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Case Report

Generalized Discoid Lupus Erythematosus with Systemic Lupus Erythematosus: A Therapeutic Challenge

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Summary

Introduction: Generalized discoid lupus erythematosus (DLE) is a rare skin manifestation; however, about 15-28% of cases may develop into Systemic Lupus Erythematosus (SLE). Generalized DLE with SLE showed a poorer prognosis and required holistic therapy.

Case Report: A 20-year-old female complained of red rash on the skin, worsen with sun exposure in the past two years. She complained of joint pain, fever, decreased appetite, and fatigue, twenty months after the skin rash onset. Skin examination on the scalp, face, trunk, hands and feet showed erythematous to hypopigmentation patches, atrophic skin, and erosions covered with crusts. Laboratory investigations revealed anemia, high titers of ANA, and anti-dsDNA. Histopathological results were consistent with lupus erythematosus. Consultation with an ophthalmologist showed no contraindications to hydroxychloroquine. She was diagnosed with generalized DLE with moderate SLE and showed an excellent response to hydroxychloroquine, methotrexate, both systemic and topical corticosteroids, and sunscreen.

Discussion: Generalized cutaneous lupus can be treated with a topical therapy such as corticosteroid, sunscreen, and systemic therapy such as hydroxychloroquine and corticosteroid. Methotrexate, as a steroid-sparing agent, has a role in treating moderate to severe SLE and lupus arthritis.

Conclusion: Early recognition of SLE in a patient with cutaneous lupus and adequate therapy in generalized DLE is essential. Combination therapy showed better efficacy than monotherapy in generalized cutaneous lupus accompanied by SLE.

Key Words: combination therapy, generalized discoid lupus erythematosus, prognosis, systemic lupus erythematosus

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Introduction

Discoid lupus erythematosus (DLE), one of the many manifestations of chronic cutaneous lupus, has a low prevalence of about 4.79/10,000 cases[1,2]. In the I. G. N. G. Ngoerah General Hospital Dermatovenereology outpatient clinic from January 2020 to March 2022, there were six cases of DLE, but only one with generalized DLE. Generalized DLE can develop into systemic lupus erythematosus (SLE) in 12.4-15% of cases[3].

Management of Generalized DLE with SLE is challenging for clinician because the poor prognosis and requires combination therapy, so collaboration with the Rheumatology department is necessary. Therefore, clinicians need to increase awareness when finding cases of cutaneous lupus to screen the systemic involvement. Thus, clinician can provide adequate therapy to prevent the progression of the disease and improve the patient's quality of life. Here we report one case of generalized DLE with SLE treated with a combination of hydroxychloroquine (HCQ), systemic corticosteroids, and methotrexate, as well as a topical therapy.

Case Presentation

A-20 years old female complained of rash on her face since two years ago, starting on both cheek. The rash felt sore and worsened when exposed to the sun. After that, the rash spread to the scalp, arms, upper back, buttocks, palms, soles, and nails. She never treated this skin complaint before. In the next 20 months, she felt joint stiffness, pain, intermittent fever, weight loss, and feeling tired easily. She seeks treatment after feeling this systemic symptom. Family history with the same symptoms was denied.

On examination of the skin only skin, there were erythematous to hypopigmented macules and patches, erosions covered with hemorrhagic crusts, atrophic scars, and alopecia in some parts of the scalp (Fig. 1). Subungual hyperkeratosis and clubbing finger was found on digits I and II of the right hand and striate leukonychia and onycholysis on the digit III of the right hand. On digit III of the left hand we found nail fold erythema. Phalanges digit II-III of the right and left hand were edematous (Fig. 1). Oral ulcer and serositis were not found. Based on the Cutaneous Lupus Erythematosus Disease Severity Index (CLASI) score, we obtained a score of 32 (severe).

Histopathological examination with hematoxylin-eosin (HE) revealed parakeratosis, epidermal atrophy, vacuolar degeneration with foci of Civatte bodies, follicular plugging, and pigment incontinence. Also, there were increase in dermal mucin deposits with a mild infiltrate of perivascular and peri-adnexal lymphocytic inflammatory cells—these features resemble discoid lupus erythematosus (Fig. 2).

