Wound Healing in Stage IV Pressure Injury With Use of Adjunct Autologous Activated Platelet-rich Plasma Therapy: A Case Report

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ABSTRACT

Introduction. Pressure injuries remain a major burden worldwide with associated morbidity and financial implications. Patients in the ICU, such as those with severe COVID-19, are especially susceptible to PI as they remain immobile for extended durations while intubated. **Objective.** This report examines a case of stage 4 PI in a senior COVID-19 survivor treated with adjunct intravenous and intralesional aaPRP therapy in addition to topical hyaluronic acid/silver sulfadiazine cream and framycetin sulphate dressing. **Case Report.** aaPRP therapy was administered via intralesional injection and intravenous infusion 4 times with 2 weeks between therapies, while the aforementioned topical cream and dressing were applied every 2 days between visits. The patient also had controlled diabetes which may affect the wound healing process. **Conclusions.** This report concludes with a discussion of how COVID-19 carries important dynamics in the pathogenesis of PI and how adjunct administration of intravenous and intralesional aaPRP, which is abundant in regenerative proteins, may be beneficial in the management of PI.

Keywords: pressure injury, COVID-19, autologous activated platelet-rich plasma

PI are lesions which are caused by prolonged pressure on a body part. Elderly, multimorbid, immobile, and paraplegic patients are at a higher risk of developing PI.[1] Patients with COVID-19 who also have ARDS are especially susceptible to PI as they remain immobile for extended durations while intubated.[2] aaPRP is an easily accessible biologic adjuvant which promotes wound healing through various bioactive factors.[3,4] This report presents a case of stage 4 PI in which intravenous and intralesional aaPRP was utilized as adjuvant therapy.

CASE REPORT

A 68-year-old male came to the outpatient clinic of Dr. Ramelan Navy Hospital, Surabaya with a gaping wound in the sacral area. The patient also had a comorbidity of type 2 diabetes, which was controlled with oral antidiabetics. He was previously bedridden in the ICU for 2 months due to severe COVID-19 and started to develop an ulcer as a result, despite existing preventive protocols such as the use of a pressure-relieving mattress, bihourly patient repositioning, and application of skin moisturizer at high-risk areas twice daily. He then continued to develop lower extremity weakness, which rendered him to be only passively mobilized by wheelchair.

Upon presentation, the wound was debrided by a general surgeon (**Figure 1**), and a referral to plastic surgery was made. Topical hyaluronic acid 2 mg per silver sulfadiazine 10 mg cream and a framycetin sulphate tulle dressing were applied to the wound.

Abbreviations: aaPRP, autologous activated platelet-rich plasma; ARDS, acute respiratory distress syndrome; ICU, intensive care unit; PI, pressure injury.

Afterward, the patient and his family were informed of adjunct aaPRP therapy. Subsequently, informed consent was gained for aaPRP administration and inclusion to this report. This study was also approved by the institutional review board.

The first dose of aaPRP was administered via intralesional injection and intravenous infusion (day 1). Subsequent aaPRP administration and evaluation were conducted approximately every 2 weeks: day 15 (**Figure 2**), day 30 (**Figure 3**), and day 44 (**Figure 4**). In between treatment visits, the patient's family applied the aforementioned cream and gauze every 2 days.

The aaPRP used was prepared with a protocol that the authors developed. The authors used 24 mL of venous blood and divided it into 8 tubes containing sodium citrate and centrifuged at 1000 rpm for 10 minutes. The separated plasma was subjected to another round of centrifugation at 3000 rpm for 10 minutes. The pellets of platelet were then isolated by discarding the excess platelet-poor plasma until 2.5 mL of plasma remained. The final step of activation, which lyses all possibly remaining thrombocytes, renders the aaPRP safe for intravenous administration.[5] This was achieved by the addition of 0.15 mL of calcium activator (H-Remedy, HayandraLab, Indonesia) to each of the tubes. After the consequent clots were removed, 10 mL of normal saline was added to each of the tubes.

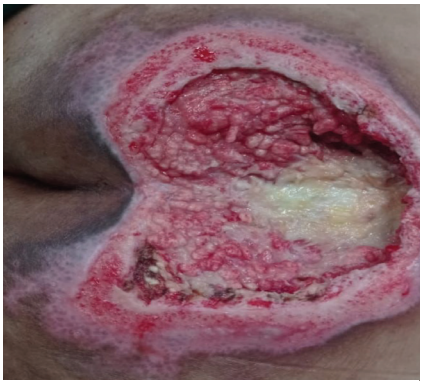

Figure 1. Stage 4 pressure injury in the sacral region after debridement. The wound measured 15×15 cm with observed sacral exposure and marginal epithelialization.

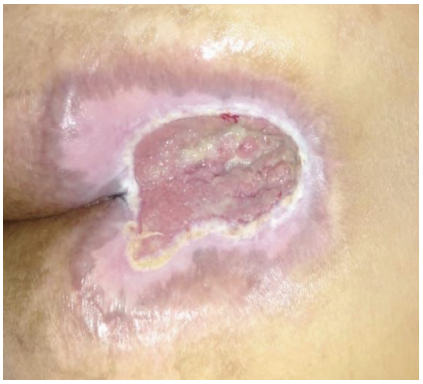

Figure 3. On day 30, the stage 4 pressure injury reduced further to a size of 8×7 cm. Further granulation, light sloughing, and modest exudation continue to be noticed.

