Complications following decompression of Chiari malformation Type I in children: dural graft or sealant?

Clinical article

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Object. Posterior fossa decompression with duraplasty for Chiari malformation Type I (CM-I) is a common pediatric neurosurgery procedure. Published series report a complication rate ranging from 3% to 40% for this procedure. Historically, many dural substitutes have been used, including bovine grafts, human cadaveric pericardium, synthetic dura, and autologous pericranium. The authors hypothesized that a recently observed increase in complications was dependent on the graft used.

Methods. Between January 2004 and January 2008, 114 consecutive patients ≤18 years old underwent primary CM-I decompression using duraplasty. Records were retrospectively reviewed for short- and intermediate-term complications and operative technique, focusing on the choice of duraplasty graft with or without application of a tissue sealant.

Results. The average age of the patients was 8.6 years. The dural graft used was variable: 15 were treated with cadaveric pericardium, 12 with Durepair, and 87 with EnDura. Tisseel was used in 75 patients, DuraSeal in 12, and no tissue sealant was used in 27 patients. The overall complication rate was 21.1%. The most common complications included aseptic meningitis, symptomatic pseudomeningocele, or a CSF leak requiring reoperation. The overall complication rates were as follows: cadaveric pericardium 26.7%, Durepair 41.7%, and EnDura 17.2%; reoperation rates were 13%, 25%, and 8.1%, respectively. Prior to adopting a different graft product, the overall complication rate was 18.1%; following the change the rate increased to 35%. Complication rates for tissue sealants were 14.8% for no sealant, 18.7% for Tisseel, and 50% for DuraSeal. Nine patients were treated with the combination of Durepair and DuraSeal and this subgroup had a 56% complication rate.

Conclusions. Complication rates after CM-I decompression may be dependent on the dural graft with or without the addition of tissue sealant. The complication rate at the authors’ institution approximately doubled following the adoption of a different graft product. Tissue sealants used in combination with a dural substitute to augment a duraplasty may increase the risk of aseptic meningitis and/or CSF leak. The mechanism of the apparent increased inflammation with this combination remains under investigation. (DOI: 10.3171/2011.5.PEDS10362)

KEY WORDS • aseptic meningitis • CSF leak • Chiari • complication • pseudomeningocele • decompression

Over one hundred years ago Hans Chiari first published his observations of autopsy patients with cerebellar ectopia involving the spinal canal.6 Since his initial observations, our understanding of Chiari malformation Type I (CM-I) has continued to evolve. Most CM-I are believed to be congenital and patients typically present with symptoms related to posterior fossa compression and/or spinal cord dysfunction.1,13 The number of pediatric patients presenting with CM-I appears to be increasing.21,22,28,29 Surgical intervention has been shown to change the clinical course of CM-I.28,31 Many different surgical treatment strategies have been described, including bone decompression with or without dural expansion, along with various algorithms for deciding whether dural expansion should be undertaken.1,5,9,11–15,17,19,20–24,26–28,30,32 However, the majority of pediatric neurosurgeons surveyed in 2000 recommended using bone decompression along with dural grafting for CM-I.18 Tissue sealants are also commonly used to augment the dural graft in an effort to obtain a watertight closure.10 A large range of complications has been reported in the literature following surgery for CM-I. Most published series have a postoperative complication rate between 3% and 40% consisting primarily of aseptic meningitis, pseudomeningocele, CSF leak, and wound infections.2,8,9,13,19,22,30,32
In 2007, the dural graft substitute commonly used by the pediatric neurosurgeons at our institution was changed due to the removal of EnDura No-React Dural Substitute (Shellhigh, Inc., Integra LifeSciences) from the market. Subsequent to the product removal, our postoperative complication rate appeared to increase dramatically. We hypothesized that the complication rate following surgery for CM-I was contingent upon the choice of expansile duraplasty material and the graft sealant used. To evaluate our hypothesis, we retrospectively reviewed 4 years of records from consecutive pediatric patients who underwent primary surgical decompression for CM-I, investigating operative technique and postoperative complications.

