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REVIEW

Mycobacterium Ulcerans soft tissue defects: reconstructive challenges

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Abstract

Background *Mycobacterium ulcerans* (*M. ulcerans*) infection is a growing concern in Australia, with several disease hotspots in south-eastern Victoria (Guest 2016). Cases at our institution, located within one such endemic area, increasingly require reconstruction of substantial mycobacterial soft tissue deficits. This article comprises a focused literature review of flap reconstruction outcomes in significant *M. ulcerans* defects and the impact of antibiotic choice, duration of antimycobacterial therapy and time to reconstruction in this context, as well as a short case series.

Methods A keyword search of Medline, Google Scholar and PubMed was conducted. In addition, four *M. ulcerans* flap reconstructions performed at our institution had case notes retrospectively reviewed for reconstruction indication, complications, outcomes and antibiotic therapy.

Results Sixteen articles met inclusion criteria, of which 11 referenced flap reconstruction of *M. ulcerans* soft tissue defects in some manner. Antibiotic regimens, peri-operative details and flap outcomes were either only briefly mentioned or not at all and were not the focus of any of the articles. We present four cases of dorsal hand *M. ulcerans* defect, which were reconstructed with fasciocutaneous anterolateral thigh flaps due to extensive soft tissue loss with extensor tendon exposure. Antibiotic regimens varied. Each procedure was undertaken with minimal complication and excellent functional outcomes.

Conclusions This review has identified the necessity of defining optimal reconstructive pathways in *M. ulcerans* soft tissue defects. Our cases demonstrate the successful use of fasciocutaneous flaps in refractory cases needing complex reconstruction. This paper presents the first review and case series on microvascular flap reconstruction of *M. ulcerans* defects. Level of Evidence Level IV, therapeutic study.

Keywords *Mycobacterium ulcerans* · Buruli ulcer · Reconstructive surgical procedures · Perforator flap · Free tissue flaps

Introduction

Mycobacterium ulcerans (*M. ulcerans*) infection is a growing concern in coastal Victoria and Queensland, with Victoria's Mornington Peninsula being one such endemic region. At our institution, the primary catchment for this region, an increasing number of patients require treatment and reconstruction of defects caused by the destructive disease process. While a range of surgical options exists for superficial defects, extensive soft tissue deficits caused by *M. ulcerans* are uncommon, and as such, there is little in the literature describing flap reconstruction in advanced cases. The nature of *M. ulcerans* defects is such that careful consideration must be given to the optimal timing of reconstruction and antibiotic duration, both of which currently remain undefined. This paper encompasses a focused literature review of flap reconstruction outcomes in significant *M. ulcerans* defects and the impact of antibiotic choice, duration of antimycobacterial therapy and time to reconstruction in this context, as well as a short case series of four microsurgical free flap reconstructions following *M. ulcerans* infection.

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Methods

The current manuscript comprises an analysis of the current literature on flap reconstruction of soft tissue defects resulting from *M. ulcerans* infection, addressing the impact of antibiotic choice and duration and timing of reconstruction on surgical outcomes. A literature search was conducted using Medline, Google Scholar and PubMed. Search terms utilised were a combination of "*Mycobacterium ulcerans*," "Buruli," "Bairnsdale ulcer," "reconstruction," "reconstructive surgery," "plastic surgery" and "flap". We limited our search to human, English studies, published between years 1950 and 2017 and identified relevant articles through bibliographic linkage. In total, 335 articles were returned in our search, with 175 articles remaining after duplicate removal. Following full-text appraisal, 16 articles met inclusion criteria, that is, these articles discussed flap reconstruction of *M. ulcerans* defects (Fig. 1) [1]. Excluded articles did not specifically address both *M. ulcerans* defects and their flap reconstruction. Interesting or relevant publications not formally included in the review are mentioned in the discussion.

We present four cases operated on between 2015 and 2017, in a single institution (Peninsula Health, Frankston, Victoria). Patient notes were retrospectively reviewed for reconstruction indication and details, complications, outcomes and antibiotic therapy. Each patient gave consent for inclusion in this paper.

