Accepted Manuscript

Submission Date: 2024-03-27
Accepted Date: 2024-04-15
Accepted Manuscript online: 2024-05-06

Journal of Reconstructive Microsurgery Open

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DOI: 10.1055/a-2320-5368

Please cite this article as: Oleck N, Erdmann R, Ravindra K et al. Synchronous Abdominal Wall and Small Bowel Transplantation: Critical Insights at Four Year Follow Up. Journal of Reconstructive Microsurgery Open 2024. doi: 10.1055/a-2320-5368

Conflict of Interest: The authors declare that they have no conflict of interest.

Abstract:
This four-year follow-up of synchronous abdominal wall allotransplantation (AW-VCA) and small bowel transplantation reveals novel insights and innovations in abdominal wall VCA. The case, involving a 37-year-old male Army veteran, showcases the benefits of AW-VCA in addressing loss of abdominal domain in intestinal transplantation (ITx). The events leading to ultimate rejection of both the AW-VCA and small bowel graft at four years highlights the complex interplay between graft survival, patient compliance, and immunosuppressive management. Notably, a significant discordance between AW-VCA and ITx rejection patterns was identified, questioning the reliability of skin components in AW-VCA as early indicators of ITx rejection. Furthermore, the behavior of the vascularized abdominal fascia, observed post-excision of the small bowel graft, offers new understanding of the immunologic response to fascia-only grafts. This follow-up emphasizes the complexities of graft survival, patient compliance, and immunosuppressive management, underscoring the need for ongoing research and innovation in the field.

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Synchronous Abdominal Wall and Small Bowel Transplantation: Critical Insights at Four Year Follow Up

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Financial Disclosure Statement: No funding was provided for this study from any individuals or organizations. Dr. Oleck, Mr. Erdmann, Dr. Ravindra, Dr. Sudan, Dr. Phillps, Dr. Mithani, Dr. Erdmann, and Dr. Atia have no personal or financial relationship that could potentially or inappropriately influence (bias) the work or conclusions of this article

This work has been presented in parts at the American Society of Reconstructive Microsurgery (ASRM) annual meeting, Nassau, Bahamas January 12-16, 2024

SUMMARY

This four-year follow-up of synchronous abdominal wall allotransplantation (AW-VCA) and small bowel transplantation reveals novel insights and innovations in abdominal wall VCA. The case, involving a 37-year-old male Army veteran, showcases the benefits of AW-VCA in addressing loss of abdominal domain in intestinal transplantation (ITx). The events leading to ultimate rejection of both the AW-VCA and small bowel graft at four years highlights the complex interplay between graft survival, patient compliance, and

immunosuppressive management. Notably, a significant discordance between AW-VCA and ITx rejection patterns was identified, questioning the reliability of skin components in AW-VCA as early indicators of ITx rejection. Furthermore, the behavior of the vascularized abdominal fascia, observed post-excision of the small bowel graft, offers new understanding of the immunologic response to fascia-only grafts. This follow-up emphasizes the complexities of graft survival, patient compliance, and immunosuppressive management, underscoring the need for ongoing research and innovation in the field.

INTRODUCTION

Abdominal wall vascular composite allotransplantation (AW-VCA) represents the highest rung on the reconstructive ladder for complex abdominal wall reconstruction. AW-VCA is performed in conjunction with intestinal transplantation (ITx) where abdominal closure is complicated by loss of abdominal domain, and history of fistula, ostomy, or abdominal fibrosis (1-4). Compared to alternative closure methods, AW-VCA avoids additional donor site morbidity and the use of prosthetic materials in an immunocompromised patient (4).

In 2018 we performed a synchronous abdominal wall and small bowel transplantation from the same donor and introduced a novel revascularization technique (1). A one year follow up was published in 2020 (5). In this report we detail the patient's course over the following three years, and the events ultimately leading to the loss of the graft. We share the insights gained from this experience, highlighting several critical aspects of AW-VCA not previously discussed in literature.