Surgical Technique

All patients were treated by 1 of 3 established pediatric neurosurgeons (H.F., T.G., and G.G.) at our institution using a standardized operative technique. All 3 surgeons applied the same surgical approach and technique to patients with CM-I. All patients were placed prone. A suboccipital decompression and C-1 laminectomy were performed. The craniectomy extended from the foramen magnum to the inferior nuchal line, taking care to provide adequate decompression of the rim of the foramen. The size of the suboccipital decompression typically measured 3 cm × 3 cm in width and height. The dura mater was opened in all cases in a Y-shaped fashion prior to the expansile duraplasty. Intradural arachnoid adhesions were sharply dissected and the pial surface of the tonsils was coagulated to restore normal CSF flow. Dural closure was accomplished with a 6-0 Prolene suture using an expansile triangular graft of cadaveric pericardium (LifeNet Health), EnDura, or Durepair Dura Regeneration Matrix (TEI Biosciences, Medtronic Neurosurgery). EnDura was used in all cases except 7 prior to its removal from the market. In the 7 cases in which EnDura was not used prior to its removal from the market, it was not in stock in the hospital, thus necessitating use of an alternative graft product. Once EnDura was removed from the market, cadaveric pericardium and Durepair were used in an approximate 1:1 ratio. The application of a tissue sealant—Tisseel (Baxter Healthcare) or DuraSeal (Covidien, Inc.)—was used on a case-by-case basis, with the overwhelming majority of grafts augmented with a tissue sealant.

Follow-Up and Complications

The patients returned routinely for postoperative visits at 2 weeks, 8 weeks, and 1 year. All patients underwent MR imaging of the brain and a cine CSF flow study was performed to evaluate the craniocervical junction at the 8-week visit. For this study, a postoperative complication was defined as any symptomatic patient who returned to the emergency department or pediatric neurosurgery clinic for medical attention. Possible complications included aseptic meningitis, a pseudomeningocele, or CSF leak. Aseptic meningitis was diagnosed most often following CSF obtained through a lumbar puncture that showed an elevated opening pressure (> 20 cm H2O), mononuclear pleocytosis, elevated protein, and a negative gram stain and culture. Two patients arrived with severe frontal headaches and neck stiffness without fever, and began treatment with steroid tapers without a spinal tap for presumed aseptic meningitis; these 2 patients improved.

Statistical Analysis

We evaluated the overall responder characteristics focusing on postoperative complications as our outcome variable of interest. Bivariate analysis of postoperative complications and dural graft/dural sealant was performed using the Pearson chi-square test. Bivariate analysis of the need for reoperation with graft type was also performed using the Pearson chi-square test. All analyses were performed using the statistical software StataIC version 10 (StataCorp LP).

Results

Patient Population

Our retrospective review of postoperative complications in patients ≤ 18 years of age after decompression for CM-I showed an average patient age of 8.6 ± 5.3 years. The dural graft used was variable: 13.2% (15 of 114) received cadaveric pericardium, 10.5% (12 of 114) Durepair, and 76.3% (87 of 114) EnDura. The tissue sealant Tisseel was used in 65.8% of patients, DuraSeal in 10.5%, and no tissue sealant in 23.7% (Table 1).

Complication Outcome

The overall complication rate was 21.1%. Results from our bivariate analyses showed complication rates for the

<p>| TABLE 1: Characteristics of the 114 children who underwent decompression surgery for CM-I |</p>
<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>age (yrs)</td>
<td>8.6 ± 5.3</td>
</tr>
<tr>
<td>graft</td>
<td></td>
</tr>
<tr>
<td>EnDura</td>
<td>76.3%</td>
</tr>
<tr>
<td>Durepair</td>
<td>10.5%</td>
</tr>
<tr>
<td>cadaveric pericardium</td>
<td>13.2%</td>
</tr>
<tr>
<td>tissue sealant</td>
<td></td>
</tr>
<tr>
<td>Tisseel</td>
<td>65.8%</td>
</tr>
<tr>
<td>DuraSeal</td>
<td>10.5%</td>
</tr>
<tr>
<td>none</td>
<td>23.7%</td>
</tr>
<tr>
<td>complication postop day</td>
<td>25.5 ± 18.1</td>
</tr>
</tbody>
</table>

