AMJ
ISSN: 0005-2523

ISSN: 0005-2523
Volume 62, Issue 09, November, 2022

Clinical Approach in Generalized Pustular Psoriasis: One Case Report

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Keywords:
Generalised Pustular Psoriasis, Psoriasis, Methotrexate.

ABSTRACT

Generalized pustular psoriasis (PPG) is a rare subtype variation of pustular psoriasis. No specific therapeutic agent for PPG has been approved in the United States and Europe yet. Standard guidelines for PPG therapy do not yet exist, so therapy is determined based on the clinical. A case is reported, a 22-year-old woman with complaints of purulent papules on almost the entire body for 1 week ago. The patient had a history of red scaly patches for 3 years ago. On generalized regional dermatological status, diffuse miliary pustules were found on an erythematous basis with desquamation. Histopathological results showed subcorneal pustules with segmented (spongiform) neutrophil inflammatory cells infiltration. The patient was diagnosed as PPG and treated with methotrexate 7.5 mg/week. The patient showed significant lesion improvement within 14 days of treatment.

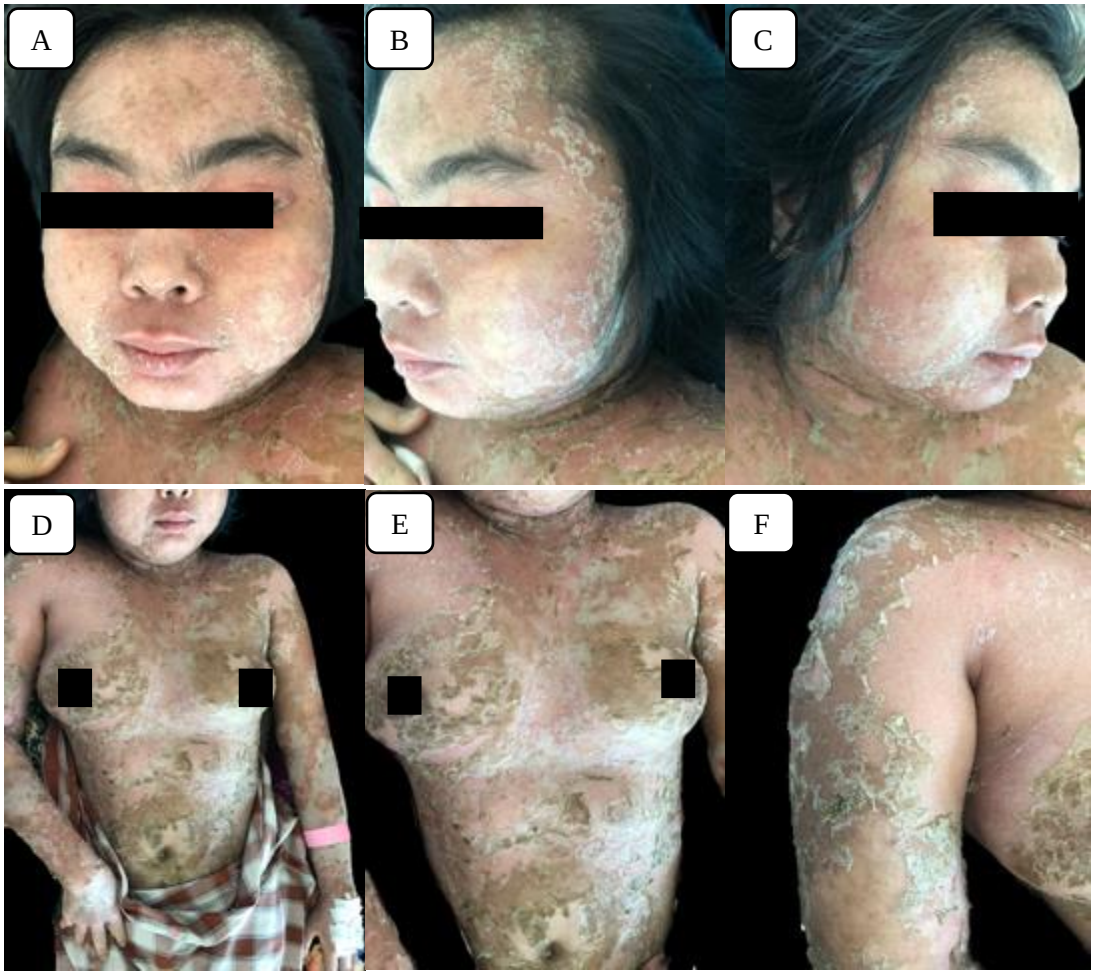
1. Introduction

Generalized pustular psoriasis (PPG) is a rare variation of pustular psoriasis. This psoriasis subtype was first reported by Leopold von Zumbusch in 1910, finding patients with plaque psoriasis to have episodes of pustular eruptions all over the body [5]. PPG can occur at any age, but usually occurs in the 5th decade. Onset may be earlier in patients with a family history of psoriasis or an *IL36RN*. In some case series, PPG was more common in women, in a 2:1 ratio, but was inconsistent [5], [9]. The prevalence of PPG is only 0.9% among individuals with psoriasis [7]. There are no specific therapeutic agents and standard guidelines for PPG therapy and determined based on the extent of the disease, the severity of the disease, and the presence or absence of risk factors. PPG therapy also often follows the guidelines for chronic plaque psoriasis [4]. *National Psoriasis Foundation Medical Board* states that the first-line therapy for PPG is acitretin, cyclosporine, methotrexate, and infliximab [5]. We report a case of a young woman with severe generalized pustular psoriasis thought to be precipitated by long-term steroid use. Methotrexate was chosen as first-line therapy.

2. CASE REPORT

A woman, aged 22 years, came for a consultation at the department of dermatology and venereology with blisters of pus appearing on most of the body 1 week before admission to the hospital. Initially, the

complaints appeared in the leg area in the form of reddish spots, then small nodules filled with pus appeared followed by peeling skin, and then spread to the chest, body, face, and whole of the body. Complaints appeared with nodules filled with pus in the mouth area. Complaints of fever are said to be present. The patient feels very itchy and painful. The patient said the complaint first appeared 3 years ago. However, it is said that 3 years ago only reddish patches followed by peeling skin. The patient has been regularly monitored for skin complaints. She has no history of drug and food allergies. The last treatment of the patient in another hospital was an antihistamine, methylprednisolone 4 mg taken once a day, and a corticosteroid ointment. The patient had a biopsy performed 2 months ago with the result of erythema multiforme. He denied a history of high blood pressure and diabetes. She has no family history with similar complaints. On physical examination found a fever with a temperature of 37.8°C with tachycardia.



