



Treatment with Platelet-Rich Plasma: an Evidence Based Case Report of Leprosy Ulcers

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Abstract

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Background : Leprosy foot ulcers occur in patients with leprosy-related neurological disorders and are classified as grade 2 disabilities. These chronic, non-healing ulcers represent a significant clinical challenge. Platelet rich plasma (PRP) application has emerged as a breakthrough treatment.

Case report : Two females (aged 48 and 58) with multibacillary leprosy presented with chronic midfoot ulcers persisting for 16 and 24 weeks. At baseline, ulcer areas were measured and biopsies were performed to assess TGF- β 1, PDGF, and collagen density. Follow-up measurements for biomarkers occurred on day 13, and ulcer area was reassessed on day 41.

Discussion : Both patients received standard therapy plus PRP, resulting in reduced ulcer area, increased TGF- β 1, and higher collagen density. PDGF levels increased in one patient but decreased in the other. PRP promotes epithelial and endothelial cell proliferation during neovascularization and stimulates extracellular matrix synthesis. Furthermore, it modulates the inflammatory response, facilitating tissue regeneration by balancing the immune system.

Conclusion : Combining standard therapy with PRP shows strong potential for healing chronic leprosy ulcers. Results demonstrated reduced ulcer area, increased TGF- β 1, and improved collagen density, though PDGF levels remained inconsistent

Keywords : platelet rich plasma (PRP), leprosy ulcer, TGF- β 1, PDGF, collagen density.

INTRODUCTION

A leprosy ulcer, traditionally termed a trophic, neuropathic, or perforating plantar ulcer, is clinically defined as a chronic, recurrent ulceration of the anaesthetic foot.¹ Thirty percent of leprosy patients experience peripheral nerve damage and 10–20% of them experience neuropathic ulcers due to peripheral nerve damage.² In clinical cohorts monitored at specialized centers, approximately 36.4% of patients are found to already have established nerve injury at the time of their initial leprosy diagnosis.³ Recent studies have found a prevalence of 60% in regional cohorts (such as Northeast Ethiopia), which closely aligns with other observed rates globally, including 55% in Toronto, 63% in India, and 67% in the United States. Depending on localized endemicity and healthcare infrastructure, rates can range from as low as 13% to 13.8% (as seen in prospective cohorts in Bangladesh and retrospective electronic health records in Colombia) to as high as 97.4% in highly endemic settings like Ecuador.⁴ Chronic wound is defined as the normal wound healing process fails within 46 weeks.⁵ Wound healing may be impaired due to a lack of growth factors and cytokines.⁶ Pathophysiological progression of leprosy ulcers include: the initiating event; neuro-invasion and neural damage (sensory, autonomic, motor neuropathy) occur, followed by mechanical shearing and micro-necrosis, and Charot neuropathy also occurs, followed by chronic inflammation, poor healing and secondary infection.⁷

The management of leprosy ulcers remains controversial, particularly regarding antibiotic use and wound care. Some studies suggest more aggressive antibiotic use, while others recommend a more conservative approach.⁸ Management of leprosy ulcers may consist of topical, physical, offloading, and preventive modalities.⁹

The purpose of this case series report is to present PRP therapy, which has only recently been used in leprosy ulcers with good results.^{10–12} Application of PRP accelerates the healing process by providing a concentrated supply of growth factors and cytokines, resulting in significant improvements in wound size reduction, increased growth factor concentration, and enhanced collagen density.¹³ The specific biological factors that undergo massive local increases, and their direct contributions to accelerating leprosy wound healing include: platelet-derived growth factor (PDGF), transforming growth factor-beta (TGF-beta1 and TGF-beta2), epidermal growth factor (EGF), fibrinogen and adhesive proteins (fibronectin, vitronectin), anti-inflammatory cytokines and anti-infective mediators.¹⁴ To measure the therapeutic superiority or non-inferiority of PRP, clinical studies compare these interventions across several key parameters: wound healing time, ulcer area and volume,^{15,16} growth factor and cytokine increase,

collagen and fibroblast density.¹⁴ Clinical research on PRP therapy has established several key findings: acceleration of wound healing,¹⁰ delivery of concentrated biomolecules, safe and painless profile.¹⁴ Despite highly encouraging case series and pilot studies, critical scientific and clinical gaps prevent PRP from becoming a globally standardized treatment for leprosy ulcers: inconclusive large-scale clinical evidence, lack of standardized preparation protocols, undetermined dosing and delivery regimens, infrastructure barriers in resource-limited settings.¹⁵

