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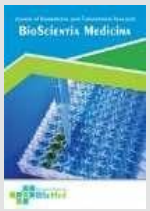

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Application of Topical Autologous Platelet-Rich Plasma for Treatment of Pemphigus Foliaceus Wounds: A Case Report

Nopriyati[1*], M. Akip Riyan Saputra[1], Yulia Farida Yahya[1], Sarah Diba[1]

[1]Department of Dermatology and Venereology, Faculty of Medicine, Universitas Sriwijaya/Dr. Mohammad Hoesin General Hospital, Palembang, Indonesia

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***Corresponding author:**
Nopriyati

E-mail address:
nopriyati@fk.unsri.ac.id

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A B S T R A C T

Background: Pemphigus foliaceus (PF) includes lesions on the skin, generally without involving the mucosa. Wounds in PF arise on the outer layer of the superficial skin, but if left untreated, the wound will not heal and will multiply. Platelet-rich plasma (PRP) containing a variety of different growth factors can be used in wound care. This study was at a time to describe autologous PRP therapy in the treatment of excoriated erosional wounds in patients with pemphigus foliaceus. **Case presentation:** A woman, 35 years old, married, a housewife living in suburban, comes to the emergency department with complaints of blisters accompanied by pain in the face, body, and back which has been increasing since 1 month ago. Examination of the skin showed palpebral blisters on the eyelids of the left and right eyes. In the anterior and posterior trunk regions, proximal 1/3rd and suprapubic extremities, there are hyperpigmented erythematous macules, multiple, nummular-plaque, discrete, partially confluent, with white to brownish scales, single layer and exfoliative. In the posterior trunk region, Nikolsky's sign was positive. Laboratory evaluation showed an increase in leukocytes and neutrophils. ANA examination showed negative results and anti-ds-DNA 54.91. Management of pemphigus in the form of topical and systemic treatment. Topical management in the form of an open compress with 0.9% NaCl solution, Intrasite gel®, and closed Cutimed sorbact® for erosion and excoriation. Topical PRP was administered on the 7th day of treatment. On the 14th day after treatment with topical PRP, the patient is allowed to go home with the repair of lesions throughout the region. **Conclusion:** PRP therapy in cases of pemphigus foliaceus is very useful in improving the clinical condition of the patient.

1. Introduction

Pemphigus is a chronic autoimmune disease characterized by vesicles and bullae on the skin due to autoantibody reactions to adhesion molecules. The incidence of pemphigus foliaceus is 0.75 to 14 cases / 1,000,000 people in 1 year in the world.[1] Pemphigus foliaceus (PF) lesions occur on the skin without involving the mucosa.[2] PF is less common than pemphigus vulgaris (PV). The incidence of PF is more common in men than women. The mean age of patients with PF ranges from 40 to 60 years.[1]

Wound healing is an active and complex process consisting of 4 phases, hemostasis, inflammation, proliferation, and remodeling. For effective wound healing, there must be a synchronization of not only interactions between cells and cells with the matrix but also the involvement of cytokines in ensuring the communication process in various processes runs smoothly. Wound healing is a dynamic process that

involves complex mechanisms mediated by various growth factors. Today there are many different types of wound care. Specific wound care depends on the characteristics of the wound. The generally accepted wound care mechanism functions as a barrier between the wound and the environment by preventing tissue drying or autolytic debridement. Several wound treatments play a role in cellular and molecular mechanisms in the wound microenvironment.[2]

Platelet-rich plasma (PRP) containing a variety of different growth factors can be used in wound care. It is extracted from whole blood using a series of centrifugation processes and, when activated, releases several antimicrobial microproteins, cytokines, and growth factors. These bioactive molecules play a role in supporting the wound healing process.[3]

Wounds in PF arise on the outer layer of the superficial skin, namely the stratum granulosum. There is not enough tissue for fluid to be trapped, and blisters form. The sores consist of crusts and reddish lesions the size of a coin, often called cornflakes. These superficial crusts are easily removed and leave superficial erosions of the skin. If not treated, the wound will not heal and more and more.[2] This study was to describe autologous PRP therapy in the treatment of excoriated erosional wounds in patients with pemphigus foliaceus.

