Acute Cutaneous and Generalized Discoid Lupus Erythematosusin Systemic Lupus Erythematosus with Neuropsychiatric Complications: A Multidisciplinary Approach

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Abstract: Acute cutaneous lupus erythematosus (ACLE) is a type of cutaneous lupus erythematosus (CLE) which presents as the characteristic malar rash and has high association with the systemic lupus erythematosus (SLE). Discoid lupus erythematosus (DLE) is a type of chronic CLE (CCLE) typically present as discoid atrophic scars with central hypopigmentation and is usually localized to skin lesions. SLE can present with a wide spectrum of complications affecting multiple organs, including neuropsychiatric involvement. We report a case of a 15-year-oldfemalepresented with the characteristic malar rash which is aggravated by sun exposure, multiple atrophic scars on the scalp and legs, and scaring alopecia. Clinical history and complete physical examination confirmed the diagnosis of ACLE and generalized DLE. She has been treated routinely for SLE since two years ago with oral methylprednisolone and mycophenolate mofetil. She also experienced psychiatric disorders, mainly depression and anxiety, and was consulted to the psychiatry clinic for neuropsychiatric complications.We focus to describe our management plan in compiling detailed regimen of topical sunscreen and corticosteroid usage which is tailored to the patient's routine activity and limitations. We also provided continuous support and established collaborative management plan with other associated departments for evaluation of other complications. This personalized and multidisciplinary approach proves to increaseher compliance andresulted in significant improvement of the disease and her quality of life.

1 INTRODUCTION

Lupus erythematosus (LE) is a term used to describe varieties of autoimmune disorders characterized by autoimmunity towards the nucleosome and ribonucleoprotein components. This disease ranges from the mildest form, with only localized cutaneous lesions, to the severe form with multiple organs involvement and high mortality rate. Based on clinical and histopathology,CLE-specific skin diseaseis divided intoACLE, subacute CLE (SCLE), and CCLE. (Costner et al., 2012)

Acute CLE is observed in 20 to 60% of LE patients, found more often in females, and it is the CLE most associated with SLE. (Costner et al., 2012). Clinically ACLE is categorized into the localized form, with erythema and edema on malar region, and the generalized form, as large morbilliform or exanthematous eruption focused on the extensor aspects of arms and hands. Patients with SCLE shows characteristic form of erythematous macules, papules, or plaques arranged annularly or polycyclic on sun-exposed body areas, with 50% systemic involvement.CCLE usually manifests only as skin lesions, most commonly DLE. (Costner et al., 2012;Oke V et al., 2013)

It is important to evaluate the possibility of systemic disease association in diagnosing CLE, including neuropsychiatric manifestation. Diagnosis can be established clinically, while laboratory and histopathology examination may help to confirm diagnosis and differentiate CLE types/ The management of CLE generally include protection

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from ultraviolet (UV) radiation, avoidance of photosensitizing agents, and topical therapy.[1] Administration of systemic immunosuppressive agent is usually reserved for CLE in generalized form or who have failed to benefit adequately. (Costner et al., 2012;Hejazi et al., 2016)

Promptdiagnosis and thorough evaluation of multiple organs involvement in ACLE and other types of CLE greatly impact the patient's prognosis and quality of life. Neuropsychiatric complications in LE patients are not commonly found and are still poorly understood. It requires holistic management and collaboration with other specialties according to the systems involved. We report a case of ACLE and generalized DLE in SLE with neuropsychiatric complications. This case report emphasizes the need to assess systemic complications and the importance of multidisciplinary approach in CLE treatment.

2 CASE

A 15-year-old female was referred to the Dermatology and Venereology clinic, Dr. CiptoMangunkusumo National Central General Hospital with the symptom of erythematous rash on both cheeks. One month ago, slightly painful erythematous patches appeared on patient's cheeks which are exacerbated by heat and sun exposure, with no pruritus. Approximately in two weeks, the lesions expanded and spread to the neck and chest areas, with multiple small erosions observed on both cheeks. There was no symptom of oral ulcer.

The patient has a history of SLE compatible with SLICC (Systemic Lupus International Collaborating Clinics) criteria since 2016. (Yu C et al, 2014). She routinely visits the Allergy-Immunology clinic of the Pediatric department since diagnosed and was being treated with methylprednisolone once daily (8 mg) and mycophenolate mofetil twice daily (540 mg in the morning and 360 mg in the evening) until present. She was also given hydroxychloroquine once daily (200 mg) but was stopped only two weeks after retinopathy developed. Warfarin was prescribed due to her antiphospholipid syndrome. She experienced multiple episodes of ACLE and DLE lesions since two years ago, and was treated with topical corticosteroid and sunscreen. The lesions sometimes were reduced, howeverone year later the lesions started to spread further accompanied by progressive hair loss on certain areas of the scalp.