Rheumatologist investigations revealed anemia (11.8 g/dl), ANA titer > 1:1000, and anti-dsDNA titer 380.7 IU/mL. Urinalysis showed no abnormalities. Using European League Against Rheumatism (EULAR)/American College of Rheumatology (ACR), we obtained a score of 16 and The Systemic Lupus Erythematosus Disease Severity Index (SLEDAI) scored 12. The ophthalmologist did not reveal any SLE abnormalities in the eye, and there were no contraindications to using HCQ. She was diagnosed with Generalized Discoid Lupus Erythematosus and moderate Systemic Lupus Erythematosus. She was treated with HCQ 200 mg/day, methylprednisolone 62.5 mg every 12 hours, methotrexate 10 mg/week, and folic acid supplementation 5 mg/week. Topical treatment with 0.25% desoximetasone cream twice daily on the body, scalp, and extremities, and 2.5% hydrocortisone cream twice daily on the face, also broad-spectrum sunscreen with a sun protection factor (SPF) 50. The methylprednisolone dosage was started at 62.5 mg every 12 hours intravenously for three days and then tapered off to 48 mg daily. Tapering off the steroid is based on the patient's clinical condition, which we evaluate every week. After five months of therapy, the patient showed improvement of skin lesions characterized by no new skin lesions, reduced crusting, and reduced hair loss, with the CLASI score was 10 (moderate degree). The symptoms of SLE are improved; reduced joint pain, no fever, and a good appetite, with SLEDAI score 4 (Fig. 3). The methylprednisolone dose was tapered off to 8 mg/day, and another systemic and topical treatment was continued.

Discussion

There are two types of DLE; localized DLE, if the lesion appears in the area above the neck, and generalized DLE, if affects the area above and below the