2. Case Presentation

A woman, 35 years old, married, a housewife, and living in suburban, comes to the emergency department with complaints of blisters accompanied by pain in the face, body, and back which has been increasing since 1 month ago. The patient was then taken to the health center for treatment and diagnosed with chickenpox. The patient received acyclovir ointment and applied it 2 times a day for 3 days, but the patient's blisters did not improve.

Three weeks earlier, the blisters on the patient's skin had begun to rupture and become blisters. The blisters do not subside and extend to the abdomen. The patient was then taken to a midwife for treatment and was given amoxicillin tablets 500 mg/8 hours, taken for 3 days. Patient complaints are not reduced by this treatment. One week later, the patient was brought by his family for treatment with non-medical alternative medicine and was advised to bathe in river water 2 times a week. The patient's blisters were given boiled water of betel leaf 3 times a day for 5 days. Because all these treatments did not work, the patient was then taken to the emergency department of Dr. Mohammad Hoesin General Hospital and hospitalized at the Department of Dermatology and Venereology.

From the anamnesis, there was no history of blisters, no history of sunburn on the face, and no known history of drug allergy. History of family members with complaints of blisters accompanied by itching, which later turned into blisters after previously being denied.

The results of the physical examination showed vital signs within normal limits. Examination of the skin showed palpebral blisters on the eyelids of the left and right eyes. In the anterior and posterior trunk regions, proximal 1/3 and suprapubic extremities, there are hyperpigmented erythematous macules, multiple, nummular-plaque, discrete, partially confluent, with white to brownish scales, single layer and exfoliative. There were also erosions to excoriations, multiple, nummular to plaques, some covered with dark brown crusts that were difficult to remove (Figure 1). The body surface area covered by the lesion was 22%, with the most widely affected region being the posterior trunk (15%). In the posterior trunk region, a positive Nikolsky sign was found. Namely, the skin was separated from the base (Figure 2).

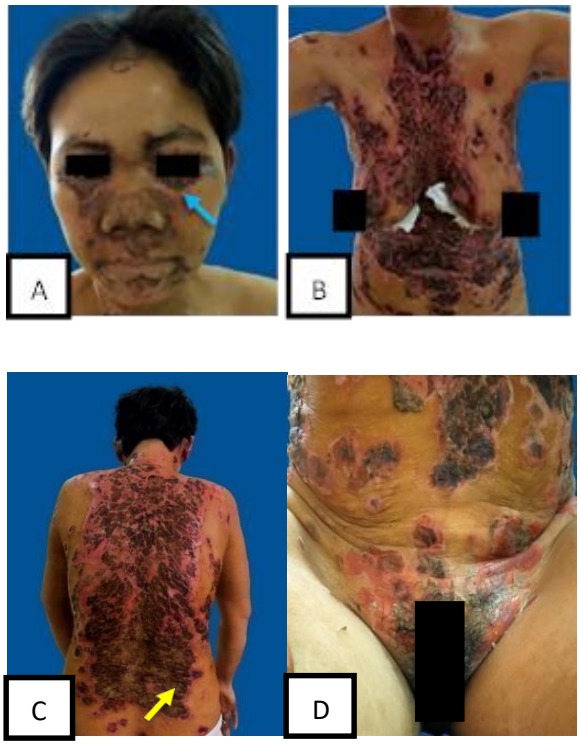

Figure 1. The clinical picture of the patient on admission to the hospital. (a) Facial region (b) Anterior trunk region (c) Posterior trunk region (d) Inguinal region.