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graft products to be 26.7% for cadaveric pericardium, 41.7% for Durepair, and 17.2% for EnDura (p = 0.128). Reoperation rates were 13%, 25%, and 8.1%, respectively. There were no infections reported in this cohort. The most common complications encountered for the graft products were aseptic meningitis (EnDura 5.7%, Durepair 41.7%, cadaveric pericardium 20%), symptomatic pseudomeningoele (EnDura 8%, Durepair 33.3%, cadaveric pericardium 13.3%), and CSF leak (EnDura 3.4%, Durepair 8.3%, cadaveric pericardium 13%). The complication rates for tissue sealants were 14.8% for no sealant, 18.7% for Tisseel, and 50% for DuraSeal (p < 0.05). The highest complication percentage for the combination group of graft and sealant in which there was more than 1 patient was 55.6% (p = 0.081), with the combination of DuraSeal and Durepair used in 9 patients (Table 2). No patients received the combination of EnDura and DuraSeal because DuraSeal was not available at our institution until after EnDura was removed from the market. However, when DuraSeal was used with either cadaveric pericardium or Durepair there was a 33.3% reoperation rate (p = 0.361; Table 3). Of interest, prior to the institutional switch from EnDura, the complication rate was 18.1% but this rate increased to 35% following the adoption of a different graft and sealant product (Table 4). All patients in the Durepair group that required reoperation secondary to chemical meningitis and elevated lumbar pressures, which did not resolve with a course of steroids, had their grafts replaced with autologous pericranium without further complications.

Timing of Postoperative Complications

Patients on average presented with postoperative complications on postoperative Day 25 (range 3–63; Table 1). Although the majority of the complications occurred within the first 21 days of surgery, there were outliers that were unexpected up to 2 months following the initial procedure. In the patients who underwent reoperation, there were no postoperative complications reported.

Discussion

In choosing a dural graft for duraplasty, “the ideal material would be available in abundance, relatively inexpensive, easy to handle, non-immunogenic, and biodegradable.” Historically, many different dural substitutes have been used for the expansile graft including bovine grafts, human cadaveric pericardium, synthetic dura, and autologous pericranium. All of these various substitutes have been shown to be potentially effective for dural grafting.3,7,8,26,36 Xenogeneic collagen-based dural graft substitutes have become increasingly popular and are typically composed of animal collagens processed to remove cellular and other immunogenic components (for example, Durepair).12 The materials used for duraplasty at our institution during the review included EnDura, Durepair, cadaveric pericardium, and autologous pericranium. No new surgical techniques were required to be learned to appropriately use the graft products, thus reducing the possibility of a lead-in learning bias. There were also 2 dural sealants used in this study, Tisseel and DuraSeal.

EnDura

EnDura is a glutaraldehyde cross-linked bovine pericardium.21 According to the product information provided at the time on EnDura, “glutaraldehyde treated tissue may deteriorate, cause inflammatory reaction, adhesions, and calcification mineralization.”21 Because of the possibility of inflammatory reaction the graft product was washed vigorously in sterile saline for at least 2 minutes prior to implantation. This dural substitute is detoxified, which is intended to prevent glutaraldehyde leaching. However, if the washing procedure was not conducted according to the instructions and leaching occurred, there is a possibility that glutaraldehyde-treated tissue could cause a local inflammatory reaction and increase postoperative complications.

<table>
<thead>
<tr>
<th>Type of Graft</th>
<th>Complication Rate</th>
<th>Total No. of Grafts</th>
<th>Total Complications</th>
<th>Complications/Total Grafts (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>EnDura</td>
<td></td>
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<tr>
<td>Durepair</td>
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<tr>
<td>cadaveric pericardium</td>
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* p = 0.081, Pearson chi-square test.
Durepair

Durepair is a collagenous implant derived from fetal bovine dermis and is processed to remove all cellular components but is not modified with cross-linking chemicals. Durepair is composed of an array of collagen fibers that form a porous matrix into which host cells and supporting blood vessels can penetrate. According to the manufacturer:

...animal study results suggest that the foreign body response associated with the use of sealants and hemostatic agents in conjunction with Durepair may be more pronounced than use of Durepair alone. This response may increase the incident rates of known risks of dural substitutes, particularly in high pressure gradient applications. If intending to use ancillary products with Durepair, ensure the products are applied in accordance with their instructions for use.16

Cadaveric Pericardium

Cadaveric pericardium is an allograft product made from human cadaveric pericardium and subsequently freeze dried. Cadaveric pericardium contains the risk of a potential immunogenic reaction or transmission of disease. Historically, the concern for infectious disease transmission was much higher as even Creutzfeldt-Jacob disease has been reported following implantation of allograft cadaveric dural substitutes.4

Autologous Pericranium

Autologous pericranium was used in our series only as a dural graft substitute at the time of the second procedure. This was a personal preference of the authors due to the increased surgical exposure required to obtain an adequate amount of pericranium in a child.