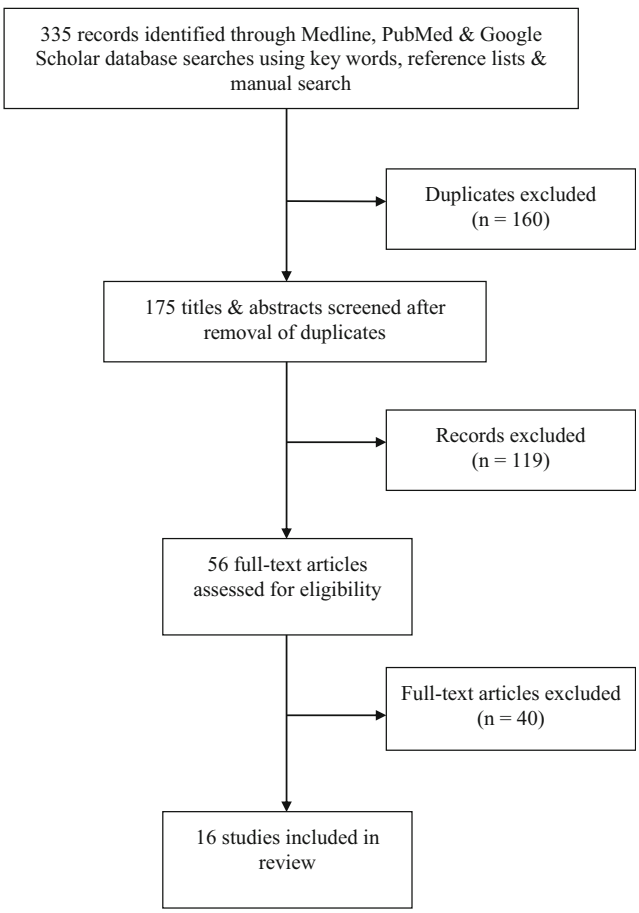

Fig. 1 PRISMA [1] attrition flow diagram

Results

Demographics

The literature review identified 16 papers mentioning flap reconstruction of soft tissue deficits following *M. ulcerans* infection (Table 1). Of these, three were case reports detailing flap reconstruction, two of which described the same case, where reconstruction was with a rectus abdominus flap [2, 3], and one paper comprised an anterolateral thigh flap reconstruction [4]. Eight papers discuss use of flap reconstruction within their cohorts without description of cases [5–12], four briefly mention flaps as a reconstructive option [5, 7, 13, 14], and one paper was unclear in its inclusion of flaps [15]. None of these papers discuss a definitive peri-operative flap reconstruction antibiotic regime, and the outcomes associated with flap reconstruction were not well-described in any article (Table 2). The papers were published between 2001 and 2017. Twelve of 16 included studies reported *M. ulcerans* in Australia, 10 in Victoria and 2 in Queensland. The remainder consisted of four African studies. There was a substantial representation of the Bellarine Peninsula (Victoria, Australia); 8 of 16 (50%) articles utilised data from Barwon Health (Geelong, Victoria, Australia), where *M. ulcerans* is also endemic [14, 16]. These studies examine overlapping datasets but focus on different facets of *M. ulcerans* disease. Notably, these authors were also the first to describe the phenomenon of paradoxical reaction in *M. ulcerans* infection, that is, the immune reconstitution inflammatory syndrome reaction following antibiotic therapy and due to *M. ulcerans* toxin mycolactone. Overall, only 11 papers describe flap reconstruction in this setting, and within these, there is no detailed discussion of peri-reconstruction antibiotic choice, duration of therapy and timing of flap reconstruction. This is the first manuscript to address this topic.

Studies discussing flap reconstruction

Generally, the studies that utilised flap reconstruction for *M. ulcerans* soft tissue defects within their cohorts did not provide great detail or focus on these cases. Agbenorku et al. [11, 12, 17] mentioned use of local transposition flaps, notably including a forehead flap to reconstruct eyelid lesions, with no detail on antibiotic therapy and only briefly commenting that there were no flap failures. O'Brien et al. and Cowan et al. noted the use of vascularised tissue flaps in six papers [5–10]. There were no specific flap timing, outcomes or peri-operative antibiotic details given; however, they reported relevant findings applicable to our research question. The group concluded that antibiotic therapy with fluoroquinolones plus rifampicin [9] in those who require major surgery (graft or flap

