Extracellular matrix graft for the surgical management of Hurley stage III hidradenitis suppurativa: a pilot case series

Objective: Surgical management of Hurley stage III hidradenitis suppurativa (HS) typically involves the excision of diseased tissue and subsequent reconstruction, potentially leading to complications or recurrence of the disease. This pilot case series sought to evaluate a decellularised ovine forestomach matrix (OFM) extracellular matrix (ECM) graft for soft tissue regeneration as part of surgical reconstruction of stage III HS of the axilla.
Method: The prospective pilot case series involved six participants and a total of eight defects. The ECM graft was used either as a dermal substitute for a staged reconstruction (n=3 defects) or as an implant under a fasciocutaneous flap (n=5 defects) following wide excision of the diseased tissue.
Results: In all cases complete healing was achieved, with no major surgical complications. When used as a dermal substitute the OFM graft was completely granulated within 2–4 weeks, with defects closing by secondary intention or following placement of a split-thickness skin graft. When used as an implant beneath a fasciocutaneous flap, healing of the surgical sites was observed after 1–3 months. At the long-term follow-up (3–12 months), all participants had excellent range of motion and none had reported disease recurrences.
Conclusion: This pilot case series explored the implementation of an ECM graft as part of the surgical management of axilla Hurley stage III HS. Although the study had a limited number of participants, long-term outcomes were promising and suggest further studies are warranted.
Declaration of interest: The graft (Myriad Soft Tissue Matrix) was provided by Aroa Biosurgery Limited (Auckland, New Zealand). AEC has received educational travel grants from Aroa Biosurgery Limited. The authors have no conflicts of interest to declare.

dermal substitute • flap reconstruction • hidradenitis suppurativa • ovine forestomach matrix

Hidradenitis suppurativa (HS) is a debilitating, chronic inflammatory disease of the dermis.[1] The causes of HS may be a combination of genetic, endocrine, environmental and microbial factors.[2] Disease progression involves follicular occlusion caused by inflammation, hyperkeratosis and hyperplasia of sweat glands, and can lead to multiple abscesses and cysts in the affected area.[2] Histological changes in HS versus normal tissue include a thickening of the epidermis, high cellular infiltration around hair follicles and disorganised collagen fibres with a decrease in collagen III.[3] Overall, systemic inflammatory markers are higher in HS than non-HS dermal diseases, such as psoriasis.[4]

Treatment of HS depends on disease severity (i.e., Hurley stage I, II and III) and includes medical treatments (for example, antibiotics, steroids and anti-inflammatories), as well as surgical interventions to remove the diseased tissue.[2] Recurrence is lower when therapeutic and surgical approaches are combined, compared with surgery alone.[5] Surgical intervention for HS depends on the severity of the disease. In mild cases, local excision or deroofing of abscesses and sinuses may be sufficient.[6] In severe cases of HS (for example, Hurley stage III) that include diffuse interconnecting tracts and abscesses across a large area, a significant surgical intervention is required, such as wide excision of the diseased tissue.[6] Following wide excision, several reconstructive approaches are possible, including primary closure, healing via secondary intention, split-thickness skin grafting, local and free flaps.[7] Recurrence rates after a wide excision appear lower than after local excision;[5] however, the extent of tissue removal means that healing time is longer and complications more likely. Bouazzi et al.[8] found that complication rates and recurrence rates remain relatively high at 25.1% and 14.0%, respectively. Ovadja et al.[9] estimated recurrence rates for wide and partial excisions at 5% and 26%, respectively, from a meta-analysis of 125 articles. Complications associated with reconstruction after wide excision may be attributed to the poor quality of the underlying tissues (for example, fibrotic or inflamed tissue), potential for dead space between the advancing flap and underlying tissues, poor vascularity of the tissues, and associated patient comorbidities.