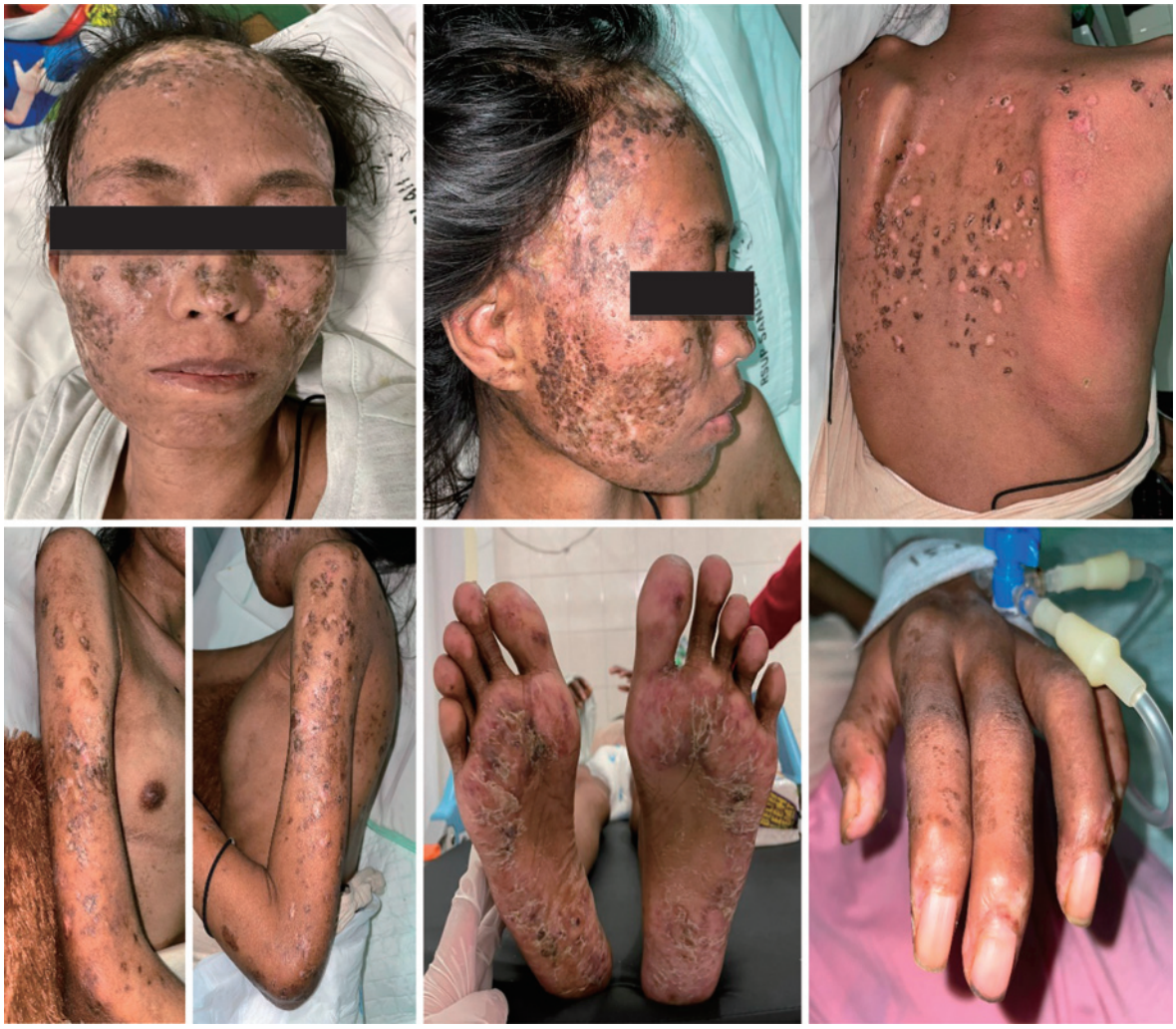

Figure 1 On the scalp, facial, thorax posterior, extremities, plantar et palmar: macules to patches of erythema, hypopigmentation and hyperpigmentation, erosions, hemorrhagic crusts, and atrophic scars.

neck[1,4,5]. Generalized DLE is reported to have a higher risk of developing SLE (15-28%) than localized DLE (5-10%)[1]. DLE can develop into SLE in 4 months to 34 years[6]. In this case, extensive lesions affected the face, scalp, back, hands and feet, and these complaints progressed to SLE within 20 months.

The main principle of managing cutaneous lupus also provides management of systemic conditions. When treating lupus, we need not only to address the acute or exacerbation phase, but also to be aware of the prevention, minimize organ damage and severe side effects of treatment to improve the patient's quality of life[7]. Based on the algorithm, all types of cutaneous lupus are treated based on the extent of skin lesions. If the lesion is localized, it can be treated topically, but if it is widespread and generalized, it should combine with systemic therapy[8].

Localized therapy includes sunscreen and topical drugs such as corticosteroids, calcineurin inhibitors, retinoids, and R-salbutamol[8-10]. Ultraviolet (UV) A and UVB exposure are precipitating factors for DLE exacerbations; broad-spectrum sunscreens with SPF $\geq$ 30 applied at least 2 mg/cm^2 routinely are essential. The effective sunscreens ingredients are octocrylene, Mexoryl SX, Mexoryl XL, parsol, and titanium dioxide. The patient was also advised to protect herself from sun exposure by wearing protective clothing when doing activities under the sun and not consuming photosensitizer drugs[11].

Topical corticosteroids work by reducing the production of immunoglobulins and tumor necrosis factor (TNF)-α, then suppress the inflammatory process. The