CASE PRESENTATIONS

Case 1

A 48-year-old female patient with a history of multibacillary leprosy complained of chronic ulcer on the midfoot of the left sole for 16 weeks. Baseline ulcer area was 3.36 cm² (Figure 1A), a biopsy of the ulcer site revealed transforming growth factor- β 1 (TGF- β 1), platelet derived growth factor (PDGF) levels, and collagen density on baseline were 18.55%, 0%, and 87.1% respectively (Figures 1B, 1C, 1D). On the 41st day after therapy, ulcer area was 2.72 cm² (Figure 1E), TGF- β 1, PDGF levels, and collagen density on day 13 were 41.71%, 7.3%, and 88.16% respectively (Figures 1F, 1G, 1H).

Case 2

A 58-year-old female with a history of multibacillary leprosy complained of chronic ulcer on the midfoot of the left sole for 24 weeks. Baseline ulcer area was 1.37 cm² (Figure 2A), a biopsy of the ulcer site revealed TGF- β 1, PDGF levels, and collagen density on day 0 were 36.90%, 19.38%, and 67.82% respectively (Figures 2B, 2C, and 2D). On the 41st day after therapy ulcer area was 0.76 cm², (Figure 2E), TGF- β 1, PDGF levels, and collagen density on day 13 were 44.34%, 16.62%, and 74.48% respectively (Figures 2F, 2G, and 2H).

Both patients have been given a combination of daily standard therapy; irrigation with sodium chloride (NaCl) solution, ulcer debridement, and use of sterile dressings, topical/systemic antibiotic treatment if needed, and applying PRP; through blood collection and processing by centrifugation, and ready-to-use PRP was administered using aseptic technique, PRP was applied on the ulcer by spreading it and a closed bandage was applied with sterile gauze and pads.¹⁰ The adjuvant therapy was given once a week for 6 weeks (Figure 3).

The result of the therapy revealed in case 1 reduction of ulcer area from baseline was 3.36 cm² (Figure 1A) to 2.72 cm² (Figure 1E) on day 41. Increased TGF- β , PDGF levels, and collagen as well from baseline were 18.55%, 0%, and 87.1% (Figures 1B, 1C, 1D) respectively to 41.71%, 7.3%, and 88.16% (Figures 1F, 1G, 1H)

