

Chronic ulcers: MATRIDERM® system in smoker, cardiopathic, and diabetic patients

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Abstract

Diabetic ulcers and pressure ulcers represent a more frequent cause of chronic wounds in aging populations. It is estimated that approximately 15% of the diabetic population will develop diabetic ulcers during their life and over half of these patients develop an infection, often osteomyelitis, with 20% requiring amputation.

The authors report a case of a 65-year-old woman affected by a post-traumatic loss of substance due to road accidents with soft tissue exposure (comprising muscle tendon) of the left knee combined with the fracture of the right fibula previously subjected to surgery and reconstruction of muscle tendon.

The patient was affected by diabetes type II, hypertension, and ischemic heart disease.

In 2008, she underwent a double bypass surgery and coronary angioplasty.

Initially, the patient was treated with cycles of advanced dressings, with fibrinolytic ointments, hydrocolloid, and subsequently, when the bottom began granulated with fibrinolytic and idrocellulosa, Hydrofibra-Ag, and Ag-alginate, three times a week for 30 days.

In the second step, the authors decided to treat the ulcer with the MATRIDERM system and auto skin graft.

Following the first treatment, 7 days after the procedure, the authors found the reduction of the loss of substance until its complete closure.

The wound's infection was evaluated by a buffer negative confirmation performed every 2 weeks four times. We obtained decrease of limb edema and full functional rehabilitation. The skin appeared renovated, with volume restoration and an improvement of the texture.

Keywords

Chronic ulcer, MATRIDERM® system, diabetes, skin grafting

Introduction

Today, a lot of causes are recognized as reasons for failure in healing of losses of substance including diabetes, heart disease, and smoking. Diabetes mellitus represents one of the most important public health problems with a worldwide impact due to its high prevalence and enormous social and economic consequences.¹ A lot of diabetic patients develop the chronic complications of diabetes: retinopathy, nephropathy, peripheral neuropathy, and atherosclerotic vascular disease; the treatment of these complications is difficult, prolonged, and often unsuccessful.² Diabetic ulcers and pressure ulcers represent a more frequent cause of chronic wounds in aging populations. It is estimated that approximately 15% of the diabetic population will develop diabetic ulcers during their life³ and over half of these patients develop an infection, often osteomyelitis, with 20% requiring amputation.⁴ Many authors⁵ described that up to 85% of lower limb amputations in diabetic patients are preceded by ulcers that fail to heal. Factors that

affect development and healing of diabetic patients ulcers include the degree of metabolic control, the presence of ischemia or infection, and continuing trauma caused by plantar pressure or the wrong choice of shoes. In addition, diabetic ulcers are frequently associated with morbidity, pain, and decreased quality of life in affected patients. Diabetic ulcers are initially a small vessel disease, which interferes with peripheral circulation leading to hypoxia of the tissue, which may result in ulceration after minor or major trauma. Peripheral gangrene may occur as a large single ulcer characteristically situated at the side or at the back of the ankle due to

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atherosclerosis. Peripheral neuropathy may coexist, with cold, swollen, and dry feet. An understanding of the processes that precipitate and propagate ulcers in diabetic patients should dictate a rational approach to therapy. Ischemic cardiopathy is a disease determined by a low blood supply to the heart by obstruction or narrowing of coronaries, which are subject to processes of hardening and fat sediment on the walls, determining atherosclerosis. The myocardial infarction causes the complete closure of the coronary artery, with irreversible tissue damage. Ischemic cardiomyopathy is the most common cause of death in the industrialized countries and medications taken hinder the physiological regeneration of tissues in view of their interactions with blood components. Patients with heart disease frequently develop different grades of congestive heart failure resulting in interstitial edema for altered venous and lymphatic drainage. It is clinically characterized by edema of the lower extremities, often symmetrical, and unilateral or bilateral swelling. It is necessary to exclude other possible causes of edema, such as venous insufficiency, connective tissue laxity, nephropathies, apoplexy, serious liver diseases with hypoproteinemia, and myxedema. Smoking is the most important risk factor in cardiovascular damage,⁷ especially if associated with additional risk factors such as diabetes mellitus, hyperlipidemia, hypertension, hyperhomocysteinemia, family history, and age. Any condition that increases the resistance to blood flow and the shearing force against the vessel walls causes intimal injury. These lesions cause the formation of atheroma (as well as diabetes and homocysteinemia).⁸ What is the mechanism through which smoking damages the arteries is not yet clear, but the metabolites of carbon monoxide and smoke components are probably toxic to the intima. Nicotine, a direct vasoconstrictor, reduces blood flow to distal end. The incidence of limb amputation is ten times higher in patients who continue to smoke after have developed arterial occlusion than in those who quit. It is also known that smoking interferes adversely in the physiological mechanisms of tissue regeneration and healing. Among patients with varicose veins, those with skin changes caused by chronic venous insufficiency and deep vein incompetence are at greatly increased risk of ulceration. However, the risk may also be increased in smoking and obese patients and in those who have restricted ankle movement and reduced calf muscle pump power.⁹