Table 1 Details of articles included in this review

Study (author, year)	Study type	Sample size (n)	Number of *M. ulcerans* cases requiring flaps	CEBM[a] Level of evidence	Use of flap reconstruction:			Location
					Detailed report of flap use	Flap used but not described	Flap not used or described, recommendation only	
Agbenorku et al., (2001)	Retrospective cohort	240	At least 6	3		✓		Ghana
Russell et al., (2002)	Case report	1	1	4	✓			Australia
Ramakrishnan et al., (2004)	Case report	1	1	4	✓			Australia
Chin-Lenn et al., (2006)	Case reports & guideline	4	0	4			✓	Australia
O'Brien et al., (2007)	Case series	40	9	4		✓		Australia
Agbenorku et al., (2011)	Retrospective cohort	38	Unknown	3		✓		Ghana
Simpson et al., (2012)	Review and opinion	N/A	N/A	3			✓	Australia
O'Brien et al., (2012)	Retrospective cohort	133	16	3		✓		Australia
O'Brien et al., (2013)	Retrospective cohort	156	3	3		✓		Australia
O'Brien et al., (2013)	Retrospective cohort	50	6	3		✓		Australia
O'Brien et al., (2014)	Review and guideline	N/A	N/A	3			✓	Australia
O'Brien et al., (2014)	Retrospective cohort	238	1	3		✓		Australia
Agbenorku et al., (2014)	Review	N/A	N/A	4			✓	Ghana
Cowan et al., (2015)	Retrospective cohort	207	5	3		✓		Australia
Guifo et al., (2016)	Retrospective cohort	101	Unknown	3		Unknown	Unknown	Cameroon
Dang et al., (2017_)	Case report	1	1	4	✓			Australia

[a] Oxford Centre for Evidence Based Medicine Levels of Evidence (OCEBM Levels of Evidence Working Group, 2011)

Table 2 Summary of clinical results of included studies, excluding review articles

Study (author, year)	*M. ulcerans* cases requiring flaps	Type, duration of antibiotic cover (days)		Defect dimensions (mm)	Flap indication	Flap choice	Complications
		Pre-operative	Post-operative				
Agbenorku et al., (2001)[14]	At least 6	N/A	N/A	N/A	Eyelid lesions	Forehead flap	Nil flap failures
Russell et al., (2002)[5]; Ramakrishnan et al., (2004)[3]	1	*Am*, *R*, *E*: at least 4	*Am*: ~26*R*, *E*, *Cla*: 90	Pre-debridement70 × 30; 10–20 deep. Post-debridement 200 × 130	Large defect, exposed joint, loss of muscle and tendon	Free rectus abdominus flap and SSG	Small area of muscle flap necrosis requiring debridement and repeat skin grafting
O'Brien et al., (2007)[10]	9	Pre- and post-operative antibiotics mentioned in overall sample but figures not specified for flap reconstruction cases Antibiotics: *R*, *Cla*, *Cip*, *E*, *Am*, *Az*		N/A	Defect unable to be primarily closed	Vascularised flap only in 6 episodes; vascularised flap + SSG in 3 patients	24% failure (recurrence) rate for "major surgery"[a]
Agbenorku et al., (2011)[13]	Unknown	*R* + *S*: overall 56 Pre- & post-operative duration not specified		N/A	Eyelid destruction; wounds unable to be closed primarily	Forehead flap for eyelids; local transposition flaps	N/A
O'Brien et al., (2012)[11]	16	Overall median 76 (in 90 patients of *n* = 133 who received antibiotics) Pre- & post-operative antibiotics mentioned but figures not specified for flap reconstruction cases		N/A	Excised wound unable to be closed primarily	Vascularised tissue flap	10% failure (recurrence) rate for "major surgery"[a]
O'Brien et al., (2013)[12]	6	Not utilised	Not utilised	N/A	Excised wound unable to be closed primarily	Vascularised tissue flap	One-third of sample experienced recurrence. Flap complications not mentioned
O'Brien et al., (2013)[8]	3	Overall median: 58 (in *n* = 156) Pre- and post-operative antibiotic regimens not mentioned Antibiotics: *R*, *Cip*, *Cla*, *M*, *Am.*		N/A	Severe paradoxical necrosis causing tendon exposure; excised wound unable to be closed primarily	Free tissue flap in 1 case; unspecified vascularised tissue flap in 1 case; flap + SSG in 1 case	Flap complications not mentioned
O'Brien et al., (2014)[9]	1	Overall median: 84 (in 17 oedematous lesions of *n* = 238) Antibiotics: *R* + *Cip or R* + *Cla* or *R* + *M.*		N/A	Oedematous lesion with significant necrosis requiring debridement	Vascularised free flap	Flap complications not mentioned
Cowan et al., (2015)[7]	5	Overall pre-operative median duration: 8 (in 39 patients of *n* = 51 treated with surgery + short-course antibiotics) Overall median duration of entire course: 29 (in *n* = 51 treated with surgery + short-course antibiotics)		N/A	Excised wound unable to be closed primarily	Vascularised tissue flap in 4 cases; vascularised tissue flap + SSG in 1	2% recurrence and non-healing rate. Flap complications not mentioned.

