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# Collagen implant with gentamicin sulphate as an option to treat a neuroischaemic diabetic foot ulcer: Case report



C.E. Costa Almeida\*

Centro Hospitalar e Universitário de Coimbra (Covões), Surgery C, Centro Hospitalar de Coimbra (Covões), Quinta dos Vales, São Martinho do Bispo, Coimbra, Portugal

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## ABSTRACT

**INTRODUCTION:** The ischaemic diabetic foot is associated with a faster evolving atherosclerosis affecting preferentially the bellow knee arteries. This distal ischemia associated with a wide distribution of multiple stenosis and occlusions throughout lower limb arteries, makes revascularization very hard or even impossible. This represents a major factor responsible for non-healing diabetic foot ulcer. In these cases all efforts should be made to find treatment alternatives that can promote ulcer healing.

**CASE PRESENTATION:** Male patient with neuroischaemic diabetic foot ulcer with exposure tendon, without possibility for endovascular or surgical revascularization, was treated unsuccessfully with prostaglandin and several types of dressings for 7 months. Skin graft failed. Weekly dressings with collagen implant impregnated with gentamicin sulphate were then started and continued in an outpatient setting. Evolution was very positive, with 99% of epithelisation in 9 months. No pain or infection since the beginning of this treatment.

**DISCUSSION:** Successful treatment of a neuroischaemic diabetic foot ulcer rests with the possibility of increasing the perfusion to the foot. Whether or not a revascularization procedure is possible will set the tone for the ensuing treatment. Using collagen implant with gentamicin sulphate, collagen is delivered to the wound bed helping in the granulation tissue formation, will increase microcirculation, and topic gentamicin will decrease bacterial load, exudate and proteases production, increasing cicatrisation.

**CONCLUSION:** In neuroischaemic diabetic foot ulcer weekly dressings with collagen implant impregnated with gentamicin sulphate can be a good option for ulcer healing.

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## 1. Introduction

Diabetic foot can have an extreme negative impact in the quality of life (Q-o-L) of patients, and is a burden to all health care systems. It will affect about 15% of all diabetic patients, and from those 18% will have a limb amputation [1]. The risk of foot ulceration in a diabetic's patient lifetime may be as high as 25% and is the most common cause of amputation [2]. In five years time 66% of them will have a contralateral amputation [1]. Diabetic foot can be neuropathic, ischaemic or septic, but most of the times combines two or more of this characteristics. The ischaemic diabetic foot has some particularities that make this patient different than the ischaemic non-diabetic one. Claudication is most of the times absent due to concomitant neuropathy (mix blessing), which gives the patient a false sense of health. Additionally atherosclerosis in a diabetic patient evolves faster, and has a wider distribution throughout lower limb arteries, affecting preferentially the bellow knee arter-

ies (distal ischemia) [3]. Because of this distal ischemia and wide distribution of multiple stenosis and occlusions throughout lower limb arteries, revascularization of an ischaemic diabetic foot can be very difficult or even impossible. This represents a major factor responsible for non-healing diabetic foot ulcer and for limb amputation [2]. In these cases all efforts should be made to find treatment alternatives that can promote ulcer healing and save limbs.

The author presents and analyze a case of a patient with an ischaemic diabetic foot ulcer without possibility for revascularization treated with collagen implant impregnated with gentamicin sulphate (Collatamp®). This case report is compliant with the CARE guidelines.

## 2. Case presentation

A 81yo male patient with non insulin-treated type 2 diabetes resorted to the emergency department in June 2014 because of a third degree burn wound with 12 × 10 cm on the right instep with exposure tendon. Additionally he had fever and inflammatory signs around the wound. Although no distal pulses were noted on physical examination, the patient did not referred claudication and blood

\* Corresponding author.

