Original Research

LIMB SALVAGE IN A NON-REVASCULARIZABLE DIABETIC FOOT USING MESENCHYMAL STEM CELLS AND HYPERBARIC OXYGEN THERAPY: A CASE REPORT

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ABSTRACT

Background: Diabetic foot ulcers (DFUs) associated with chronic limb-threatening ischemia (CLTI) significantly increase the risk of major amputation, especially in patients unsuitable for revascularization. In such cases, alternative limb salvage strategies are essential.

Case Presentation: A 75-year-old male with type 2 diabetes mellitus, hypertension, and coronary artery disease presented with a 6-month history of non-healing, infected wounds at the amputation stumps of the left first, second, and third toes. Clinical examination revealed chronic ulceration with poor perfusion. Imaging demonstrated diffuse infrapopliteal arterial disease with poor distal runoff, and the limb was deemed non-revascularizable.

Intervention: The patient underwent staged surgical debridement to remove necrotic tissue and reduce infection. This was followed by a multimodal adjunctive approach including intramuscular administration of allogeneic bone marrow-derived mesenchymal stem cells (MSCs), serial applications of platelet-rich fibrin matrix (PRFM), and 19 sessions of hyperbaric oxygen therapy (HBOT). Supportive management included culture-directed antibiotics, glycaemic optimization, nutritional support, and offloading.

Outcome: The patient showed progressive wound healing with formation of healthy granulation tissue. Complete epithelialization was achieved by 12 weeks, and major limb amputation was avoided. No significant adverse events were observed during treatment or follow-up.

Conclusion: A multidisciplinary approach combining surgical debridement, mesenchymal stem cell (MSC) therapy, platelet-rich fibrin matrix (PRFM), and hyperbaric oxygen therapy (HBOT) may facilitate limb salvage and enhance wound healing in selected patients with non-revascularize diabetic foot ulcers. Mesenchymal stem cells, through their angiogenic, immunomodulatory, and regenerative properties, may play a significant role in improving tissue repair and avoiding major amputation in complex ischemic diabetic foot wounds. Further studies are required to validate efficacy and establish standardized treatment protocols.

Keywords: Diabetic Foot Ulcer, Chronic Limb-Threatening Ischemia, Limb Salvage, Mesenchymal Stem Cells, Hyperbaric Oxygen Therapy, Platelet-Rich Fibrin.

INTRODUCTION

Diabetic foot ulcers (DFUs) are a major complication of diabetes mellitus and a leading cause of lower-limb amputation worldwide [1]. The coexistence of peripheral arterial disease (PAD), particularly chronic limb-threatening ischemia (CLTI), significantly worsens prognosis by impairing tissue perfusion, delaying wound healing, and increasing the risk of infection and tissue necrosis [2].

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Revascularization remains the cornerstone of management for ischemic DFUs, as restoration of blood flow improves limb salvage rates [3]. However, a subset of patients presents with extensive distal arterial disease, poor distal runoff, or unfavourable anatomy, making revascularization technically unfeasible [4]. These non-revascularizable cases represent a significant therapeutic challenge and are associated with high rates of major amputation [5].

In such patients, management is focused on limb salvage through a multidisciplinary approach that includes surgical debridement, infection control, optimization of glycaemic status, and pressure offloading [6]. Despite these measures, outcomes are often suboptimal due to persistent ischemia and impaired tissue regeneration [7].

Recent advances in adjunctive therapies have shown promise in addressing these limitations. Mesenchymal stem cell (MSC) therapy has been investigated for its potential to promote angiogenesis and modulate inflammation [8,9]. Platelet-rich fibrin matrix (PRFM) provides a scaffold rich in growth factors that support tissue repair [10], while hyperbaric oxygen therapy (HBOT) enhances tissue oxygenation and improves host immune response [11,12].

This case report highlights the role of a combined multimodal approach integrating surgical, regenerative, and oxygen-based therapies in achieving limb salvage in a patient with a non-revascularizable diabetic foot [13–15].

CASE PRESENTATION

A 75-year-old male with a known history of long-standing type 2 diabetes mellitus, hypertension, and coronary artery disease presented with a 6-month history of non-healing wounds over the amputation stumps of the left first, second, and third toes. The patient reported intermittent purulent discharge, localized pain, and progressive difficulty in ambulation despite prior conservative treatment. He also had a significant past history of contralateral below-knee amputation, indicating advanced peripheral vascular disease.