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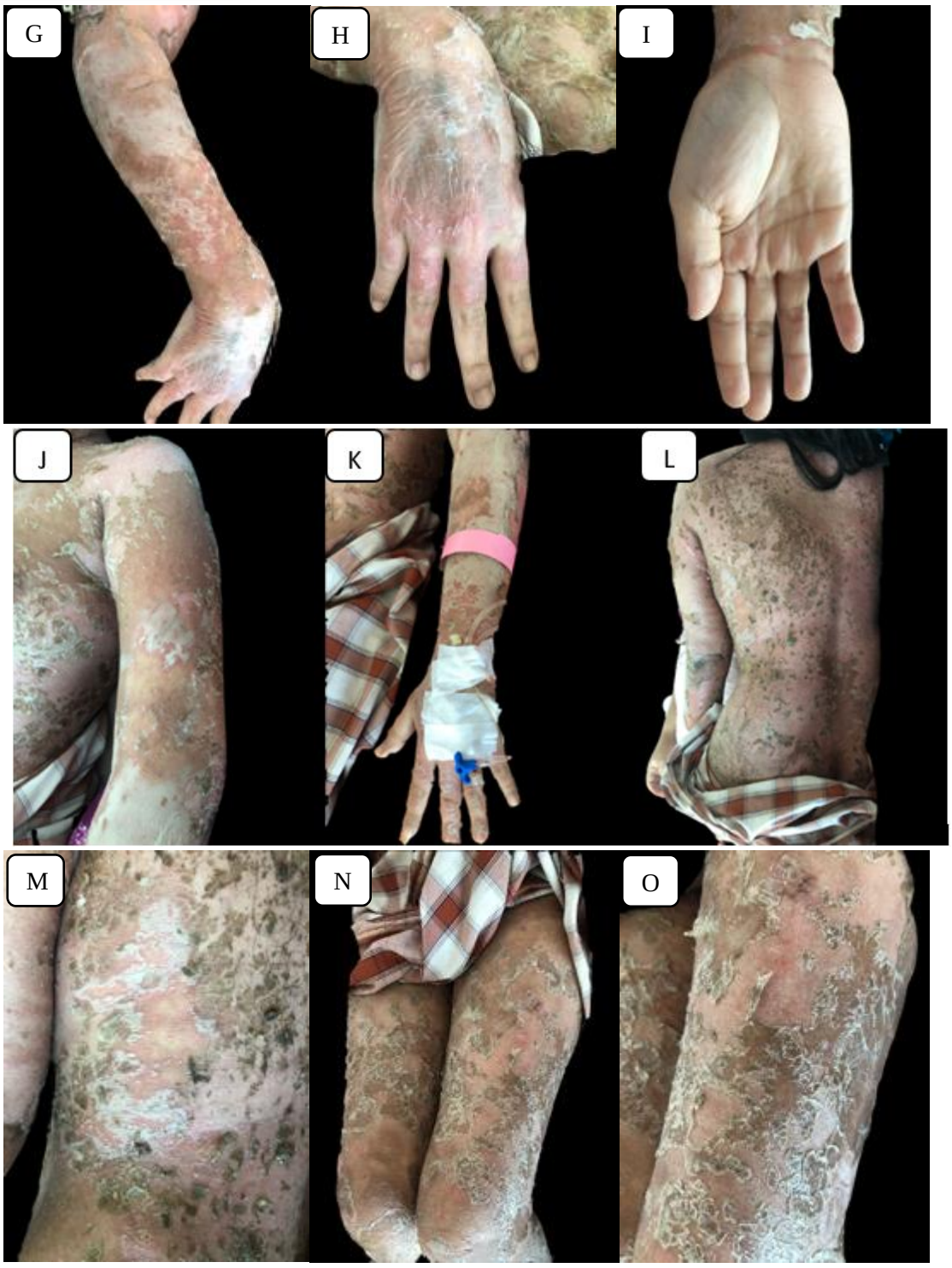