The healing of chronic ulcers needs a multifaceted approach. Every diabetic patient should be adequately controlled by the overall state of health. It is important to create a systematic program evaluation that includes both the general control and topical wound. Today, chronic ulcers can be treated using a wide range of therapeutic methods: traditional, new, and experimental ones, each one with different indications, efficacy, and side effects.

Moreover, ulcer treatment's success depends largely on the detection, treatment, and resolution of predisposing causes. This very debilitating condition, which reduces significantly the quality of life, causes social discomfort and generates considerable costs, not only to the patient, but also to the society.¹⁰

Our study is designed to analyze the results obtained with the use of the system MATRIDERM[®] and the autologous skin graft, in the surgical treatment of loss of substance of different etiopathogenesis.^{11–15}

Case report

The study protocol was approved by the research ethics board of our institution. Patient's anonymity was respected and informed consent was drafted before the surgical procedure and the production of digital images.

A 65-year-old woman was admitted to our department because of a post-traumatic loss of substance due to road accidents, which occurred on 22 December 2010. Clinical examinations show the presence of soft tissue exposure (comprising muscle tendon) of the left knee combined with the fracture of the right fibula, which has been subjected to surgery and reconstruction of muscle tendon.

Physical examination showed no flexion contracture, with a loss of substance of a maximum size of 30 cm in width, 40 cm length, and 0.5 cm depth (Figure 1(a)–(c)).

The wound appeared fibrinous, necrotic, malodorous, and secreting. The patient was affected by diabetes type II, hypertension, and ischemic heart disease. In 2008, she underwent a double bypass surgery and coronary angioplasty (percutaneous transluminal coronary angioplasty (PTCA) + stent on the circumflex artery (CX) and descending artery (DA)) for a myocardial infarction (left ventricular ejection fraction = 40%). She smokes, an average of about 30 cigarettes a day for 50 years. She was subjected to the following therapy: unfractionated heparin (UFH) 4000 IU (insulin), targosid 200 mg/3 mL (teicoplanin antibiotic), nekacin 1000 mg (amikacin antibiotic), and ramipril 5 mg (angiotensin-converting-enzyme (ACE)-inhibitor). She had never been subjected to surgery for the wound.

Initially, the patient was treated with cycles of advanced dressings, with fibrinolytic ointments, hydrocolloid, and subsequently, when the bottom began granulated with fibrinolytic and idrocellulosa, Hydrofibra-Ag, and Ag-alginate, three times a week for 30 days.

Periodically, a swab culture of the wound was performed, which showed the presence of *Citrobacter freundii* and *Corynebacterium striatum* infections. On the basis of the results of the antibiogram, the patient was treated with piperacillin and tazobactam for 15 days.

The echo-color Doppler of lower limb showed medium-to high-grade arteriovenous insufficiency.

In the second step, we decided to treat the ulcer with the MATRIDERM system and auto skin graft (Figure 1(d)–(g)).