On clinical examination, the distal left forefoot demonstrated chronic ulceration at the digital amputation sites, characterized by macerated margins and seropurulent discharge. There was no clinical evidence of proximal spread of infection such as cellulitis or deep abscess formation. Peripheral vascular assessment revealed diminished dorsalis pedis and posterior tibial pulses, with delayed capillary refill, suggestive of compromised distal perfusion. Handheld Doppler examination showed monophasic waveforms in the infrapopliteal vessels, consistent with severe peripheral arterial disease.

Laboratory investigations on admission revealed Leukocytosis (white blood cell count 12,860/µL), indicating active infection, along with anemia (hemoglobin 10.4 g/dL). Glycaemic control was moderately maintained, with a glycated hemoglobin (HbA1c) level of 7.0%. Wound swab and intraoperative tissue samples were obtained for microbiological evaluation to guide targeted antimicrobial therapy.

Computed tomography peripheral angiography demonstrated diffuse infrapopliteal atherosclerotic disease with long-segment narrowing of the anterior tibial, posterior tibial, and peroneal arteries, along with poor distal runoff. These findings indicated advanced peripheral arterial disease with limited options for distal revascularization. Following multidisciplinary evaluation by the vascular surgery team, the limb was classified as non-revascularize chronic limb-threatening ischemia based on anatomical and technical considerations.

Microbiological cultures revealed heavy growth of *Klebsiella pneumoniae*, which was resistant to ampicillin and first-generation cephalosporins but sensitive to carbapenems and selected fluoroquinolones. Accordingly, antibiotic therapy was tailored to sensitivity results.

Overall, the clinical presentation was consistent with an infected, ischemic, non-healing diabetic foot ulcer in the setting of non-revascularize chronic limb-threatening ischemia, placing the patient at high risk for major limb amputation.

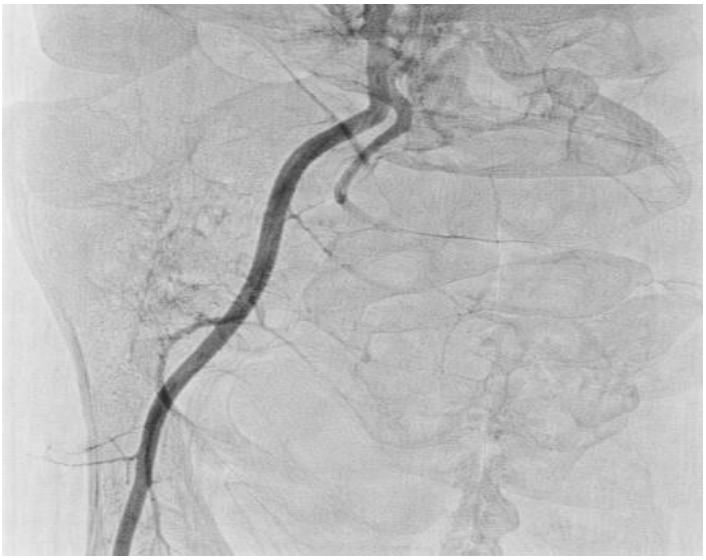

Figure 1: Digital Subtraction Angiography Demonstrating Severe Infrapopliteal Arterial Disease with Marked Luminal Narrowing Of the Tibial Vessels and Poor Distal Runoff, Consistent With Advanced Peripheral Arterial Disease

Figure 1 Notes: The angiographic image shows diffuse atherosclerotic involvement of the anterior and posterior tibial arteries with reduced contrast opacification distally, indicating compromised blood flow. These findings support the diagnosis of non-revascularizable chronic limb-threatening ischemia**.**

