Managing a challenging diabetic foot ulcer in a patient with end-stage renal disease



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The formation of infected and hypergranulation tissue in diabetic foot ulcer (DFU) in a patient with end-stage renal failure (ESRF) created a complex and challenging situation for the clinicians involved. Hypergranulation is defined as overgrowths of granulation tissue to prevent cell proliferation from occurring as the inflammatory phase is altered. The hypergranulation tissue is above the level of the surrounding skin. It is friable, prone to bleeding and can get easily infected. In this case study, the authors used Retro Tech Dressing (RTD™) foam to treat the infected hypergranulation tissue which presented inside the DFU in a patient with ESRF. Debridement therapy and the application of RTD, as well as addressing the underlying condition, was found to effectively heal the wound without complications.

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End-stage renal failure (ESRF) is an independent risk for developing wound in patients with diabetes mellitus (Behan and Reyzelman, 2018). There is about 15–40% risk of developing diabetic foot ulcer (DFU) amongst individual with ESRF and diabetes mellitus (Kaminski, 2015). Peripheral neuropathy that occur in ESRF with diabetes mellitus exposes patients to insensible trauma or injury to their feet and, as a consequences, DFUs will arise. Apart from that, peripheral arterial disease that emerges due to atherosclerosis as well as calcification of calcium and phosphate deposits contribute to the development of DFU in ESRF. The uremic toxins presented in ESRF affect the local wound healing mechanism as well as influence the function of multiple systems in the human body (Scholnick, 2016). Uremic toxins that appear due to ESRF cause the accumulation of interleukin-6 which impacts on the healing process in chronic inflammation (Behan and Reyzelman, 2018). This prolonged chronic inflammatory response triggers hypergranulation although the accelerating mechanisms are not fully understood (McGrath, 2011).

Hypergranulation is defined as an excessive granulation tissue above surrounding healthy tissues and it is caused by an altered cell sequel inflammatory response (Stephen Haynes and Hampton, 2010). Hypergranulation tissue is often friable and produces an increased level of exudate and hence is difficult to manage clinically. The risk of infection in hypergranulation tissue is due to the vertical proud flesh characteristic of the tissues that prevent standard healing mechanism to occur. Hypergranulation carries the risk of increased infection by the nature of its exuberant tissue that is moist and highly vascular. The delayed healing is a result of structural deformity that rendered re-epithelialization.

The objective of this study is to evaluate the effect of Retro Tech Dressing (RTD) in managing infected hypergranulation tissue in DFU with ESRF. RTD is a foam that has been designed to stimulate healing in chronic wounds by employing silver ion, gentian violet and methylene blue to the wound bed. These three active ingredients have effective antimicrobial and antifungal functions. The active ingredients also have early and sustained antimicrobial protection that help to prevent biofilm. The active ingredients are integrated into a polyurethane foam matrix which is soft, surface-conforming and easy to use (Keneric Healthcare, 2014). RTD can holds exudate vertically, maintain moisture and prevent maceration. RTD absorbs excess protein-rich exudates from the wound, hence creating a favourable wound healing environment (Keneric Healthcare, 2014).

Figure 1. The wound before the application of the new dressing.

Case report

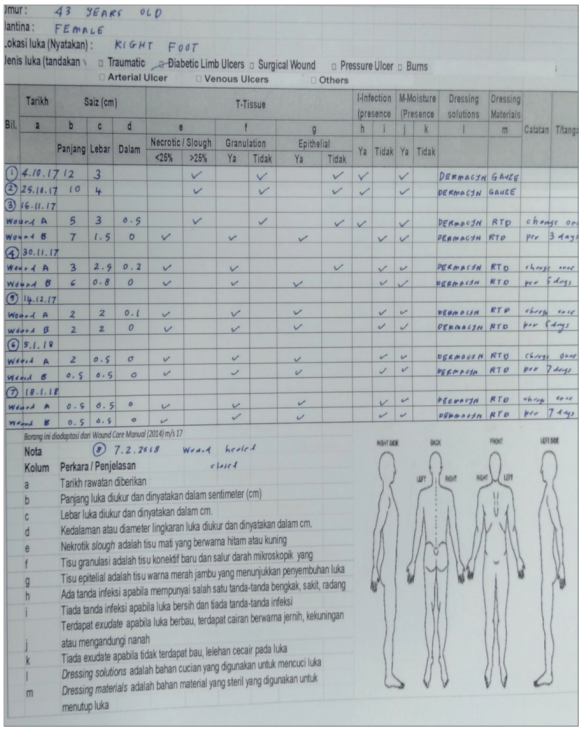
This case study presents a 43-years-old female who has had Type 2 diabetes mellitus and hypertension for the last five years. She was diagnosed with ESRF in August 2017, and since then underwent haemodialysis three times per week. On September 2017, she developed DFU on her right foot due to traumatically tight shoes after a period of prolonged walking. She came to the authors' clinic in October 2017 for the continuation of care after surgical wound debridement was done at the Seremban General Hospital, Malaysia. After a six-weeks treatment with multiple dressing products, her wound still showed poor healing. On top of this, it was noted that there was new hypergranulation tissue on the wound bed.

