Received: 1 July 2019 | Revised: 26 July 2019 | Accepted: 11 August 2019

DOI: 10.1111/dth.13062

THERAPEUTIC HOTLINE: SHORT PAPER

DERMATOLOGIC THERAPY WILEY

Use of injectable platelet-rich fibrin in the treatment of plasma cell mucositis of the oral cavity refractory to corticosteroid therapy: A case report

Roberta Gasparro | Daniela Adamo | Michele Masucci | Gilberto Sammartino | Michele Davide Mignogna

Department of Neuroscience, Reproductive Science and Odontostomatology, University of Naples Federico II, Naples, Italy

Correspondence
Roberta Gasparro, Department of Neuroscience, Reproductive Science and Odontostomatology, University of Naples Federico II, Via Pansini, 5, 80131 Naples, Italy.
Email: roberta.gasparro@unina.it

Abstract

Plasma cell mucositis (PCM) is a rare benign disease affecting adults characterized by an erythematous mucosa, an epithelial hyperplasia, and a dense submucosal infiltration of mainly mature plasma cells. PCM has been treated with topical, intralesional, and systemic corticosteroids, antibiotics, and topical cyclosporin with unreliable results and questionable benefits. Here, we present a case of PCM, refractory to previous treatments, treated with i-PRF (injectable platelet-rich fibrin) injections. The infiltrations were performed once a week for 2 months. There were no adverse reactions to the treatment. The pain gradually reduced until the score of zero at the fourth infiltration, and the patient remained free of pain during the whole study period. Clinically, we did not obtain a complete healing of the lesion, but a reduced perilesional inflammatory infiltrate was observed at a distance. Therefore, we can conclude that i-PRF has been effective in the management of pain in PMC but does not result in complete healing of the disease.

KEYWORDS

corticosteroids, pain, plasma cell mucositis, platelet-rich fibrin, tissue repair

1 | INTRODUCTION

Plasma cell mucositis (PCM) is a rare poorly defined disease entity of the upper aerodigestive tract, not yet completely understood in its pathogenesis, usually seen in elderly patients (Heinemann, Fischer, Barta, Michaelides, & Elsner, 2006). PCM is considered a benign disease of adults not associated with the development of plasma cell neoplasms (Solomon, Wein, Rosenwald, & Laver, 2008). The diagnosis is made based on clinical and pathological findings, such as an erythematous mucosa with a surface papillomatous "cobblestone" pattern, an epithelial hyperplasia, and a dense submucosal infiltration of mainly mature plasma cells (Smith, Crighton, Chisholm, & Mountain, 1999). The disease is associated with intense pain, dysphagia, and an impaired quality of life. Therefore, the management is focused, mainly, on providing symptomatic relief.

PCM has been treated with topical, intralesional, and systemic corticosteroids, antibiotics, and topical cyclosporin with unreliable results and questionable benefits (Solomon et al., 2008). PRF (platelet-rich fibrin) is a blood-derived product that contains cytokines and growth factors, such as platelet-derived growth factors (PDGF), transforming growth factor beta (TGF-beta), and vascular endothelial growth factor, involved in the processes of hemostasis, wound healing, and tissue repair (Cabaro et al., 2018; Gasparro et al., 2018). PRF was initially developed as a fibrin clot. In the last few years, the need for an infiltrative use of PRF has led to a new product, the injectable PRF (i-PRF), a liquid blood derivative rich in leucocytes and growth factors (Miron et al., 2017).

The purpose of this case report is to evaluate the efficacy of i-PRF injections in the treatment of PCM, refractory to previous treatments.

Roberta Gasparro and Daniela Adamo contributed equally to the study.

To the best of our knowledge, this is the first report of the use of i-PRF in PMC.

2 | CASE PRESENTATION

In January 2016, a 78 -year-old woman presented at the Department of Oral Medicine of the University of Naples Federico II in Italy, with the complaint of intense oral pain localized on the left side of the buccal mucosa.