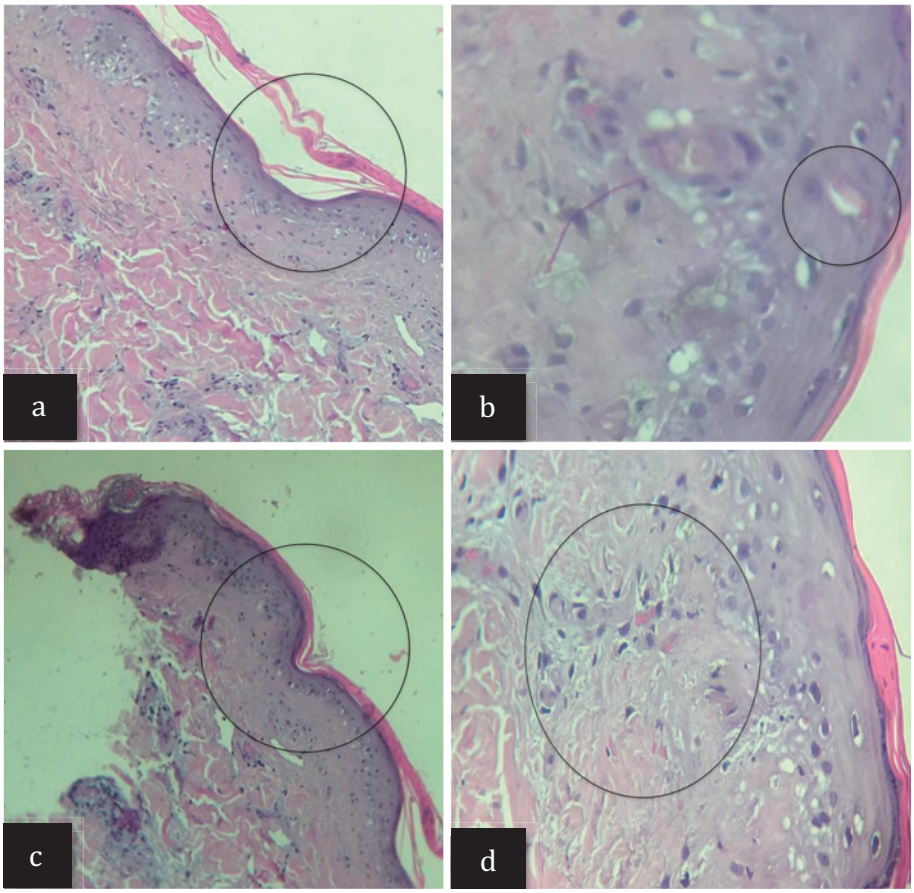

Figure 2 Histopathology section with hematoxylin-eosin stains showed findings of **a.** Epidermal atrophy (×40), **b.** Vacuolar degeneration with foci of Civatte bodies (×400), **c.** Follicular plugging (×40), and **d.** Pigment incontinence (×100)

selection of topical corticosteroids is determined based on the location of the lesion. Facial lesions should be treated with low to medium potent. Lesions on the trunk, arms, palms, soles, and scalp can be treated with medium to high potency[12,13]. To minimize the side effects, topical steroids can be used for two weeks, then enter the drug-free phase every two weeks, or decrease the frequency of use[1,8,10]. A topical combination of steroids and calcineurin inhibitors can be used in cases of lupus refractory to topical therapy[11]. In this case, patient was treated with 2.5% hydrocortisone cream on the face, and 0.025% desoximetasone cream for thick skin lesions, followed by a drug-free phase every two weeks. The drug unavailability limits the choice of topical calcineurin inhibitors in this case. A broad-spectrum sunscreen with SPF 50 was also given for long-term use.

Systemic therapy is given if there is no improvement with localized therapy, generalized skin lesions, or systemic involvement. If cutaneous lupus coexists with SLE, treatment is initially based on SLE's severity[5,14]. Therapy in the acute phase reduces systemic inflammation and achieves remission. Maintenance therapy is to maintain remission and reduce relapse. Assessment of SLE disease activity can be calculated with the SLEDAI score. In the acute phase of moderate SLE, methylprednisolone 250 mg intravenously daily for three days, methotrexate 10-25 mg/week, and HCQ 6.5 mg/kg/day are given. In the maintenance phase, prednisolone 7.5 mg/day, HCQ 200 mg/day, and methotrexate 10 mg/week are used[4].

HCQ is the first-line drug for all types of cutaneous lupus. This drug can lower lysosomal pH, suppress immune cell chemotaxis/phagocytosis, and induce suppression of autoantigen release. HCQ also stimulates anti-inflammatory function and inhibits cytokines such as interleukin (IL)-1, IL-2, interferon (INF)-γ, and INF-α. Generally, HCQ is given in doses of 200-400 mg/day. Another study stated that 200-800 mg/day administration proved effective in 55-82% of cases[15,16]. Side effects

Figure 3 Skin progress after five months of therapy

are retinopathy, xerosis, hyperpigmentation, gastrointestinal intolerance due to high doses, and renal toxicity at a cumulative dose of 1000 grams. Several risk factors that can increase the likelihood of retinopathy include dose > 5 mg/kg BW, duration of use > 5 years, abnormal glomerular filtration rate, and concurrent use of tamoxifen[5]. Before using HCQ and after five years of HCQ treatment, it is recommended for an eye screening. When compared with other drugs, HCQ is a drug with minimal side effects, so it is recommended for lifelong use to control disease activity[5,11].

