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Comprehensive Treatment Approaches in a Unique Case of Generalized Pustular Psoriasis

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Abstract

Psoriasis is an immunological inflammatory disease characterized by skin inflammation and epidermal hyperplasia. One type of psoriasis is Generalized Pustular Psoriasis (GPP), which is usually preceded by other diseases. A 56-year-old woman presented to the Department of Dermatology and Venereology with a recent onset of red spots accompanied by pustules distributed across her body. The initial manifestation of these symptoms occurred approximately one month prior, and the condition has progressively worsened over the past three days. Physical examination of dermatological status showed erythematous plaques with smooth, well-defined scales with irregular, round edges, lenticular size, multiple, discrete, and confluent distribution, generalized distribution in the pedis dextra et sinistra, manus dextra et sinistra, and femoral regions. Skin biopsy examination results showed skin tissue with hyperkeratosis, acanthosis, and parakeratosis, with PMN inflammatory cells (Munro's micro abscess). The conclusion of the skin biopsy is pustular psoriasis. The patient was diagnosed with GPP. Patients were given Methotrexate, calcitriol tablets 0.25 mcg twice a day, cetirizine tablets 10 mg twice a day, and topical cream. After one week of treatment, the patient's lesions improved. Treatment continues, and patients are given education to avoid trigger factors such as stress, excessive activity, extreme temperature changes, and focal infections. The management must consider various influencing factors, including genetic factors, skin barriers, predisposing factors, and trigger factors. Prevention is also important. The patient needs to be educated about the details of the disease, how to prevent a recurrence, and treatment when the disease recurs.



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1. Introduction

Psoriasis is an immunological inflammatory disease characterized by skin inflammation and epidermal hyperplasia. This disease can increase the risk of

destructive arthritis, cardiovascular morbidity, and psychosocial problems. The economic and health burden on the country due to this disease is enormous. One type of psoriasis is Generalized Pustular Psoriasis (GPP), which is usually preceded by other diseases [1, 2].

GPP can occur at any age but is most common at ages >50 years. The risk of GPP in women is greater than in men. GPP is a rare disease so specific diagnostic explanations regarding GPP are very limited to determine the prevalence of this disease. The incidence of GPP in France is 1.76 per 1,000,000 people, in contrast to Japan, which is 7.46 per 1,000,000 people, and in Korea, it is around 88-124 per 1,000,000 people [1].

Symptoms of GPP begin with a fever that lasts several days and the eruption of sterile pustules with a diameter of 2-3 mm that appear suddenly and completely. Pustules are distributed on the trunk and extremities, including the nail beds, palms of the hands, and soles of the feet. GPP has prominent systemic symptoms and there are potentially life-threatening complications such as hypocalcemia, bacterial infection, sepsis, and dehydration. Severe pustular psoriasis requires robust treatment with a rapid onset of action to avoid life-threatening complications [3].

The etiology of GPP is unclear, but GPP may occur due to a combination of certain genetic loci, particularly inflammatory cytokine signaling, and environmental risk factors, including viral infections, medications, and corticosteroid withdrawal. The pathogenesis of GPP is associated with the interleukin (IL)-36 cytokine pathway that regulates the innate immune system. Uncontrolled expression and activation of the cytokine IL-36 can lead to a persistent inflammatory cascade in the epithelium. This can lead to the induction of chemokines such as CXCL1 and CXCL8 (IL-8), resulting in a chemokine gradient that draws large numbers of neutrophils into the epidermis [4].

Histological examination of GPP lesions reveals parakeratosis, substantial mononuclear and neutrophilic infiltration into the epidermis, as well as epidermal edema and hyperplasia. Spongiform pustules of Kogoj, suprapapillary capillary hyperplasia, and Munro's microabscesses typical of plaque psoriasis are also seen. GPP can occur together with plaque psoriasis which can hinder the diagnosis of this disease [5].