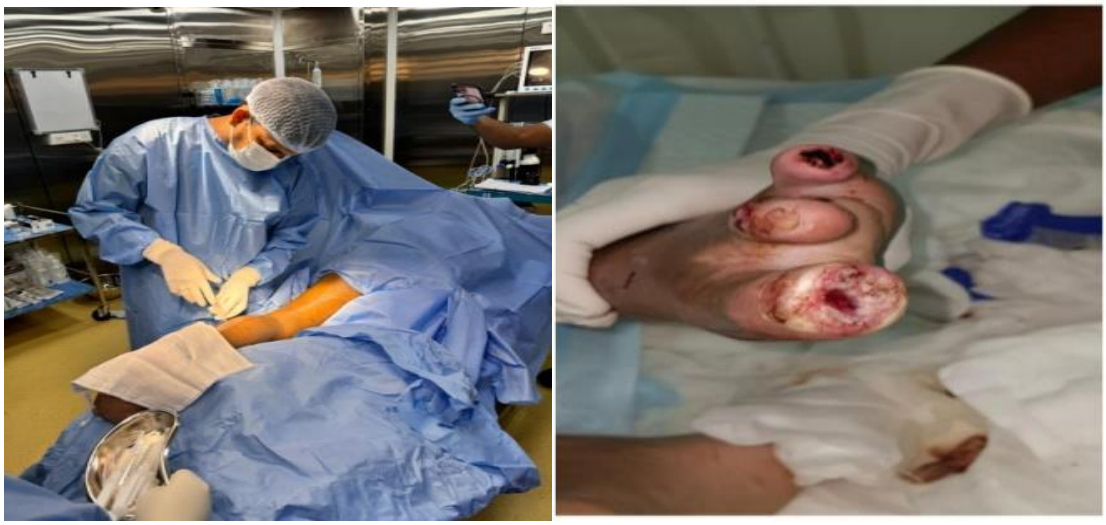

Figure 2: Preoperative Close-Up View of the Forefoot Demonstrating Multiple Infected, Non-Healing Wounds at the Digital Amputation Sites Prior To Surgical Intervention.

Notes: The image shows ulcerated amputation stumps with surrounding maceration, seropurulent discharge, and inflamed margins, consistent with an infected ischemic diabetic foot ulcer.

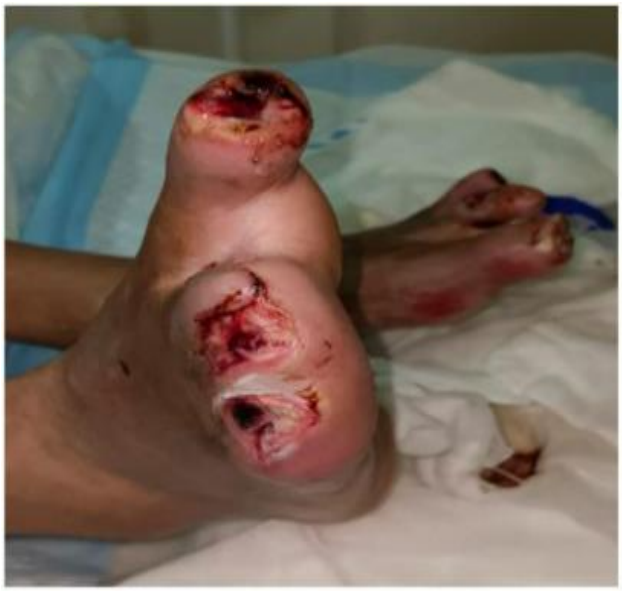

Figure 3: Preoperative Plantar View of the Foot Demonstrating Ulcerated Amputation Stumps With Necrotic Tissue and Surrounding Inflammation

Notes: The image highlights areas of tissue necrosis with inflamed margins and surrounding soft tissue involvement, consistent with an infected ischemic diabetic foot ulcer prior to surgical debridement.

INTERVENTION

A multidisciplinary limb-salvage strategy was undertaken in a staged manner to control infection, promote tissue regeneration, and avoid major amputation.

1. Surgical Debridement

The patient initially underwent staged surgical debridement under regional anesthesia. All necrotic, infected, and non-viable soft tissue was meticulously excised until healthy bleeding margins were achieved while preserving viable surrounding structures. The procedure was performed to reduce bacterial burden, control local infection, and optimize the wound bed for subsequent regenerative therapies. Deep tissue and bone samples were

obtained intraoperatively for microbiological evaluation and assessment of underlying osteomyelitis.

2. Mesenchymal Stem Cell Therapy

Following adequate wound bed preparation, allogeneic bone marrow–derived mesenchymal stem cells (MSCs) were administered via intramuscular injections into the ipsilateral calf musculature. The therapy was aimed at promoting angiogenesis, improving microvascular circulation, modulating inflammation, and enhancing tissue regeneration in the ischemic limb. MSC therapy was considered particularly beneficial in this patient due to the absence of feasible revascularization options and the high risk of major limb amputation.

3. Platelet-Rich Fibrin Matrix (PRFM)

Platelet-rich fibrin matrix (PRFM) was prepared and serially applied to the wound bed at two-week intervals on four occasions. PRFM served as a biologically active scaffold enriched with growth factors that promoted cellular proliferation, angiogenesis, granulation tissue formation, and extracellular matrix deposition. The therapy contributed to enhancement of wound healing and progressive reduction in ulcer size and local inflammation.

