


From CLE to SLE: A Case Report from Local Hospital

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ABSTRACT

Introduction: Lupus erythematosus (LE) is a combination of various interrelating autoimmune clinical diseases. Cutaneous lupus erythematosus (CLE) is a spectrum of typical autoimmune skin features of systemic lupus erythematosus (SLE). A good recognition of the typical appearance of this skin lesion (CLE) enables diagnosis and good management of SLE. **Case**: A 26-year-old female with SLE with *acute skin lessions* (ACLE) skin lesions. Suspicion of SLE became stronger when the antinuclear antibody (ANA) titer reached 1:3,200. The main therapy is methylprednisolone injection followed by a gradual dose reduction. The patient was treated for 6 days in hospital and all lesions improved. **Conclusion**: The patient in this case had SLE with 6 clinical domains in the EULAR/ACR 2019 criteria and a total score of 34 (>10). Earlier and more accurate diagnosis of SLE can make therapy more effective, especially if CLE is already present.

Keywords: Autoimmune disease, cutaneous lupus erythematosus, SLE.

ABSTRAK

Pendahuluan: Lupus eritematosus (LE) merupakan penyakit yang merupakan gabungan dari berbagai penyakit klinis autoimun yang saling berkaitan. Lupus eritematosus kulit (CLE) adalah spektrum kulit ciri khas dari lupus eritematosus sistemik (SLE). Pengenalan gambaran khas lesi kulit (CLE) ini memungkinkan diagnosis dan penatalaksanaan SLE yang baik. **Kasus:** Wanita berusia 26 tahun penderita SLE dengan lesi kulit akut (ACLE). Kecurigaan terhadap SLE makin kuat karena titer antibodi antinuklear (ANA) mencapai 1:3.200. Terapi utamanya adalah injeksi *methylprednisolone* dilanjutkan dengan pengurangan dosis secara bertahap. Pasien dirawat selama 6 hari di rumah sakit dan semua lesi membaik setelah perawatan. **Kesimpulan**: Pasien pada kasus ini mengalami SLE dengan 6 domain klinis pada kriteria EULAR/ACR 2019 dan skor total 34 (>10). Diagnosis yang lebih dini dan tepat terhadap SLE dapat membuat terapi jadi lebih efektif, terutama jika sudah ada CLE. **Kelvin, Louis Rianto, Linda Julianti Wijayadi. Dari CLE Menjadi SLE: Sebuah Kasus di Rumah Sakit Lokal.**

Kata Kunci: Penyakit autoimun, lupus eritematosus kulit, SLE.

Introduction

Lupus erythematosus (LE) is a combination of various clinical disosders.[1] The incidence rate of systemic lupus erythematosus (SLE) is 5.14 (1.4-5.13) per 100,000 people per year.[2] Several risk factors can influence the incidence of SLE, namely genetics, drugs, viruses, UV rays, and tobacco.[1] The initial presentation of SLE is often similar to the constitutional viral syndrome, such as weight loss, fatigue, low-grade fever, and arthritis.[3] SLE diagnosis must fulfill several criteria that evolved over time.[4] Cutaneous lupus erythematosus (CLE) refers to LE-specific skin disease. A good detection of CLE is the first step in diagnosing SLE, as CLE can develop into SLE.[1] Symptoms in CLE are often influenced by several risk factors, especially cigarette smoke or sunlight.[5]

Management of SLE is especially with antimalarial therapy, typically hydroxychloroquine (HCQ). HCQ is generally well tolerated and has been shown to lower the risk of disease flares, improve life expectancy, decrease thrombosis risk, and have positive effects on skin disease and manifestations of SLE.[5] Glucocorticoids are also used to control disease activity.[6] Prevention, such as using sunscreen and avoiding direct sunlight, can be beneficial.[1] This case report aims to recognize CLE early to prevent its development into SLE and the management of CLE and SLE.[7]

Case

A 26-year-old female came to the hospital emergency room (ER) with shortness of breath accompanied by a cough with phlegm since a week ago. The patient complained of recurring joint pain for 4 months and was self-treated with herbal medicine and piroxicam. Red spots appeared on the face 3 months ago, reddening on both sides 1 month later (Figure 1). The patient also experienced oral ulcers, hair loss, and weight loss from 42 kg to 34 kg. In the ER, the vital signs were blood pressure 110/70 mmHg, pulse 139x/minute, respiration 24x/minute, a high temperature (39^{0}C), and O_2 saturation 97%. Physical examinations found anemic conjunctivae in both eyes, stomatitis, and signs of fluid in the lungs.

