® for dural repair, no signs of graft rejection, CSF leaks, or other complications were noted [5].

While a formal cost evaluation was not feasible due to the retrospective nature of this project, we believe that the increased costs associated with the use of such products during craniotomy are easily offset by the time saved during closure. Primary or secondary closure of dural openings with or without synthetic products increases the duration of the case by approximately 20-60 minutes whereas dural closure with such onlay products may be performed in a matter of minutes. In addition, harvesting of autograft (galea, pericranium) further lengthens surgical times and may also increase the risk of subsequent bleeding or wound healing issues if galea is used.

The average hospital costs for operating room time range between $100-136 for performing a craniotomy. DuraMatrix costs $500-1000 depending on the size of the implant and purchasing agreement with the vendor. With these costs, the breakeven point for the product would be the reduction of operative time by 5-9.5 minutes. As a primary closure of dura may take between 30-50 minutes, DuraMatrix would be predicted to be financially favorable assuming that the use of such products does not increase the risk of secondary complications as in our study.

One of the most commonly cited reasons against the use of such products is due to fears regarding infectious disease transmission especially prion diseases. Human allografts have been associated in the transmission of Creutzfeldt-Jakob Disease, cadaveric materials may be infected with human immunodeficiency virus, and bovine spongiform encephalopathy has drawn attention to bovine dura mater substitutes [15]. DuraMatrix is manufactured from collagen derived from bovine Achilles tendon which is classified by European Standards as a Class IV material and by US Food and Drug Administration as a Class II medical device. In this respect, there is no detectable infectivity for Bovine Spongiform Encephalopathy (BSE). The procedure involves treatment with sodium hydroxide which inactivates the SE pathogens [7, 14]. An independent laboratory conducted a viral inactivation study for the product's manufacturing process and concluded that the process was successful in inactivating the viral strains of Bovine Viral Diarrhea and Porcine Parvoviradae. DuraMatrix-Onlay™ is contraindicated for those individuals with a known history of hypersensitivity to bovine derived materials.

Conclusion

We have found that the use of DuraMatrix-Onlay™ as an onlay product for dural reconstruction is safe and effective. Complication rates demonstrated in this series of 100 patients were no higher than historical controls documented in other studies. The safety concerns of this product have been alleviated through extensive testing to confirm that no detectable infectivity for BSE exists following treatment with sodium hydroxide. DuraMatrix™ serves as a cost efficient and reliable product that offers a valuable alternative to primary dural closure.

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