Revascularization of AlloDerm Used during Endoscopic Skull Base Surgery

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Abstract

Keywords

- AlloDerm
- skull base surgery
- skull base reconstruction
- acellular dermal matrix
- revascularization

Objectives AlloDerm is an acellular dermal matrix often used for reconstruction throughout the body. AlloDerm has been shown to undergo revascularization when used to reconstruct soft tissue such as in abdominal wall reconstruction. In this study, the authors review the literature on revascularization of AlloDerm and demonstrate the histologic findings of AlloDerm after implantation during skull base reconstruction.

Study Design Literature review and case reports.

Setting Tertiary Care Institution

Participants Patients from a tertiary care institution

Main Outcome Measures Histologic slides are evaluated and compared with non-implanted AlloDerm.

Methods The authors review a case of explanted AlloDerm that had been used for skull base reconstruction after endoscopic skull base surgery.

Results Upon reviewing the histologic slides of explanted AlloDerm to nonimplanted AlloDerm, we demonstrate revascularization of AlloDerm when used in skull base reconstruction. Representative slides will be included.

Conclusions AlloDerm undergoes revascularization when used for skull base reconstruction.

Introduction

Acellularized human dermal matrices such as AlloDerm (Lifecell, Branchburg, New Jersey, United States) are becoming more prevalent for use in medical applications. A graft made of human acellular dermal matrix components can provide a scaffold for wound healing that is durable, flexible, and integrates well into surrounding tissues. Used first in the treatment of burn wounds, AlloDerm has been found to have utility in periodontal surgeries, dural replacements in neurosurgery, and abdominal, breast, and head and neck reconstruction surgeries, among other uses.^{1–4}

AlloDerm is an acellular dermal matrix made of collagen, elastin, and laminin that is fabricated from human cadaver skin. During production, a high ionic strength solution

separates the epidermis from the dermis, and sodium deoxycholate is used to remove dermal cells. These steps have also been shown to reduce major histocompatibility class I and II molecules reducing the likelihood of immune rejection.⁵ The final product is freeze dried and, ultimately, rehydrated in the operating room before application.

While multiple studies have examined the revascularization of AlloDerm in animal models, there has not been much exploration into revascularization in human applications. Scarano et al assessed acellular matrix integration in gingival augmentation, and observed revascularization within 2 weeks and complete graft substitution within 10 weeks.⁶ This study aims to histologically assess the revascularization of AlloDerm when used for skull base reconstruction in endoscopic skull base surgery in humans.

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Methods

This was a retrospective review of two cases at our institution in which AlloDerm was placed during an initial surgery and explanted at a later procedure. Histologic studies were done on the explanted AlloDerm by a senior pathologist at our institution to determine whether revascularization occurred in the specimens. The explanted AlloDerm was directly compared with nonimplanted AlloDerm. Given the retrospective nature of this study, Institutional Review Board approval was not required.

The first case is a 33-year-old woman who initially presented with galactorrhea to an outside institution in February 2016. A magnetic resonance image (MRI) brain revealed a 2.5 cm sellar mass impinging on the optic chiasm and involving the carotid arteries bilaterally. She was placed on bromocriptine for suspected prolactinoma and referred to our institution for surgical evaluation. On March 6, 2016, she underwent an uncomplicated transsphenoidal hypophysectomy (TSH). During follow-up as an outpatient, her 1-year postoperative MRI revealed significant recurrence, and patient was suffering from headaches and worsening vision. In February 2017, she underwent revision TSH. Part of the AlloDerm that was used for the initial skull base reconstruction was explanted and sent for pathologic evaluation. Intraoperatively, the AlloDerm was grossly incorporated into the surrounding dura and adherent to the surrounding bony defect.

The second is a case of a 56-year-old male with a known history of craniopharyngioma status post initial resection in May 2016 at an outside institution who presented to our institution ~18 months later due to a syncopal episode and decreased visual acuity. On MRI, he was found to have a large cystic craniopharyngioma. He subsequently underwent ventriculoperitoneal shunt as well as endoscopic resection of the compressive suprasellar cyst. During the procedure, the AlloDerm from his first procedure was explanted and sent to pathology for evaluation. The AlloDerm was noted to be well-incorporated with the surrounding dura and adherent to the surrounding bone.

Results

Upon reviewing the pathologic slides of explanted AlloDerm and nonimplanted AlloDerm, it is evident that AlloDerm undergoes revascularization when used for skull base reconstruction. Explanted AlloDerm from patient 1 (►Fig. 1) demonstrates clear revascularization. The time between its initial use and explantation was 11 months. The specimen had newly formed vascular channels, hemosiderin as well as spindle cells within the AlloDerm matrix, indicating the formation of new vessels within the AlloDerm.

Similarly, the AlloDerm from patient 2 also clearly demonstrates the ingrowth of new vessels (►Fig. 2). This AlloDerm was explanted after 17 months. We see newly formed vascular channels and a mixed cellular infiltrate within the AlloDerm. This specimen was also stained for CD34 with immunoperoxidase, which highlights the newly formed vascular channels.

Fig. 1 The image showing newly formed vascular channels (arrows) within the AlloDerm. Rare hemosiderin-laden macrophages are also present (arrowheads). In addition, spindle cells consistent with organization are noted (stars) (hematoxylin and eosin stain, x200).