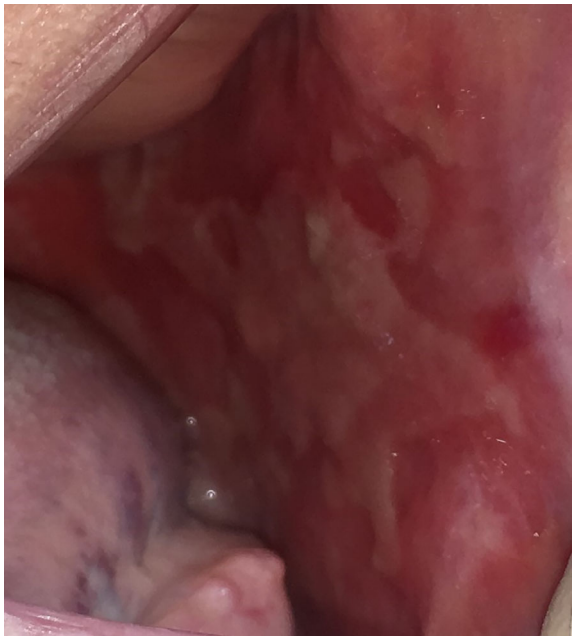

FIGURE 1 Clinical view of the left side of the buccal mucosa showing an intense diffuse erythema, ulcerations, and erosions

The intra-oral examination showed an intense diffuse erythema, ulcerations, and erosions of that area, whereas the other side of the buccal mucosa was clinically normal (Figure 1).

The medical history revealed hypertension without any immunological and autoimmune disease, and the patient denied using chewing gum, cinnamon, or other topical substances; blood examination, serum protein electrophoresis, biochemical screening, and liver, kidney, and thyroid function tests revealed serum, iron, and vitamin B12 levels within normal limits. Pemphigus and pemphigoid antibody tests, ANA, and polymerase chain reaction were negative.

The histopathological examination of an incisional biopsy taken from the lesion showed a wide subepithelial inflammatory infiltrate with a predominance of plasma cells without evidence of oral epithelial dysplasia. Direct immunofluorescence was negative (IgA, IgG, IgM, fibrinogen, C3 antibodies).

Immunohistochemical assay using CD3, CD20, and CD138 antibodies confirmed the diagnosis of PMC of the oral mucosa (Figures 2a,b).

The patient was initially treated with systemic corticosteroids (prednisone 50 mg/day in a single morning dose); however, after 15 days, the treatment was stopped due to the occurrence of side effects (increase of blood pressure, increase of intraocular pressure, tachycardia, and insomnia).

Hence, we decided to periodically treat the patient with topical corticosteroids (clobetasol propionate ointment 0.05% in Orabase-B directly on the lesion three times per day for 20 days), intralesional corticosteroid injections (triamcinolone acetonide 40 mg/mL; four injections in four equal sites of lesion once a week every 2 weeks for a maximum of 3 months), topical tacrolimus (0.1% for 2 months using it in a topical form as a cream twice a day every 12 hours), and topical cyclosporine (oral solution 100 mg/mL as a "swish and spit" medication, three times daily for five weeks) without any results in terms of clinical findings and symptoms. The last treatment was terminated 4 months before the use of i-PRF.