The problem of GPP is very complex, so management needs to consider various influencing factors, including genetic factors, skin barriers, predisposing factors, and trigger factors. Therefore, preventive efforts are important. Dermatologists need to communicate with patients and their families, provide information and education about the disease, teach how to treat and prevent recurrence, and control and eliminate the itch-scratch cycle. The purpose of writing this case report is to describe a generalized pustular psoriasis to find out how

to handle and manage it appropriately to prevent worsening and complications.

2. Cases

A 56-year-old woman came to the Department of Dermatology and Venereology with complaints of red spots with pustules almost all over the body. Complaints of red spots containing pustules on the right and left upper arms, front of the chest, and back. Meanwhile, on the forearms, thighs, and legs there are red spots without pustules. The onset of these symptoms began a month ago, and there has been a notable exacerbation in the last three days. The reddish spots are accompanied by itching and burning so that the patient scratches them and the reddish spots immediately spread throughout the body. These spots then turn into pustules. Some pustules merge into one called "the lake of pus", and there are some pustules that burst and peel. Itching is felt erratically, it can be morning, afternoon, or night.

The itching also feels worse when the weather changes. Complaints of itching also appear when patients consume foods such as chicken and eggs. Apart from that, patients also admit that complaints can arise if the patient is having a lot of thoughts and emotional stress. The patient also complained of having cavities in his teeth since approximately one month ago and the patient underwent treatment at the dental and oral clinic and was diagnosed as aggressive periodontitis. The patient had complained about the same thing four times. Complaints arise every time the patient feels anxious and stressed. It first felt after giving birth, but the patient did not see a doctor and it disappeared by itself. Then the patient felt the same thing when she felt stressed because she was going to marry his child in 2016. The patient had no history of diseases such as diabetes melitus and hypertension. No family members had the same complaints as the patient.

Physical examination of dermatological status showed erythematous plaques with smooth, well-defined scales with irregular, round edges, lenticular size, multiple, discrete, and confluent distribution, generalized distribution in the pedis dextra et sinistra, manus dextra et sinistra, and femoral regions. There are also pustular lesions with a well-defined erosion surface with regular round edges, nummular to plaque size, multiple herpetiform, and regional distribution (Figure 1). The calculation of body surface area (BSA) was 38% and the calculation of psoriasis area and severity index (PASI) was 23,2. Laboratory examination revealed an increase in ESR (61 mm/hour), a decrease in neutrophils (0%), and an increase in monocytes (10%). Skin biopsy examination results showed skin tissue with hyperkeratosis,



Figure 1. Clinical photograph of the patient when she first came to the Polyclinic Dermatology at RSUDZA with a PASI score of 23.2 (dated 18-07-2022).



Figure 2. Follow up at 14 days, the lesions showed improvement, scaling and pustules began to decrease and disappear from all over the body with a PASI score of 17.8 (dated 09-08-2022).



Figure 3. Follow-up at four months, the patient's lesions improved with a PASI score of 9.4 (dated 16-11-2022).

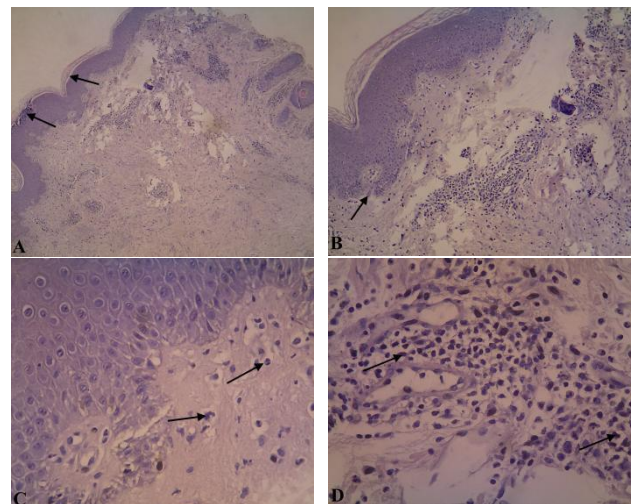


Figure 4. On histopathological examination with HE staining (A) 10x magnification shows Munro's micro abscess (upper arrow) and parakeratosis (lower arrow), (B) 20x magnification shows elongation of the rete ridges (C, D) 40x magnification shows perivascular PMNs (upper and lower arrow).

acanthosis, and parakeratosis, with PMN inflammatory cells (munro's abscess). In the dermis, there are perivascular PMNs and PMN pollutants. No malignancy was found. The conclusion of skin biopsy is pustular psoriasis (Figure 4). The patient was diagnosed with GPP.