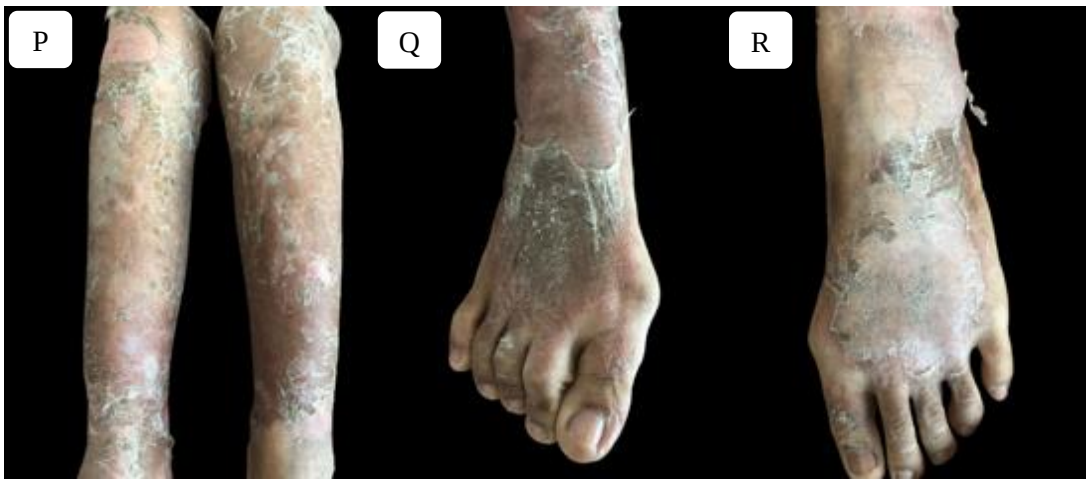
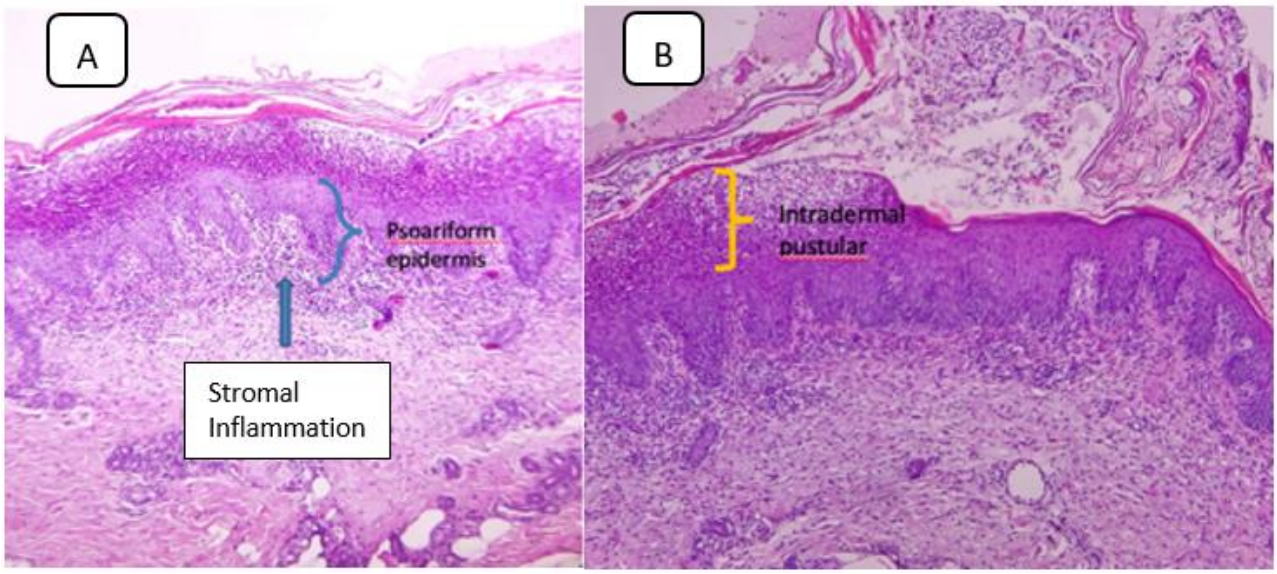




