Case Report

Infected Nonhealing Wound in a Kidney Transplant Recipient: Successful Treatment With Topical Homologous Platelet-Rich Gel

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Abstract

Impaired would healing is a known adverse effect of chronic immunosuppression. Solid-organ transplant recipients undergoing major abdominal surgery have an increased risk of wound-related complications compared with the general population. In this subset of patients, surgical site infections and wound dehiscence must be aggressively treated to avoid sepsis, graft loss, and death.

Recently, topical application of platelet-rich plasma has been proposed as an alternative therapeutic option to enhance wound healing in difficult cases. Unfortunately, randomized controlled trials evaluating the efficacy of platelet-rich plasma compared with standard or advanced wound management are lacking, and the literature mostly refers to anecdotal reports in patients with no evidence of wound infection.

This report documents a kidney transplant recipient who experienced spontaneous bladder rupture because of gangrenous cystitis. After an exploratory laparotomy and bladder repair, the patient developed a deep surgical site infection by multidrug resistant Acinetobacter baumannii and extensive wound dehiscence. Advanced wound management and vacuum-assisted closure therapy were ineffective. Topical homologous platelet-rich gel was used resulting in significant wound healing, without infections or immunologic complications.

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Introduction

Impaired would healing is a well-known adverse effect of chronic immunosuppression. Solid-organ transplant recipients undergoing major abdominal surgery have an increased risk of wound-related complications compared with the general population.[1] In this subset of patients, surgical site infections and wound dehiscence must be aggressively treated to avoid sepsis, graft, loss, and death.[2]

Recently, topical application of platelet-rich plasma (PRP) has been proposed as an alternative therapy to enhance wound healing in difficult cases. Unfortunately, randomized controlled trials evaluating the efficacy of PRP compared with standard or advanced wound management are still lacking and the current literature mostly refers to anecdotal reports in patients with no evidences of wound infection.[3]

This case report documents a kidney transplant recipient who experienced spontaneous bladder rupture because of gangrenous cystitis. After an exploratory laparotomy and bladder repair, the patient developed a deep surgical site infection by multidrug resistant *Acinetobacter baumannii* and extensive wound dehiscence. Advanced wound management and vacuum-assisted closure therapy were ineffective. Topical homologous platelet-rich gel (PG) was used resulting in significant wound healing, without infections or immunologic complications.

Case Report

A 58-year-old male kidney transplant recipient with chronic cervical and lumbar spondylotic myelopathy was admitted to our institution for elective spinal

decompression in June 2013. Comorbidities included end-stage renal disease of uncertain cause, antiphospholipid syndrome, hypertension, and dyslipidemia. He received his first deceased-donor kidney transplant in 2004 and at the time of hospitalization, was on a triple-agent immunosuppressive regimen (cyclosporine, mycophenolate mofetil, steroids). The main reason for surgical referral was impaired bladder function with urinary retention and recurrent urinary tract infections.

A few hours after admission, he started complaining of severe abdominal pain and suddenly became anuric. On examination, the abdomen was distended and tender, body temperature was 39°C, mean arterial blood pressure was 70 mm Hg, and heart rate was 100 bpm. Urgent blood tests showed neutrophil leukocytosis (white cell count, $12 \times 10^3/mm^3$) and acute kidney injury (serum creatinine, 7.8 mg/dL; potassium, 6.3 mEq/L; pH, 7.35). Fluid resuscitation was promptly initiated, and a bladder catheter inserted, but urinary output did not improve.

An urgent abdomen and pelvis computed tomography scan with intravenous and intravesical dilute contrast was performed. It showed multiple intraabdominal fluid collections and a perforated bladder because of gangrenous cystitis. Cyclosporine and mycophenolate mofetil were stopped, empiric intravenous antibiotic treatment was started, and the patient was brought into the operating suite for surgical exploration. The abdomen was fully inspected, a perivesical purulent collection was evacuated and extensive debridement performed. The bladder was edematous and fragile, with multiple intraparietal abscesses and 4 major perforations at the dome. Lacerations were repaired with 2 layers of polyglycolic acid interrupted sutures, and the peritoneal cavity washed with warm normal saline. After the procedure, the patient's general condition and renal function improved rapidly.