Tisseel

Tisseel, a human fibrin sealant, contains fibrinogen as the main active ingredient and also contains thrombin (derived from pooled human plasma), calcium chloride, and fibrinolysis activator (aprotinin). Although Tisseel is not approved for use in neurosurgery, it has been widely adopted for off-label use. According to the manufacturer's insert, contraindications include avoiding injection into the circulatory system, not using with hypersensitivity to aprotinin, and avoidance of use with brisk arterial bleeding. Because Tisseel contains pooled human plasma, there are potential risks for viral transmission.

DuraSeal

DuraSeal is 100% synthetic and consists of 2 dilute aqueous precursor liquids that cross-link within 1–2 seconds of spraying to form a hydrogel network. This sealant has the potential to absorb fluid and swell following application. The hydrogel matrix then breaks down by hydrolysable linkages in the polyethylene glycol matrix and is absorbed within 4–8 weeks. According to the manufacturer's insert, contraindications to its use include a history of allergy, penetration of an air sinus, renal/hepatic/immune dysfunction, head trauma, and infection. It is also to be avoided in cases of hydrocephalus, and those involving a ventricular drain or lumbar drain. DuraSeal is FDA-approved for use in cranial and spinal surgery, and has been evaluated in several animal-based and clinical studies, but was associated with quadriplegia and cauda equina syndrome in 2 patients.

Characterization of Postoperative Complications With Combined Dural Graft and Sealant

A retrospective review25 of a single-institution experience with DuraSeal sealant in combination with nonautologous duraplasty materials revealed 44 cases in which DuraSeal was combined with a collagen matrix allograft, and 10 cases in combination with bovine pericardium. Overall, in 154 cases, there were 13 cases of CSF leak (8.4%), 6 cases of pseudomeningocele (3.9%), and 5 surgical infections (3.2%). There were 5 cases of CSF leak (11.4%), 3 pseudomeningoceles (6.8%), and 1 infection (0.6%) in the collagen matrix subgroup, and there was 1 CSF leak (10%), 1 pseudomeningocele (10%), and no infections in the bovine pericardium group. In a multidisciplinary historical cohort study, a retrospective review was performed of 66 patients (> 15 years of age) who underwent cranial operations that were closed using DuraSeal with nonautologous duraplasty and compared with 50 patients who were enrolled in the DuraSeal Pivotal Trial treated with autologous material. The complications from both groups were similar within 90 days of surgery, although there were very few patients with Chiari malformations in this adult series. The incidence of postoperative CSF leakage was 7.6% in the study group (retrospective population) and 6.0% in the Pivotal Trial population. The incidence of meningitis was 0% and 4.0% in the retrospective and Pivotal Trial groups, respectively.

In our retrospective review of postoperative complications in 114 consecutive patients ≤ 18 years old undergoing surgical decompression for CM-I, we found that the complication rate may be dependent on the dural graft with or without the addition of tissue sealant used. Because of the relatively few number of patients in some of the combination groups of graft/sealant, it was difficult for any of our analyses to reach a significance level of p < 0.05; although even with such small group sizes, there are trends toward significance that should be investigated further.

The results from this series suggest that the association of a higher complication rate for the combination of Durepair and DuraSeal, although not statistically significant, might be clinically significant. The reasons behind this are unclear. Foy et al.12 reported a severe allergic reaction to Durepair in the lumbar spine associated with a positive antigen skin test, along with eosinophilic and chronic lymphocytic graft infiltration. This inflammation resolved after removal of the graft. Following this report, one of the patients in the current series developed a severe postoperative aseptic meningitis and symptomatic pseudomeningocele. His lumbar puncture revealed spinal pressures that were markedly elevated (> 50 cm H2O), and CSF analysis revealed a profound lymphocytosis. Pathology showed nongranulomatous inflammation (Fig. 1), but without eosinophilic graft infiltration. The initial Chiari malformation repair in this patient was made using a Durepair graft augmented with DuraSeal. This patient had a
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A negative antigen skin test to Durepair placed on the skin. A complete reversal of the elevated lumbar pressures and chemical meningitis occurred rapidly with the replacement of the dural graft with autologous pericranium.

