

The Coexistence of Systemic Lupus Erythematosus and Psoriasis: Is It Possible?

Hendra Gunawan, Awalia, Joewono Soeroso

Department of Internal Medicine, Faculty of Medicine, Airlangga University - Dr. Soetomo Hospital, Surabaya, Indonesia

Corresponding Author:

Prof. Joewono Soeroso, MD., M.Sc, PhD. Division of Rheumatology, Department of Internal Medicine, Faculty of Medicine, Airlangga University - Dr. Soetomo Hospital. Jl. Mayjen. Prof. Dr. Moestopo 4-6, Surabaya 60132, Indonesia. email: joewono.soeroso4@gmail.com; sylvester.gunawan@gmail.com.

ABSTRAK

Lupus eritematosus sistemik (LES) adalah penyakit autoimun kronik eksaserbatif dengan manifestasi klinis yang beragam. Psoriasis vulgaris adalah penyakit kulit yang menyerang 1-3% dari populasi. Patofisiologi mengenai tumpang tindihnya penyakit tersebut belum sepenuhnya diketahui. Hal ini menyebabkan adanya tantangan tersendiri dalam tatalaksana kedua penyakit tersebut. Dua orang laki-laki dengan LES dan psoriasis vulgaris dilaporkan dengan manifestasi klinis eritroderma berulang dengan fotosensitif. Perbaikan klinis dicapai setelah terapi kombinasi metilprednisolon dengan metotrexat. Adanya LES yang tumpang tindih psoriasis vulgaris merupakan suatu fenomena klinis yang langka. Hubungan kedua penyakit tersebut dapat berupa saling mendahului atau tumpang tindih pada suatu waktu yang sama dan memiliki hubungan dengan adanya anti-Ro/SSA. Adanya tumpang tindih dari dua penyakit tersebut memberikan paradigma baru dalam patofisiologi, diagnosis, dan tatalaksana di masa mendatang.

Kata kunci: lupus eritematosus sistemik, psoriasis vulgaris, psoriatic arthritis, overlap syndrome.

ABSTRACT

Systemic lupus erythematosus (SLE) is a chronic autoimmune disease with various clinical disorders and frequent exacerbations. Psoriasis vulgaris is a common skin disorder which affect 1-3% of general populations. The pathophysiology regarding the coexistence of these diseases is not fully understood. Therapeutic challenges arise since the treatment one of these diseases may aggravate the other. We reported two cases of SLE with psoriasis vulgaris with clinical manifestations as recurrent erythroderma with photosensitivity. Improvement in clinical condition was observed after treating the patients with methylprednisolone combined with methotrexate. The coexistence SLE and psoriasis are considered very rare. The presence of this overlap syndrome may precede one another or occur simultaneously and is closely related with the presence of anti-Ro/SSA. Thus, it raises new challenge regarding its relationships, diagnosis, therapeutic, and management.

Keywords: systemic lupus erythematosus, psoriasis vulgaris, psoriatic arthritis, overlap syndrome.

INTRODUCTION

Systemic Lupus Erythematosus (SLE) is a chronic exacerbative autoimmune disease with various clinical disorders. Cutaneous manifestations are frequent in SLE, as much as 70-80% patients develop skin lesions during the disease progression and approximately 20% of SLE patients have skin lesions as initial presentation. Cutaneous manifestations in SLE can be divided into acute, subacute, and chronic cutaneous lupus erythematosus (CCLE). The most common cutaneous manifestations are malar rash, photosensitivity, discoid lesions, and alopecia. Other manifestations such as Raynaud phenomenon, livido reticularis, panniculitis, bullous lesions, vasculitic purpura, and urticaria may be related but not specific to SLE.^{1,2}

Subacute cutaneous lupus erythematosus (SCLE) distribution is more extensive than chronic cutaneous lupus erythematosus. SCLE also has the tendency to spare the face with minimal or no scarring. The most common types are papulosquamous and annular polycyclic lesion. Other SCLE presentations such as erythroderma, erythema multiforme, toxic epidermal necrolysis like lesion (Rowell syndrome), and generalized poikiloderma are uncommon and considered as rare type of SCLE.^{3,4} Majority of patients with SCLE are associated with anti-Ro antibodies but only 50% of patients meet criteria for SLE. Patients with SCLE usually have mild systemic symptoms with arthritis and myalgia are the most common symptom. Other more severe symptoms such as lupus vasculitis, CNS lupus, and nephritis are scarce and only occur in less than 10%.²

