Peripheral blood mononuclear cells enhance sacral wound healing in a patient with spinal cord injury: a case report

Le cellule mononucleari del sangue periferico migliorano la guarigione della ferita sacrale in un paziente con lesione al midollo spinale: un caso clinico

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ABSTRACT

Pressure ulcers are one of the biggest problems in people with Spinal Cord Injury (SCI); this could affect both acute patients and people with chronic SCI, and in the same way bed-ridden patients and people with greater autonomy due to friction and shear mechanisms they are subjected during wheelchair bed transfers. The occurrence of a pressure injury also limits the rehabilitation potential and functional self-recovery. In this case, we reported the story of a 50-year-old man with paraplegia who developed a sacral pressure ulcer in the first days after SCI. Despite the many types of advanced dressings used, the efforts made, the care in positioning, we were unable to close the wound for 5 months. According to plastic surgeons, we decided to use autologous Peripheral Blood Mononuclear Cells (PBMNC) injections to accelerate the process of healing and in a few weeks it led to the complete closure of the sacral wound. PBMNC could be an interesting tool to reduce closing times in addition to advanced dressing; it could be used both in patients during the first period of rehabilitation after SCI and in out-patient settings.

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Introduction

Pressure Ulcers (PU) are chronic wounds associated with significant morbidity and are a substantial burden to the healthcare system affecting 6–18% of hospitalized patients, with significantly higher prevalence in chronically ill or bedridden individuals, such as patients in the intensive care unit or those with spinal cord injury.[1] Patients who develop pressure ulcers have significant prolonged hospital stays and increased risk of infection.[2]

Increasing scientific evidence suggests that autologous Peripheral Blood Mononuclear Cells (PBMNCs), consisting in monocytes/macrophages and lymphocyte, play a key role in tissue regeneration because of their dual ability: high angiogenic and immuno- modulatory capacity, actually this cell concentrate may represent a treatment for complex pressure ulcers. In a clinically relevant murine model study of ischemia-reperfusion-induced PU showed for the first time, that induced M2-like macrophage polarization is a promising strategy to protect against PU formation and promote PU repair.[3]

The mechanism of action of PBMNCs is based on the induction of therapeutic angiogenesis with collateral vessel formation through the paracrine activities of growth factors, cytokines, messenger molecules, and exosomes.[2,4-6] PBMNCs play a key role in tissue regeneration in persistent trophic lesions through their ability to shift inflammatory macrophage M1 to the M2 regenerative phenotype.[6,7] It has also been shown that

some subpopulations of lymphocytes T (Th1, Th2, Tregs) are able to activate macrophage polarization and exhibit flexibility and plasticity never observed.[8-10]

Already Danon *et al.* in 1989 published in PNAS that local injections of macrophages into experimentally induced ulcers in old mice accelerates healing to levels almost comparable to that which occurs physiologically in young animals.[11]

Zuloff-Shani *et al.* publishes data on more than 1000 patients with refractory ulcers treated with allogeneic macrophages showing that the use of a macrophage suspension is a safe and effective therapeutic strategy that shortens the healing period, reduces the risk of complications and morbidity, and improves the quality of life of patients.[12] Moreover, a controlled clinical trial on the efficacy of macrophage injection in stage III-IV pressure ulcers versus control group (standard care) on 100 consecutive patients with a total of 216 pressure ulcers showed that the rate of completely healed wounds was significantly higher ($p<0.001$) in all patients treated with macrophages than in the group treated with standard therapy.[13] Rigato *et al.* in an extensive meta-analysis, showed that autologous PBMNC were effective in significantly reducing amputations in critical limb ischemia patients.[14]

Spinal Cord Injury (SCI) results in motor paralysis and sensory loss that places individuals at particularly high risk of pressure injuries. Multiple comorbidities associated with autonomic, cardiovascular, pulmonary, endocrine, gastrointestinal, genitourinary, neurological, and musculoskeletal dysfunction makes it even more likely that pressure injuries will occur.[18]

While early education about pressure-injury prevention, including appropriate support surfaces, wheelchair and seating systems, frequent repositioning, optimal transfer techniques, nutrition, physical activity, weight management, and smoking cessation may provide the best strategy for pressure-injury treatment in the form of prophylaxis,[19,20] once a pressure injury occurs, early wound care is essential to promote timely wound-healing.[21]

Management requires multidisciplinary intervention to determine and fix the cause of the pressure injury, optimize psychosocial support, provide complete pressure relief of the wound, optimize nutrition, minimize wound bioburden, optimize support surfaces and wheelchair seating systems, eradicate infections, and if necessary, provide surgical intervention.[18]

Case Report

In April 2022, a 50 years old man had onset of paraplegia with absence of sphincter control, neurogenic bladder and bowel.

He immediately underwent a surgical dorsal decompression with a corpectomy and placement of titanium mesh at the level of D6-D7 with thoracic access.