Ovine forestomach matrix (OFM) is an extracellular matrix (ECM) bioscaffold widely used in wound management and implant procedures.[10–13] OFM has excellent biophysical performance,[14] is anti-inflammatory,[15,16] recruits mesenchymal stem cells,[17] stimulates angiogenesis,[18] aids tissue infill and undergoes complete remodelling.[18] OFM is available as a graft (Myriad Soft Tissue Matrix, Aroa Biosurgery Limited, New Zealand) designed as a dermal substitute

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for the surgical management of deep partial or full-thickness defects in plastic and reconstructive surgery and for implant procedures to reinforce soft tissues. Given OFM's anti-inflammatory properties and ability to quickly build new tissue, we hypothesised that the OFM graft may have utility as part of surgical reconstruction of HS. In this pilot case series, patients with Hurley stage III HS of the axilla were surgically reconstructed using the OFM graft, either as a dermal substitute or as an implant as part of a flap reconstruction of the affected areas.

Methods

Informed consent was obtained from all participants. All procedures were performed in accordance with the ethical standards of the respective institutions involved and the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Participants who were unwilling to follow the study protocol or unable to provide informed consent were excluded from it.

A total of six patients consented to participate in this case series (Table 1). All patients had a history of axillary HS and had previously been managed with various interventions, including standard wound care, topical antibacterials, minor surgical deroofings, laser treatments, antibiotics and anti-inflammatory therapies. Of the patients, two (Participants 2 and 6) presented with bilateral lesions that were simultaneously managed as part of the case series. None of the patients were receiving pharmacotherapies for their HS management at the time of the surgery or during the follow-up period. Reconstruction proceeded either using the OFM graft (Myriad Soft Tissue Matrix) as a dermal substitute or as part of a flap reconstruction (Table 1). When used as a dermal substitute (Participants 1 and 2), lesions were resected including the deep subcutaneous fat layer down to the fascia. OFM graft was cut to size and rehydrated, then sutured to the perimeter of the defect. Either the three-layer ('Thin') or five-layer ('Thick') OFM graft was used (Table 1). A non-adherent dressing (Adaptic, KCI Corporation, US) was placed, then negative-pressure wound therapy (NPWT) was maintained for 1–2 weeks (continuous 125mmHg). Once the OFM graft had fully granulated, the defects were managed with either a combination of ECM (Endoform Natural Dermal Template, Aroa Biosurgery Limited, New Zealand) and gentian violet/methylene blue (GV/MB) foam dressing (Hydrofera Blue, Hydrofera

Table 1. Participant summary including demographic, surgical management and outcomes

Participant, gender, age, comorbidities	HS stage III duration	Location	Surgical management	Time of last follow-up
Participant 1 Male, 29 Deep vein thrombosis (DVT)	2 years	Right axilla	• Resected down to fascia, ~12×7cm defect • ECM graft applied as a dermal substitute • Fully granulated at 4 weeks • ~80% epithelialised at 6 weeks	Minor complication at 1 week – resolved week 2 11+ months No further complications No recurrence
Participant 2 Male, 39 Uncontrolled diabetes Smoker HbA1c=12.6%	15 years	Right and left axilla	• Wide resection down to fascia, ~12×17cm (right) and ~12×20cm (left) defects • ECM graft applied as a dermal substitute • Fully granulated at 3 weeks • STSG at 22 weeks, 100% graft take at 23 weeks	7+ months No complications No recurrence
Participant 3 Female, 31	5 years	Right axilla	• Partial axillary resection, ~15x15cm defect • ECM graft placement, then fasciocutaneous flap reconstruction • Fully healed at 1 month	12+ months No complications No recurrence
Participant 4 Female, 26 HIV	5 years	Right axilla	• Entire hair-bearing axillary resection, ~10x20cm defect • ECM graft placement, then fasciocutaneous flap reconstruction • Fully healed at 3 months	Minor complication at week 3 – resolved week 6 10+ months No further complications No recurrence
Participant 5 Female, 37 Gout	10 years	Right axilla	• Entire hair-bearing axillary resection, ~15×20cm defect • ECM graft placement, then fasciocutaneous flap reconstruction • Fully healed at 3 months	7+ months No complications No recurrence
Participant 6 Female, 30 Lupus, rheumatoid arthritis	10 years	Right and left axilla	• Entire hair-bearing axillary resection, ~8×12cm defects • ECM graft placement, then fasciocutaneous flap reconstruction • Fully healed at 1 month	3+ month No complications No recurrence