Psoriasis vulgaris is a skin disease which affects approximately 1-3% in general population.⁵ It is a chronic inflammatory skin disease. Inflammatory arthritis is a common clinical manifestation in psoriasis patient, approximately affecting 25% psoriasis patient. It affects both men and women equally and at the age of 30-50 years old. Psoriatic arthritis (PsA) is a seronegative spondyloarthritis due to the potential of axial joint involvement and enthesitis as its pathogenesis. The presentation is variable and can range from mild to debilitating, erosive arthropathy.⁶

The coexistence of SLE and PsA is very rare with a prevalence of 0.6%.⁷ Psoriasis generally precedes the SLE. Phototherapy which is common management in patient with psoriasis may act as a trigger for SLE. Common problems are diagnostic problem and therapeutic management as SLE is a seropositive arthritis while PsA is a seronegative arthritis, and hydroxychloroquin as well as systemic corticosteroids may exacerbate psoriasis.⁸ Therefore, we reported a case series of patients with psoriatic-like skin lesion presenting as erythroderma.

CASE ILLUSTRATION

Case 1

A 45-year-old male came into the emergency department with persistent scaling and redness of the skin. History taking revealed persistent scaling and redness of the skin had occurred since 7 months before. Scaling of the skin was preceded by redness, and skin eruptions in extensor area of extremities. History of taking antibiotics, non-steroid anti-inflammatory drugs, and pain killer drugs was not reported. There were no constitutional symptoms like fever, fatigue, nausea, shortness of breath, vomiting, and weight loss. He was anxious about his medical condition and had insomnia since 2 months before. Joint pain was felt on both hands, fingers, and knees. Previous medication history revealed the presence of psoriasis vulgaris based on skin biopsy which did not improve with methotrexate 15 mgs weekly, type 2 diabetes mellitus with insulin, and depression. He worked as an officer in a construction company and had a history of photosensitivity with sun exposure. Family histories of psoriasis and connective tissue diseases were negative.

Physical examination revealed a fully alert with normal, vital signs, thorax, and abdominal examinations. Extremities examinations revealed the presence of joint swelling without tenderness in PIP and DIP I-II-III-IV-V, as well as bilateral knees. Erythroderma presenting as generalized maculae with squamae was evident in $\geq 10\%$ of his Body Surface Area (BSA) (**Figure 1**). Psoriatic nail was evident in fingers and toes. Laboratory parameter showed hemoglobin



Figure 1. Physical appearance of the patient. The right side showed the presence of psoriatic nail with erythematous maculae and squamae.

13.5 g/dL, leukocytes 13.14 μ /L, neutrophils 62.3%, platelets 345 μ /L, albumin 2.86 g/dL, fasting glucose level 200 mg/dL, 2-hours post prandial glucose level 315 mg/dL, and low level of potassium 3.0 mEq/L. Renal and liver function tests are within normal limit.

Immunology parameter revealed ANA test was positive 1:151.4, ANA profile showed the presence of anti Ro/SSA (Ro-52 recombinant), rheumatoid factor, and IgM anti MCV. Radiology examination revealed seagull appearance in PIP and DIP joints in both sides of hands (**Figure 2**), degenerative disease of the spine without sacroilitis. Skin biopsy revealed the presence of elongated rete ridges, parakeratosis, acanthosis concurrent with psoriasis. His Dermatology Life Quality Index (DLQI) score was 24. Systemic lupus erythematosus (SLE) and psoriatic arthritis



Figure 2. The presence of seagull-like appearance showed the evidence of psoriatic arthritis in both hands

were diagnosed in this patient based on SLICC criteria which showed the presence of depression, skin lesion, skin rash (erythroderma), arthritis, along with the presence of ANA and anti Ro/SSA as the immunology criteria, SLE and psoriatic arthritis were assessed in this patient.