We conducted the following preoperative tests, in addition to videat anesthetic:

- Blood tests that showed fasting blood glucose of 110 mg/dL;
- X-ray chest, which showed an accentuation of the plot of the whole field;



Figure 1. (a) Preoperative view after curettage: medial view, (b) preoperative view after curettage: frontal view, (c) preoperative view after curettage: lateral view, (d) intraoperative view: MATRIDERM® application, (e) intraoperative view: medial view, (f) intraoperative view: frontal view, (g) intraoperative view: lateral view, (h) postoperative view at 30 days: medial view, (i) postoperative view at 30 days: frontal view, (j) postoperative view at 30 days: lateral view, and (k) postoperative view at 30 days: donor site.

- Echocardiography (ECG)-cardiology consultation, which showed intermediate cardiac risk.

After surgery, the patient was treated with antibiotics for 7 days. Seven days after the surgical treatment, the skin graft showed an engraftment of 100%.

Materials and methods

MATRIDERM system

MATRIDERM is a single-use three-dimensional matrix composed of native structurally intact collagen fibrils and elastin for supporting dermal regeneration. The collagen is

obtained from bovine dermis and contains the dermal collagen types I, III, and V. The elastin is obtained from bovine nuchal ligament by hydrolysis. MATRIDERM serves as a scaffold in the skin reconstitution and modulates scar tissue formation. Moreover, MATRIDERM has an excellent hemostatic property and thus reduces the risk of split-skin sub-graft hematoma. The non-use of chemical crosslinking of the collagen results in a matrix that is especially biocompatible. In addition, MATRIDERM is a collagen matrix of acellular nature. The collagen serves as a “scaffold” to promote cell growth and vascularization.

MATRIDERM system and autologous skin grafting procedure

With previous asepsis and local anesthesia (1% lidocaine without adrenaline), the ulcer is first surgically debrided, until the wound bed is well perfused. Careful hemostasis is carried out before the application of MATRIDERM. Inadequate control of the bleeding could lead to the separation of the MATRIDERM. MATRIDERM® may be applied using a single-stage or a two-stage procedure, depending on the treatment regimen: in our study, we used the single-stage procedure. MATRIDERM is immediately covered with split skin through the 1-mm thick matrix by diffusion. The patient benefits in particular from the fact that a second operation is not necessary. MATRIDERM is supplied in sterile double-bagged packs, and these may only be opened under sterile conditions. Before use, it must be rehydrated in physiological saline solution. MATRIDERM should be laid on the surface of the water and not immersed to avoid trapped pockets of air (air pockets can hinder the diffusion and thus jeopardize the attached graft). The matrix is ready for use as soon as the appearance of the entire surface has changed from white to translucent. To apply MATRIDERM, it should be cut to the exact size of the ulcer. Our experience shows that skin grafting flourishes better if the two layers overflow approximately to 0.3 cm. We applied the matrix manually, and it is crucial that MATRIDERM is in complete contact with the whole area of the ulcer bed and adheres to it. Air bubbles between the ulcer bed and the matrix should therefore be carefully removed by smoothing them out the margins of the matrix. A split-thickness cutaneous was harvested from an uninvolved area (the inguinal region whenever possible) using a Zimmer dermatome (Zimmer, IN, USA). The split skin is grafted into the ulcer area directly on the top of MATRIDERM; an additional attachment of MATRIDERM with the split skin is achieved by sutures. A slight pricking is recommended to avoid the formation of seromas. To cover the ulcer, we use a nonocclusive silicon film or paraffin gauze. Medication was performed with nonadhering dressings (Adapttec–Johnson and Johnson Wound Management, Ethicon, Somerville, NJ, USA) and gauzes on the affected area. It is recommended to apply a slight pressure to prevent the formation of seromas.

Follow-up evaluation

After 7 days, the medication was removed. Patient was treated with a prophylactic antibiotic (ciprofloxacin 500 mg), twice a day for 1 week starting the day before surgery.

The postoperative follow-up consisted of four visits during the first month—once a week—and two additional visits in the third and the sixth months.