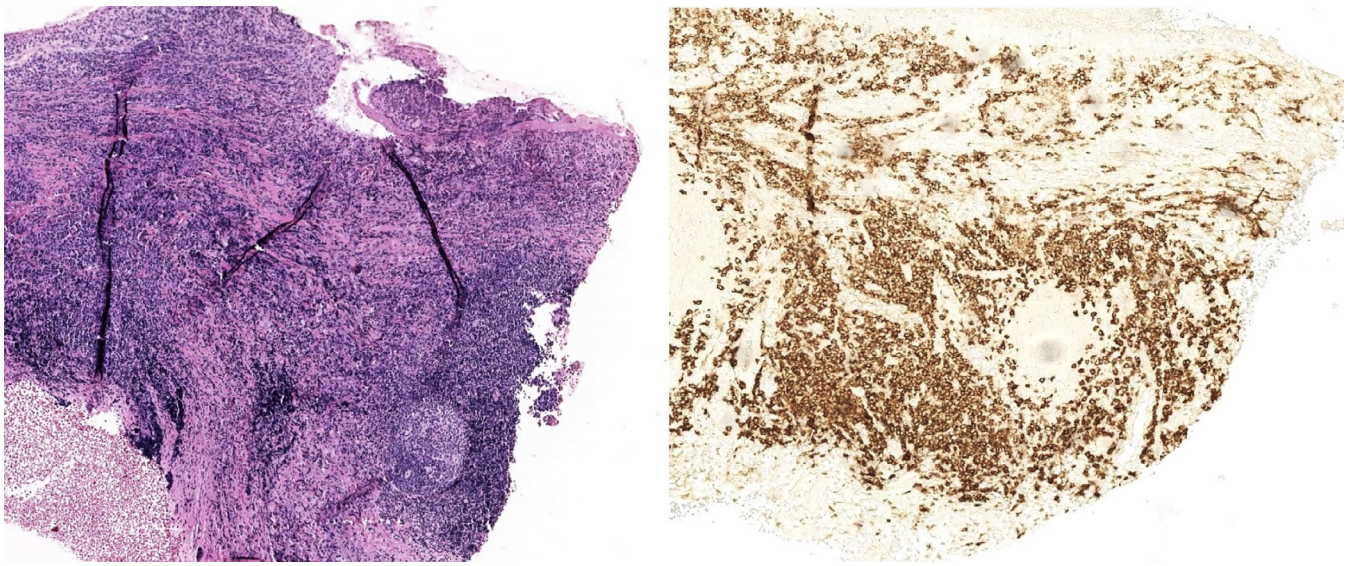

FIGURE 2 (a) Hematoxylin and eosin–stained section showed dense infiltration of plasma cells in the oral mucosa; (b) immunohistochemistry-stained section with anti-CD138 confirmed prevalent plasma cells infiltration (CD138, clone MI15, Dako omnis, ×4)

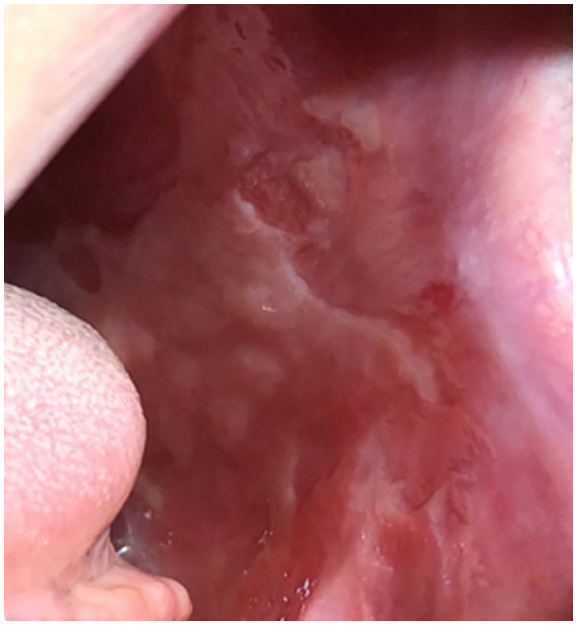

FIGURE 3 Six-months follow-up

For the i-PRF preparation, 20 mL of whole blood were collected from the antecubital vein in two sterile plastic tubes without anticoagulant (Process for PRF, Nice, France) and centrifuged at 700 rpm for 3 minutes with a Duo-centrifuge (Process for PRF, Nice, France) according to the manufacturer's instructions. At the end of the process, the i-PRF was easily detectable at the top of the tube with the remaining blood below. The tubes were carefully opened, and 1 mL per tube was collected in an insulin syringe connected to a 29G needle (Insu/Light 1 ml, Rays, Italy). The PRF was injected while still in a liquid state using the same syringe. The infiltration was made without anesthesia at four points of the peripheral area of the buccal lesion. The infiltration was performed once a week for 2 months. There were no adverse reactions to the treatment.