Pulse dose of 500 mg methylprednisolone was administered in 3 days, methotrexate 15 mg po/weekly along with folic acid supplementation and basal bolus insulin regimen. Intravenous methylprednisolone was tapered to 1 mg/kgBW after pulse dose. Scaling of the skin was improved there was no new episode of scaling, and joint pain was improved by the 6th day after pulse dose of methylprednisolone. He was discharged from hospital with methylprednisolone, methotrexate, basal bolus insulin, and education about his current condition.

Case 2

A 79-year-old male came into emergency department with scaling of the skin since 3 days ago. He had a history of generalized erythematous lesion 3 weeks before admission. Scaling of the skin was preceded with redness and itch in all areas of his body. Constitutional symptoms like fever, dyspnea, and joint pain was reported. Joint pain in both knees, fingers, and toes were reported since 4 months ago. Morning stiffness were also felt for 40 minutes. History of photosensitivity, recurrent painless oral thrush since 6 months ago were reported. There was no history of weight loss, nausea, vomiting, nor diarrhea. Skin biopsy revealed the presence of psoriasis vulgaris. He is a retired clerk, with 9 children spent his time mostly by gardening. There was no family history of autoimmune nor metabolic diseases.



Figure 3. The presence of generalized erythroderma in this patient

Physical examination revealed the presence of edema in bilateral pretibial. Dermatological examination revealed the presence of Auspitz's sign and erythroderma in $\geq 10\%$ BSA (**Figure 3**). Laboratory parameter showed hemoglobin 11.5 g/dL, leukocytes 8,500 μL , neutrophils 45%, eosinophils 11.9%, lymphocytes 51%, platelets 42,000 μL , albumin 2.9 g/dL, CRP 80 mg/dL, AST 44 IU/L, and ALT 65 IU/L. His ANA-IF revealed the nucleoplasm speckled pattern $\geq 1:1000$, cytoplasmic homogenous 1:100, whereas anti Ro/SSA was negative.

Bilateral knee x-ray examinations revealed the presence of bilateral entesopathy (**Figure 4**) and gull wing appearance in both PIP II-III-IV-V. His DLQI score was 7. Based on his age, the presence of, skin rash, thrombocytopenia, arthritis, photosensitivity, and ANA-IF, SLE was assessed in this patient. Therefore, SLE + psoriatic

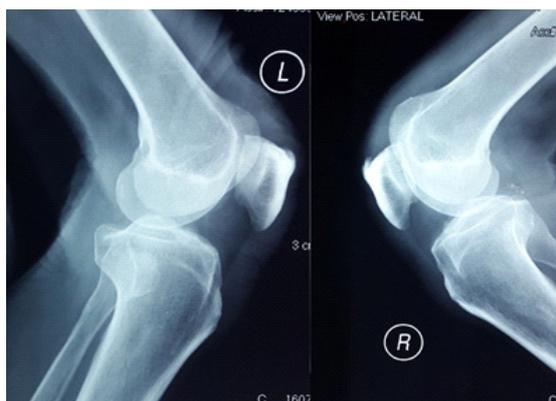


Figure 4. The presence of entesopathy bilateral.

arthritis was assessed in this patient. Supportive treatment was given due to recent pneumonia and older age. Intravenous methylprednisolone 1 mg/kgBW was administered for 7 days and methotrexate 10 mg/weekly. Upon treatment, symptoms were gradually improved including no new rash, increased platelets (68,000 μL) and he was discharged after 10 days of hospitalization.