We compare these two specimens with nonimplanted AlloDerm (►Fig. 3), which demonstrates an acellular and avascular collagen architecture.

Discussion

In this article, we investigate the characteristics of AlloDerm used for skull base reconstruction during endoscopic skull base surgery that was subsequently explanted during revision surgery.

Desired qualities of a dermal replacement are strength, revascularization, and integration into host tissues. Early revascularization is especially important in preventing infection, a complication which could necessitate removal of the graft. Prosthetics, while widely used, are not well integrated into native tissue and have a high risk of infection. Autologous fascial grafts are another option that perform well as tissue replacements, and have been shown to become well vascularized and integrated.⁷ However, autologous donor tissue is limited, and extraction can cause donor site morbidity, including scar, hematoma, seroma, or wound dehiscence.⁸ AlloDerm provides tissue that performs similar to previously used materials and without morbidity of a harvest site.

The performance of acellular dermal matrices has been found equal to, if not better than prosthetics and autologous tissue in animal models. The grafts have been shown to perform well in wound closure with a few post-surgical complications and comparable strength to prosthetics.^{9–11} They have also been found to perform as well as autologous tissue in maintaining volume and minimizing fibrosis which is important in assessing overall wound healing and aesthetic outcome, especially in applications involving the head and neck.⁵

Histological analysis of acellular dermal matrix confirms its rapid revascularization and reintegration into animal host tissue, and suggests that its integration parallels normal wound healing.¹² An initial inflammatory phase is characterized by a cellular infiltrate composed of mostly

Fig. 2 (A, C) The image showing newly formed vascular channels (arrows) and a mixed cellular infiltrate (stars) within the AlloDerm. (B, D) CD34 immunostains highlight the newly formed vascular channels (immunoperoxidase, B X50; D X200).

macrophages and histiocytes. A proliferative phase follows, in which the number of inflammatory cells decreases while myofibroblast and endothelial cells increase in correspondence to revascularization. Multiple studies have found almost complete revascularization after 7 days in subcutaneous models,^{5,9,11–13} but longer in less vascularized tissues such as breast reconstruction models and tracheal scaffolds.^{10,14} Eppley found that subcutaneous revascularization occurred from both surfaces regardless of the orientation of the graft's original basement membrane and that revascularization takes longer to complete when multilayered grafts are used.¹⁵ Lymphatic channels also form once a mature vascular network is established.¹² Later, the graft undergoes

tissue and collagen remodeling. Within a few months, grafts resemble original tissue grossly and histologically and have minimal adhesions and stretching.^{5,9} Wei et al showed that the allograft itself does not have the capability to direct cytodifferentiation, and remodeling is dependent on surrounding tissue types.¹⁶

In terms of infection rates, AlloDerm is only considered aseptic and not sterile. Infection rates in acellular dermal matrices have been studied extensively in breast reconstruction cases where rates range from 0 to 14%, with an increased likelihood in patients that smoked or underwent additional radiation therapy. Infection rates in cases using acellular matrices trended higher than in those that did not; however,

Fig. 3 The image showing nonimplanted acellular AlloDerm.

none of the studies found these differences statistically significant.^{17–24} Maintenance of AlloDerm viability and formation of granulation tissue was seen even if the site was infected after incorporation of the AlloDerm into the host tissue. This suggests that the revascularization process is adequate to eliminate the bacterial load.¹⁹ Awad et al studied AlloDerm complications when used in contaminated sites. They found a 24% infection rate when AlloDerm was used for abdominal wall closure in the context of intra-abdominal sepsis or necrotizing fasciitis. The cultured organism always originated from the organism present in the infected abdomen at the time of surgery, showing that AlloDerm is susceptible to infection at its placement site.²⁵

Of note, Nahabedian describes an occasional erythematous reaction that occurs overlying the AlloDerm that is self-limiting and refractory to antibiotics. This reaction is not thought to be infectious, but rather an inflammatory response to the AlloDerm preservatives. This reaction can be minimized by washing the matrix twice in a saline bath before application.¹⁹

Chaplin et al⁵ used Xenoderm, an acellular dermal graft made from Yucatan minipigs to perform dural repairs on Yucatan minipigs to represent a true allograft in this species. In their study, they found that the acellular allograft was an ideal dural replacement and therefore postulated that AlloDerm is similarly ideal for dural repairs. This is due to several characteristics of the acellular dermis, including revascularization of the graft and low infection rates.

AlloDerm is now widely used for endoscopic skull base reconstruction. It is unclear how early AlloDerm becomes revascularized when used for this purpose as this study evaluated AlloDerm that was explanted remotely from the initial surgery. However, in the authors experience, AlloDerm has been found to be adherent to the surrounding bone in as little as 72 hours after placement. Revascularization is likely responsible for the low infection rate when used for endoscopic skull base reconstruction, as well as its high success rate in effectively repairing the skull base and preventing postoperative cerebrospinal fluid leaks.

Conclusion

AlloDerm undergoes revascularization when used in endoscopic skull base reconstruction, similar to what has been shown in other areas of the body and in animal models. This helps to account for its effectiveness for skull base reconstruction and low infection rate.

Conflict of Interest

None.

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