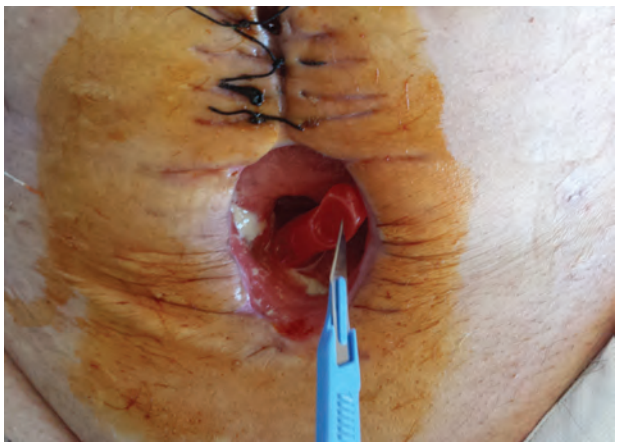
Postoperatively, on day 5, a complete dehiscence of the lower abdominal wall developed with a cloudy exudate. A trial of vacuum-assisted closure therapy was attempted, but it was immediately stopped after recurrent urinary leakage, probably worsened by the application of continuous negative pressure. Nutritional supplementation was administered to boost recovery, and the wound was dressed daily with silver-impregnated alginate. After 30 days, there was little improvement, the urinary leak settled but wound healing remained poor. Surgical site infection by multidrug-resistant Acinetobacter baumannii was detected and a course of intravenous colistin was administered.

After a multidisciplinary meeting, on postoperative day 39, topical treatment with PG was started. Usually, autologous whole blood is used as a source of platelets, but since the patient was frankly anemic and on chronic immunosuppression, homologous platelets were preferred.

Platelet-rich gel was prepared as described. Four hundred fifty mL of whole blood from multiple donors was collected into a triple-bag system (TERUFLEX with CPD/SAGM, Terumo Corp., Rome, Italy). It was fractionated into PRP and packed red blood cells centrifuging the bag at $462 \times g$ for 10 minutes at 22°C (Cryofuge 6000i, Heraeus Instruments, AHSI SpA, Massa Martana, Italy). To obtain a platelet concentrate with a final platelet count of at least $1 \times 10^6 \pm 2 \times 10^5$ platelets/μL, PRP was further centrifuged at $3932 \times g$ for 6 minutes at 22°C. Several tubes (Vacutainer Plus, 367817, Becton Dickinson, Plymouth, UK) were filled with 5 mL of platelet concentrate, and the component mixed with 5 National Institute of Health units of thrombin and 2 mL of calcium gluconate 1:20 (Bioindustria Laboratorio Italiano Medicinali SpA, Novi Ligure, Italy). The mixture was allowed to coagulate for 5 minutes at 37°C and stored at -80°C.

Wound preparation and PG application were performed every 48 hours as follows. A 5-mL tube of frozen PG was collected and allowed to thaw for 15 minutes at room temperature. The wound was

Figure 1. Postoperative Day 39: Baseline



A cylinder of platelet-rich gel is applied to the wound bed (the abdominal wall dehiscence, the rectus sheath and the anterior surface of the bladder can be easily seen at the bottom).

cleaned with normal saline and all debris removed mechanically. When dry, the wound bed was filled with PG and dressed with silver-impregnated alginate (Figure 1).

Wound healing dramatically improved and the infection resolved (Figure 2). Colistin was stopped and from postoperative day 84, the dressing was changed weekly. Twenty-eight days later, the patient was discharged. At that time, the wound was completely healed, skin swabs were negative, and graft function was excellent (Figure 3). Neither adverse events nor acute immunological reactions were observed during the treatment.