ECM—extracellular matrix; HS—hidradenitis suppurativa; STSG—split-thickness skin graft

Corporation, US), or polyhexamethylene biguanide (PHMB) dressing (Bioguard, Integra Life Sciences Corporation, US). Of the patients, one (Participant 1) closed via secondary intention, while another received a split-thickness skin graft (STSG) (Participant 2). Flap reconstruction (Participants 3–6) used a wide excision of the affected tissue as well as lateral margins down to the fascia. OFM graft was cut to size, rehydrated and placed into the defect, before a fasciocutaneous flap advancement and closure. Iodoform gauze was packed between sutures, and a non-adherent dressing placed, followed by GV/MB foam and silver alginate dressings. Sutures were removed at week five. All surgical sites were monitored weekly by the investigators.

Results

Patients with Hurley stage III HS of the axilla underwent wide excision of the hair-bearing area of the axilla down to the fascia, leaving defects with sizes ranging from ~100–300cm^2 (Table 1). Where the OFM graft was used as a dermal substitute (Participants 1 and 2; n=3 sites), the OFM grafts became infiltrated and vascularised after ~1 week, and completely granulated at 2–4 weeks. Where the OFM graft was implanted under a fasciocutaneous flap (Participants 3–5), the surgical sites were healed after 1–3 months. Of the patients, one (Participant 4) experienced mild wound dehiscence at three weeks that closed with standard management. Of the six patients reported in the case series, none experienced a recurrence at the last postoperative visit at 3–12 months.

Patient 1

A 29-year-old male patient presented with two years of Hurley stage III HS of the right axilla. Full-thickness wide excision down to the fascia was performed, leaving a defect of ~12×7cm (Fig 1). The defect was reconstructed using OFM graft ('Thick', 10×20cm) as a dermal substitute to build granulation tissue in the defect and enable closure via secondary intention. The OFM graft was dressed with a non-adherent dressing and NPWT (125mmHg, continuous) used for the first 1.5 weeks, then a PHMB dressing used until closure. At day four, the OFM graft was visibly integrating as granulation tissue formed, with only the distal portion that was not contacting the underlying tissue not showing vascularity. At one week the outer layers of the graft had become contaminated and had sloughed from the remainder of the defect. These were removed via gentle debridement. The surface of the graft was lightly debrided at 1.5 weeks to reveal a well vascularised granulation bed and NPWT was discontinued. At week four the granulated defect had started to epithelialise and by week eight the defect was 80% epithelialised and the patient returned to work. There was no recurrence at the last follow-up, at 7.5 months, and the patient had good range of motion and acceptable cosmesis.

Fig 1. Reconstruction of axilla hidradenitis suppurativa using ovine forestomach matrix (OFM) graft as a dermal substitute following wide excision of the axilla (Participant 1). Initial defect site (**a**). Surgical excision of damaged tissue (~12×7cm) (**b**). OFM graft placement and fixation with staples (**c**). Day 4 post-operation, small areas of granulation tissue present (**d**). Day 10, granulation tissue apparent (**e**). Week 4 post-operation (**f**). Week 8 post-operation (**g**)