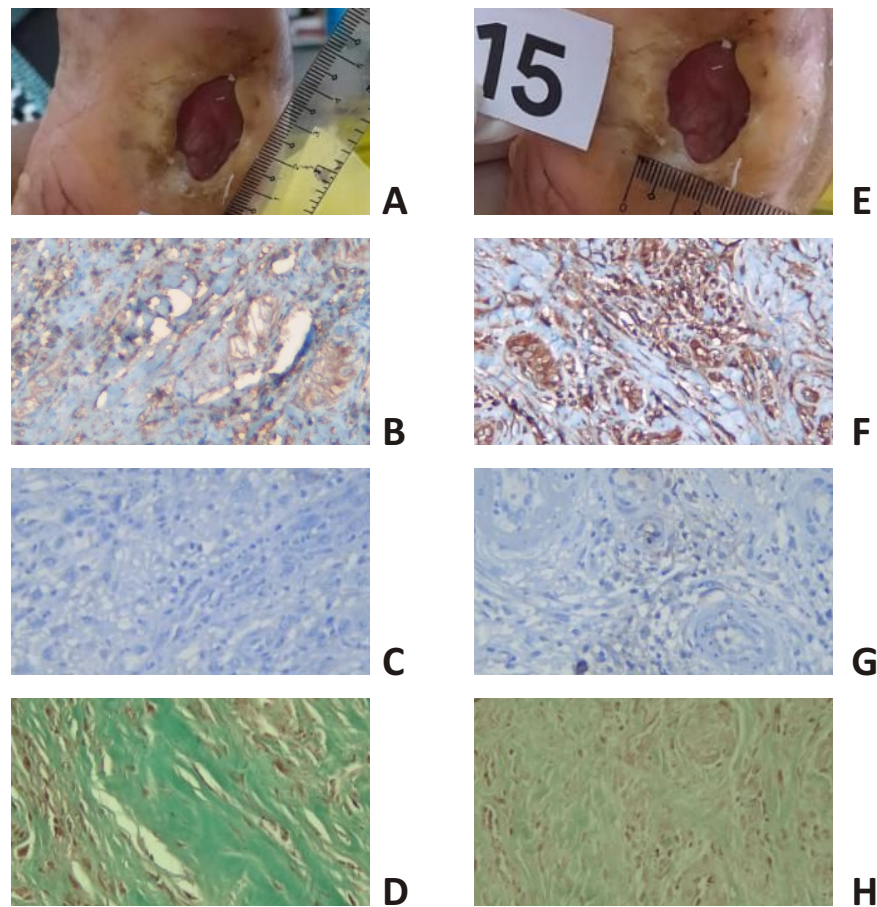


Figure 1.

- | | |
|---|---|
| A. Ulcer area on baseline (3.36 cm ²) | E. Ulcer area on day 41 (2.72 cm ²) |
| B. TGF-β1 on baseline (18.55%) | F. TGF-β1 on day 13 (41.71%) |
| C. PDGF level on baseline (0%) | G. PDGF level day 41 (7.3%) |
| D. Collagen density on baseline (87.1%) | H. Collagen density day 13 (88.16%) |

respectively. The similar result also found in case 2 reduction of ulcer area from baseline was 1.37 (Figure 2A) cm² to 0.76 cm² (Figure 2E) on day 41. There was only an increasing TGF-β1 levels, while PDGF levels decreased and collagen increased from the baseline of 36.90%, 19.38%, and 67.82% (Figures 2B, 2C, and 2D) respectively to 44.34%, 16.62%, and 74.48% (Figures 2F, 2G, 2H) respectively.

The problem faced is a leprosy patient with grade 2 disability, namely chronic plantar ulcers. Will PRP administration accelerate ulcer healing? Can PRP administration reduce wound area, increase TGF-beta and PDGF levels, and collagen density?

The search for evidence is traced through scholarly articles (including systematic reviews, clinical trials, randomized controlled trials, and case reports published in English). Data were searched through PubMed, ResearchGate, Scopus, Proquest, and Google Scholar specifically keywords used Platelet-Rich Plasma (PRP),

autologous blood products (L-PRF), and treatment of leprosy ulcers (trophic ulcers) or related are relatively scarce. There are 9 manuscripts provided (Table 1).

If Platelet-Rich Plasma (PRP), autologous blood products (L-PRF), and treatment of leprosy ulcers (trophic ulcers) used as keywords, there were eight manuscripts, consisting of four cohort studies,^{10,11,17,19} one randomized control trial,¹² two case reports,^{14,20} and one case series¹⁸ (Table 1).

DISCUSSION

World Health Organization (WHO) data, in 2023 at least 182,815 which corresponds to a new case detection rate of 22.7 per million population, 5% higher than new cases in 2022 reported globally, the largest number of new cases 131,425 (71.9%) in the South East Asia region, and grade 2 leprosy lesions of 1.2 per million population, with 9,729 patients reported from 184 countries. In Indonesia,