DISCUSSION

Subacute cutaneous lupus erythematosus clinical manifestations occurred mostly in females. Its lesions present with erythematous macules and papules that evolve into scaly papulosquamous (psoriasiform) or annular/

polycyclic plaques. Other forms, such as erythroderma, erythema multiforme-like lesions, and generalized-poikiloderma may occur and regarded as a rare type of SCLE.³ The presence of SCLE is closely associated with the presence of anti-Ro/SSA.⁹ The key mechanism in SLE is the production of autoantibodies which are produced by polyclonal B cell activation or autoantigen directed immune stimulation. Several factors such as genetic, environmental, and hormonal factors are the trigger of SLE.¹⁰

The presence PsA is approximately 25% in patients with psoriasis. It is characterized by stiffness, pain, swelling, and tenderness of the joints as well as surrounding areas, such as ligaments and tendons. It affects both male and female equally and typically presents at the age of 30 to 50 years. The presence of cutaneous symptoms usually precedes the onset of PsA. It is considered as a seronegative spondyloarthritis. The clinical manifestations ranges from mild arthritis to severe, debilitating, and erosive arthropathy.^{6,11} Imaging examinations such as conventional radiography, computed tomography, magnetic resonance, skeletal scintigraphy, positron emission tomography, and fluoroscopic optical imaging are helpful in making diagnosis, evaluating, and monitoring disease progression. Conventional radiography may reveal the combination of destructive changes such as erosions, tuft resorption, and osteolysis with bone proliferation including periostitis, ankylosis, spur formation, as well as non-marginal syndesmophytes. Though less sensitive than the others, conventional radiography remains highly specific compared to CT in detection of joint erosions.¹²

The etiology and pathogenesis of psoriasis are not yet understood, but it is thought to be a multifactorial disease comprises of genetic disposition and environmental risk factors which act as trigger factors, such as stress, trauma, infections, and drugs. Psoriasis shares both immunologic and genetic risk factors with other autoimmune diseases such as rheumatoid arthritis (RA) and SLE. The role of novel CD4 T effector cells (TH17) plays an important role in autoimmune inflammatory response. The main cytokines secreted by TH17 is IL-6, IL-17, IL-

21, and IL-22. Keratinocytes hyperproliferation is induced by IL-21 and IL-22. Thus, the current postulate that in a genetically predisposed an unknown stimulus are needed on epidermal keratinocytes to produced tumor necrosis factor (TNF)- α , interferon (IFN)- α , and IFN- γ . These mediators will activate dendritic cells and induce the differentiation of naïve T cells into TH1 and TH17 which would migrate to skin, acting as antigen presenting cells and releasing cytokines, such as TNF- α , IFN- γ , IL-23, IL-22, and IL-17. Those cytokines induced proliferation of keratinocytes and alter their maturation, resulting the epidermal hyperproliferation, together with inflammatory T cell infiltration are the fundamental basis psoriatic lesions.¹⁰

The presence of SLE and psoriasis itself is very rare. The association between these two disease is not yet fully understood even though there should be the trigger that induce the development of both diseases.¹³ It is known that T cells play a central role in the development of psoriasis whereas B cells do in SLE. This fact leads to the view that superantigens might be the common mediator, but it is known that alterations of TH17 may occur in both diseases. The presence of IL-17 and IL-23, cytokines which are produced by TH17 subset play a role to the renal damage in SLE patients.¹⁰ The onset of both diseases might precede one another or occur simultaneously in a person. Patients with overlap syndrome of SLE and psoriasis have an increased risk for photosensitivity which was evident in both cases.^{5,13}

The presence of SLE and psoriasis raises question about how to diagnose both diseases. The coexistence of these diseases is associated to ANA and anti-Ro/SSA (52-recombinant). Cozzani et al.¹⁴, reported that ANA was present in 98% SLE patients and 57% psoriasis patients. Anti-Ro/SSA's presence were reported in psoriasis and SLE. Silvy et al.¹⁵, reported that Anti-Ro/SSA was present in 3 out of 200 psoriasis cases, whereas Johnson et al, reported its prevalence was 2% in biologically agent naïve psoriatic arthritis patients. Anti-Ro/SSA's presence was also reported in SLE patients. Cozzani et al.¹⁴, reported its prevalence was 80% in SCLE patients, another report by

Lopez-longo et al.¹⁶, showed that anti-Ro/SSA was detected in 88% patients with SCLE.^{9,14-17} Though antibodies to Ro/SSA was pivotal in the diagnosis of SLE and psoriasis, some cases reported with this overlap syndrome reported the absence of antibody to Ro/SSA antibody. Thus, detailed medical history taking, including the history of previous medication, photosensitivity, and other constitutional symptoms must be done meticulously.¹⁰