Table 2 (continued)

Study (author, year)	*M. ulcerans* cases requiring flaps	Type, duration of antibiotic cover (days)		Defect dimensions (mm)	Flap indication	Flap choice	Complications
		Pre-operative	Post-operative				
			Antibiotics: *R* + one of *Cip*, *Cla*, *E* or *M*; *Cla* + one of *E or Cip*; or *Cla* alone				
Dang et al., (2017)[6]	1	N/A		N/A	150 × 200	Large defect with exposed extensor tendons, cutaneous nerve branches and extensor retinaculum	Anterolateral thigh free flap	No flap complications

Am amikacin, *R* rifampicin, *Cip* ciprofloxacin, *Cla* clarithromycin, *M* moxifloxacin, *E* ethambutol, *S* streptomycin, *Az* azithromycin, *SSG* Split-thickness skin graft

[a] "Major surgery": split-thickness skin grafts and/or vascularised tissue flaps

reconstruction) may effectively reduce recurrences [8, 10], as well as indicating that cure is usually achieved with 8 weeks of antibiotics [9]. Regarding paradoxical reactions [6], the need to be mindful of misdiagnosis as antibiotic therapy failure is raised, especially as this may impact timing and outcomes of reconstruction. O'Brien et al. also discussed a rare sub-type of *M. ulcerans* infection, the oedematous lesion [7], where the authors note that despite antibiotic therapy, such lesions almost always required extensive surgical debridement for necrosis, which may produce the need for a different reconstructive and antibiotic approach in these cases. Lastly, Cowan et al. [5] demonstrated that adjuvant surgical excision plus reconstruction where necessary can decrease the duration of antibiotic therapy required for resolution of infection, by reducing bacterial load and hence improving treatment success rates.

Chin-Lenn et al. [13] and Simpson et al. [14] both proposed management algorithms for *M. ulcerans*, recognising the need for flap reconstruction in larger soft tissue defects to minimise disability and maximise cosmesis. Their management strategies differ in approach to excision and debridement, which may be attributed to the evolution of World Health Organisation (WHO) guidelines and discoveries over the past decade. O'Brien et al. [16] published an Australian consensus guideline update in 2014, addressing, among other things, the combination of surgery and antibiotic therapy. The authors acknowledged the necessity for vascularised flap reconstruction in extensive defects and recommended 4–8 weeks of antibiotic treatment prior to surgical repair. Their antimycobacterial therapy suggestion is rifampicin plus ciprofloxacin, moxifloxacin or clarithromycin, in preference to intramuscular antibiotics.

Additionally, Guifo et al. [15] investigated all chronic wound cases at their centre in Cameroon, including a subset of 101 *M. ulcerans* cases (51% of sample). Three flap reconstructions were reported; however, it is unclear whether these were performed on *M. ulcerans* cases.

Case reports on flap reconstruction

Russell et al. [2] and Ramakrishnan et al. [3] described the same paediatric case of *M. ulcerans*, sustained in tropical Queensland and reconstructed at a Victorian hospital. A rectus abdominus muscle and adipofascial free flap was used to reconstruct a composite defect of the dorsal elbow, including the triceps tendon. The deficit measured 200 by 130 mm. With 3 months of antibiotics (rifampicin, amikacin, ethambutol, clarithromycin) and physiotherapy, the patient regained full function of the joint.

Dang et al. [4] reported use of an anterolateral thigh flap to reconstruct a dorsal hand *M. ulcerans* defect. Published in 2017, the paper discussed an operation performed by

one of our senior authors and is included as one of our case reports below.