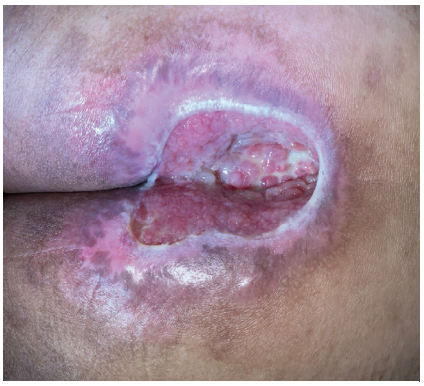

Figure 2. On day 15, the stage 4 pressure injury reduced to a size of 10×7 cm with observed granulation. There was minimal exudation and sloughing. The sacrum is no longer exposed and further epithelialization was noted.

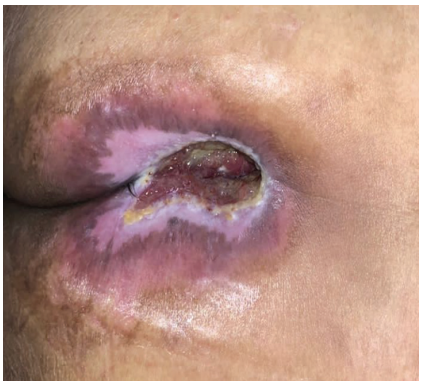

Figure 4. On day 44, the grade 4 pressure injury reduced to a size of 5×3 cm. Minimal sloughing and exudation are observed. The wound continued to heal in an ongoing healthy granulation process.

DISCUSSION

PI remains a major burden worldwide, with an incidence of up to 3 million patients in the United States alone.[6] The treatment of PI is also costly and may be a financial burden to patients. In the United States, treatment of hospital-acquired stage 4 PI and its related complications can cost over $120 000 during one admission. This may also be due in part to the increased length of stay. Conditions prevalent among patients with PI include pain, depression, infection, osteomyelitis, and sepsis.[7]

In this case, the patient was admitted to the ICU during a nationwide surge of COVID-19 cases. While ICU patient protocols do exist, they are difficult to uphold when staff in the ICU are severely shorthanded. Staff shortages may have hindered the ability to moisturize and reposition the patient properly.[8] Various types of pressure-relieving mattresses exist in the market that aim to optimize the distribution of body pressure. However, a 2021 systematic review stated that current evidence is still insufficient to determine the best type of mattress in preventing PI incidence. Nevertheless, the study concluded that alternating pressure (active) air surfaces are more cost-effective than reactive (static) foam surfaces in terms of preventing new PI.[9]

The cytokine storm may be a key player in PI pathogenesis in patients with COVID-19. Heavy systemic inflammation and cardiopulmonary dysfunction may cause local microthrombi in patients. At the same time, proinflammatory cytokines such as interleukin-6 and tumor necrosis factor-alpha from the storm also exacerbate the inflammation and ischemia in the PI-afflicted region.[10] Therefore, simultaneous control of systemic and local inflammation in PI is essential in the management of PI in patients with COVID-19.

The presence of diabetes may also lower wound healing rates due to growth factor deficiency.[11] In the TIMERS model of wound healing, deficiency of growth factors may impede wound edge advancement.[12] Intravenous and intralesional

aaPRP achieves systemic and local inflammation control through various proteins such as interleukin-1 receptor antagonist, vascular endothelial growth factor, platelet-derived growth factor, and epidermal growth factor.[3,4] As such, aaPRP administration also provides much-needed growth factors to the lesion.

Although other groups have previously treated PI with intralesional/intradermal platelet-rich plasma, the current authors believe their group is the first to also administer it intravenously. They have also previously utilized intravenous aaPRP to curb inflammation in patients with severe COVID-19 infection.[13]

Throughout the healing process, no infection was observed in the patient. Besides the application of framycetin, adjunct administration of aaPRP may also play a role in preventing infection as it has been shown to exhibit synergism with antibiotics.[14]

LIMITATIONS

The sole subject reported in this study design translates to a clear weakness. Furthermore, no analysis was conducted in determining the association between the corticosteroid dose nor the frequency of administration with the observed outcome. The optimal dose of aaPRP is also yet to be determined.

CONCLUSIONS

While reports of improved PI healing with platelet-rich plasma are abundant, the current case adds evidence to the existing literature and demonstrates the potential that adjunct systemic and local administration aaPRP has in delivering a highly satisfactory result of PI healing. As prevention is always better than cure, the authors also encourage health care practitioners to take preventive measures with regards to PI. The adjunct administration of aaPRP would not have been optimal without diligent repositioning and meticulous care from the patient's family. The administration of intravenous and intralesional aaPRP in PI patients should be further researched in well-designed clinical trials.

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