E-mail address: [carloscostaalmeida@yahoo.com](mailto:carloscostaalmeida@yahoo.com)



**Fig. 1.** A—Neuroischaemic diabetic foot ulcer with exposure tendon before starting Collatamp® dressings. B—After 5 months of weekly dressings evolution is positive, with epithelisation coming from the edges, and without pain or infection.

flow was noted on doppler. Started empirical antibiotic therapy with meropenem and was admitted to general surgery department for wound care. Exudate was sent to microbial culture, and it was positive for staphylococcus aureus and pseudomonas aeruginosa. Clindamycin was then added to meropenem to treat infection.

During this period a vascular study was performed. Right ankle-brachial index was 0,52. Lower limbs angioCT scan revealed multiple stenoses along femoral and popliteal arteries, with severe occlusions in the arteries below knee. A diagnosis of a neuroischaemic diabetic foot with distal ischemia without outflow was made (TASC D classification of femoropopliteal lesions). Because of this severe distal ischemia without outflow no revascularization was possible, and iloprost was initiated and prolonged for 28 days. After 25 days in hospital he was submitted to surgical debridement of fibrin and dead tissue, and continued dressings with several products (including Dakin solution, hydrofibers with Ag, vacuum therapy). No clinical signs of infection at this time, and microbial cultures were negative.

Although granulation tissue was slowly growing on the wound bed, no significant healing was being achieved with all these treatments, and wound was almost the same size with exposure tendon. Because of that a skin graft was tried in November 2014 (6 months in-hospital) even knowing it was an ischaemic foot. Only 15% of the graft was viable on the 10th post-operative day. One month later (December 2014) infection recurred with a positive culture for staphylococcus aureus gentamicin sensitive. Treatment decision was made for collagen implant impregnated with gentamicin sulphate (Collatamp®) dressings on a weekly basis, and he was discharged home in the 19th December 2014 (Fig. 1A).

During follow-up in outpatient consultations, dressings with Collatamp® were made on a weekly basis. No dressings between consultations. A good evolution was noted, with granulation tissue growing on the wound bed and epithelisation coming from the wound edges. After 5 months evolution was amazing, with fast granulation tissue formation and skin growing (Fig. 1B). At 8 months of outpatient dressings cicatrization was 95% completed

(Fig. 2A). After 9 months of Collatamp® dressings, wound is now 99% epithelized (Fig. 2B). Patient himself is happy with the evolution and the limb salvage. No infection and no pain during Collatamp® treatment. No recurrence till now.

### 3. Discussion

There is an association between diabetes mellitus and the development of peripheral arterial disease (PAD). In the diabetic patient PAD is more aggressive compared to the non-diabetic, and the need for major amputation is five- to ten- times higher for diabetics than non-diabetics. Sensory neuropathy and decrease resistance to infection are contributors to this increase risk of amputation in the diabetic patient [4]. PAD is more aggressive in diabetics because atherosclerosis evolves faster, and has a wider distribution throughout lower limb arteries, affecting preferentially the below knee arteries with multiple stenosis and occlusions (distal ischemia) [3].

In these setting the successful treatment of a foot ulcer rests with the possibility of increasing the perfusion to the foot. Whether or not a revascularization procedure is possible will set the tone for the ensuing treatment [4]. The low inflow due to multiple stenosis and occlusions in femoral arteries coupled with the low outflow associated to the distal ischemia will be responsible for a poor graft postoperative patency, making revascularization surgery impossible due to expected bad outcome [4]. Predictors of successful outcome in endovascular treatment include a shorter length of occlusion and a lesser number of vessels treated [4]. In the diabetics (like the case presented) this is the opposite [3]. Because they have multiple stenosis throughout lower limb arteries, most of the times in the below knee territory with small calibre vessels, endovascular treatment has limited indications. In the case reported, surgical team decided not to proceed to revascularization because there was no outflow enough to obtain a good outcome (TASC D classification of femoropopliteal lesions). These factors associated with



Fig. 2. A—Cicatrization continues after 8 months of outpatient dressings with Collatamp®. B—With 9 months of evolution epithelisation is 99% completed.

sensory neuropathy and decreased resistance to infections make the neuroischaemic diabetic foot ulcers very difficult to treat [4].