Since May 2017, she started to experience psychiatric disorders, mainly depression and anxiety, and was consulted to the Psychiatry clinic. She was diagnosed with neuropsychiatric systemic lupus erythematosus (NPSLE) and was treated with sertraline once daily (25 mg) and aripiprazole once daily (7.5 mg), however she did not visit the clinic routinely and did not take the medications as instructed. She is currently on the 10th grade and lives with her parents. From our interview with her and her father, we found that since diagnosed with SLE, she became less talkative and often seclude herself from her peers. She often felt less confident and has trouble concentrating while studying at school. She described that she did not apply sunscreen routinely because she was not convinced that it helps.

Physical examination revealed the characteristic malar or butterfly rash on her face, as well as multiple discoid atrophic scars on both supraorbital areas and multiple small erosions with telangiectasia (Figure 1). Moon face appearance was observed. There are also multiple erythematous nummular patches on neck and chest, multiple atrophic scars on the lower legs and scalp, with alopecia and hair thinning on the surrounding areas (Figure 2). Assessment of lesions using the Revised Cutaneous Lupus Erythematosus Disease Area and Severity Index (RCLASI) showed total activity score and total damage score of 13 and 11, respectively. Laboratory test showed increased anti ds-DNA (268.6 IU/mL), increased ACA IgM (34 MPL), and decreased C3 and C4 levels (37.2 and 7.66 mg/dL, respectively).No histopathological or direct immunofluorescence examination were performed.

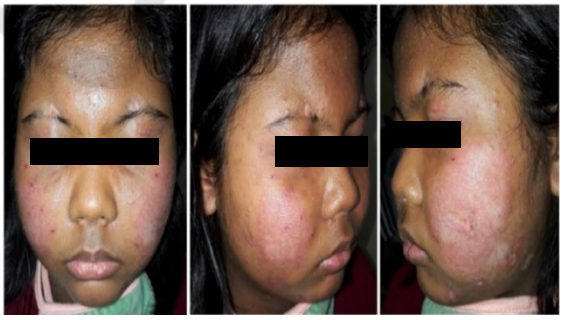

Figure 1.Classic ACLE and DLE lesions. Typical early erythematous plaque demonstrating hyperkeratosis and accentuation of follicle orifices and multiple sharply demarcated, round-to-ovoid slightly indurated erythematous plaque on both cheeks and eyebrows.

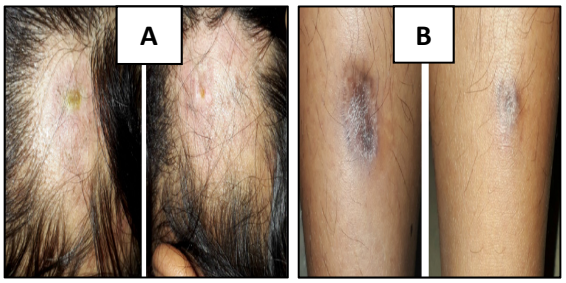

Figure 2.(A) Multiple atrophic scars and alopecia on the occipital areas of the scalp; (B) Multiple atrophic scars on the anterior lower legs.

She was diagnosed with ACLE and generalized DLE in SLE with neuropsychiatric complications. She was treated with a strict regimen of sunscreen application (every two to three hours on sun-exposed areas) on sun-exposed areas, which was adjusted to her school schedule of indoor and outdoor activities to prevent overuse and increase compliance. Topical corticosteroid was also added while the systemic therapy was supervised by the Pediatry clinic. We also advised the patient and her father about the importance and potential benefits of routine visit to the Psychiatry clinic. After six weeks of treatment, the erythematous plaques on cheeks subsided, while the DLE lesions and alopecia remain the same. Several new erosions and excoriations emerged. Previous wounds expanded, some covered with dark crusts and produced yellowish pus. Gram stain examination was performed and showed bacterial infection. After managing the infection with wet dressing and systemic antibiotic the skin lesions showed marked improvement, confirmed by the decrease of RCLASI total activity score from 13 to 9. Routine visit to the Psychiatry clinic greatly improved the patient's compliance and quality of life. This shows the importance of recognizing systemic complications and multidisciplinary management in CLE patients.

3 DISCUSSION

The patient showed characteristic clinical appearance of localized ACLE. However, other possible differential diagnosis that have similar features should be excluded, such as acne rosacea, dermatomyositis, polymorphous light eruption (PMLE), or photoallergic contact dermatitis.[1] In rosacea we usually find characteristic erythematous papules or pustules, while cutaneous lesions such as Gottron papules, pruritus and erythematous patches distributed on the extensor aspects and muscle weakness are commonly found in dermatomyositis, thus both are excluded. (Costner et al., 2012; Okon et al., 2013). She was not diagnosed as PMLE because there were no pinkish or erythematous papules, and other sun-exposed area besides the face, neck, and chest were not involved.(Lehmann et al., 2011). Photoallergic contact dermatitis could be considered, due to the history of regular topical sunscreen usage since 2016 which contains photo-allergenic substances, especially butylmethoxy-dibenzoylmethane, octylmethoxycinnamate, and methylbenzylidene camphor. (Goncalo et al., 2013) However, her lesions were transient and only appeared on certain areas, which makes this diagnosis unlikely.