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Laboratory examination **(Table 1)** revealed anemia, leukopenia, hypoalbuminemia, and proteinuria. The ANA test was positive with a titer of 1/3,200. A right pleural effusion was found in the chest x-ray **(Figure 3).** The diagnosis is SLE with constitutional, hematologic, mucocutaneous, serosal, musculoskeletal, and renal involvement. The treatment was 125 mg methylprednisolone IV twice daily with dose titration for 6 days. On the third day, several coin-like lesions appeared on both palms **(Figure 2)** and under the neck; all lesions improved after treatment. A drip of 25% albumin, 100 mL for 3 consecutive days, accompanied by oral albumin, folic acid, and $CaCO_3$ three times a day, was also given. The systemic symptoms persisted even after the skin symptoms had decreased; she was referred to a type A hospital for further treatment.

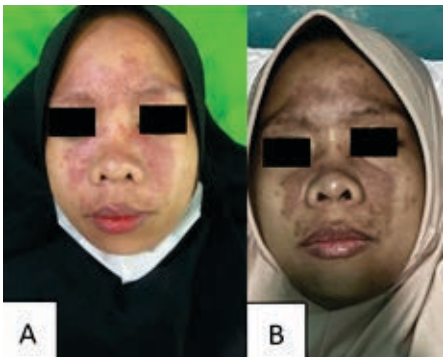

Figure 1. Lenticular to plaque-sized erythematous plaques in the facial region or "butterfly/malar rash" on the 1st day of hospitalization (A) and become hyperpigmented after 2 weeks (B).

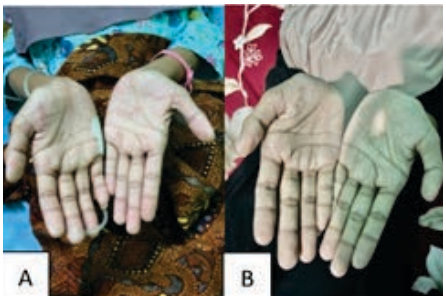

Figure 2. Miliary to lenticular erythematous macules on both palms on the 3rd day of hospitalization (A) and become hyperpigmented after 2 weeks (B).

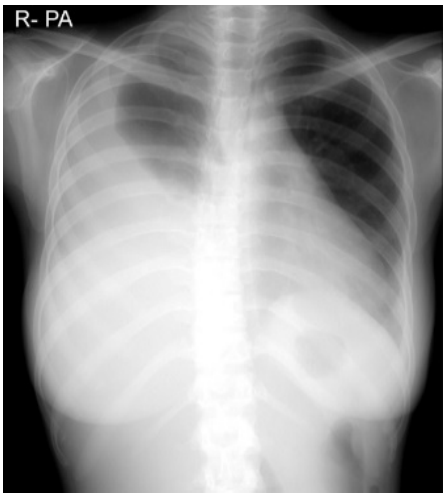

Figure 3. Right pleural effusion.

Discussion

Lupus erythematosus (LE) is a combination of various clinically interrelated autoimmune diseases, especially against nucleosomes and ribonucleoproteins.[1] The etiopathogenesis is multifactorial, consisting of several genetic, immunological, endocrine, and environmental factors. Females are ten times more at risk of developing SLE than males, and the risk of SLE is 14 times higher in Klinefelter Syndrome (47, XXY).[8] Many factors play a role in the pathophysiology of lupus erythematosus. Innate and adaptive immune responses play an important role in the development of lupus erythematosus. Activation of the innate immune system can be Toll-like receptor-dependent or independent. T and B lymphocytes also play a role in the emergence of lupus erythematosus.[9] Systemic lupus erythematosus is caused by aberrant activity of the immune system; the immune system attacks healthy cells and tissues. Early genetic studies observed familial SLE aggregation and high concordance in monozygotic twins, implicating HLA and early complement component genes.[10]