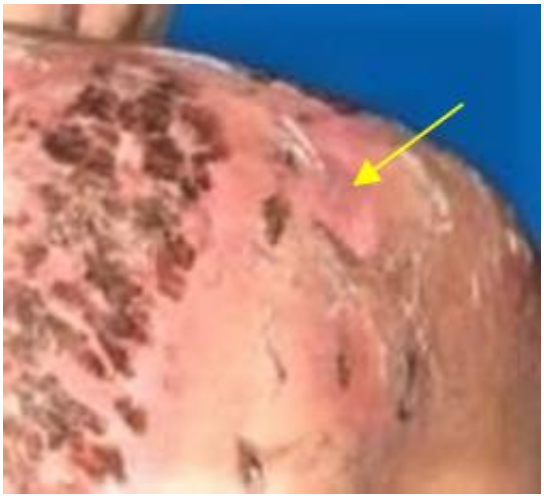

Figure 2. In the posterior trunk region, there is the separation of the skin from the base (positive Nikolsky sign).

Complete blood count showed hemoglobin 14.3 g/dL, platelets 427,000/µL, increased leukocyte count (13,270/mm^3) and neutrophils (72%), and decreased lymphocytes (13%). Clinical chemistry examination showed a decrease in total protein (5.9 g/dL), albumin (3.4 g/dL), globulins (2.5 g/dL) and blood sugar (89 mg/dL). The results of the anatomical pathology examination showed a gap in the subcorneal because the acantholysis process contained lymphocyte cells. In the superficial dermis, there is a perivascular lymphocytic infiltrate; effects of pemphigus foliaceus. ANA examination showed negative results and anti-ds-DNA 54.91. This patient was diagnosed with pemphigus foliaceus.

Management of the patient includes general and specific management. General management includes educating the patient and family that the disease is caused by an autoimmune process and is not contagious, the patient is not allowed to scratch the lesion, an explanation of wound compresses, and how to use drugs. Specific management includes topical and systemic management. Topical management in the form of open compresses with 0.9% NaCl solution for 30 minutes every 12 hours, Intrasite gel® every 12 hours, and then closed with Cutimed sorbact® for erosion and excoriation. Systemic treatment in the form of 0.9% NaCl: Ringer lactate intravenous (1:1) 20 drops per minute, injection of dexamethasone 5 mg every 24 hours (1-0-0) on day 1, injection of ceftriaxone 1 gram every 12 hours on day 1 and tablets Cetirizine 10 mg every 24 hours orally. The patient's prognosis was dubia ad bonam. The patient was planned to be given a topical platelet-rich plasma treatment on the seventh day of treatment. On the 14th day after treatment with topical PRP, the patient was discharged home with a repair of lesions throughout the region (Figure 3).

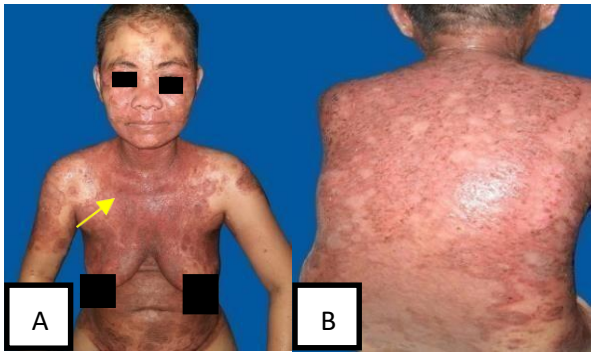

Figure 3. Clinical features of the patient on the 14th day of treatment; (a) facial region and anterior trunk (b) posterior trunk region 14 days after starting PRP therapy.

Three months after treatment with PRP, there was clinical improvement in the pemphigus lesions. In the facial region, trunk anterior et posterior, upper extremity 1/3 proximal, supra pubis, there are erythematous-hyperpigmented macules, multiple, nummular-plaque, discrete partially confluent.

3. Discussion

Pemphigus is an intraepidermal bullous autoimmune dermatosis that occurs in lesions of the skin and or mucous membranes.[4-7] Based on clinical and histopathological characteristics, the 2 main forms of pemphigus are pemphigus vulgaris (PV) and pemphigus foliaceus (PF). Pemphigus foliaceus is a chronic autoimmune bullous disease characterized by intraepidermal bullae and acantholysis of the skin.[7] In this case, pemphigus foliaceus occurred in a 35-year-old woman.