Pain was assessed using the visual analogic scale, and clinical images were documented every week. Before the treatment, the mean pain score was 7, gradually reducing until 0 at the fourth infiltration; the patient remained free of pain during the whole study period.

Clinically, we did not find a complete healing of the lesion, but a reduced perilesional inflammatory infiltrate was observed 6 months after (Figure 3).

Follow-up examinations were scheduled once a month during the first 6 months after the treatment. During the follow-up, the patient received no further treatment.

The protocol was approved by the Ethical Committee of the University of Naples Federico II (protocol number 347/16), and the patients signed a written informed consent form. This article was written following the CARE statement guidelines (Consensus-based Clinical Case Reporting Guideline Development, Riley et al. [2017]).

3 | DISCUSSION

The tissue regeneration or repair process requires a harmonious reaction of various types of cells, including immune cells (neutrophils, macrophages, and lymphocytes), epithelial cells, fibroblasts, and stem cells. The rationale for the use of hemocomponents is the acceleration in the healing of soft and hard tissues by increasing the concentration of growth factors, in particular for the treatment of chronic wounds (Martinez-Zapata et al., 2016).

In particular, several in vitro studies have shown the effect of i-PRF on cells. i-PRF has revealed an increase in the migration and proliferation of osteoblasts compared to platelet-rich plasma (Wang, Zhang, Choukroun, Ghanaati, & Miron, 2018). PRF injections allow angiogenesis and activation of fibroblasts with neocollagenesis and adipogenesis (Fortunato, Barone, Bennardo, & Giudice, 2018). Furthermore, i-PRF has induced a significantly higher cell migration of mRNA, PDGF, TGF-beta, collagen 1, and fibronectin by gingival fibroblast on a titanium implant surface in vitro, inducing a potential soft tissue regeneration (Wang, Zhang, Choukroun, Ghanaati, & Miron, 2017).

The use of liquid blood-derived products is widespread in orthopedics and in plastic surgery (Dohan Ehrenfest et al., 2014; Sommeling et al., 2013).

Because PRF has angiogenetic proprieties and induces the cell proliferation, it is suggested to avoid its use when malignancy is suspected.

Oral applications have been described in the treatment of ulcerative oral lichen planus by using an infiltration of PRGF (plasma rich in growth factors) in cases refractory to corticosteroid therapy. Piñas, Alkhraisat, Fernández, and Anitua (2017) reported a complete healing of lesions in four patients treated with PRGF. In two of these cases, the lesion healed completely immediately after the first application, and in the other two cases, it healed after the second application.

In relation to PRF, blood is collected without any anticoagulant and immediately centrifuged. There is no need for any biochemical modification of blood because no anticoagulants, thrombin, or calcium chloride are required, making the procedure easily exploitable. Ease of preparation, low cost, and outpatient use make PRF also an optimal scaffold for tissue healing processes (Fortunato et al., 2018).

4 | CONCLUSION

The PCM is a complex rare disease with a poor response to treatment. i-PRF has been effective in the management of pain in PCM but does not result in a complete healing of the disease. We suggest using i-PRF in cases unresponsive to conventional treatment as an adjuvant therapy, particularly in older patients to avoid the side effects related to corticosteroid therapy. However, this is a preliminary report; therefore, larger scale studies, including RCTs, are needed to confirm this protocol in the treatment of PMC.

CONFLICT OF INTEREST

The authors declare no potential conflict of interest.

ORCID

Roberta Gasparro https://orcid.org/0000-0001-6175-7806

REFERENCES

Cabaro, S., D'Esposito, V., Gasparro, R., Borriello, F., Granata, F., Mosca, G., … Riccitiello, F. (2018). White cell and platelet content affects the release of bioactive factors in different blood-derived scaffolds. *Platelets*, *29*(5), 463–467.