Patient 2

A 39-year-old male patient, with uncontrolled diabetes and a heavy smoker presented with bilateral HS lesions to the axilla (Fig 2). The patient underwent a wide excision down to the fascia, leaving excision sites of 17×12cm (right) and 20×12cm (left). OFM graft ('Thin') was trimmed to size, rehydrated and placed into the defect. The grafts were sutured to the perimeter of the defect and additional mattress sutures placed in the centre of the graft to tightly approximate this to the underlying tissue. The grafts were dressed with a non-adherent contact layer, then NPWT (125mmHg, continuous) used for 1.5 weeks. The grafts were 100% granulated at three weeks, but an STSG was deferred until the patient's diabetes and nicotine use were controlled. Instead, ECM wound dressing (Endoform Natural, Aroa Biosurgery Limited) was applied weekly to aid epithelialisation of the granulation tissue, covered with a GV/MB foam. At 15 weeks the right and left defects had reduced to 5.6×11cm and 3.5×11cm, respectively, and at 22 weeks STSGs were placed on the bilateral axillae, with 100% graft take at 23 weeks. Both defects were healed by week 26.

Patient 3

A 31-year-old female patient presented with five years of Hurley stage III HS of the axilla. Full-thickness excision down to the fascia was performed under general anaesthetic leaving a defect of ~15×15cm (Fig 3). OFM graft was trimmed to size, rehydrated in saline then applied to the excision site and sutured in place with absorbable sutures before fasciocutaneous

Fig 2. Bilateral reconstruction of axilla hidradenitis suppurativa using ovine forestomach matrix (OFM) graft as a dermal substitute (Participant 2). Surgical sites on the right (R) and left (L) axilla. Defect sizes were 17×12cm and 20×12cm, respectively (**a**). Surgical excision (**b**). OFM graft placement and fixation with sutures at the periphery and mattress sutures at the centre (**c**). At three weeks post-operation, 100% granulation tissue (**d**). At 15 weeks post-operation and weekly extracellular matrix (ECM) treatment, defects reduced in size to 5.6×11cm (R) and 3.5×11cm (L) (**e**). At 22 weeks post-operation, before placement of split-thickness skin graft (not shown) (**f**)

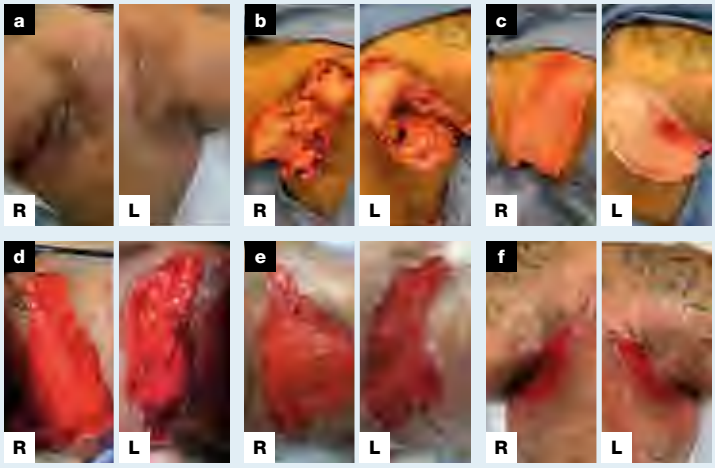
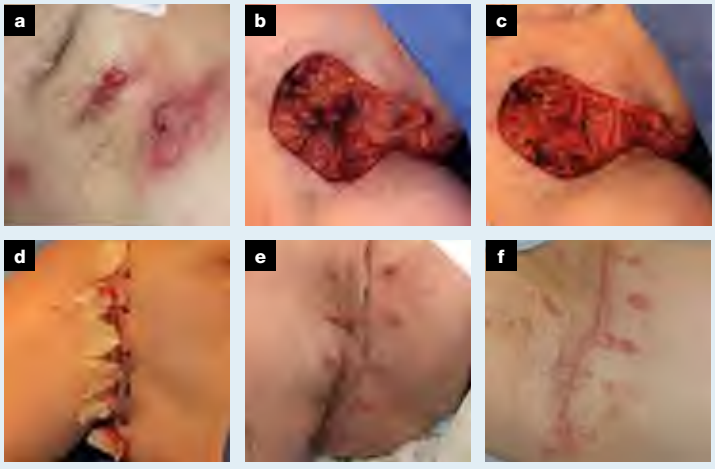