4. Hyperbaric Oxygen Therapy (HBOT)

The patient underwent a total of 19 sessions of hyperbaric oxygen therapy (HBOT), with each session lasting approximately 90–120 minutes at therapeutic pressures. HBOT was administered to enhance tissue oxygenation in the ischemic limb, improve leukocyte-mediated bacterial killing, stimulate neovascularization, and accelerate wound healing. The therapy also contributed to reduction of edema, improved infection control, and overall enhancement of tissue repair in the non-healing diabetic foot ulcer.

5. Supportive Care

Comprehensive supportive care was provided throughout the treatment course, including culture-directed systemic antibiotic therapy, optimization of glycaemic control, nutritional supplementation, analgesia, and strict pressure offloading. Regular wound assessment and dressing changes were performed to maintain a healthy wound environment and monitor healing progression. Management was coordinated through a multidisciplinary team involving podiatry, vascular surgery, infectious disease, and endocrinology specialists to maximize the likelihood of successful limb salvage and prevent recurrence.

TIMELINE

Time Point	Clinical Events
6 months before presentation	Development of non-healing wounds at the amputation stumps of the left first, second, and third toes, associated with pain and intermittent purulent discharge.
At presentation	Clinical examination revealed chronic infected ulcers with poor distal perfusion. Laboratory investigations showed Leukocytosis and anemia.
Initial evaluation	CT peripheral angiography demonstrated diffuse infrapopliteal arterial disease with poor distal runoff. Limb classified as non-revascularize CLTI.
Week 0	Staged surgical debridement performed; tissue samples obtained. Culture grew *Klebsiella pneumoniae* and antibiotic therapy was tailored.
Weeks 1–2	Initiation of adjunctive therapies including intramuscular mesenchymal stem cell (MSC) injections and first application of platelet-rich fibrin matrix (PRFM).
Weeks 2–8	Serial PRFM applications at two-week intervals. Hyperbaric oxygen therapy (HBOT) initiated and continued (total 19 sessions).
Weeks 4–10	Progressive wound healing with reduction in discharge, development of granulation tissue, and decrease in ulcer size.
Week 12	Complete epithelialization achieved; no complications observed.
Follow-up	Continued multidisciplinary care with no recurrence of ulceration and successful avoidance of major amputation.

Outcome and Follow-Up

The patient tolerated all interventions without perioperative complications or adverse events related to mesenchymal stem cell therapy or hyperbaric oxygen therapy. Over the course of treatment, there was a gradual reduction in local pain, wound discharge, and surrounding inflammation. Serial clinical assessments demonstrated progressive improvement in the wound bed, with the formation of healthy granulation tissue and reduction in ulcer dimensions. By the end of the treatment period, there was clear evidence of infection control, supported by clinical resolution of purulence and favorable response to culture-directed antibiotic therapy. The patient was able to transition to protected weight-bearing with

improved ambulatory capacity and reduced discomfort.

Complete epithelialization of the wound was achieved approximately 12 weeks after initiation of the multimodal therapy. No signs of recurrent infection, tissue necrosis, or wound breakdown were observed during follow-up. Importantly, major limb amputation was successfully avoided in this high-risk, non-revascularize patient.

At subsequent follow-up visits, the patient remained clinically stable, with intact skin coverage and no evidence of ulcer recurrence. Long-term management included regular wound surveillance, strict glycaemic control, optimization of cardiovascular risk factors, and customized footwear with pressure offloading to prevent recurrence.

This favorable outcome highlights the potential benefit of a combined surgical and regenerative approach in achieving durable limb salvage in complex ischemic diabetic foot ulcers.