Case Report

A description of the patient’s pre-transplant course has been detailed in our one year follow up (5). In brief, the patient is a 37-year-old male Army veteran with a complex abdominal surgical history related to perforated appendicitis in early childhood. He ultimately

developed short bowel syndrome and recurrent small bowel enterocutaneous fistulae. His care was transferred to Duke University Hospital (DUH) in 2014. After several unsuccessful attempts at fistula takedown and abdominal wall reconstruction, the patient was enrolled under an IRB-approved protocol for abdominal wall transplantation in conjunction with a small bowel transplantation which was performed on October 12, 2018. A novel revascularization technique was performed with an arteriovenous loop created using the saphenous vein and common femoral artery, bilaterally (1). Throughout the one-year postoperative period the patient experienced four discrete episodes of abdominal wall rejection that required admission and treatment. During this time only one questionable episode of mild intestinal rejection was identified.

Between May 2019 and November 2020, the patient did not experience any episodes of rejection requiring additional immunosuppression. He continued with standard immunosuppression including tacrolimus (goal trough 12-15 ng/dl), mycophenolate mofetil 1000 mg BID, and prednisone 20 mg daily. In December of 2020 the patient developed an episode of Banff III rejection of the AW-VCA after a period of noncompliance with immunosuppression. This was managed as an inpatient with high dose steroids with significant resolution to Banff I on biopsy one month later. During this time initial small bowel biopsy demonstrated mild acute cellular rejection. This improved rapidly with no clear evidence of rejection several days later on follow up biopsy. The patient experienced two similar AW-VCA rejection episodes over the following two years managed with topical Clobetasol and high dose IV steroids. Again, small bowel biopsies were deemed “mild” or “indeterminate for acute cellular rejection” and no additional treatment was indicated. These findings are displayed graphically in Figures 1 and 2.

The patient presented to DUH in January of 2023 after a several month period of inconsistent follow up. He complained of persistent abdominal pain and 30lb weight loss, and imaging revealed a partial small bowel obstruction. AW-VCA biopsy at this time demonstrated findings consistent with chronic rejection. Small bowel biopsy demonstrated mild acute cellular rejection and high dose steroids were initiated. Over the following month,

the small bowel graft demonstrated poor function with persistent obstructive symptoms and minimal contrast transit on imaging. Ultimately in February of 2023, small bowel biopsy demonstrated evidence of chronic rejection and the decision was made to proceed with graft excision.

On 2/16/23 the small bowel graft was excised, a gastrostomy was performed, and the patient was left in discontinuity. Approximately 50% of the AW-VCA was excised at this time. The skin and subcutaneous tissue of the remaining AW-VCA was removed, but healthy appearing graft fascia was left in situ and repaired to native fascia without tension. Post-operatively the patient's immunosuppression regimen was adjusted with discontinuation of mycophenolate and gradual taper of prednisone. Single agent therapy with tacrolimus was continued with a new goal of 4-6 ng/ml. During his postoperative course the fascia of the remaining AW-VCA developed progressive superficial fibrinous debris which was managed with bedside debridement. After several readmissions for dehydration and acute kidney injury, the decision was made to discontinue all immunosuppression. Over the next three months the patient developed degradation of his abdominal wound, ultimately resulting in full thickness wound breakdown at the interface between the graft and native abdominal fascia. The AW-VCA was excised in its entirety on 8/3/2023 - four years, nine months, and twenty-two days after initial transplantation. The native fascia was able to be partially closed primarily and the remainder of the defect was bridged with a biologic mesh.

DISCUSSION

This case details our experience with synchronous AW-VCA and ITx and the events leading to chronic rejection and graft excision. The ITx graft survival of four years and four months aligns with the 2023 Intestinal Transplant Registry 5-year graft survival rate of 44% (6). The incidence of ITx rejection must be taken into consideration when planning synchronous abdominal wall reconstruction. In our opinion, AW-VCA should be strongly considered in these cases as it avoids donor site morbidity associated with free tissue transfer and prosthetic materials used in tissue expansion and mesh repair.