Initial assessment revealed two wounds at the right plantar *[Figure 1]* described as wound A (forefoot area) and wound B (midfoot area). The size of wound A (hypergranulated area) is 5 x 3 x 1.0 cm with friable bleeding tissue and pus. Wound B size is 7 x 1.5 cm with granulation tissue.

Wound progression was assessed using the standard wound evaluation form provided by Malaysia Ministry of Health (MOH) *[Figure 2]*. A standard protocol for wound management using modern dressing was accomplished. Sharp wound debridement was done as indicated. The wound was cleansed with super-oxidised solution (Dermacyn™) and combined with RTD foam, which acts as both a primary and secondary dressing. At the same time, the patient was given education on the method of diabetic self-control; appropriate nutrition and fluid intake and foot care including offloading therapy. In addition, her medication was optimized and adherence to dialysis advocated.

Her blood pressure was monitored and optimized with anti-hypertensive medication. The authors referred her to occupational therapy for foot care and offloading therapy of her DFU. Offloading was optimized as she used a wheel chair most of the time when travelling and crutches for short-distance walking. No orthosis was needed as the patient was not walking much since she had the DFU. The authors referred the patient to a nutritionist because of the patient's underlying chronic anaemia, which was the result of ESRF. Anaemia is one of the causes that impedes wound healing in ESRF as there is not enough oxygen to supply the tissues.

She used insulin as a medication for her diabetes mellitus treatment and despite of the good glycaemic index, the wound at her foot showed poor healing. *Table 1* shows the HbA1c level when she first arrived on October 2017, which is considered within good glycaemic control for diabetes mellitus with ESRF. The anaemia improved on referring to a nutritionist besides haematinics prescription. This together with the regular dialysis balanced the excess of uremic toxins that existed in her body. In fact, her initial haemoglobin level was not severe enough to disrupt the healing mechanism process *[Table 2]*.


umur : 43 YEARS OLD
Jantina : FEMALE
Lokasi luka (Nyatakan) : RIGHT FOOT
Jenis luka (tandakan √) : Traumatic, Diabetic Limb Ulcers, Surgical Wound, Pressure Ulcer, Burns, Arterial Ulcer, Venous Ulcers, Others

Bil.	Tarikh	Saiz (cm)			T-Tissue						I-Infection (presence)		M-Moisture (Presence)		Dressing solutions	Dressing Materials	Catatan	Titangi
	a	b	c	d	e		f		g		h	i	j	k	l	m		
		Panjang	Lebar	Dalam	Necrotic / Slough <25%	Necrotic / Slough >25%	Granulation Ya	Granulation Tidak	Epithelial Ya	Epithelial Tidak	Ya	Tidak	Ya	Tidak				
1	4.10.17	12	3			✓	✓		✓		✓		✓		DERMACYN	GAUZE		
2	25.10.17	10	4			✓	✓		✓		✓		✓		DERMACYN	GAUZE		
3	16.11.17																	
	Wound A	5	3	0.5		✓		✓		✓	✓		✓		DERMACYN	RTD	change on	
	Wound B	7	1.5	0	✓		✓		✓			✓	✓		DERMACYN	RTD	Pro 3 days	
4	30.11.17																	
	Wound A	3	2.9	0.2	✓		✓			✓		✓	✓		DERMACYN	RTD	change once	
	Wound B	6	0.8	0	✓		✓		✓			✓	✓		DERMACYN	RTD	pro 5 days	
5	14.12.17																	
	Wound A	2	2	0.1	✓		✓		✓			✓	✓		DERMACYN	RTD	change once	
	Wound B	2	2	0	✓		✓		✓			✓	✓		DERMACYN	RTD	pro 5 days	
6	9.1.18																	
	Wound A	2	0.5	0	✓		✓		✓			✓	✓		DERMACYN	RTD	change once	
	Wound B	0.5	0.5	0	✓		✓		✓			✓	✓		DERMACYN	RTD	pro 7 days	
7	18.1.18																	
	Wound A	0.5	0.5	0	✓		✓		✓			✓	✓		DERMACYN	RTD	change once	
	Wound B	0.5	0.5	0	✓		✓		✓			✓	✓		DERMACYN	RTD	pro 7 days	