Gambar 1 (A-R). Clinical finding on the first day.

Dermatological status showed miliary pustules on an erythematous, desquamated base all over the body. Blood laboratory results obtained normal results. The working diagnosis in the patient was generalized pustular psoriasis (PPG) with a differential diagnosis of Acute Generalized Pustulosis Exanthema (PEGA). The patient underwent an excisional biopsy with the results on day 4 supporting a diagnosis of generalized pustular psoriasis. The patient was given initial therapy on the first day using dexamethasone 5 mg twice daily intravenously, diclofenac sodium 50 mg twice daily, cetirizine 10 mg once daily, and petrolatum jelly which in the morning and evening throughout. On day 2 of therapy, dexamethasone was replaced with methotrexate 7.5 mg/week. On the 6th day of treatment, the skin on the whole body was dry and peeling. Small white nodules on the abdomen and left arm are minimal with no new lesions appearing. The itching is still felt but has reduced. The patient was then discharged and laboratory tests were carried out again with normal results on the 14th day of control. Methotrexate therapy 7.5 mg/week was continued for 2 weeks and folic acid 1 mg/24 hours/orally and 10% urea was applied morning and evening to the skin as a moisturizer.



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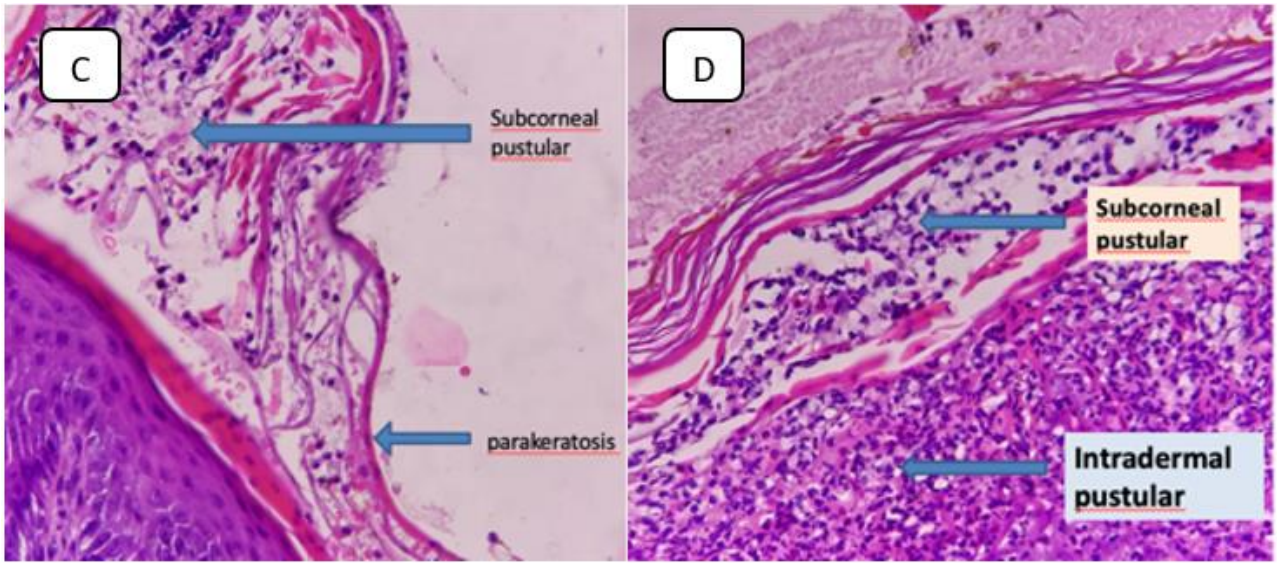
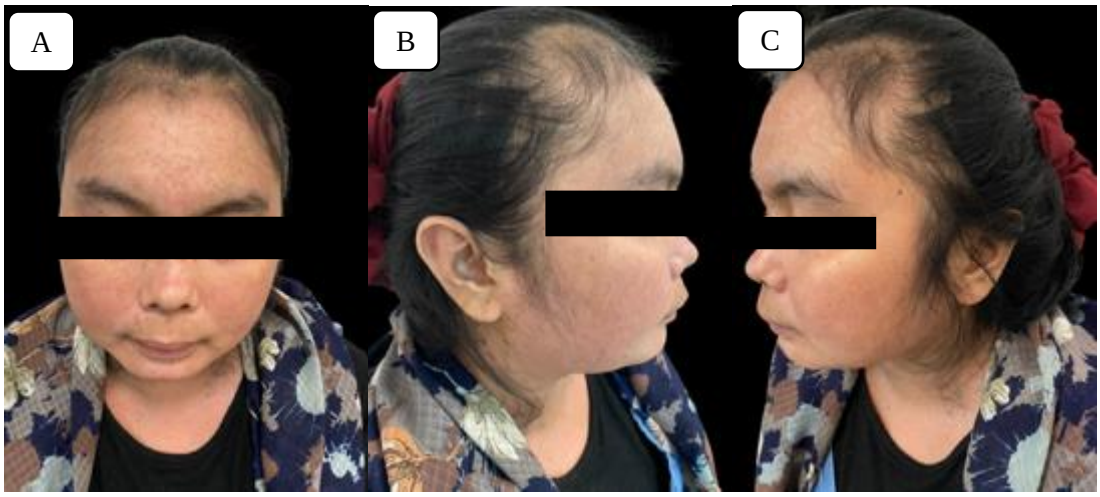
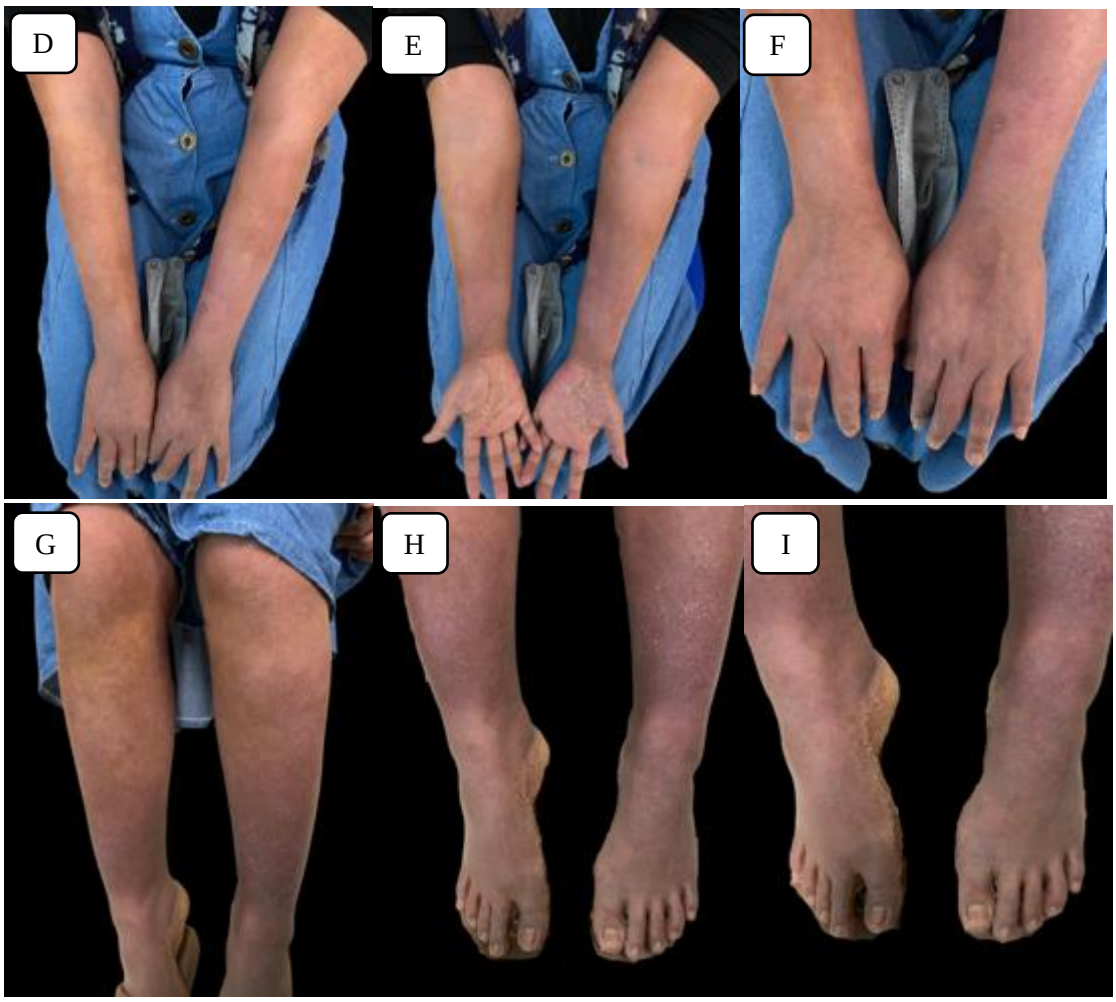