Case series (Table 3)

We describe four cases of advanced of *M. ulcerans* infection where reconstruction was performed by one or two of the senior authors, between 2015 and 2017. The mean age of the sample ($n = 4$) was 65 years (range 17–86), with 3 males and 1 female. *M. ulcerans* infection was diagnosed by acid fast bacillus culture and polymerase chain reaction (PCR) for *M. ulcerans*. All four defects were of the dorsal hand, with the indication for reconstruction uniformly being extensive soft tissue loss with exposure of extensor tendons. Antibiotic regimens varied, with an average of 7.5 weeks (range 3–12) of pre-operative antibiotic therapy and 12.5 weeks (range 10–15) total therapy.

Case 1

As mentioned, Dang et al. have previously reported this case [4] of an 86-year-old male with dorsal hand *M. ulcerans* infection and a radiocephalic arteriovenous fistula (AVF) directly adjacent to the defect. Here, we present additional unpublished details regarding antibiotic therapy. *M. ulcerans* was diagnosed after a 2-week history of an expanding ulcer of the dorsal left hand. Rifampicin and clarithromycin were commenced. Following debridements, failed skin grafts and ongoing antibiotic therapy, the resulting defect was 150 by 200 mm and encroached onto tissues of the AVF site. Indications for reconstruction were exposed extensor tendons, cutaneous nerve branches, extensor retinaculum and open metacarpophalangeal joints. Main reconstructive aims were sufficient tissue coverage and AVF preservation, which an anterolateral thigh (ALT) flap was deemed to best address. Six weeks following antibiotic commencement, microvascular flap reconstruction was performed, consisting of a single end-to-end arterial anastomosis using the dorsal branch of the ulnar artery and two venous end-to-end anastomoses with a tributary of the basilic vein and a vena comitans. Intraoperative transduction of recipient venous pressure was undertaken to reduce chance of venous flap congestion in the setting of higher venous pressure in the AVF site. There were no complications, and the AVF was successfully preserved. Rifampicin and clarithromycin were continued for 7 weeks post-reconstruction. At 6 months, debulking of the flap was undertaken. Ultimately, the patient regained full range of movement with good functional and aesthetic outcomes, as well as successful ongoing use of the AVF.

Case 2

A 76-year-old male was diagnosed with *M. ulcerans* following a 10-week history of chronic intermittent infection on his dorsal right hand. He was commenced on rifampicin, ciprofloxacin and sodium fusidate. After 6 weeks and multiple debridements, he underwent a full thickness skin graft, which failed 3 weeks later due to widespread paradoxical reaction extending to the volar distal phalanx in all digits and through to the palm, with fat and skin necrosis on the dorsum and web spaces, for which he was commenced on prednisolone. Ultimately, exposure of the extensor tendons (Fig. 2) led to an ALT flap reconstruction 9 weeks post-antibiotic commencement, with one arterial anastomosis to the ulnar artery, and two venous anastomoses to a vena comitans and a superficial dorsal vein. There were no complications. Antibiotics were continued post-operatively for 6 weeks, and prednisolone was weaned and ceased 9 weeks post-operatively, at which time the flap was well healed. At 6 months, the hand displayed only slight restriction in range of movement, secondary to flap bulkiness. Debulking and revision was carried out at 9 months (Fig. 3). At 12 months, the patient regained

Table 3 Case series, summary

Case number	Age, Sex	Flap choice	Defect location	Recipient vessels		Type, duration of antibiotic cover	
				Arterial	Venous	Pre-operative	Post-operative
1	86, M	ALT	Dorsal left hand	Dorsal branch of ulnar artery	Tributary of the basilic vein; vena comitans	6 weeks *R*, *Cla*	7 weeks *R*, *Cla*
2	76, M	ALT	Dorsal right hand	Ulnar artery	Vena comitans; superficial dorsal vein	9 weeks *R*, *Cip*, *SF*	6 weeks *R*, *Cip*, *SF*
3	82, F	ALT	Dorsal right hand	Radial artery	Radial artery vena comitans; cephalic vein	3 weeks *R*, *Cla*	7 weeks *R*, *Cla*
4	17, M	ALT	Dorsal right hand	Radial artery	Radial artery vena comitans; cephalic vein	3 months *R*, *Cip*	Prophylactic *Cli* only.