During the procedure was revealed the presence of spondylodiscitis with pulmonary abscess, so the abscess was cleared and the spondylodiscitis curettage, followed by placement of interbody mesh. Another surgical procedure was performed after a week with posterior stabilisation of D4-D5 and D8-D9.

In May 2022 he was transferred to Rome Spinal Unit with a diagnosis of non-traumatic spinal cord injury due to spondylodiscitis.

He was assessed with the International Standards for Neurological Classification of Spinal Cord Injuries (ISNCSCI) with a neurological level of D4 and Asia Impairment Scale (AIS) C with an incomplete paraplegia.

On admission to our ward, we found a pressure ulcer lesion in the sacral region.

The lesion presented as an eschar, and he underwent an escharotomy in the following days.

In the following weeks he was treated with advanced dressings of various types: collagenase, greasy gauze dressing, iodoform gauze.

He was submitted to curettage several times, but despite nursing care, the postural changes in bed every 2/3 hours and in a wheelchair, the pressure ulcer didn't show any signs of improvement (Figure 1).

At the end of August, we found a saccate collection 7 cm deep with abundant and purulent discharge under the pressure ulcer, it was washed with Betadine and hydrogen peroxide and dressed in a soft polyurethane foam.

At the end of September, we applied a Negative Pressure Wound Therapy (NPWT) for 3 weeks and we discussed the case with our plastic surgeons who gave the advice to plan PBMNCs for a cycle of three injections approximately every 30 days.

The first injection was made the 19th of October, the second the 14th of November and the last one the 12th of December. The patient was discharged home in January 2023 with a significant reduction of the sacral lesion (Figure 2).

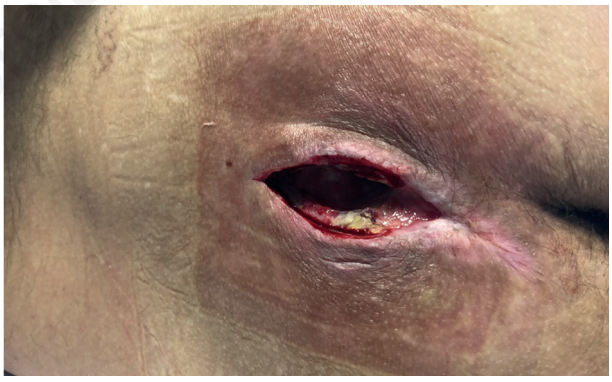

Figure 1. September 2022 before PBMNC injections.

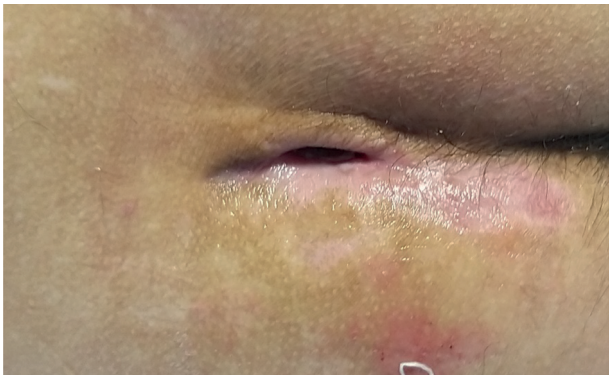

Figure 2. January 2023 after 3 PBMNC injections.

After a month after the last PBMNC implant the sacral lesion was completely healed. After one year the sacral area is still healed, and the patient does not report any skin problems.

Materials and Methods

The concentration of autologous PBMNCs was produced by selective filtration point of care device (MonoCells Solution – Athena Cell Therapies Technology). Briefly, 120 ml of acid-citrate-dextrose (ACD)-anticoagulated peripheral blood was loaded in the upper blood bag, and filtration was performed. The PBMNCs were harvested in 10 ml of sterile saline back flush and immediately implanted using ten 1 ml 21G syringes.

The cell product obtained has been extensively characterized in terms of composition, recovery, and FACS cell population analysi.[15] After appropriate surgical debridement of the wound bed, multiple injections of 10 mL PBMNC cell suspensions (0.2–0.3 mL in boluses) were injected perilesional using a 21 G needle.

All the procedures were performed in the patient room. Cells were implanted at the edge of the wound in equally spaced points, injected using a retrograde technique perilesional and intra-lesional.

Gentle pressure was applied to promote hemostasis for approximately 2 minutes.

The patient underwent three implant procedures, with the second implant occurring 21 days after the first and the third occurring 42 days after the first. A silver alginate dressing was applied during the treatment.

Conclusions

The use of PBMNCs could be a effective therapeutic option in the management of pressure ulcers in patients with SCI.

This procedure could be promoted a resolutive treatment in the indwelling pressure ulcers but we could also consider it as a first option when we don't achieve any improvement in the first period with conservative treatment, anyway we need further studies to identify the perfect timing of treatment.

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