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CASE REPORT

When amputation is not the end of the challenge: A successful therapy for osteomyelitis and soft tissue infection in a patient with type 1 diabetes

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ABSTRACT

Infection is a common complication in patients with diabetic foot ulcer, leading to lower extremities amputation and healing failure. In this article, we report the case of a 39-year-old man with diabetes who developed a severe soft tissue infection and osteomyelitis after experiencing a major amputation for wet gangrene of both the foot and the ankle.

INTRODUCTION

Diabetic foot ulcer (DFU) represents the result of several harmful conditions, including peripheral arteriopathy, neuropathy and infection, which might significantly benefit from the coordinated expertise of multiple specialists. Among DFU complications, bone and soft tissues' infections are related to a high risk of lower limb amputation[1]. Furthermore, the infection might hinder the healing process and require prolonged care, if not treated with specific antibiotics for an adequate amount of time[2–4]. The isolation of resistant pathogens, such as methicillin-resistant *Staphylococcus aureus* (MRSA), represents a major health issue and a difficult challenge for clinicians, often associated with a history of previous hospitalization[4]. MRSA infection requires a prolonged parenteral treatment, as it might rapidly spread through fascial planes, determining necrotizing infections and formation of sinus tract wounds[3,5].

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CASE REPORT

This case is about a 39-year-old male patient affected by type 1 diabetes who was admitted to our Division (Division of Endocrinology and Metabolic Diseases at University of Campania Luigi Vanvitelli), Naples, Italy, in September 2020 with a recent history of major amputation carried out below the knee 3 months before. The surgery was required as a consequence of wet gangrene of the right foot and ankle, due to a neuropathic burn injury that was complicated by MRSA infection. Informed consent was obtained from the patient. The Research Ethical Committee of University of Campania Luigi Vanvitelli did not require other specific approval for the publication of case reports.

The patient had poorly controlled diabetes (glycated hemoglobin 8.9% [74 mmol/mol], fasting glucose 256 mg/dL) and positivity to infection/inflammation markers (C-reactive protein 4.16 mg/dL, fibrinogen 735 mg/dL, white blood cells 13.87 × 10^3/μL). The clinical examination of the residual limb showed signs of infection, particularly purulent discharge, and several tunneled wounds confluent into a cavity with exposure of the tibia (Figure 1a). Magnetic resonance imaging confirmed

a wide erosion of the soft tissues with severe inflammation/infection of the tibia (Figure 1b,c,d). The bone biopsy was diagnostic for a MRSA infection. We hence started a specific antibiotic therapy with vancomycin 1,000 mg administered by intravenous infusion twice a day for the first day and then at the dosage of 500 mg twice a day. Furthermore, the limb was daily debrided and medicated, with hydrogen peroxide for the first 4 days, and later with saline solution and sterile dressings.

After 3 weeks, the patient underwent elective surgery, which consisted of the surgical debridement of the bone, aimed at avoiding an additional shortening of the residual limb. Furthermore, the tunneled lesions were filled with Integra Flowable Wound Matrix (Integra LifeScience Corp., Plainsboro, NJ, USA), closed with stitches, and covered with wet gauze and an elastic bandage for compression. During hospitalization, strict glucose monitoring of the patient was carried out to optimize insulin therapy and improve glycemic control.

At hospital discharge, vancomycin administration was suspended and replaced with dalbavancin, which was administered at the dosage of 1,500 mg. A second infusion was practiced after 1 week at the same dosage, to ensure an appropriate duration of targeted antibiotic therapy. After 6 weeks, the residual limb was clinically healed (Figure 2a), and the magnetic resonance imaging showed a significant reduction of the inflammation involving the bone and the soft tissues (Figure 2b,c,d).

DISCUSSION

Diabetes is strictly related to lower extremities complications, which represent a major health issue in terms of mortality, costs and quality of life[6,7]. Clinical trials have shown that chronic hyperglycemia is responsible for healing failure due to the deficiency of fibroblast proliferation and growth factors production, and impaired immune and inflammatory response to infection[6]. Furthermore, patients with DFU have a high risk of recurrence, even after the complete resolution of the wound, which increases over the years[6,7].

In addition to the detrimental effects of hyperglycemia, we should consider that both DFU risk factors and complications, such as infections or the structural alteration of the tissues, might persist after DFU remission[7]. Indeed, osteomyelitis represents a difficult challenge for clinicians, often requiring both medical and surgical approaches[8]. The choice of the procedures and their timing should be established on specific patients' characteristics, considering the most conservative and holistic approach to improve the prognosis[8,9]. In the present patient, the original MRSA infection that contributed to the major amputation was never completely resolved, and the tunneled wounds affecting the residual limb represented the perfect soil for the pathogens' growth and spread. A multidisciplinary and progressive approach was necessary to treat all the factors involved in the healing failure of the DFU and the residual surgical wound.