Histologic examination, serology, and immunofluorescence test (lupus band test) are useful to search for the deposit of immunoglobulin and complement components in dermoepidermal junction which is seen in SLE patients. The most frequent immunoglobulin class deposited is IgM, seen in 90% of lesional skin biopsies. It is helpful in diagnosing SCLE or Chronic Lupus Cutaneous from other type of SLE since it is only positive in skin lesion. The disadvantages are the presence of antibody is found in 60-100% biopsy samples and its wide range of sensitivity (10.5-78.9%) as well as specificity (47.8-97.8%) depending on the criteria used.^{18,19} We thought there was a strong indication to perform lupus band test to confirm SLE diagnosis in both cases, but we could not do that due to lack of equipment. Therefore, we diagnosed SCLE in case 1 based on refractory erythroderma which was unresponsive to psoriasis medication. Thrombocytopenia can be found in psoriasis patient after receiving anti-TNF therapy, and case 2 was naïve to psoriasis medication.²⁰ Therefore, based on his age, thrombocytopenia, arthritis, photosensitivity, and ANA test, we diagnosed this patient with SLE and psoriasis.

The coexistence of these diseases raises question about the management to control both diseases simultaneously. The control of SLE requires the administration of systemic corticosteroid, especially in SLE with renal or central nervous system involvement. Failure in corticosteroid tapering may induce rebound flare of psoriasis or psoriatic erythroderma. Phototherapy though favorable for psoriasis in most cases must be put into consideration as it can trigger SLE flare. Antimalarial agents which widely used in cutaneous and joints manifestations may aggravate or precipitate

psoriasis. Patients with cutaneous SLE who develops psoriasis after the administration of antimalarial agents should be evaluated for the possibility of drug-induced psoriasis.^{10,13}

Biologic agents, like etanercept or infliximab may be used to control psoriasis but its adverse effect such as anti-TNF α induced lupus (ATIL) must be considered. Though reversible through withdrawal of therapy, the clinical manifestations may involve renal and central nervous system. Systemic corticosteroids or immunosuppressants often needed to control moderate-to-severe psoriasis. Moderate-to-severe psoriasis is defined as the presence of skin lesion >10% BSA and DLQI score >10. Glucocorticoid pulse is indicated in severe psoriasis.^{21,22} Methotrexate is the only agent that is known successfully treating the coexistence of these diseases. In our cases both patients were administered systemic corticosteroids.¹⁰

We administered pulse dose of 500 mg intravenous methylprednisolone in case 1 because of the severe psoriasis which presented as recurrent generalized erythroderma in \geq 10% of his BSA and DLQI score was 25. We did not administer pulse dose of corticosteroids to case 2 because he was an elderly patient and the history of recent infection. Therefore, we used intravenous methylprednisolone 1 mg/kgBW with close monitoring to the platelet counts. Methotrexate was given to both cases. The clinical condition of case 1 improved dramatically after pulse dose of corticosteroids and methotrexate 15 mg/weekly. There was no new rash and he could resume his daily activities. Patient in case 2 had a worse prognosis because of his age and many comorbid factors, such as history of infection in previous hospital admission.

CONCLUSION

It has been reported a case series of coexistence of SLE and psoriasis with erythroderma as its manifestation. The coexistence of both diseases is rare and poses new challenge in discovering its relationships, therapeutical management, and education. The presence of this overlap syndrome may precede one another or occur simultaneously and is closely related

with the presence of anti-Ro/SSA. Lupus Band test is helpful to search for immune complex deposition in skin lesion. Therapeutic challenges occur in which suppression of SLE activity with corticosteroids or antimalarial agents may aggravate or precipitate psoriasis and phototherapy or biologic agents may trigger SLE flare. Thus, proper history taking should be performed in order to diagnose this rare phenomenon and giving comprehensive managements are key to suppress the activities of both diseases.

COMPETING INTEREST

The authors declare that there is no conflict of competing interest regarding the publication of this article.

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