R rifampicin, *Cla* clarithromycin, *Cip* ciprofloxacin, *SF* sodium fusidate, *Cli* clindamycin

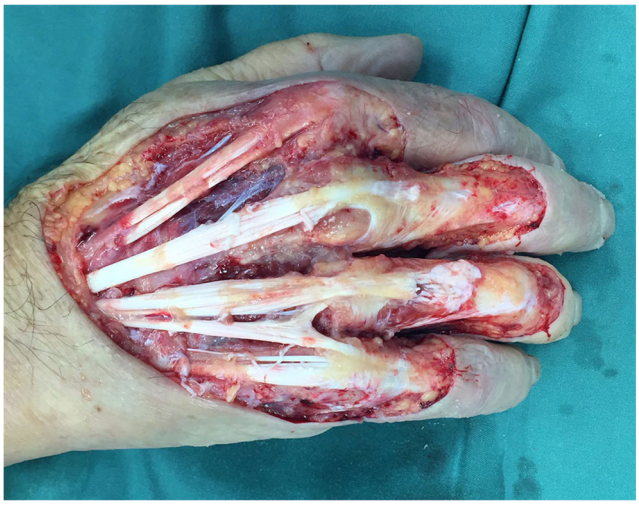

Fig. 2 Case 2, mycobacterial soft tissue defect, dorsum of right hand and digits, with extensor tendons on view

full range of motion, with satisfactory functionality and cosmesis.

Case 3

An 82-year-old female with a 2-week history of a dorsal right hand wound was diagnosed with *M. ulcerans*. She was prescribed rifampicin and clarithromycin, and debridement revealed the ulcer to be deep with extensor tenosynovitis. Again, an ALT flap was deemed the most suitable reconstructive option. Three weeks following antibiotic commencement, flap reconstruction was undertaken, with arterial anastomosis to the radial artery and two venous anastomoses to a radial artery vena comitans and the cephalic vein. Additionally, the lateral cutaneous nerve of the thigh was anastomosed to the dorsal branch of the radial nerve. There were no intraoperative complications. Antibiotics were continued for 7 weeks postoperatively. Two weeks following reconstruction, the distal-ulnar and mid-radial flap edges developed inflammatory slough, which was diagnosed as paradoxical reaction. This was managed with prednisolone, given for a total of 6 weeks, and resolved without surgical intervention. At 6 months, the patient had regained full range of motion and function and is planned for flap debulking.

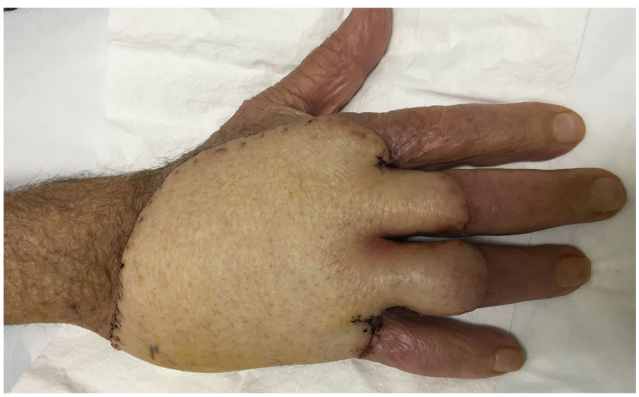

Fig. 3 Case 2, post flap division for digital inset

Case 4

A 17-year-old male with a 7-week history of an oedematous, erythematous right dorsal hand and wrist, which was unresponsive to antibiotics given by his general practitioner, was diagnosed with *M. ulcerans* infection. Rifampicin and ciprofloxacin were prescribed, and debridements were required for extensive fat and skin necrosis, leaving a defect 80 mm × 120 mm in size, exposing the extensor tendons (Fig. 4). Reconstruction with a split thickness skin graft was unsuccessful due to tethering to exposed extensor tendons, leading to unacceptable restriction in range of movement. Consequently, an ALT flap was deemed the reconstructive method of choice. At 5 months post-diagnosis of *M. ulcerans* infection, and after successful antimycobacterial treatment with a 3-month course of rifampicin and ciprofloxacin, flap reconstruction was performed using a single end-to-end arterial anastomosis to the radial artery and two venous anastomoses to a radial artery vena comitans and cephalic vein. A small split thickness skin graft was used on the radial flap border. There were no complications. Post-operative prophylactic clindamycin cover was given. At 2 months, the flap was bulky but well healed (Fig. 5) and the patient had regained full active range of movement. Debulking and revision are scheduled.