Other series of duraplasties for CM-I report CSF leak rates of 0%–12%. Among 74 combined patients from 3 different series undergoing duraplasty with xenogeneic pericardium, 1 patient developed a CSF leak and no patients developed a pseudomeningocele or required reoperation. Fischer and Vanaclocha and Saiz-Sapena combined reported no pseudomeningocele or CSF leak in 32 patients who underwent a duraplasty with pericranial autograft. In another study by Danish et al., 56 patients underwent a duraplasty with a suturable synthetic collagen graft (DuraGen) and 5 patients developed a pseudomeningocele, 1 patient developed a CSF leak, and 4 required reoperation. In the same series, 45 patients underwent a duraplasty with acellular human dermis, 5 developed a pseudomeningocele, and 1 had a CSF leak. Finally, Attenello et al. reported on 77 patients who underwent a duraplasty with pericranial autograft (40 patients) or polytetrafluoroethylene graft (27 patients). No patient in either group developed a CSF leak or symptomatic pseudomeningocele. In the current series, however, there was a 21.1% overall complication rate, which included symptomatic pseudomeningocele and CSF leak.

Time Course of Postoperative Complications

It was also of interest to evaluate the time course of postoperative complication presentation. In comparing the various dural graft products and tissue sealants, those patients who received Durepair and DuraSeal did not present until after postoperative Day 16 (Fig. 2). It is difficult to evaluate whether this relates to Durepair alone, DuraSeal alone, or the combination, because our series had only 3 patients who received Durepair but not DuraSeal, and only 3 patients who received DuraSeal but not Durepair. Biocompatible hydrogels such as polyethylene glycol hydrogel in DuraSeal do not typically allow cells to migrate through, which may actually delay postsurgical inflammation and healing. This delay in cell migration may explain why the CSF leaks presented much later in the patients who underwent closure using Durepair and DuraSeal.

On February 2, 2009, Medtronic issued a recall of Durepair in Canada, stating that “preliminary data suggests that the foreign body reaction of concomitant use of some ancillary products with Durepair is more pronounced than Durepair alone and may increase rates of other known risks.” While evaluating the use of tissue sealants, we were surprised that the lowest complication rate occurred when no tissue sealant was used (14.8%) compared with DuraSeal (50%) or Tisseel (18.7%). Although the majority of patients in our series underwent graft augmentation using a tissue sealant, it is unclear as to why a sealant was not used in those cases involving no sealant. It is possible the surgeon believed an excellent watertight primary closure was obtained in those cases, and thus, no sealant augmentation was warranted. This result questions the need and efficacy of using tissue sealants to augment a watertight closure. It appears that a good primary dural closure is just as effective and may have less morbidity than the addition of a tissue sealant. At the current time, pediatric neurosurgeons at our institution have switched to using cadaveric or autologous pericranium with Tisseel, and the complication rate dropped to 5% in the next 40 consecutive decompressions of CM-I, which is comparable to the historical rate.

Conclusions

Complication rates from decompression of CM-I in children may be dependent on the dural graft with or without the addition of tissue sealant. Our complication rate approximately doubled following the adoption of a different graft product. The use of tissue sealants to aug-

![Fig. 1. Photomicrograph of the junction of synthetic dura graft (upper) and native dura (lower) showing moderate chronic nongranulomatous inflammation. H & E. original magnification × 20.](image)

![Fig. 2. Bar graphs of postoperative complications for graft type (upper) and sealant type (lower).](image)
ment duraplasty may not provide any additional benefit. A complete reversal of the chemical meningitis can occur with replacement of the dural graft, although the source of the increased inflammation and complication rate, graft versus sealant, or combination of the two, remains under investigation.

Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author contributions to the study and manuscript preparation include the following. Conception and design: Parker. Acquisition of data: Parker, Cotton, Cummings, George, Fuchs. Analysis and interpretation of data: Parker. Drafting the article: Parker. Critically revising the article: Grant. Reviewed submitted version of manuscript: all authors. Statistical analysis: Parker. Administrative/technical/material support: Cummings. Study supervision: Grant.

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This work was presented in part as proceedings at the CNS Annual Meeting, Orlando, Florida, September 2008, and the American Society of Pediatric Neurosurgeons Annual Meeting, Hawaii, January 2009.

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