The level of active and passive movement in a single plan was evaluated with the assistance of a physiotherapist in the first and sixth month after surgery.

The presence of infections, inflammation, or any other complication, especially medicines taken and the postoperative pain (evaluated by visual analogical scale), were observed. Images were captured in each control. The postoperative period was regular, and in the short-term postoperative results has been highly satisfactory for both, the surgeon and patient.

Results

Following the first treatment, 7 days after the procedure, we found the reduction of the loss of substance until its complete closure.

The enhancement of cutaneous conditions in addition to the reduction of the pain was a great achievement for the patient, as well as a reduction of wound secretion. The wound's infection was evaluated by a buffer negative confirmation performed every 2 weeks four times. We obtained decrease of limb edema and full functional rehabilitation. The skin appeared renovated, with volume restoration and an improvement of the texture (Figure 1(h)–(k)).

Discussion

Diabetes is a chronic multisystemic disease. People with diabetes have a 12%–25% of risk to develop ulcers. To reduce arteriosclerotic vascular risk in these patients, it is important to maintain good hygiene and good glycemic control, which reduce the incidence of lower limb neuropathy. It is important that the patient is advised to quit smoking, and to submit patients to a proper treatment for hypertension and dyslipidemia and to use anticoagulants in selected patients. It is also important to prevent the infectious complications that may cause sepsis. Deep infections require a rapid aggressive surgical debridement in combination with antibiotic therapy. The choice of antibiotic depends on the results of bacterial culture. It is important to keep in mind that the aim of antibiotic treatment is to cure infection but not to heal the wound, which usually requires a much longer period. The primary principles of wound care include a regular debridement in order to remove necrotic material from the site of the ulcer and application of advanced medications. Alternatively, hyperbaric oxygen therapy is used as adjunctive therapy for ulcers. A series of small studies showed a more rapid healing and reduction of the

amputations in patients treated with hyperbaric oxygen compared with control subjects.¹⁶ The actual consensus recommendation is that hyperbaric oxygen therapy may be useful as adjuvant to standard presidium approach in the treatment of wounds in patients, but this field needs further investigation. Another treatment is the vacuum assisted closure (V.A.C.[®]) therapy. Surgical techniques are possible with grafting or the use of local or remote flaps. An emerging field is regenerative surgery including the use of growth factors (such as those derived from platelets), mesenchymal stem cells derived from adipose tissue, system of monocytes–macrophages of the peripheral blood, and also tissue engineering.

There are many options for the treatment of ulcers in diabetic patients. In the past, in our clinical experience, we have used Integra[®], a temporary dermal substitute. When compared with this dermal substitute, MATRIDERM is better for many reasons:¹⁷ it is composed of native collagen, it does not contain glutaraldehyde (which has no chemical bonds and makes the matrix particularly biocompatible), it allows a one-step procedure, and it is economically advantageous.¹⁸ From a clinical perspective, we found that the benefits of the use of MATRIDERM, with respect to skin graft alone, were as follows: easy integration with the receiving bed, best dermal architecture and flexibility, and a higher wound contraction. MATRIDERM is used for reconstruction of full thickness defects of the skin combined with autologous grafts. The aim of this treatment is to give immediate coverage of the wound, and therefore, it can be well used in chronic ulcer treatment of different etiology.^{11–15}

Conclusion

Frequent causes of failure in the healing of substance loss are diabetes, cardiopathy, and smoke. Our study shows that a combination of MATRIDERM tissue auto graft can be used in order to cover loss of substance with excellent functional and esthetic results. For the success of the operation, it is essential to have an appropriate wound bed preparation. We want to highlight that in patients with severe complications, it is essential to enable a rapid and multidisciplinary approach to reduce comorbidities that can lead to the chronicization of the ulcer. In selected patients, a fast one-step approach, as the procedure described here, seems to be a rapid and effectively therapeutic option, especially in those patients in whom chronic ulcer is the last manifestation of a variety of preexisting medical conditions.

Declaration of conflicting interests

The authors declare that they have no conflicts of interest.

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