

Use of allogeneic platelet gel in the management of chemotherapy extravasation injuries: a case report

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Abstract: The allogeneic platelet (PLT) gel offers to be a valid supportive measure in the management of chemotherapy extravasation injuries. We report a case of a 58-year-old patient with multiple myeloma enrolled for high-dose chemotherapy and autologous stem cell transplantation. As pretransplant therapy, the patient received induction therapy with bortezomib, adriablastina, and desametasone. A port was inserted in the vein on the back of the hand. After three cycles, the patient reported rapid development of redness, pain, and necrotic tissue in the left hand, and a diagnosis of extravasation was addressed. The patient presented a raw area on the back of the hand caused by cytotoxic/chemotherapeutic drug leakage because of the malposition of venous access devices. Skin ulcer was debrided, and the wound was reconstructed with a combination of local random rotational flap and abdomen skin graft. Two weeks later, a 20% skin flap necrosis was observed. In the context of wound healing, topical plasma-rich PLT gel is able to accelerate the regeneration and repair of tissue, so it was set out to assess PLT gel efficacy in this case. The PLT gel was applied topically once every 5 days, for a duration of 60 days on average. There were no adverse reactions observed during the topical therapy. Complete wound healing was observed after 12 PLT-rich plasma applications. No ulcer recurrence was noted in the patient during the follow-up period of 2–19 months.

Keywords: growth factors, platelet gel, chemotherapy, management, extravasation

Introduction

Extravasation is an important complication in cancer patients under chemotherapy.^{1–4} Currently, chemotherapy extravasation management remains controversial,³ and there is no definitive standard procedure to solve the problem. We report the management of a patient with massive skin necrosis after extravasation of bortezomib, adriablastina, and desametasone. In addition to surgical debridement of necrotic tissue and skin grafting, we used platelet (PLT) gel, rich in growth factors (PDGF, EGF, VEGF, and TGF- α and - β) to stimulate healing of skin ulceration and wound closure.⁵

Case report

A 58-year-old man with multiple myeloma,⁶ Durie–Salmon stage III,⁷ was enrolled for high-dose chemotherapy and autologous stem cell transplantation. As pretransplant therapy, the patient received induction therapy with bortezomib, adriablastina, and desametasone. A port was inserted on the back of the hand. The patient reported rapid development of redness and pain in the left hand, 2 weeks after the completion of the third cycle. The patient presented a raw area on the back of the hand because of leakage of cytotoxic/chemotherapeutic drugs from the malposition of venous access devices. Skin ulcer was debrided, and the wound was reconstructed with local

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Figure 1 Skin lesion after surgical debridement of necrotic tissue.

random rotational flap and abdomen skin graft. Two weeks later, a 20% skin flap necrosis was observed. In the context of wound healing, numerous studies and clinical findings have demonstrated that topical, nontransfusional plasma-rich PLT gel is able to accelerate the regeneration and repair of the tissue, through the action of the various growth factors within the alpha granules of the PLTs.^{8–12} The PLT gel treatment has been used based on biological and clinical results reported in literature. According to the standard current approach,¹³ the lesion management included the surgical removal of necrotic material and cleansing of margins of the wound bed before PLT gel application (Figure 1). After moist saline dressing, the wound was covered with allogeneic platelet-rich plasma (PRP) and fatty gauze. In our case, a blood component (thrombin) was produced from allogeneic whole blood using a “homemade” system.

The PLT gel was prepared the day of the treatment. Samples of whole blood (total 40 mL) were collected in 10-mL acid-citrate-dextrose vacutainers (Becton Dickinson Labware, Franklin Lakes, NJ, USA) from periodic donors. The whole blood was centrifuged at 180 g for 10 minutes to obtain concentrated erythrocytes and PRP. PRP were centrifuged again at 1,800 g for 10 minutes to separate PLT concentrate from PLT-poor plasma.

To activate the PRP homologous and to accelerate the gelling process, thrombin autologous was prepared by adding calcium gluconate to the PLT-poor plasma (ratio 0.2:1 mL). After 15–40 minutes of incubation at 37°C, the product was centrifuged at 1,800 g for 10–15 minutes. One milliliter of thrombin-containing supernatant and 0.50 mL of ionized Ca⁺⁺ were added to the previously separated PRP, in a Petri dish (Falcon, Becton Dickinson Labware), and mixed until a gelatinous mixture was obtained (from 2 minutes to 5 minutes). All the procedure has been performed under a laminar-flow hood (Faster Bio48).

The nonhealing ulcer measured 3×4 cm (Figure 1). Three days after adjusting debridement, the wound was covered with allogeneic PRP (Figure 2A). The PLT gel was applied topically once every 5 days. The healing time was 60 days on average. The wound healed completely after 12 applications (Figure 3). The presence of granulation tissue was observed and recorded by digital photography in the patient after the second application of PLT gel. Figure 1 illustrates the ulcer before the treatment; Figures 2B and 3 show the same lesion, respectively, after 20 days and 60 days. No adverse reactions were observed during the topic therapy. No ulcer recurrence during the follow-up period of 2–19 months in the patient was noted.



Figure 2 (A) First application of platelet gel. **(B)** Skin photograph 20 days after the start of therapy.



Figure 3 The previous ulceration photograph 60 days posttreatment showing complete closure of the lesion and re-epithelialization tissue with no inflammation.

Discussion

Accidental extravasation of chemotherapy into surrounding tissue is a frequent event. Indeed, the phenomenon is estimated at a rate of between 0.1% and 6%.^{14–16} Treatment of extravasations depends on the quantity extravasated, the delay until therapy is started, and the size of the resulting necrotic injury. Historically, a number of local treatments have been used, such as dimethyl sulfoxide^{17,18} cooling and intralesional injection of corticosteroids¹⁹ with either no proven benefit or even detrimental effect. However, if the condition is missed, the consequences may be dramatic, with massive necrosis and ensuing tissue destruction. Here we have described the case of a patient with multiple myeloma and severe skin necrosis induced by chemotherapy, who was treated with PLT gel. PLT gel rapidly repaired the ulceration damage, blocked the progression of lesion, reduced the intensity of pain, and restored the patient's ability to move the hand. Greppi et al demonstrated the efficacy of PLT gel to treat recalcitrant ulcers in geriatric and hypomobile patients with chronic skin ulcers unresponsive to previous treatment with advanced medications.¹³ A meta-analysis review had revealed PRP as an advanced wound therapy in hard-heal acute and chronic wounds, favored significantly for complete healing.^{20,21} This process was regulated by PLTs, not only for their hemostatic function but also for their ability to repair and regenerate damaged tissues.^{22–27} These mechanisms are regulated by cytokines and growth factors released by activated PLTs. The cytokines and growth factors contained within PLT- α granules act via an endocrine, paracrine, and autocrine mechanism, binding to the tyrosine kinase-activated membrane receptors found on the various tissue effectors, thereby regulating chemotaxis, cell proliferation, angiogenesis, and the synthesis and degradation of

extracellular matrix proteins.^{28–30} Although in several clinical studies, topical therapy seems to exhibit no clear adjuvant effect on wound healing,^{31,32} based on our experience we suggest that the use of PLT gel, together with conventional therapies, could be considered as an effective treatment for the management of chemotherapy-induced damage and tissue necrosis in oncologic patients.

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Patient consent

Patient consent was obtained for this study.

Disclosure

The authors declare no conflicts of interest in this work.

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