The patient was given Methotrexate, calcitriol tablets 0.25 mcg twice a day, and cetirizine tablets 10 mg twice a day. The patient was also given a mixture of 3% salicylic acid

cream, 0.1% mometasone furoate cream, and vaseline album to be applied all over the body. For the scalp, a mixture of 3% salicylic acid cream, 5% LCD, and 0.05% clobetasol propionate cream to be applied to the scalp in the evening. The patient also received narrowband ultraviolet B (NB-UVB) phototherapy twice a week. After receiving treatment, the lesions showed improvement. Redness, crusts and pustules began to decrease and disappear all over the body with a PASI score from 23,2 to 9,4 after 4 months of therapy (Figure 2 and 3). Treatment continues and patients are given education to avoid trigger factors such as stress, excessive activity, extreme temperature changes, and treating focal infections with consultation at the Dental and Oral Department.

3. Discussions

The findings obtained in the patient from the history, physical examination, and supporting examinations point to GPP where the patient came with the main complaint in the form of erythematous spots accompanied by pustules that felt itchy, painful, and burning for one month all over the body. Manifestations of GPP can be accompanied by acute fever and erythematous rash on the skin accompanied by sterile pustules 2 mm-3 mm in diameter. Pustules are scattered on the body and extremities, including the nail beds, palms, and soles of the feet. Pustules usually appear on erythematous skin. The rash on the skin first appears as a patch and then becomes confluent as the disease becomes more severe. The Patient also have cavities in their teeth which can be a port of entry for bacteria. The certain etiology of GPP is still not known. A study has identified streptococcal infection as a still unknown trigger of psoriasis although it has been suspected in attacks of GPP. Psoriasis has previously been associated with streptococcal infections in epidemiological and immunological studies. A case-control study showed that recent streptococcal infection was associated with a seven-fold increased risk of psoriasis, even without identifying an infectious agent [6].

On examination of liver function, current blood sugar, and kidney function, no abnormalities were found. A complete blood count showed an increase in ESR, namely 61 mm/hour, a decrease in rod neutrophils, and an increase in monocytes. This is in accordance with the theory where laboratory abnormalities are often found in the form of leukocytosis with neutrophilia, increased erythrocyte sedimentation rate, hypocalcemia, increased levels of transaminases, alkaline phosphatase, and bilirubin [7].

Generalized Pustular Psoriasis is difficult to control and requires potent therapy with a rapid onset to avoid life-threatening complications. Successful management of GPP is difficult to achieve because even with multiple drug regimens, the rate of recurrence of pustular eruptions remains high. Salicylic acid is a traditional agent used in psoriasis therapy. This substance is often combined with LCD or sulfur in Vaseline vehicles. Salicylic acid has several benefits such as keratolytic and desmolytic effects, keratoplastic effects, anti-pruritic effects, anti-inflammatory effects, analgesic effects, and bacteriostatic effects [8].

Salicylic acid preparations have long been known to have anti-inflammatory properties. As is known, aspirin (acetyl salicylic acid) has been widely used as an analgesic, antipyretic, and systemic anti-inflammatory. Salicylic acid inhibits prostaglandin synthesis and has anti-inflammatory effects in topical preparations at a concentration of 0.5-5%. At a concentration of 0.5-2%, salicylic acid has stabilization of the stratum corneum which causes keratoplastic effects. The mechanism is not yet known with certainty, but it is thought to be a homeopathic adaptation phenomenon, namely salicylic acid causes weak keratolytic stimulation which causes increased keratinization [9].