Figure 2. (A) Postoperative Day 60. The Abdominal Wall Is Completely Closed and Granulation Tissue Covers the Rectus Sheath; **(B)** Postoperative Day 105. Progressive Re-Epithelialization of the Wound; **(C)** Postoperative Day 131. The Wound Is Completely Healed

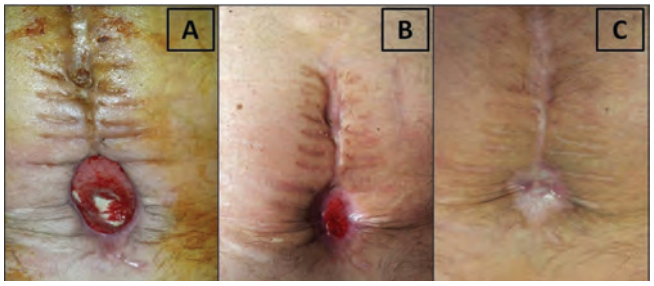
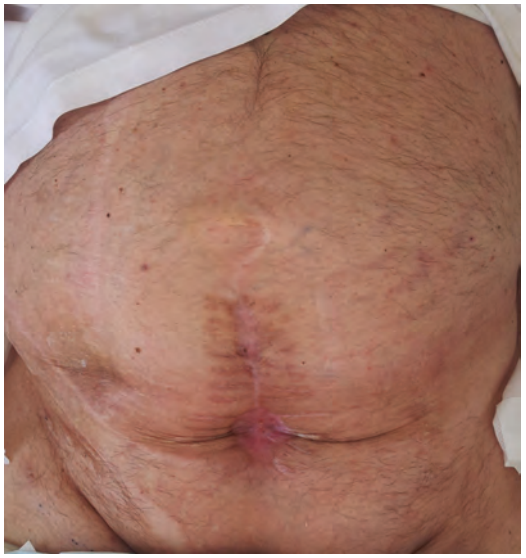


Figure 3. Final Scar Overview



Discussion

It is well accepted that platelets start the wound healing process by releasing locally active growth factors and essential cytokines that attract mesenchymal cells and promote their differentiation and proliferation. In vitro studies demonstrated that PRP triggers the proliferation of endothelial cells and fibroblasts through the release of platelet-derived growth factor, transforming growth factor beta 1, vascular endothelial growth factor, epidermal growth factor,[4] basic fibroblast growth factor, type-1 insulinlike growth factor, and hepatocyte growth factor.[5] Data from histologic examination suggests that platelet derivatives may curb inflammation, reduce matrix metalloproteinase activity, induce neovascularization, and promote granulation tissue formation. Recent findings support the hypothesis that platelets help the immune system fight several pathogens by releasing signaling proteins that attract and activate monocytes and macrophages to the site of injury.[6,7]

Platelet-rich preparations have been proposed as an alternative option to enhance wound healing when other strategies fail, and papers showing encouraging results with the use of PRP and PG are available.[3]

Randomized clinical trials comparing platelet-rich derivatives to standard or advanced wound management are lacking, and to date, there is a paucity of studies that assess the role of PRP and PG in infected wounds.[8] Moreover, most of the data refer only to platelet mixtures obtained from autologous whole blood. Homologous components are deemed less safe owing to the risk of infections, adverse reactions, and sensitization.

To our knowledge, this is the first report describing a kidney transplant recipient with an infected wound dehiscence successfully treated with topical application of homologous PG. Our personal experience suggests that PG can be safely and effectively used to treat difficult and infected wounds in solid-organ transplant recipients on chronic immunosuppression. When autologous whole blood is not available, homologous platelets may be considered as the risk of sensitization or adverse reactions remains extremely low.

This is a single case report that warrants further research on (1) PRP and PG topical application as an additional treatment of surgical site infections in immunocompromised patients; (2) allogenic blood derivatives topical application in high immunologic risk patients; and (3) cost analysis comparing topical platelet-rich derivatives versus advanced wound management versus vacuum-assisted closure system in nonhealing infected wounds.

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