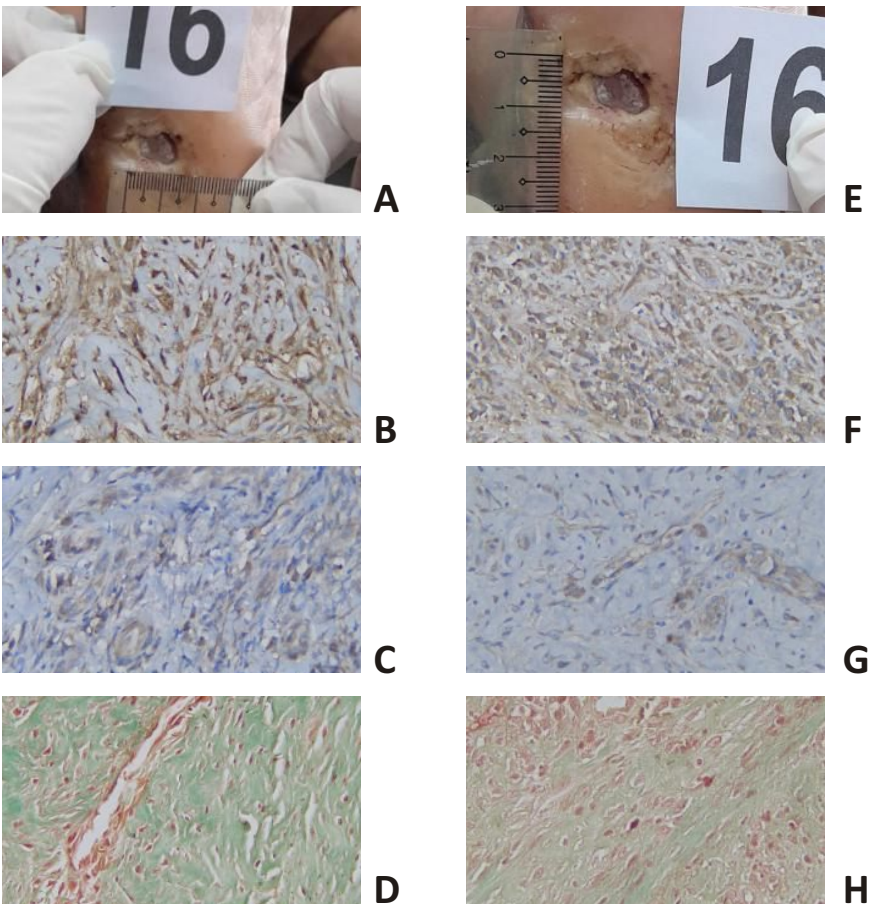


Figure 2.

- A. Ulcer area baseline (1.37 cm²)
- B. TGF-β1 on baseline (36.90%)
- C. PDGF level on baseline (19.38%)
- D. Collagen density baseline (67.82%)
- E. Ulcer area on day 41 (0.76 cm²)
- F. TGF-β1 day 13 (44.34%)
- G. PDGF level day 13 (16.62%)
- H. Collagen density day 13 (74.48%)

Treatment procedure						
Week 1st	Week 2nd	Week 3rd	Week 4th	Week 5th	Week 6th	
Natrium chloride dressing was change everyday						
Day 1	Day 7	Day 14	Day 21	Day 28	Day 36	Day 42
Irrigation with NaCl, administration of PRP	Irrigation with NaCl, administration of PRP	Irrigation with NaCl, administration of PRP	Irrigation with NaCl, administration of PRP	Irrigation with NaCl, administration of PRP	Irrigation with NaCl, administration of PRP	Irrigation with NaCl, administration of PRP
ulcer size			ulcer size			
TGF-β, PDGF levels		TGF-β, PDGF levels				

