Platelet-rich plasma as a treatment for lymphoedema

Authors (clockwise from left): *Bachu Abraham, Rabiah Hasan, Syed Ahsan and Muhammad Sharif Kaz Kaz*

Platelet-rich plasma (PRP) is an autologous concentrate enriched in growth factors. Its tissue-repairing effects have made PRP the focus of attention for use in tissue regeneration. PRP has been safely used in many fields, including orthopaedics and sports medicine. In the case examined here, a 67-year-old woman had left shoulder pain after a motor vehicle accident. She had long-standing post left lumpectomy upper-limb swelling due to breast cancer, which had been diagnosed well over a decade before. She developed stage 3 lymphoedema of the left arm and hand, which was refractory to comprehensive decongestive therapy and compression garment therapy. MRI of the left shoulder demonstrated a small partial-thickness tear of the rotator cuff. After failure of initial treatment with physical therapy and corticosteroid injection, she was referred for PRP treatment. Five days after the first PRP injection, the patient reported a complete resolution of lymphoedema in her left hand.

Bachu Abraham *is Director of Rehabilitation Medicine, Michigan Institute of Musculoskeletal Medicine, Michigan, US;* ***Rabiah Hasan*** *is Medical Research Assistant, Detroit Institute of Musculoskeletal Medicine, Michigan, US;* ***Syed Ahsan*** *is Vascular Medicine Specialist, Henry Ford Health System, Michigan, US;* ***Muhammad Sharif Kaz Kaz*** *is Student Research Assistant, Detroit Institute of Musculoskeletal Medicine, Michigan, US*

Platelet-rich plasma (PRP) is an autologous concentrated preparation of human platelets contained in a small volume of plasma that is characterised by haemostatic and tissue-repairing effects. PRP is enriched by various growth factors and its tissue-repairing effects have made it the focus of attention for use in tissue regeneration. PRP has been safely used in many different fields, including orthopaedics, sports medicine and dentistry. Current evidence from *in vitro* and animal studies suggests PRP as potential source to regenerate injured lymphatic vessels to treat or prevent lymphoedema (Akgül et al, 2016).

While performing a PRP injection, the authors noted incidentally that there was improvement of lymphoedema. Based on the findings, the authors undertook a literature survey to identify and explain the association between lymphoedema and PRP.

Case presentation

A 67-year-old woman was seen in a pain management and rehabilitation clinic for left shoulder pain 2 years after a motor vehicle accident. Her medical history included breast cancer diagnosed over a decade ago in her left breast, which was treated with lumpectomy, along with axillary node dissection, radiation and chemotherapy. Post-treatment, she developed stage 3 lymphoedema of the left arm and hand. Her lymphoedema was noted to be refractory to comprehensive decongestive therapy and compression garment therapy.

An MRI of the left shoulder demonstrated a small partial-thickness tear that extended through approximately 50% of the thickness of the rotator cuff. After failure of initial treatment with physical therapy and corticosteroid injection, she was referred for PRP treatment. The course of action is dependant on the severity of injury and it varies from person to person, although quite often the authors begin with conservative care. Five days after the first PRP injection, the patient reported a complete resolution of lymphoedema in her left hand.

Treatment

Approximately 4cc of PRP, which was harvested from the patient's blood, was injected into her supraspinatus interval under fluoroscopy.

Outcome and follow-up

The patient was re-examined 18 months later and continued to report resolution of the left-hand lymphoedema along with improvement in the functional capacity of the left hand.

Figure 1. Post-treatment changes: left forearm versus left hand.

Discussion

Lymphoedema is a common disorder of the lymphatic system, which usually manifests as swelling of the affected region. The lymphatic vessels play a quintessential role in the interstitial fluid homeostasis maintains and immune response.

Anatomical or functional disruption of the lymphatic vessels can result in the progressive accumulation of lymph fluid in the interstitial spaces. Lymphoedema is characterised not only by progressive swelling but also by progressive fibrosis, delayed immune response resulting in recurrent cellulitis and permanent non-pitting oedema (Saito et al, 2013).

Current treatment modalities are divided into medical management and, more recently, microsurgical options. Conservative treatment includes complete decongestive therapy, manual lymphatic drainage, compression therapy, exercise, advanced pneumatic compression therapy, compression garments and skin care; surgical treatments include lymphovenous shunts, vascularised lymph node transplant/transfer, direct excision and liposuction (Kayıran et al, 2017).

Platelets play a fundamental role in coagulation, immune response, angiogenesis and healing. Numerous proteins are contained in the alpha-granules of platelets: platelet-derived growth factor (PDGF), transforming growth factor, platelet factor interleukin, platelet-derived angiogenesis factor (PDAF), vascular endothelial growth factor (VEGF), epidermal growth factor (EGF), insulin-like growth factor IGF and fibronectin (Lubkowska et al, 2012).

PDGF has been shown to have an angiogenic effect due to PDGF receptors being expressed on capillary endothelial cells. It stimulates mitogenicity and chemotaxis of fibroblasts, and smooth muscle cells and chemotaxis of neutrophils and macrophages; hence, it helps in wound healing and improves immune response (Lacci and Dardik, 2010).

Moreover, PDGF has been shown to stimulate production of several matrix molecules, such as fibronectin, collagen, proteoglycans and hyaluronic acid. The production and secretion of collagenase by fibroblasts suggests a role in the remodelling phase of wound healing. Due to the angiogenesis effect and wound healing properties, it has been suggested as a potential treatment option in lymphoedema (Heldin and Westermark, 1999).

VEGFs that stimulate cellular responses by binding to their endothelial tyrosine kinase receptors are important regulators of angiogenesis, in particular, lymphangiogenesis. VEGFR-1 is expressed on haematopoietic stem cells, monocytes and vascular endothelial cells, and is required for the migration of monocytes and macrophages. VEGFR-2 is expressed on vascular endothelial cells and lymphatic endothelial cells, and regulates vascular endothelial function. VEGFR-3 is only expressed on lymphatic endothelial cells and is responsible for lymphatic endothelial cell function. Activation of both VEGFR-2 and VEGFR-3 might be needed for efficient lymphangiogenesis. VEGF-C improves lymphoedema by promoting lymphangiogenesis, stimulating the recanalisation of injured lymphatic vessels, restoring the lymph flow, promoting the organisation of lymphatic endothelial cells into functional lymphatic vessels and ameliorating the pump activity of the collecting lymphatics through the activation of VEGFR-2 and VEGFR- 3 (Akgül et al, 2016).

This effect was studied in a murine tail lymphoedema model. The authors studied the effects of injected PRP and adipose stem cells on angiogenesis (anti-CD31 staining), microcirculation (laser Doppler imaging), lymphangiogenesis (anti-LYVE1 staining), microvascular architecture (corrosion casting) and wound healing (digital planimetry). PRP significantly increased lymphangiogenesis, while the application of adipose stem cells did not induce any significant change (Ackermann et al, 2015).

Conclusion

The effect of PRP on lymphangiogenesis and lymphoedema development represents a promising approach to improving the regeneration of lymphatic vessels, restoring disrupted lymphatic circulation and treating or preventing lymphoedema. In the future, more clinical trials are needed to evaluate the effect of PRP in lymphoedema. WME

Ethical consent

Consent to publish this case report and photo was received from the patient.

Disclosures

None of the authors report a conflict of interest related to this article.

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