The incidence rate of SLE is 5.14 (1.4-5.13) per 100,000 people per year.[2] The prevalence of SLE in Indonesia reaches 0.5% of the total population.[11] Several risk factors can influence the incidence of SLE, namely genetics, drugs, viruses, UV rays, and tobacco.[1] The initial presentation of SLE is often similar to constitutional viral syndromes, such as weight loss, fatigue, and low-grade fever, usually followed by arthralgias or arthritis. Arthritis in SLE is characterized by morning stiffness and mild to moderate joint swelling. It is non-erosive, may be symmetrical or asymmetrical, and may affect large or small joints. If constitutional symptoms with arthralgias or arthritis are not accompanied by other characteristic manifestations of lupus, such as photosensitive rash on the face, neck, or extremities, it is appropriate to conduct a clinical and laboratory evaluation for infection before diagnosis of SLE.[3] Chronic inflammation, such as SLE, can increase catabolism, and albumin is broken down more rapidly. Redistribution of albumin can occur in overhydration or when albumin moves into the interstitial space; dilutional hypoalbuminemia is common in SLE.[12]

In 1997, the American College of Rheumatology (ACR) established 11 criteria for SLE. Four of the 11 criteria are skin disorders, namely malar rash, discoid rash, photosensitivity, and oral ulcers.[13] It is difficult to differentiate SLE from cutaneous lupus erythematosus (CLE). In 2019, the European Alliance of Associations for Rheumatology (EULAR)/ACR collaboration SLE criteria included an increase in antinuclear antibodies (ANA) of ≥1:80 followed by seven clinical domains (constitutional, hematologic, neuropsychiatric, mucocutaneous, serosal, musculoskeletal,

Table. Laboratory data.

Variables	Value	Reference Range
Hemoglobin (g/dL)	9.3	11.7-15.5
Leukocytes (/uL)	3,200	5,000-10,000
Hematocrit (%)	26.4	35-47
Platelet (/uL)	275,000	150,000-450,000
LED (mm/Hr)	66	0-15
Albumin (g/dL)	2.2	3.4-4.8
Protein (urine test)	Positive 1	Negative


and renal) and three immunological domains (antiphospholipid antibodies, complement proteins, and SLE-specific antibodies), with a total score of at least 10 points **(Figure 4)**.[1,13,14] The majority of SLE patients (97.8%) had a positive ANA, at least previously.[15]

This case presented various systemic signs indicating a change from CLE to SLE. The SLE criteria total score for this patient is 34, with constitutional domain (fever), hematologic domain (leukopenia and autoimmune hemolysis from the anemia), mucocutaneous domain (non-scarring alopecia, oral ulcers, and acute cutaneous lupus), serosal domain (pleural effusion), musculoskeletal domain (arthritis), and renal domain (proteinuria +1). This patient has a right pleural effusion with shortness of breath accompanied by a cough with phlegm for a week. Autoimmune conditions cause inflammation, leading to increased vascular permeability and diminished pleural fluid absorption. Another systemic condition in this patient includes fever, arthritis, hematological abnormalities such as anemia and leukopenia, high ESR, proteinuria and hypoalbuminemia, and high ANA titer (1:3,200), indicating systemic SLE.

Entry criterion

Antinuclear antibodies (ANA) at a titer of ≥1:80 on HEp-2 cells or an equivalent positve test (ever)

If absent, do not classify as SLE

If present, apply additive criteria

Additive criteria

Do not count a criterion if there is a more likely explanation than SLE.

Occurrence of a criterion on at least one occasion is sufficient.

SLE classification requires at least one clinical criterion and ≥ 10 points.

Criterion need not occur simultaneously.

Within each domain, only the highest weighted criterion is counted toward the total scores.

Clinical domains and criteria	Weight
Constitutional	
Fever	2
Hemotologic	
Leukopenia	3
Thrombocytopenia	4
Autoimmune hemolysis	5
Neuropsuhiatric	
Delirium	2
Psychosis	3
Seizure	5
Mucocutaneous	
Non-scarring alopecia	2
Oral ulcers	2
Subacute cutaneous OR discoid lupus	4
Acute cuteneous lupus	6
Serosal	
Pleural or pericardial effusion	5
Acute pericarditis	6
Musculoskeletal	
Joint involvement	6
Renal	
Proteinuria >0,5g/24h	4
Renal biopsy Class II or V lupus nephritis	8
Renal biopsy Class III or IV lupus nephritis	10

Immunology domains and criteria	Weight
Anthiphospholipid antibodies	
Anti-cardiolipin antibodies OR	
Anti-β2GP1 antibodies OR	
Lupus anticoagulant	2
Complement proteins	
Low C3 OR Low C4	3
Low C3 AND Low C4	4
SLE-specific antobodies	
Anti-ds DNA antibody* OR	
Anti-Smith antibody	6

Total Score:

Classify as Systemic Lupus Erythematosus with a score of 10 or more if entry criterion fulfilled.