Figure 3. Treatment Procedure

TABLE 1
Manuscript provided

No.	Keywords: Platelet-Rich Plasma (PRP), autologous blood products (L-PRF), and treatment of leprosy ulcers (trophic ulcers) or related	Keywords: Platelet-Rich Plasma (PRP), autologous blood products (L-PRF), and treatment of leprosy ulcers (trophic ulcers)	Note
1	Anandan V <i>et al.</i> did a study, focus on a study of 50 leprosy patients showing 92% complete healing with autologous PRP over a mean time of 4.38 weeks. ¹⁰	Anandan V <i>et al.</i> did a study, focus on a study of 50 leprosy patients showing 92% complete healing with autologous PRP over a mean time of 4.38 weeks (10).	Cohort study
2	Rather PA, <i>et al.</i> did a study , focus on investigated the efficacy and safety of PRP in a tertiary care setting. ¹⁷	Rather PA, <i>et al.</i> did a study , focus on investigated the efficacy and safety of PRP in a tertiary care setting. ¹⁷	Cohort study
3	Saha S <i>et al.</i> did a study focus on RCT showing PRP + total contact casting (TCC) is more effective than TCC alone (91% reduction in area vs 79%). ¹²	Saha S <i>et al.</i> did a study, focus on RCT showing PRP + total contact casting (TCC) is more effective than TCC alone (91% reduction in area vs 79%). ¹²	Observer-blind randomized controlled study
4	Vendan <i>et al.</i> wrote a case series, focus on prospective study of 11 patients (18 ulcers) showing success with L-PRF, with healing achieved in 4 weeks. ¹⁸	Vendan <i>et al.</i> did a case series, focus on prospective study of 11 patients (18 ulcers) showing success with L-PRF, with healing achieved in 4 weeks. ¹⁸	Case series
5	Conde-Montero E, <i>et al.</i> wrote a case report, focus on a case report highlighting success with intralesional PRP. ¹⁴	Conde-Montero E, <i>et al.</i> wrote a case report, focus on a case report highlighting success with intralesional PRP. ¹⁴	Case report
6	<u>Napit</u> <i>et al.</i> did a study, focus on trial evaluating L-PRF/PRP on leprosy neuropathic foot ulcers, noting that while L-PRF is used in ILC-2022, evidence is still developing. ¹⁹	<u>Napit</u> <i>et al.</i> did a study, focus on trial evaluating L-PRF/PRP on leprosy neuropathic foot ulcers, noting that while L-PRF is used in ILC-2022, evidence is still developing. ¹⁹	Cohort study
7	<u>Napit</u> <i>et al.</i> did a study, focus on trial evaluating L-PRF/PRP on leprosy neuropathic foot ulcers, noting that while L-PRF is used in ILC-2022, evidence is still developing. ¹⁹	<u>Napit</u> <i>et al.</i> did a study, focus on trial evaluating L-PRF/PRP on leprosy neuropathic foot ulcers, noting that while L-PRF is used in ILC-2022, evidence is still developing. ¹⁹	Case report
8	Sari <i>et al.</i> did a study, focus on the effects of platelet rich plasma topical gel on chronic plantar ulcer healing in leprosy patients. ¹¹	Sari <i>et al.</i> did a study, focus on the effects of platelet rich plasma topical gel on chronic plantar ulcer healing in leprosy patients. ¹¹	Cohort study
9	Napit <i>et al.</i> wrote a systematic review focus on systematic review confirming that, although evidence is limited, L-PRF and PRP show potential in treating chronic ulcer. ¹⁵	—	Systematic review

14,376 new cases of leprosy were reported in 2023, ranking 3rd in the world. Approximately 30% of new leprosy patients already have some degree of nerve function impairment when they are first diagnosed. If the disease goes untreated, up to 70% of people with leprosy

can develop nerve function impairment, which is a hallmark of the disease. The vast majority of ulcers in patients with leprosy are a direct consequence of the peripheral nerve damage.²¹ Predisposition to the front of the foot is 79%, the middle of the foot is 7% and the back of

the foot is 14% of plantar ulcers.²² Both patients had leprosy ulcers in the middle of the foot.

The use of PRP for leprosy ulcers (specifically chronic plantar ulcers) is an emerging therapy aimed at overcoming the stagnant healing process caused by neuropathy and poor vascularity. Recommendation of the use of PRP for leprosy ulcer is level B and evidence level is level 2 (2a – 2b). Only eight articles were found regarding PRP and leprosy ulcers, consisting of four cohort studies,^{10,11,17,19} one randomized control trial,¹² two case report,^{14,20} and one case series.¹⁸ The therapy is recommended as an adjunctive treatment (additional to standard care when conventional off-loading and wound dressing fail after 46 weeks.²²

This case series describes the potential of PRP in improving the healing of chronic leprosy ulcers. The observed reduction in ulcer area and elevated level of TGF- β 1 in both patients, but PDGF level increased in 1 patient meanwhile in other patient decreased generally in line with the known mechanism of action of PRP that contains growth factors, namely encouraging the proliferation of epithelial cells, endothelium in the process of neovascularization, and the synthesis of extracellular matrix components, as well as modulating the inflammatory response which tissue repair and regeneration occurs when there is balance and control of the immune system needed to clean debris and pathogens from wounds.^{23,24}