Figure 2. Histopathological results obtained tissue appears to be lined by *squamous* with hyperkeratosis, parakeratosis, and achanthosis, with an elongated rete redge, localized spongiosis. Intradermal and subcorneal pustules were seen with *segmented* (*spongiform*) neutrophil inflammatory cells infiltration (Figs A, B). In the dermis layer, an infiltration of inflammatory cells of mature lymphocytes was seen. No eosinophilic inflammatory cell infiltration was found. Stroma of fibrous connective tissue and collagen (figure A). Skin derivatives were found. No signs of malignancy were found in this preparation. This has the effect of supporting a generalized pustular psoriasis.





Gambar 3 (A-L) Clinical finding on day 14.

3. DISCUSSION

Using guidelines from Japan (2018), a definitive diagnosis of PPG can be made, ie if all four parameters in the guidelines are met. Meanwhile, a suspect diagnosis is made if two or three parameters are met. These parameters are systemic symptoms such as fever and fatigue; Systemic or extensive redness with multiple sterile pustules that may confluent into a *lake of pus;* neutrophilic subcorneal pustules, histopathology characterized by spongiform pustules of kogoj; and recurrence of these clinical and histological findings. European guidelines (2017) define PPG as primary, sterile, nonacral skin pustules that present with or without systemic inflammation, with or without plaque psoriasis, and may be recurrent (more than one episode) or persistent (more than 3 months) [4]. Based on the clinical findings in this patient, the diagnosis of PPG was established according to the guidelines in Japan and Europe. Clinical findings in patients are still possible to be diagnosed with PEGA [5]. The difference between PPG and PEGA is in previous psoriasis history, medication history, duration of clinical symptoms, lesion characteristics, disease recurrence, and histopathological findings. In PPG, a previous history of psoriasis may be found. Fever and lesions have a long duration, lesions are usually monomorphic and last longer, up to 10-14 days before resolution occurs. Lesions rarely involve the flexural areas than PEGA [5], [10- 12]. PEGA is one form of drug reaction. Therefore, there is a history of taking the drug several hours to days before the sudden onset of the lesion. PEGA lesions are nonfollicular pustules several millimeters in size, polymorphic, spreading with erythema or edema. Lesions begin on the face and flexure before spreading to the trunk and extremities. Manifestations resolve after discontinuation of the drug and do not recur. Drugs that often