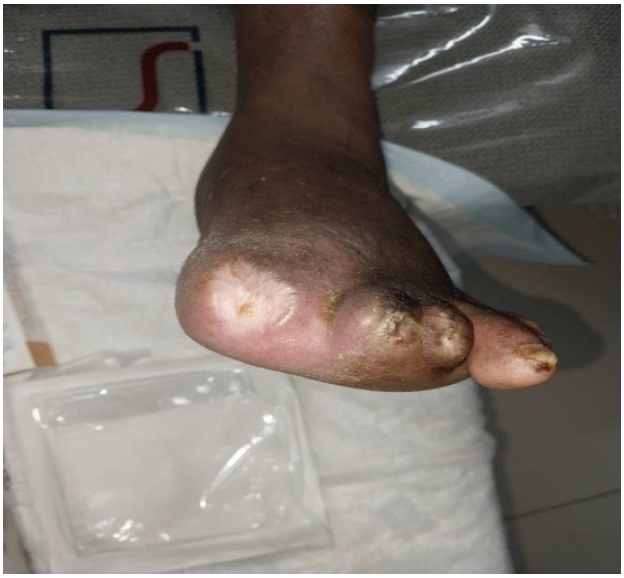

Figure 4: Follow-Up Photograph at 12 Weeks Postoperatively Demonstrating Complete Epithelialization of the Wound Following Multimodal Treatment.

Notes: The image shows intact skin coverage with resolution of infection and absence of necrotic tissue. The favorable outcome reflects progressive healing achieved through serial wound care, including debridement, offloading, and adjunctive therapies.

DISCUSSION

This case highlights the challenges associated with managing diabetic foot ulcers (DFUs) complicated by chronic limb-threatening ischemia (CLTI) in patients who are not candidates for revascularization. Such cases are associated with poor healing outcomes and a high risk of major amputation due to persistent ischemia, infection, and impaired tissue regeneration [2,3].

Surgical debridement remains the cornerstone of management, as it removes necrotic tissue, reduces bacterial load, and prepares the wound bed for healing [4]. However, in the presence of severe ischemia, conventional measures alone are often insufficient. Therefore, adjunctive therapies that target the underlying pathophysiological barriers to healing are increasingly being explored [14].

Mesenchymal stem cells (MSCs) have shown promise in the management of ischemic wounds due to their ability to promote angiogenesis, modulate inflammation, and enhance tissue repair [5,6]. Similarly, platelet-rich fibrin matrix (PRFM) provides a scaffold enriched with growth factors that supports cellular proliferation and extracellular matrix formation [8]. Hyperbaric oxygen therapy (HBOT) further complements these modalities by increasing tissue oxygen tension, improving leukocyte function, and enhancing antimicrobial activity [7,9,15].

In the present case, the combination of surgical debridement with MSC therapy, PRFM application, and HBOT resulted in progressive wound healing and complete epithelialization within 12 weeks, despite the absence of revascularization options. This suggests a potential synergistic effect of these therapies in addressing multiple barriers to healing, including hypoxia, impaired angiogenesis, and chronic inflammation [5,7].

However, this report has several limitations. As a single case, the findings cannot be generalized, and the relative contribution of each intervention cannot be determined. Additionally, standardized protocols for MSC therapy and HBOT in DFUs are not yet well established, and long-term outcomes remain uncertain [6,7].

Despite these limitations, this case supports the role of a multidisciplinary and multimodal approach in

selected patients with non-revascularizable DFUs. Further prospective studies and controlled trials are required to evaluate the efficacy, safety, and cost-effectiveness of these combined therapies and to establish standardized treatment guidelines [3,14].

CONCLUSION

This case demonstrates that limb salvage is achievable in selected patients with non-revascularize diabetic foot ulcers through a comprehensive, multidisciplinary approach. The combination of staged surgical debridement with adjunctive regenerative therapies, including mesenchymal stem cells and platelet-rich fibrin matrix, along with hyperbaric oxygen therapy, may enhance wound healing by addressing key pathophysiological factors such as ischemia, infection, and impaired tissue regeneration.

The favorable outcome observed in this patient, including complete wound epithelialization and avoidance of major amputation, highlights the potential synergistic role of these modalities in complex ischemic wounds where conventional revascularization is not feasible.

However, given the limitations of a single-case report, further prospective studies and controlled trials are necessary to validate the efficacy, safety, and cost-effectiveness of such combined therapeutic strategies and to establish standardized treatment protocols.

Patient Perspective

The patient reported marked reduction in pain and wound discharge following treatment. He expressed satisfaction with limb preservation, especially given his prior amputation on the opposite side. He noted improved mobility and ability to perform daily activities. The patient remains compliant with follow-up and preventive care.

Informed Consent

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. The patient was assured that all personal identifiers would be kept confidential.

Ethical Approval

This case report was conducted in accordance with the ethical standards of the institutional and national research committee and with the Declaration of Helsinki. Formal ethical approval was not required as this is a single case report with informed consent obtained from the patient.

Conflict of Interest

The authors declare that they have no conflicts of interest regarding the publication of this case report.

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