PRP is safe and increases the healing time of chronic wounds.^{10–12,20,24–29} Making PRP requires separating red blood cells and leukocytes. There are no standard guidelines for the making of PRP, single or double centrifugation can be carried out and the length of time and speed of centrifugation can vary.²⁹ There are two variations of PRP that exist, namely: PRP with minimal leukocytes and rich in leukocytes. The centrifugation process allows the extraction of some isolate cells and higher concentrations of growth factors.³⁰ According to the procedure for making PRP it is possible to make various types of PRP such as leukocyte-platelet rich fibrin (L-PRF),¹⁰ platelet-rich fibrin matrix (PRFM).³¹

Both cases obtained reduction of ulcer area similar with almost all other studies or case reports,^{20,26,29} in both cases the location were on midfoot, different with Anandan *et al.*¹⁰ study in which leprosy ulcer patients were more prone on forefoot. PRP administration can stimulate granulation, accelerate wound healing, and reduce hospital stay and morbidity.¹⁰ Sari *et al.*¹¹ gave PRP gel to leprosy ulcers, giving good results in improving wound size, increasing macrophages, neovascularization and granulation tissue.

Transforming growth factor- β 1 (TGF- β 1) regulates cellular processes, differentiation, extracellular matrix formation and immunosuppression.²⁹ TGF- β has 3 isoforms, namely TGF- β 1, TGF- β 2, and TGF- β 3. TGF- β 1 secreted as inactive precursors and activation is

required before binding to the TGF- β 1 receptor. The process of recruiting fibroblasts and immune cells from the circulation and wound edges to the wound area is stimulated by several growth factors such as TGF- β 1, TGF- β 2 and TGF- β 3. Granulation tissue, angiogenesis and collagen synthesis and production will then be formed. Barriers to the formation of matrix metalloproteinases (MMPs) will stimulate the buildup of collagen fibers, the main ones being type I fibroblasts by TGF- β 1. Reduction of TGF- β 1 can explain the failure of healing in chronic wounds and in general can represent a chronic condition.³² Both patients revealed increasing TGF- β 1 level, but based on the available studies, it is more accurate to state that the scientific literature does not show an increase in TGF- β 1 after effective leprosy ulcer treatment.³³ Only one study showed an increase TGF- β 1 in ozone therapy in diabetic foot ulcers,³⁴ more studies needed to determine whether application of PRP can increased TGF- β 1 level.

Cell growth and division are regulated by growth factors, one of which is PDGF. PDGF is a mitogenic agent, it is also a chemoattractant for fibroblasts and smooth muscle cells.³⁵ The presence of neutrophils and monocytes is influenced by PDGF.³⁶ Several cells produce PDGF including smooth muscle cells, activated macrophages, and endothelial cells.³⁷

Platelet-rich plasma (PRP), which is rich in growth factors including PDGF, helps in chronic ulcers. This study has shown that the direct application of PRP leads to accelerated wound healing, increased granulation tissue formation, and faster wound closure in patients with chronic wounds, including those from leprosy and diabetes. This demonstrates that increasing the concentration of PDGF at the wound site is an effective therapeutic strategy.³⁸ Both patients showed different PDGF levels. One patient showed an increase, the other showed a decrease PDGF levels. The scientific literature does not show an increase in PDGF after effective leprosy ulcer treatment, only one study showed an increase PDGF in ozone therapy in diabetic foot ulcers.³⁴

Evaluation of ulcer healing correlates with collagen deposits which can be measured from collagen density, in accordance with the study by Yumun *et al.*³⁹ which showed that combination therapy of hyperbaric oxygen and PRP or separate therapy had an effect on angiogenesis and proliferation of new collagen fibers, also with Duran's study⁴⁰ which found increasing collagen in wound healing proses in rat treated with PRP.

CONCLUSION

The combination of standard and PRP therapies has shown potential in promoting the healing of chronic leprosy ulcer, as revealed reduction in ulcer area can increase TGF- β 1 level, and improved collagen density PDGF level inconsistency result. The findings in both

patients warrant larger randomized clinical trials and longer treatment durations.

CONFLICT OF INTEREST

All authors certify that they have no affiliations with or involvement in any organization or entity with any financial or non-financial interest in the materials discussed in this manuscript.

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