Steroids are a therapy that is often used in various inflammatory diseases because they are antiproliferative, anti-inflammatory, vasoconstrictive, and immunosuppressive so when used on psoriasis lesions they can reduce plaque thickness and reduce erythema lesions. Steroids are an option for treating spots in lighter areas such as the face and armpits. But strong steroids are preferably used to remove thickened plaques on the palms. Potent topical steroids are corticosteroids, clobetasol propionate, or betamethasone propionate which are applied once or twice daily. Long-term use of topical steroids that cause skin atrophy, hair growth, and hypopigmentation. Different new formulations are available to increase the penetration of topical corticosteroids. Betamethasone valerate and clobetasol propionate have better efficacy for scalp psoriasis compared to lotion [10].

The Liquor carbonis detergent (LCD) compound is a keratoplastic drug. It works by releasing dead cells from the epidermis and slowing the growth of skin cells. This compound has a soothing effect on scaly and dry skin. Apart from that, it can also relieve itching from this skin condition. In GPP, LCD has the effect of suppressing DNA synthesis so that it can inhibit keratinocyte proliferation. Tar preparations are very helpful in removing scales and available in the form of creams, ointments, and shampoos. Because it has a detergent formula, this drug

can cause side effects in the form of mild skin irritation or skin rashes [9].

The patient was given clobetasol propionate therapy to treat complaints on the scalp, as it is known that steroids are anti-inflammatory so they can remove plaque and reduce erythema lesions. Patients also receive a mixture of antibiotics and steroids which are anti-inflammatory and anti-bacterial. Then the patient also received salicylic acid plus LCD and corticosteroids to remove scale on the lesions and also to increase the anti-inflammatory effect. Methotrexate is also administered to these patients for autoinflammatory and autoimmune conditions. Patients also receive calcitriol to inhibit excessive skin cell proliferation, increase skin cell differentiation, and modulate immunologic factors. Cetirizine is an antihistamine drug that has antipruritic properties which are useful for treating inflammation of the skin. Cetirizine is a second-generation non-sedating antihistamine that has a very good level of safety. In addition, this drug has anti-inflammatory properties. This drug works by blocking histamine, which is a compound that increases in quantity and causes allergic symptoms and reactions when the body is exposed to an allergen (allergy-triggering substance) [11]

Psoriasis is characterized by an increase in the number of mast cells in the upper dermis and in the epidermis. Degranulated mast cells are seen in the earliest stages of psoriatic inflammation in the skin. The role of mast cells is the main histamine producer in humans. Antihistamines are commonly used to treat itching in psoriasis patients, especially the first generation due to their additional sedative effects. Cetirizine significantly reduced levels of tryptase-positive mast cells and resulted in clinical improvement in erythema, indicating multilevel immunopharmacological modulation of this antihistamine in psoriasis sufferers. Antihistamines aim to reduce the itching that occurs due to the allergic process. The mechanism of action of antihistamines is that the histamine H1 receptor antagonist binds to the H1 receptor without activating the receptor, which prevents the binding and action of histamine¹⁰

The therapy we gave to the patient gave satisfactory results as indicated by the patient's clinical improvement from the first time she came to the 4th month and a decrease in the PASI score. By providing adequate and holistic therapy, the patient's prognosis is good and the patient's quality of life can improve. It is hoped that patients will have regular check-ups at the hospital to prevent recurrence of their psoriasis.

4. Conclusions

Generalized pustular psoriasis is a rare disease so specific diagnostic explanations regarding GPP are very limited to determine the prevalence of this disease. GPP also difficult to control and requires potent therapy with a rapid onset to avoid life-threatening complications. The problem of GPP is very complex and requires comprehensive handling. The management needs to consider various influencing factors including genetic factors, skin barriers, predisposing factors, and trigger factors. Preventive is also important.

Patient need to be educated about their disease in detail, how to prevent recurrence and treatment when their disease recurs. In this patient, the diagnosis of GPP was made based on clinical and histopathological examination. Adequate therapy provides better outcomes for patients. It is hoped that in the future there will be more research regarding establishing diagnoses and other therapies for GPP.

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