Discussion

Over the past two decades, there has been an evolution of treatment recommendations for *M. ulcerans* infection. In 2001, World Health Organisation (WHO) guidelines focused on surgery as the mainstay of treatment, with little weight given to the role of antibiotics. These were only given for super-infection or as adjuncts to surgery. Wide local excision was considered the only curative method,

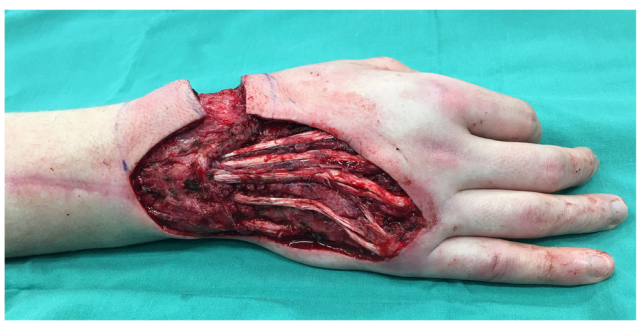

Fig. 4 Case 4, mycobacterial soft tissue defect, dorsum of right hand, with extensor tendons on view

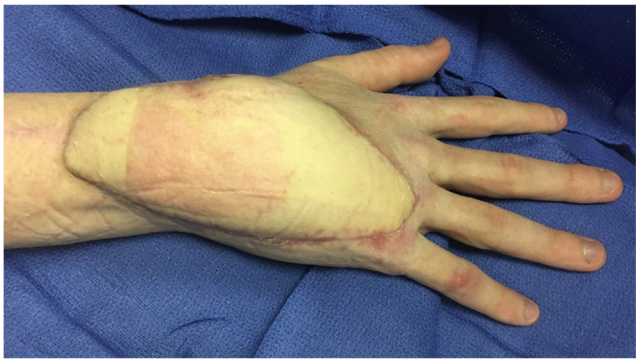

Fig. 5 Case 4, at 6 weeks post-anterolateral thigh flap reconstruction of mycobacterial soft tissue deficit

with split-skin grafting to larger wounds [18]. WHO's following publication, in 2004, acknowledged the growing evidence supporting antibiotic therapy for *M. ulcerans* with rifampicin and an aminoglycoside for 8 weeks, plus simple debridements to remove dead tissue only. Radical debridement was recommended sparingly, as antibiotics had been found to reduce the necessity for extensive excision [19]. Currently, WHO recommends surgery as an adjunct therapy to antibiotics in *M. ulcerans* infection, where reconstruction, if necessary, is by skin graft or flap [20]. Based on our experiences in this endemic region, the extensive defects resulting from soft tissue destruction by this mycobacterium and mycolactone toxin can surpass the level of simple reconstruction, especially in the hand, requiring the use of free fasciocutaneous flaps. While the current guideline of conservative debridement reduces the number of complex reconstructions required by enabling soft tissue conservation, we have found that in spite of this, a small minority of our patients still require microvascular flap reconstruction. However, skin grafting or local flaps remain the most commonly used reconstructive methods in this population.