The diagnosis of PF in this patient was established by history, physical examination, and supporting examinations. Pemphigus guidelines based on the European Academy of Dermatology and Venereology (EADV) state that in history, patients may complain of loose blisters that break easily, leaving erosions covered with crusts in the seborrheic areas (chest, scalp, face, and interscapular areas) accompanied by pain or burning. The patient may not be aware of the presence of bullae because they break easily, and only secondary lesions are found in the form of superficial blisters with scales accompanied by exudate that easily dries into scabs with a reddish base accompanied by burning or pain.[8,9]

Physical examination of primary lesions in the form of vesicles or superficial sagging bullae on the skin of the face, head, and body. The primary lesion may not be found on examination because it ruptures easily.

Secondary lesions in the form of shallow erosion are more common. The scale of the lesion is often found to indicate the detachment of the stratum corneum from the area of intraepidermal acantholysis, the stratum granulosum. Most lesions occur on the chest and back. On the face and scalp, exudate from erosive lesions dries faster, leaving a scab with a reddish base.

Nikolsky's sign is common in pemphigus foliaceus.[9] The mechanism of occurrence of Nikolsky 's sign is a loss of intercellular adhesion of keratinocytes in the upper epidermis (acantholysis), which results in the formation of shallow vesicles/bulls that do not occur in other types of pemphigus. So Nikolsky's sign can be considered quite sensitive for the diagnosis of pemphigus. On physical examination, the scales of the lesions did not match the literature, where the scales on the lesions were medium in size and dark brown in color due to manipulation of the lesions by soaking betel leaf in boiled water, but they could still be distinguished clinically from the scales of seborrheic dermatitis.

On investigation, PF on histopathological examination contained acantholytic keratinocytes, neutrophils, and fibrin with varying amounts in the blisters. Older lesions exhibit chronic inflammation, including acanthosis, hyperkeratosis, and parakeratosis. Keratinocytes in the granular layer show dyskeratotic changes. There is an increased amount of pigment in basal melanocytes. Capillaries become dilated. Edema in the upper layers of the dermis may appear to vary degrees. Inflammatory cell infiltration consisting of neutrophils, eosinophils, and lymphocytes may be seen in small numbers and varied distribution.

The general management of PF consists of systemic corticosteroid therapy to inhibit antibody production, combined with the use of topical agents to prevent infection, protect areas of erosion and promote epithelialization.[10,11] Topical therapy for PF focuses on proper skin care and the use of topical medications. Grada, et al. explained that the main purpose of wound healing is to prevent infection, maintain skin moisture, protect the wound and prevent scar formation.

Cleansing the wound gently by compressing using saline every 12 hours is a top priority for wound care in pemphigus. The use of moisture-retentive dressings, both occlusive and semi-occlusive, helps accelerate the re-epithelialization process and restores the skin barrier. Nonadherent gauze, transparent film, hydrocolloid, and hydrogel dressings can be applied to the wound directly. Choosing a dressing is something that needs to be considered, not only the characteristics of the wound but also the specific type of dressing, such as absorption capacity, hydration quality, adhesion quality, and comfort.[8,12-14]

In patients for topical therapy, it is given by cleaning the lesion with 0.9% NaCl compressed for 30 minutes every 12 hours and applying hydrocolloid, namely Intrasite gel®15,16. Intrasite® consists of 2.3% carboxymethylcellulose polymer, 20% propylene glycol, and 77.7% water. Carboxymethylcellulose acts as an autolytic debridement, and propylene glycol enhances wound penetration. PRP is also applied to the patient's wound to accelerate wound healing in the patient. Wounds in PF are superficial in the granular stratum in the form of wounds covered with crusts that are easily removable and leave superficial erosions but in patients, the crusts are difficult to remove. If the lesion is not treated, the lesion will not heal and will increase in size.[2,8,15]