Fig 3. Fasciocutaneous flap reconstruction of axilla hidradenitis suppurativa using ovine forestomach matrix (OFM) graft as an implant device (Participant 3). HS of axilla tissue pre-operation (**a**). Partial excision of axilla tissue (~15×15cm) (**b**). OFM graft sutured to fascia underneath flap advancement (**c**). Flap advancement and closure with Iodoform packing between adjacent sutures (**d**). Week 3 post-operation, sutures removed (**e**). Week 11, wound healed (**f**)



flap advancement and closure. Iodoform was packed between adjacent sutures to enable any fluid to wick from the defect. The site was dressed with a non-adherent and GV/MB antibacterial foam dressing. Sutures were removed at week three and by week 11 the surgical site was completely healed. No complications or recurrences were noted, and the surgical site was covered with a secondary dressing. Healing of the surgical site was observed at three weeks and no complications or recurrence was noted at seven months.

Patient 4

A 26-year-old female presented with five years of Hurley stage III HS of the axilla with multiple draining and interconnected sinuses. The patient had well-controlled HIV, and had previously managed HS with topical antibiotics and laser treatments. Full-thickness excision of the affected area was performed leaving a defect of ~20×10cm (Fig 4). OFM graft ('Thick', 10×20cm) was placed in the defect and fixed in place with absorbable sutures before a fasciocutaneous flap advancement and closure. Iodoform was packed between pledgeted retention sutures and the defect covered with a non-adherent GV/MB dressing. The patient presented at week three with a wet cover dressing after trying to self-manage dressing changes, resulting in minor dehiscence of the closure and maceration. The area of dehiscence was gently debrided and granulation tissue was noted in the base of the defect. The area of dehiscence was managed with ECM and GV/MB. By week six, only a small (~2×2cm) area of dehiscence remained open and by week 12 the entire area was fully healed. The patient's axilla remains lesion free at seven months.

Discussion

This case series gave preliminary insights into the successful surgical management of Hurley stage III HS using OFM graft either as a dermal substitute or as part of a flap reconstruction. Surgical removal of diseased tissue in a Hurley stage III HS patient results in a large tissue deficit at the surgical site, leaving patients at risk of postoperative complications. Additionally, many patients with HS display comorbidities, such as obesity, metabolic syndrome and insulin resistance, which can reduce normal healing rates post-surgery.[19] Tissue within HS lesions presents many histological findings that are associated with uncontrolled inflammation, such as lymphocyte infiltration and scar tissue, including a decrease in collagen III.[3] Interestingly, circulating matrix metalloproteinases (MMPs) are increased in the blood of an HS patient and it is thought that MMPs facilitate the rupture of neighbouring follicles within lesions, leading to tunnelling and abscess formation.[20] As such, HS-affected tissues may be predisposed to poor healing and present a real challenge in surgical reconstruction.

Decellularised ECM bioscaffolds, such as OFM, that are typically produced from human or animal tissues, have been shown to increase the rate of healing in hard-to-heal wounds, and it is thought that this is due to the material's ability to promote angiogenesis, control inflammation and provide a structural scaffold for remodelling.[15,16,18,21] As it relates to the pathology seen in HS, studies have shown that an important factor in ECM bioscaffold-mediated healing is the impact on chronic inflammation.[22] ECM bioscaffolds can promote constructive remodelling by changing the

phenotype of inflammatory cells, leading to an increase in the population of macrophages that display a remodelling anti-inflammatory phenotype (M2) versus a pro-inflammatory phenotype (M1).[15,23] The OFM bioscaffold has been shown to inhibit MMPs and neutrophil elastase,[16] and undergoes constructive remodelling *in vivo*, consistent with an anti-inflammatory response.[15,18,24]