Dohan Ehrenfest, D. M., Andia, I., Zumstein, M. A., Zhang, C. Q., Pinto, N. R., & Bielecki, T. (2014). Classification of platelet concentrates (platelet-rich plasma-PRP, platelet-rich fibrin-PRF) for topical and infiltrative use in orthopedic and sports medicine: Current consensus, clinical implications and perspectives. *Muscles, Ligaments and Tendons Journal*, *4*(1), 3–9.

Fortunato, L., Barone, S., Bennardo, F., & Giudice, A. (2018). Management of facial pyoderma gangrenosum using platelet-rich fibrin: A technical report. *Journal of Oral and Maxillofacial Surgery*, *76*(7), 1460–1463.

Gasparro, R., Qorri, E., Valletta, A., Masucci, M., Sammartino, P., Amato, A., & Marenzi, G. (2018). Non-transfusional hemocomponents: From biology to the clinic—A literature review. *Bioengineering (Basel)*, *5*(2), E27. http://doi.org/10.3390/bioengineering5020027

Heinemann, C., Fischer, T., Barta, U., Michaelides, A., & Elsner, P. (2006). Plasma cell mucositis with oral and genital involvement—Successful treatment with topical cyclosporine. *Journal of the European Academy of Dermatology and Venereology*, *20*(6), 739–740.

Martinez-Zapata, M. J., Martí-Carvajal, A. J., Solà, I., Expósito, J. A., Bolíbar, I., Rodríguez, L., … Zaror, C. (2016). Autologous platelet-rich plasma for treating chronic wounds. *Cochrane Database of Systematic Reviews*, *5*, CD006899.

Miron, R. J., Fujioka-Kobayashi, M., Hernandez, M., Kandalam, U., Zhang, Y., Ghanaati, S., & Choukroun, J. (2017). Injectable platelet-rich fibrin (i-PRF): Opportunities in regenerative dentistry? *Clinical Oral Investigations*, *21*(8), 2619–2627.

Piñas, L., Alkhraisat, M. H., Fernández, R. S., & Anitua, E. (2017). Biological therapy of refractory ulcerative oral lichen planus with plasma rich in growth factors. *American Journal of Clinical Dermatology*, *18*(3), 429–433.

Riley, D. S., Barber, M. S., Kienle, G. S., Aronson, J. K., von Schoen-Angerer, T., Tugwell, P., … Gagnier, J. J. (2017). CARE guidelines for case reports: Explanation and elaboration document. *Journal of Clinical Epidemiology*, *89*, 218–235.

Smith, M. E., Crighton, A. J., Chisholm, D. M., & Mountain, R. E. (1999). Plasma cell mucositis: A review and case report. *Journal of Oral Pathology & Medicine*, *28*(4), 183–186.

Solomon, L. W., Wein, R. O., Rosenwald, I., & Laver, N. (2008). Plasma cell mucositis of the oral cavity: Report of a case and review of the literature. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontics*, *106*(6), 853–860.

Sommeling, C. E., Heyneman, A., Hoeksema, H., Verbelen, J., Stillaert, F. B., & Monstrey, S. (2013). The use of platelet-rich plasma in plastic surgery: A systematic review. *Journal of Plastic, Reconstructive & Aesthetic Surgery*, *66*, 301–311.

Wang, X., Zhang, Y., Choukroun, J., Ghanaati, S., & Miron, R. J. (2017). Behavior of gingival fibroblasts on titanium implant surfaces in combination with either injectable-PRF or PRP. *International Journal of Molecular Sciences*, *18*(2), E331. http://doi.org/10.3390/ijms18020331

Wang, X., Zhang, Y., Choukroun, J., Ghanaati, S., & Miron, R. J. (2018). Effects of an injectable platelet-rich fibrin on osteoblast behavior and bone tissue formation in comparison to platelet-rich plasma. *Platelets*, *29*(1), 48–55.

How to cite this article: Gasparro R, Adamo D, Masucci M, Sammartino G, Mignogna MD. Use of injectable platelet-rich fibrin in the treatment of plasma cell mucositis of the oral cavity refractory to corticosteroid therapy: A case report. *Dermatologic Therapy*. 2019;e13062. https://doi.org/10.1111/dth.13062