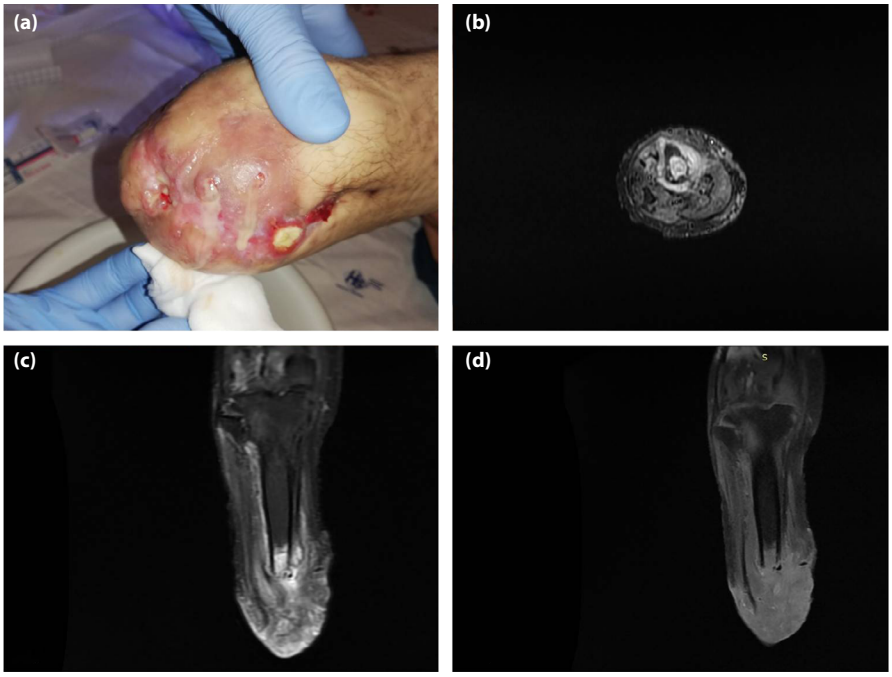

Figure 1 | (a) Clinical signs of infection of the patient's residual limb during hospitalization (phlogosis and purulent discharge after light pressure). (b,c) Hyperintense signal of the tibia and the soft tissues in axial and coronal short tau inversion recovery magnetic resonance imaging sequences. (d) Contrast impregnation of the tibia and the soft tissues in coronal T1-weighted Fat suppressed (FS) sequence after gadolinium administration.

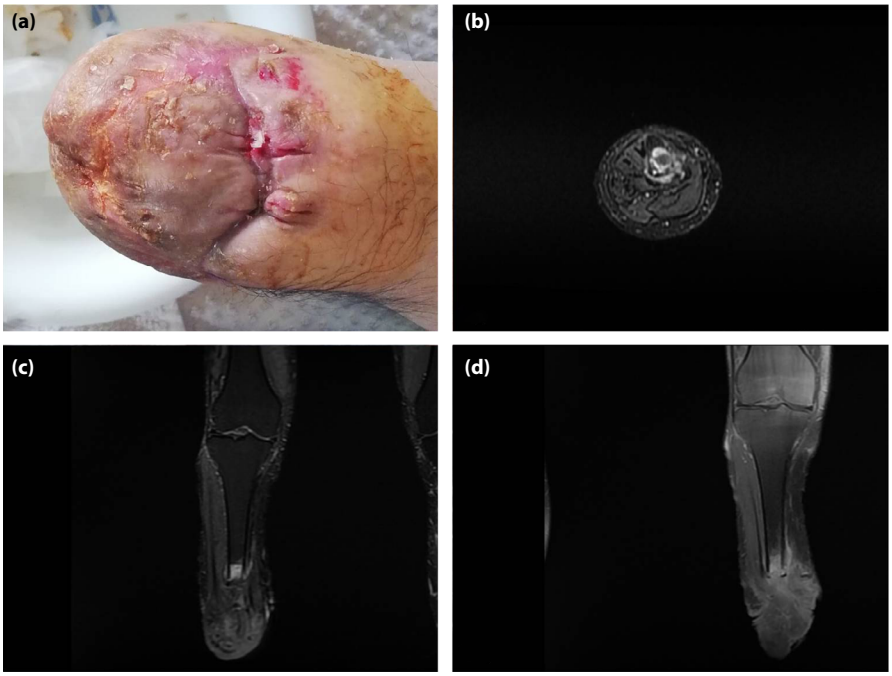

Figure 2 | (a) The residual limb after the removal of the stitches with no signs of phlogosis and purulent discharge. (b,c) Significant volumetric reduction of the hyperintense signal of the tibia and the soft tissues in axial and coronal short tau inversion recovery magnetic resonance imaging sequences. (d) Reduction of the contrast impregnation of the tibia and the soft tissues in coronal T1-weighted FS sequence after gadolinium administration.

After the diagnosis, the first step was to reduce both the infection and the inflammation, as well as to debride the injury bed, promoting the local granulation process. The second step involved the tissue engineering, which offers an important contribution to DFU treatment: the Flowable Wound Matrix is a gel matrix of type I collagen, acting as a tridimensional scaffold well adaptable to irregular wounds. The development and the application of reliable and innovative biomaterials on a thoroughly debrided tissue might provide the stimulus for regeneration and healing[10]. The final step implicated the adequate duration of the antibiotic therapy, according to the Clinical Practice Guidelines for the Diagnosis and Treatment of Diabetic Foot Infections released by Infectious Diseases Society of America[5]. Dalbavancin is a lipoglycopeptide antibiotic, available for intravenous use, with long administration interval and half-life, which acts through the inhibition of polymerization and cross-linkage of peptidoglycan[11]. Dalbavancin is currently indicated for skin and soft tissue infections, although it reaches a good distribution in bone and has been administered successfully in osteomyelitis[12].

In conclusion, this clinical report emphasizes the importance of the multidisciplinary approach in patients with DFU, which might now benefit from several therapeutic tools. These include off-label antibiotic therapy and tissue engineering, supporting traditional surgery and medical care. Dealing with DFU requires a wide knowledge of all therapeutic options to promote the healing process and avoid traumatic surgery. The combined application of the appropriate treatments might be essential to guarantee the best standard of care to our patients.

DISCLOSURE

MG received honoraria for speaking at meetings from Mundi Pharma. KE received honoraria for speaking at meetings from Novartis, Sanofi-Aventis, Lilly, AstraZeneca, Boehringer Ingelheim, Novo Nordisk and Mundi Pharma. The other authors declare no conflict of interest.

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