Discordance between AW-VCA and ITx Rejection in Surveillance Biopsies

We experienced significant discordance between the surveillance biopsy results of the AW-VCA and ITx. This was evident during the first year after transplantation and continued throughout the lifespan of the graft. Several instances of Banff Grade II-III rejection were identified in the AW-VCA without commensurate rejection of the small bowel. Three episodes of Banff III AW-VCA rejection required IV steroid therapy. Small bowel biopsy at this time demonstrated mild or indeterminate levels of rejection and did not require additional escalation of immunosuppression.

Skin is considered the most immunogenic component of a VCA, leading to a more rapid and robust immune response relative to other tissue types. (7,8). Because of this, prior literature has suggested that the skin component of a VCA may serve as a sentinel marker of rejection (9). However, in this case we found that skin and intestinal biopsies frequently did not correlate. Similarly, reports of ITx rejection not preceded by AW-VCA have been demonstrated in the literature (8,10,11). With this in mind, we believe that reliance on the skin component of an AW-VCA as a surveillance tool may be unreliable.

Immunologic rejection of Vascularized Abdominal Fascia

A unique aspect of this case was the partial preservation of the AW-VCA fascia at the time of small bowel graft resection. This allowed observation of the immunologic response to the AW-VCA graft in the absence of skin and subcutaneous tissue. Despite low dose single agent immunosuppression, the graft demonstrated slow, progressive degradation with worsening superficial fibrinous debris. Ultimately immunosuppression was discontinued, and the graft progressed to full thickness necrosis requiring complete graft excision. This demonstrates that vascularized fascia is robustly rejected in the absence of immunosuppression.

Fascia is generally considered poorly immunogenic (12), and preservation of vascularized fascia through the falciform ligament has been demonstrated in multivisceral transplantation

without alterations in immunosuppression (12,13). However, in these cases a separate microvascular anastomosis is not performed, and the vascularized fascia cannot be assessed independent of the visceral graft. Our case provides a unique insight into the behavior of a vascularized fascia-only graft which has not been previously reported in the literature.

CONCLUSION

In this report, we present a four-year follow-up of a patient who underwent synchronous AW-VCA and ITx, culminating in graft excision due to chronic rejection. Our findings highlight a distinct discordance between AW-VCA and ITx rejection patterns, offer new insights into the immunologic response to vascularized abdominal fascia, and underscore the importance of ongoing investigation in this field.

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Figure 1. ITx biopsy results from one-year post-transplant to final biopsy prior to graft excision. Severity of rejection (none, mild, moderate, severe, chronic) was graded by pathologic analysis.

Figure 2. AW-VCA biopsy results from one-year post-transplant to final biopsy prior to graft excision. Severity of rejection was graded by pathologic analysis according to the Banff Classification (14).

Figure 3. Abdominal wall VCA (AW-VCA) appearance at the time of small bowel graft excision. Before bowel graft excision (left). After bowel graft excision, half of abdominal wall

graft has been excised in a full thickness manner (middle). After removal of skin and subcutaneous tissue of the remaining AW-VCA, with preservation of ~50% of the graft fascia (right).

Figure 4. Postoperative course following small bowel graft excision with gradual tapering of immunosuppression. AW-VCA eleven days after graft excision, tacrolimus and prednisone (left). AW-VCA ten weeks after bowel graft excision, tacrolimus only (middle). AW-VCA three months after bowel graft excision, immunosuppression discontinued (right).

Figure 5. Clinical appearance of the abdominal wall at the time of AW-VCA excision demonstrating full thickness necrosis (left). Mesh repair of resultant abdominal wall defect after AW-VCA excision (middle left and middle right). Three weeks after AW-VCA excision, primary skin closure (right).