ISSN: 0005-2523
Volume 62, Issue 09, November, 2022

trigger PEGA are macrolides and beta-lactams. In addition, quinolones, sulfonamides, terbinafine, antimalarials, calcium channel blockers, NSAIDs can also trigger PEGA [10- 12]. In this case, the appearance of the lesions started from the feet, not the face and flexural areas and the onset was not triggered by treatment. Complaints of red spots with repeated scales have been felt by the patient. The clinical features of the patient lead to the diagnosis of PPG. Discontinuation of systemic corticosteroids in patients with plaque-type psoriasis may precipitate a PPG.[2] Skin lesions appear rapidly. In many patients, all lesions appear within 3 days. The lesion starts distally and then spreads centripetally. The lesions are symmetrical, with distribution on the extensor surfaces of the extremities, face, and neck, and very rarely involving the thighs, buttocks, and trunk. The appearance of the lesion is in the form of a target lesion, which is in the form of an erythematous papule or plaque resembling a *wheal*. circular, regular, The center becomes purplish and dark, while the edges still give an erythematous and edematous appearance. In addition, the center may turn into purpuric or necrotic or tense vesicles. Mucosal lesions occur in 70% of patients, especially in the oral cavity [6]. Laboratory examinations of PPG patients usually found an increase in *C-reactive protein* (CRP), leukocytosis and neutrophilia, liver function abnormalities and an increased erythrocyte sedimentation rate (ESR), antistreptolysin O antibody[level] [4], [5]. Therefore, the diagnosis in this patient was re-evaluated clinically and then histopathologically re-examined. The findings of parakeratosis, acanthosis, and elongation of the rete ridges as well as neutrophil infiltration of the stratum corneum, subcorneal and psoriasiform pustules in this case, are consistent with the features of pustular psoriasis. The absence of eosinophilic infiltration in the dermis helps differentiate pustular psoriasis from PEGA [1- 3]. PPG treatment aims to control the pustules quickly and prevent new eruptions; control itching, redness, and edema; control fever and pain; prevent cardiac complications, acute respiratory distress, and kidney failure; control comorbid cholangitis and arthritis. The National Psoriasis Foundation Medical Board makes several lines of treatment based on age group (adults and children) and special conditions (pregnancy). The first-line treatment for PPG in adults is acitrecin, cyclosporine, methotrexate, and infliximab. Second-line treatment includes adalimumab, etanecept, psoralen plus ultraviolet light (PUVA), topical corticosteroids, topical calcipotriene, and topical tacrolimus [5]. Various literature reviews mention that the consideration of the choice of therapy is mostly based on the patient's comorbidities and possible side effects. There are no specific provisions regarding the severity and PASI score that are considered in the selection of therapy [4], [8]. The patient was given methotrexate 7.5 mg/week. Guidelines from the National Psoriasis Foundation recommend an initial dose followed by examination for hematological abnormalities 7 days later. The commonly used dose is 7.5-25 mg per week [7]. The dose of MTX in this patient has been adjusted. Methotrexate (MTX) is a dihydrofolate reductase inhibitor that is often used in inflammatory conditions as a *steroid-sparing agent.* MTX is contraindicated in pregnancy because it is stimulating abortion, mutagenic and teratogenic; the drug should be discontinued at least 3 months before conception in both men and women; potential to cause hepatotoxicity and hematological toxicity; Drug onset lasts up to several weeks [4], [7], [8]. Acitrecin has the highest efficacy among the first-line therapeutic options. Patients who are unresponsive or intolerant to acitrecin can use methotrexate. Methotrexate has a slower onset and potential for hepatotoxicity and haematological toxicity. Cyclosporine is used in severe and acute disease because of the rapid onset of the drug. One case demonstrated the use of cyclosporine in a case that was resistant to other treatments. This drug must be considered for side effects in the form of hypertension, nephrotoxicity, and an increased risk of infection. Infliximab also has a rapid onset, ie resolution of pustules within 1 – 3 days, so it is considered first-line therapy in patients with severe and acute PPG. Infliximab increases the risk of serious infections, lymphoma and other malignancies, and can trigger *flares* PPG [4], [5], [7], [8].

4. Conclusion

Because there are no standard recommendations for establishing the diagnosis of generalized pustular

psoriasis, the clinical presentation must be known to make a diagnosis.

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