Wide excision of HS-affected tissue leaves a significant full-thickness defect which, left to heal via secondary intention, may result in significant scar contracture and loss of functional status of the affected area. Dermal substitutes have been part of the reconstructive ladder for many years, although their use in HS reconstruction is limited relative to their widespread use in applications such as burns, necrotising fasciitis, trauma and wounds. Iida et al. reported a two-stage procedure using a bovine dermal substitute (Terudermis, Terumo Corporation, Japan) following wide excision of axillary HS in three patients.[25] Gonzaga et al. took a similar two-stage approach in four patients using a bi-layer dermal matrix (Integra, Integra Life Sciences Corporation, US), but included NPWT to aid regeneration of the neodermis, prior to STSG.[26] The largest case report included 18 patients (33 lesions) using a bi-layer dermal matrix (Integra) followed by STSG, though local infection was observed in 45% of patients following use of the bi-layer dermal matrix.[27] Nicoli et al. combined the use of platelet rich plasma and a hyaluronic acid dermal substitute (Hyalomatrix Fidia Advanced Biopolymers, Italy) following wide excision, leaving the defect to close via secondary intention.[28] When used as a dermal substitute, the OFM graft showed rapid granulation tissue formation (~1 week), and defects went on to close either via secondary intention (Participant 1) or received an STSG (Participant 2).

The OFM graft was alternatively used as an implant as part of a fasciocutaneous flap reconstruction (Participants 3–5). The option for a flap reconstruction was dependent on the availability of proximal tissues. Flap reconstructions of HS have been widely reported, but often suffer complications.[5,8,9] Flap dehiscence and associated complications may be explained by the chronicity of the underlying tissues, poor vascularity, and potential for dead space between the flap and the underlying fascial layer. It was hypothesised that placement of an ECM bioscaffold as an implant under the fasciocutaneous flap may reduce these complications as the graft would be infiltrated and remodelled to provide a deeper layer of well-vascularised new tissue. All patients managed using this approach healed well.

Fig 4. Flap reconstruction of axilla hidradenitis suppurativa (HS) using ovine forestomach matrix (OFM) graft as an implant under the fasciocutaneous flap (Participant 4). HS tissue of the axilla (**a**). Full-thickness excision of damaged tissue (~20×10cm) (**b**). OFM graft placement and fixation before flap advancement (**c**). Flap advancement and primary closure with Iodoform packed between pledgeted retention sutures (**d**). Week 1, post-operation (**e**). Week 3, minor post-operation dehiscence treated with ECM (**f**). Week 5 post-operation (**g**). Week 6, small area of dehiscence open (~2×2cm) (**h**). Week 12, entire area fully healed (**i**)

A patient (Participant 4) had dehiscence of the closure at week three, due to poor dressing management.

Conclusion

Patients with HS experience significant challenges with regard to their quality of life, such as an increased risk of cardiovascular disease and suicide, sexual dysfunction, irritable bowel syndrome, depression and anxiety.[29] Surgical intervention can risk further challenges without appropriate tools to reduce the number of complications and recurrence of lesions. Our initial findings, using the OFM graft as part of our surgical reconstruction of these affected patients, is very encouraging. A larger case study with long-term follow-up of patients treated with OFM graft would be a valuable tool to access improvements in the rate of recurrence of the disease and complications after surgical intervention with OFM. JWC

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Reflective questions

- Hidradenitis suppurativa (HS) has a significant impact on patients' quality of life and often patients with HS simply manage the symptoms associated with HS lesions. Should surgical intervention be considered more often for these patients, especially in instances of stage III HS?
- Surgical reconstruction involving inflamed tissue like that seen in HS often suffers from increased complication rates (eg infection, dehiscence or seroma). Should the inclusion of advanced ECM technology to counteract tissue inflammation be considered more often for these types of surgeries?

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