With reference to our hand defect cases, duration of antibiotic therapy and timing of reconstruction is exceedingly relevant, as illustrated by the following. At least 4–8 weeks of antibiotic therapy is recommended [9, 16, 20] before reconstruction in order to render a lesion cured and facilitate best outcomes in terms of non-recurrence of infection, therefore lessening wound healing complications in the setting of a flap reconstruction. This advantage, however, is held in balance with the ongoing exposure of tendons for the duration of antibiotic therapy, which can lose viability over time if treated improperly. In conjunction with the cost and inconvenience of regular dressings and loss of function during this time, an argument can be made for earlier rather than later reconstruction. Further, there remains the complication of the paradoxical reaction, which can occur both during and following antibiotic treatment, and has the potential to disrupt flap outcomes regardless of both duration of antibiotic therapy and timing of reconstruction. From our limited sample, we have experienced success with 3–12 weeks of pre-reconstruction antimycobacterial therapy, and while one of our cases was reconstructed earlier than guidelines may suggest, a reduced time frame in this particular situation was deemed necessary to prevent ongoing injury to unprotected tendons. Although this case was unfortunately affected by paradoxical reaction post-operatively, as discussed, this may occur at any point during or after antibiotic therapy and is not necessarily an indication of treatment failure. O'Brien et al. [16] list oedematous lesions and age greater than 60 years to be risk factors for paradoxical reaction in Australians, and as such, these points should be taken into consideration when deciding on both antibiotic duration and timing of reconstruction. Overall duration of antibiotic therapy in our cases ranged from 10 to 15 weeks, which begs the question: when is the earliest point within this overall duration that we can reconstruct, hence preserving tendon health, while still having a low enough bacterial load for the flap to remain viable? There is no information regarding this in the literature, nor do our case reports have the power to provide any robust findings on this topic. Further research into the area is warranted. Regarding antibiotic choice, it is essentially a question of which agent to use in conjunction with rifampicin, and while our literature review reveals several generalised antibiotic recommendations, there are currently no publications on antibiotic selection specific to flap reconstruction in *M. ulcerans.* The use of ciprofloxacin, moxifloxacin or clarithromycin with rifampicin is clearly effective; however, it remains to be seen whether one of these agents produces better outcomes in microvascular flap reconstruction.

Our key reconstructive aims were to minimise deformity, maximise functional and aesthetic outcomes and ultimately allow the patient to return to their regular activities of daily living. It was deemed most appropriate to achieve these goals with fasciocutaneous free flaps. As mentioned in our case series, grafting was unsuitable in these defects due to tendon exposure and graft tethering, causing restriction of movement, loss of function and poor cosmesis. While a pedicled groin flap could have fulfilled similar criteria, the increased oedema, associated stiffness and periods of immobilisation, plus the absence of contraindication to microvascular reconstruction, led to our use of the anterolateral thigh flap. The choice to utilise a fasciocutaneous flap, over fascia- or muscle-only flaps, was to maximise hand function by facilitating optimal tendon gliding and allow for simpler post-operative monitoring and revision.

Notably, there were four Ghanaian papers, published between 2000 and 2013, which utilised reconstructive surgery not for initial *M. ulcerans* deficits but for its sequelae. Agbenorku et al. [21] used radial forearm flaps to reconstruct skin and tissue deficit following release of elbow and wrist contractures from *M. ulcerans* infection. Adu et al. [22–24] details the use of pedicled flaps to repair these contractures.

The authors iterate that *M. ulcerans* infection treated with antibiotics alone leaves ulcers to heal by secondary intention, which can cause significant deformity in extremities. Hence, they advocated for early excision and reconstruction with grafting or flaps, to prevent or minimise such sequelae [22]. Additionally, they note that antibiotic treatment has limited benefit in advanced cases of *M. ulcerans* with contracture, as often, the reason for the development of contracture is late diagnosis, and in such situations, there is no longer active *M. ulcerans* infection which will respond to antibiotics [24, 25]. To our knowledge, there is no Australian literature on contracture sequelae post-*M. ulcerans* infection, which we believe may be due to different access to healthcare, lower infection rates in Australian versus African populations and differing levels of health awareness.

Conclusion

There is a paucity of literature regarding microvascular flap reconstruction of *M. ulcerans* deficits, in the context of reconstructive timing, antibiotic choice and duration. We have recognised, through the volume of cases at our institution located in an endemic *M. ulcerans* region, that there is an increasing need for a detailed reconstructive protocol. Our case series demonstrates the successful use of fasciocutaneous perforator flaps to reconstruct soft tissue defects remaining after *M. ulcerans* infection; however, further research must be undertaken to define the optimal antibiotic choice, overall therapy duration, and timing of reconstruction while achieving key reconstructive aims. This paper comprehensively presents the first review and case series on microvascular flap reconstruction of advanced *M. ulcerans* defects.

Compliance with ethical standards

Conflicts of interest Rachael Leung, Daniel Reilly, George Miller, Marc A. Seifman, David J. Hunter-Smith and Warren M. Rozen declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

For this type of study formal consent is not required.

Informed consent Informed consent was obtained from all individual participants included in the study.

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