Systemic corticosteroids are also the first line of therapy in generalized cutaneous lupus. However, clinicians need to be careful when lowering the dose, not too fast or too slow, because it is associated with relapse and increased steroid toxicity. In cases of moderate SLE, starting with intravenous methylprednisolone (≤ 250 mg for 1-3 days) followed by oral prednisolone ≤ 0.5 mg/kg/day and then gradually decreasing it by 5-10% every 1-2 weeks. In DLE, the steroid dose required is >1 mg/kg/day to get better results[12]. Side effects include diabetes, hypertension, cataracts, osteopo-

rosis, and Cushing's syndrome, so monitoring is necessary every three months[4,7].

Methotrexate (MTX) is the primary choice in cutaneous lupus and lupus arthritis among all immunosuppressive agents[4,7]. The action of MTX in lupus is through its anti-inflammatory effect, which stimulates adenosine release and further suppresses the inflammatory function of neutrophils, macrophages, and lymphocytes[4]. MTX can decrease the expression of skin lymphocyte antigens on mononuclear cells and cause downregulation of endothelial E selectin and decrease mononuclear leukocyte infiltration in skin lesions. A retrospective trial by Wenzel et al. on 43 patients with refractory cutaneous lupus found that 98% of cases improved after low-dose MTX administration, of which 12 were DLE who responded well to methotrexate 7.5-25 mg/week[7,17]. Side effects include myelosuppression, liver fibrosis, cirrhosis, and pulmonary infiltrates. Monitoring can be done every 2-4 weeks[4].

Combination therapy gives better results in preventing recurrence and complications when compared to monotherapy[4,9]. Based on EULAR recommendations, immunosuppressants should be considered in the acute phase of moderate and severe SLE to reduce the side effects of steroids. A study in Toronto reported that the combination of HCQ and MTX can reduce corticosteroid use and reduce SLE exacerbations in more than 60% of SLE cases in the first five years[13].

The goals for DLE therapy is a clinical improvement observed every two weeks, and therapy can be discontinued if there is no erythema and scales (a sign of inactive disease)[6]. The target of SLE therapy is achieving remission (SLEDAI 0) or mild disease activity (SLEDAI 1-5). If the condition is stable/in remission, it is recommended to stop all drugs except HCQ[4]. Our case was given a methylprednisolone starting dose of 62.5 mg every 12 hours intravenously and then tapered off into 48 mg daily. Tapering down of steroid, in this case, is based on the patient clinical condition, which we evaluate every week. After five months of therapy, it tapered off to 8 mg daily. The patient also took HCQ 200 mg once daily, methotrexate 10 mg weekly, and folic acid supplementation 5 mg/week. During five months of observation, the CLASI score decreased to 10, and arthritis was improved with SLEDAI 4.

Discoid lupus Erythematosus is cutaneous lupus with the most prolonged remission[18]. Discoid lupus Erythematosus is not life-threatening, but it is cosmetically disturbing due to the scars experienced so which can interfere with the patient's quality of life. Prompt treatment of the initial lesion can help prevent or reduce the severity of scarring and atrophy[8,11]. In scarring conditions, other therapies may be considered, including dermabrasion, autologous fat transfer, pulsed dye laser therapy, and Erbium: YAG 2940 nm[20]. Arthritis is not life-threatening but can interfere with the patient's quality of life[19]. Treatment for scars, in our case, can be considered if the patient is cosmetically disturbed and the patient's condition is stable.

Conclusion

Early recognition of SLE in patients with cutaneous lupus and adequate therapy in generalized DLE is essential. Combination therapy showed better efficacy than monotherapy in generalized cutaneous lupus accompanied by SLE. In this case, we present a generalized DLE with moderate SLE and was treated with systemic treatment, including HCQ, methylprednisolone, and methotrexate; topical therapy consists of a corticosteroid and a broad-spectrum sunscreen with SPF 50. On five months of observation, there was an improvement in CLASI and SLEDAI scores. The patient responded well to therapy, and there were no side effects. Treatment of atrophic scars can be considered after patients are in remission.

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Author's Contribution

All authors have contributed to the preparation and writing of this case report.

Competing Interest

The author declares there is no conflict of interest.

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