Figure 4. EULAR/ACR 2019 SLE criteria.[14]

Abbreviations: SLE: Systemic lupus erythematosus; DNA: Deoxyribonucleic acid; IV: Intravena.

The term CLE refers to LE-specific skin disease, which is divided into four types according to the Duesseldorf classification, consisting of acute cutaneous LE (ACLE), subacute cutaneous LE (SCLE), chronic cutaneous LE (CCLE), and intermittent CLE (ICLE).[16] Systemic involvement occurs in nearly 90% of ACLE cases, 20%–30% of SCLE cases, and <5% of chronic localized discoid LE (CDLE) cases.[17] ACLE has two types: local and general. In localized ACLE, a "butterfly" rash usually occurs, covering the cheeks, forehead, front of the neck, and bridge of the nose. SCLE usually occurs in white women with an average age of 50 years. As many as 10%-30% of SCLE patients are drug-induced; most people at that age already have comorbid diseases that require routine medication. CCLE has three types: discoid LE (DLE), LE profundus/panniculitis (LEP), and chilblain LE (CHLE). DLE is the most common (80%) with a coin (discoid) shape.[1,16,18] The fourth type (ICLE) is different from the other types because the prognosis is better than the other types of CLE, so it is considered a separate entity from CLE in the Duesseldorf classification. Lupus erythematosus tumidus (LET) is included in ICLE. Clinically, LET is characterized by single or multiple indurated, weeping, urticarial-like plaques with a smooth reddish or bright purple surface on sun-exposed areas. The swelling and the absence of epidermal involvement are the most important features of LET.[16] This case was a housewife who sometimes went out for a walk in the daytime. SLE was diagnosed because of specific cutaneous ACLE typical symptoms, such as a "butterfly" rash for 2 months and coin-shaped lesions on the palms of both hands and lower neck. The patient also experienced oral ulcers and hair loss but no alopecia.

Standard SLE treatment utilizes antimalarial therapy, typically hydroxychloroquine (HCQ). HCQ is generally well tolerated and has been shown to lower the risk of disease flares, improve life expectancy, decrease thrombosis risk, and have positive effects on skin disease and manifestations of SLE.[5] Glucocorticoids are also used for controlling the disease activity. The dosage depends on the severity of the disease; 5–10 mg prednisone equivalent is usually sufficient for mild manifestations. More severe disease may require higher dosing: up to 0.5–1 mg/kg prednisone equivalent with or without initial pulse


intravenous (IV) methylprednisolone for lupus nephritis, severe hematologic involvement, or central nervous system disease.[6] Because of hypoalbuminemia, a drip of 25% albumin 100 mL for three consecutive days accompanied by oral albumin, folic acid, and $CaCO_3$ three times a day was given. Maintaining the albumin levels was necessary to prevent edema.[12] Other therapies, such as topical steroids and topical calcineurin inhibitors, dapsone, methotrexate, lenalidomide, or mycophenolate mofetil (MMF), can be used.[6] In the management of CLE, first-line local therapy is class 1 topical glucocorticoids and topical calcineurin inhibitors, as well as intralesional triamcinolone acetonide at a dose of 2.5-10 mg/mL. If local therapy fails, one or a combination of aminoquinoline antimalarial drugs can be given, which is effective in 75% of CLE patients.[1,19] To prevent CLE or SLE, sunscreen with a minimum SPF of 30 is recommended.[1] CLE must be immediately treated to prevent SLE progression. However, the patient already had SLE, treated with methylprednisolone 125 mg IV twice a day, and tapered off gradually. We do not use HCQ due to the unavailability of the drug. After 2 weeks, the patient experienced hyperpigmentation on both faces. Increased sun exposure and regular sunscreen noncompliance may be the cause, as hyperpigmentation in the same previous butterfly lesion and sunscreen can prevent hyperpigmentation.[20,21]

Conclusion

We report the case of a 26-years-old female who was confirmed to be suffering from SLE with involvement of constitutional, hematologic, mucocutaneous, serosal, musculoskeletal, and renal. The appropriate clinical symptoms, a supportive physical examination, accompanied by examination tests that led to the diagnosis of SLE. From EULAR/ ACR 2019 criteria, this patient have 6 clinical domains. The total score for this patient is 34 (>10). The therapy was carried out for 6 days of patient treatment. Sunscreen with SPF 30 can be useful for prevention of CLE or SLE with CLE. Our suggestion is that close follow-up is needed regarding the recovery of this patient from skin to systemic lesions.

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