In these cases, like the one presented, treatment with prostaglandins can be of good help increasing skin vascularization. However it may not be sufficient to heal an ischemic diabetic foot ulcer. Additionally, skin grafts in an ischaemic limb without possibility for surgical or endovascular revascularization will have low chances of success. That is why in the case presented only 15% of the skin graft was viable one week after surgery.

For ulcer healing, a good and healthy granulation tissue on the wound bed is mandatory, which will allow epithelisation to occur starting from the wound edges. Bacterial load of a chronic wound will have a negative impact on healing because of proteases production from polymorphonuclear cells, which will degrade collagen and decrease cicatrization [5,6]. Keeping the ulcer uninfected, not contaminated, and lowering bacterial load is crucial for a good healing process. The use of collagen implant impregnated with gentamicin sulphate (Collatamp®) has not been fully studied in diabetic foot ulcers, except when osteomyelitis exists. However Collatamp® has shown to reduce surgical site infection (SSI) in cardiac surgery [7], orthopaedics [8], general surgery [8,9] and vascular surgery [10]. Additionally there are reports of good results in promoting venous ulcer healing and decreasing local pain [5]. Ischemia and diabetic microangiopathy impair blood supply to soft tissues in a diabetic foot. Because of this, systemic administration of antibiotics will lead to local concentrations below minimum inhibitory concentration (mic), which causes failure to resolve infection and sustains development of resistant stains. [2]. With topic application of Collatamp® a local gentamicin concentration high above mic is reached (active against staphylococcus and gram-negative germs), and without toxic effects since there is no systemic absorption. A rapid fall-off in local gentamicin concentration prevents long-term sub-inhibitory concentrations and reduces risk of antibiotic resistance. There are no reports of resistance with long-term use [5,10]. Additionally, using collagen as a carrier has effects on healing, helps on haemostasis, minimizes scarring, has low antigenicity, and it is a well-tolerated implant without side effects [6,11].

Using collagen implant with gentamicin sulphate, collagen is delivered to the wound bed helping in the granulation tissue formation, will increase microcirculation, and topic gentamicin will decrease bacterial load, exudate and proteases production, increasing cicatrization [5]. These were the reasons for our choice in the case presented, choice that was proved to be of worth. The healing process was faster after the use of Collatamp® as a weekly dressing, and the wound was kept painless, non-infected, and without exudate. Allowing the patient to see the good progress week after week in the healing process, will have a positive impact in his Q-o-L.

The good results that were achieved in this case match other studies data. In a multicentre randomized controlled trial published by Lipsky et al. comparing diabetic foot ulcer treatments, a treatment group with gentamicin-collagen sponge had a significantly higher healing rate than did the control group [12]. Varga et al. in a randomized trial concluded that the application of collagen impregnated with gentamicin sulphate shortened wound healing duration after minor amputations in diabetics by almost two weeks [2]. The new idea that this case report adds is the fact that using this sponge in a diabetic patient with chronic ischemia of lower limbs without possibility for revascularization who develops an ulcer, granulation tissue formation and epithelization can be achieved. Ischemia increases the amputation rate of a diabetic patient, so every effort must be made to reduce it, and Collatamp® is probably a possibility.

#### 4. Conclusion

In neuroischemic diabetic foot ulcer weekly dressings with collagen implant impregnated with gentamicin sulphate can be a good option for ulcer cicatrization. A RCT will be necessary for comparison with other treatment options and validate these results.

#### Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy

of the written consent is available for review by the Editor-in-Chief of this journal on request.

### Fundings

No sources of funding.

### Conflict of interests

Has been invited by EusaPharma to give lectures in clinical sessions about his own experience using Collatamp in general surgery and vascular surgery.

### Author contribution

CE Costa Almeida—study design, data collection, data interpretation, writing, review.

### Ethical approval

No need for ethics committee approval in this case.

### Guarantor

CM Costa Almeida, MD, Ph.D., chairman of general surgery department from Surgery C of “Centro Hospitalar e Universitário de Coimbra”.

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