Platelet-rich plasma (PRP) is an endogenous therapeutic technology that has the potential to stimulate and accelerate wound healing. PRP is defined as an autologous biological product derived from the patient's blood where after the centrifugation process, a blood fraction with a higher platelet count is obtained than the circulating blood. Platelets have an important role in the wound healing process thanks to their hemostatic function and the content of cytokines and growth factors. There are several growth factors that play a role in the wound healing process, platelet-derived growth factor (PDGF), epidermal growth factor (EGF), fibroblast growth factor (FGF), insulin-like growth factor (IGF 1, IGF 2), and vascular endothelial growth factor (IGF). VEGF), transforming

growth factor (TGF-β) and keratinocyte growth factor (KGF).[16-18]

The use of growth factor (GF) in assisting skin wound healing has been around since the 1940s and can be applied in various ways, both topically and intralesionally, using specific media or gene therapy. Successful trials of skin ulcers, acute skin wounds, burns, and plastic and cosmetic surgery in animals and humans have been reported. Growth factors play an important role in the complex process of wound healing and tissue regeneration. Growth factors provide protein signals to influence cellular metabolic processes. Each GF has more than one effect on the wound healing process and plays a role in binding to specific receptors on target cell membranes. These effects include triggering chemotactic (signaling cells to enter the wound), induction of cell migration and proliferation, and stimulation of cells to up-regulate protein production. GF not only regulates cell migration and proliferation but also plays a role in extracellular matrix remodeling and triggers angiogenesis, creating an ideal environment that promotes wound healing.[3,18] In this case, topical PRP was administered with a duration of every 48 hours. The administration of PRP was carried out after wound care and the removal of crusts on the patient. The results of the therapy that has been carried out are improvements in the wounds on the face and body of the patient, and the patient is allowed to be outpatients. The prognosis of skin disorders in this patient is good. During 4 weeks of therapy, the patient experienced remission, which lasted for 3 months of treatment.[3,18,19]

Systemic therapy for pemphigus foliaceus based on the European Academy of Dermatology & Venereology (EADV), namely the administration of steroids equivalent to prednisone 1-1.5 mg/kgBW every 24 hours, has been shown to be effective in cases of pemphigus foliaceus, this is possible because of the mechanism of action of steroids. PF occurs in patients who have a specific HLA genotype in which specific autoantibody-producing B cells are present. The complex interaction with Th2 CD4+ cells activates B cells, and these Th2 cells' over-activation results in the production of autoantibodies in pemphigus vulgaris and pemphigus foliaceus. Th2 cells are known to cause the secretion of many cytokines, one of which is IL-4 which plays a major role in the humoral immune response in pemphigus. IL-4 increases antibody production through activated B cells and can convert IgG1 to IgG4, which is important in the active forms of pemphigus vulgaris and pemphigus foliaceus. IL-4 is also able to maintain disease continuity through the conversion of naive T cells into Th2 cells. Production of autoantibodies and epitope binding causes loss of adhesion between desmosomes, resulting in the separation of keratinocytes, which is directly related to pemphigus foliaceus disease.[8,19]

Systemic corticosteroids with adjuvant immunosuppressants are the mainstay of therapy in moderate to severe cases. Clinical response can be observed within a few days after starting treatment.[15] After disease control is achieved, the next dose of the drug used to promote disease control is given. The end of this phase is when 80% of the lesions have healed, both mucosal and skin, and there are no new lesions for at least 2 weeks. This phase may be relatively short but may be considered longer if there is extensive skin ulceration. In this phase, start reducing the dose of corticosteroids. In the maintenance phase, treatment is gradually reduced to minimize side effects and remain effective in controlling the disease. The ultimate goal of treatment is to maintain remission on prednisolone 10 mg daily or less.

4. Conclusion

PRP therapy in cases of pemphigus foliaceus is very useful in improving the clinical condition of the patient.

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