Borang ini diadaptasi dari Wound Care Manual (2014) m/s 17

Nota Kolum	Perkara / Penjelasan
	7.2.2018 Wound healed closed
a	Tarikh rawatan diberikan
b	Panjang luka diukur dan dinyatakan dalam sentimeter (cm)
c	Lebar luka diukur dan dinyatakan dalam cm.
d	Kedalaman atau diameter lingkaran luka diukur dan dinyatakan dalam cm.
e	Nekrotik slough adalah tisu mati yang berwarna hitam atau kuning
f	Tisu granulasi adalah tisu konektif baru dan salur darah mikroskopik yang
g	Tisu epitelial adalah tisu warna merah jambu yang menunjukkan penyembuhan luka
h	Ada tanda infeksi apabila mempunyai salah satu tanda-tanda bengkak, sakit, radang
i	Tiada tanda infeksi apabila luka bersih dan tiada tanda-tanda infeksi
j	Terdapat exudate apabila luka berbau, terdapat cairan berwarna jernih, kekuningan atau mengandungi nanah
k	Tiada exudate apabila tidak terdapat bau, lelehan cecair pada luka
l	*Dressing solutions* adalah bahan cucian yang digunakan untuk mencuci luka
m	*Dressing materials* adalah bahan material yang steril yang digunakan untuk menutup luka

Figure 2. Malaysia Ministry of Health (MOH) wound evaluation form

Table 1. Results of the patient's glycaemic index

Date	20.10.2017	15.1.2018
HbA1c level	7.0%	6.4%
Fasting blood glucose	6.0 mmol/L	5.3 mmol/L

Table 2. Results of the patient's haemoglobin

Date	20.10.2017	15.1.2018
Haemo-globin level	10.2 g/L	11.8 g/L
Fasting blood glucose	6.0 mmol/L	5.3 mmol/L

Table 3. Results of the patient's total white cell count

Date	20.10.2017	15.1.2018
Total white cell count	22x109/L	7.8x109/L

Figure 3. After 4 weeks of treatment with RTD

Figure 4. After 12 weeks of treatment with RTD

The level of TWBC actually increased in October 2017, indicating a high inflammatory index, although clinically the patient did not present with systemic manifestation such as fever. The patient was not on oral antibiotics.

RESULTS

Upon appropriate wound management with RTD dressings and an approximately bi-weekly follow up, the wound had attained complete re-epithelialization within 12 weeks of treatment. *Figure 3* represents the wound after four weeks application of RTD. The authors focused on the patient's adherence issue to foot hygiene abd explained to her the importance of foot care. *Figure 4* shows the wound outcome after 12 weeks application of RTD; revealing a dramatic improvement in wound healing without any complications. *Table 3* shows a significant reduction of infection as a result of RTD application. The total white cell count decreased soon after the wound had healed. There was no need to administer systemic or local antibiotics throughout this period of treatment.

Discussion

The presence of infected hypergranulation tissue prevent cell epithelization and, as a consequence, it remains a challenge for wound management. Altered chemical messengers in the human body with ESRF prevent wound healing progression despite the holistic approaches given. Gentian violet and methylene blue within the RTD decrease the bacterial load and absorb exudates as well as inhibit further development of hypergranulation tissue (Edwards, 2016).

It is possible that the presence of methylene blue and gentian violet as well as silver polyurethane foam inside had a positive effect in managing infected hypergranulation tissues (Edwards, 2016). The gentian violet, methylene blue and polyurethane foams are highly absorbent and non-cytotoxic, enhancing antibacterial activity against a broad spectrum of yeast and bacteria commonly found in wounds, for example *methicillin-resistant Staphylococcus aureus (MRSA)* and *Pseudomonas aeruginosa* (Kevin and Heil, 2017).

Gentian violet works as an antifungal, antimicrobial and mild analgesics. Methylene blue, which is bound to the foam matrix, has the ability to absorb excess exudate but is capable of maintaining the moist environment of the wound. Silver ions has the ability to kill bacteria in the wound fluid that has been absorbed by the foam dressing. Silver ions in the dressing provide antimicrobial activity where it can reduce and prevent infection in the wound bed (Thomas Hess, 2003). The three components in the RTD dressing attain the net beneficial result towards wound healing process (Keneric Healthcare, 2014). Nevertheless, the exact mechanisms are poorly understood and therefore further trials are needed.

There was no sample of tissue culture and sensitivity taken initially and, as a consequence, the exact microorganism that caused the infection is unknown. However, the exact mechanism of why hypergranulation occurs in the first place is not clearly understood. Hypergranulation can be due to an aberrant inflammatory allergic response (McGrath, 2011) and the patient may have had an allergy to the materials used in her previous dressings. The authors are looking forward by continue to follow up this patient twice per year in view of a possible recurrence of a DFU in the future.

Conclusion

Although this is only one case study and further research and evidence is needed, the authors believe that using RTD helped to prevent complications such as amputation and an increased risk of morbidity and mortality. Debridement as well as RTD proved effective in managing the infected hypergranulation in this patient's DFU. WAS

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