Physical examination also revealed multiple discoid atrophic scars with peripheral hyperpigmentation and central hypopigmentation on scalp and lower legs, which are characteristic of classic DLE lesions. DLE lesions on hairy areas usually show follicular keratotic plug and may cause scarring alopecia, also found in this patients. (Cortner et al., 2012). She experienced alopecia from one year ago and did not show any improvement until recently, which support the assessment that it is scarring alopecia caused by DLE. (wang et al., 2011). This can highly impact the patient's quality of life, especially in female teenager, highlighting the importance of specialized evaluation and treatment in this case.

Evaluation of CLE lesions can be very difficult, due to the chronic nature of the disease and low response towards therapy. The extent and severity of CLE lesions in this patient were not evaluated thoroughly, which may contribute to herlong-lasting lesions.In 2005, there was a tool developed to evaluate the activity and damage of the disease in CLE patients, termed CLASI (cutaneous lupus erythematosus disease area and severity index).[9]However in 2010 this tool is revised and termed Revised CLASI (RCLASI).This revised tool allow for a more complete and thorough evaluation of all lesions as it consider different form of CLE lesions, such as superficial or adherent scaling, and the type of dyspigmentation. It also assesses the presence of mucous membrane lesions and alopecia (Kuhn et al., 2010).

Since May 2017, she was diagnosed with neuropsychiatric SLE, which is a form of neurological involvement in SLE. Clinical manifestations of NPSLE could appear as neurological symptoms, such as epileptic seizure, headache and cerebrovascular disease, or cognitive and psychiatric disorders. (Souirti et al., 2013).The

prevalence of depression in SLE patients was found to be six times higher than healthy subjects, which was correlated with serum IL-10 concentrations, relationship assessment, and fatigue severity.(Figueiredo-Braga et al., 2018) Psychiatric disorder could also be triggered by corticosteroid usage in 10% of patients that manifest as mood disorder in 93% of those patients.(Bertsias et al., 2010). In this patient, NPSLE manifested more clearly as psychiatric disorder, which are mood disorder, depression, and anxiety, prompting her referral to the Psychiatry clinic. She was treated with antidepressant (sertraline) and antipsychotic (aripiprazole), complemented by supportive psychotherapy for depressive symptom. This is consistent with the European League Against Rheumatism (EULAR) recommendation for the management of SLE with neuropsychiatric manifestations in 2014. .(Bertsias et al., 2010).

Treatment of CLE is still a major challenge because there is still no specific therapy approved for CLE. The purposes of CLE management are educating the patient about the disease and prevention by avoiding trigger factors.(Hejazi et al., 2016) These can be achieved by minimizing ultraviolet (UV) exposure, physical protection, and application of water-resistant broad-spectrum sunscreen that contain sun protection factor (SPF) ≥ 30 dan UVA-blocking agents.[1]This patient has already used SPF≥ 30 sunscreen since 2016 and was also given vitamin D3(cholecalciferol) supplementation 1 tablet per day. However, she admitted that she only applied the sunscreen two to three times per day. This frequency could not provide adequate photoprotective effect, considering the sunburn dosage percentage after 30 minutes of sun exposure, and the sunscreen actual usage concentration of 0.5–0.8 mg/cm^2, to achieve adequate photoprotection the sunscreen must be reapplied every 1.25–2 hours for SPF 30, and every 2.5–4 hours for SPF 45. The vitamin D3 dosage given was also not enough, as one tablet of the patient's supplement only contain 133 IU of cholecalciferol. It is recommended to give vitamin D3 supplementation of at least 400 IU per day for all CLE patients.(Hejazi et al., 2016)

For a more comprehensive treatment of this patient, we need to pay attention to the risk of the development of other diseases associated with SLE and CLE. Cerebrovascular disorders affect 2–15% SLE patients, most commonly acute ischemic stroke. Moreover, this patient has a history of antiphospholipid syndrome which increase the risk of thrombosis, another risk factor of cardiovascular disease. (Souirti et al., 2013). The risk of cardiovascular disorder is apparently also higher in CLE patients compared to the general population.(Hesselvig et al., 2017). Considering those conditions, thorough cardiologic evaluation should be one of the priorities in the management plan of this patient.

4 CONCLUSION

Management of CLE and SLE is quite challenging. Diagnosis can be made by clinical basis, however the assessment of affected areas and disease severity must be performed thoroughly. The RCLASI is a reliable tool for that purpose and should be used anytime possible to allow efficient and accurate treatment plan. Protection from sun exposure using topical sunscreen is still the most important aspect of CLE management. Clinicians should allocate adequate time to educate the patient and caretaker regarding the correct method of sunscreen application, as well as other methods of sun protection. Neuropsychiatric complication is a rare manifestation of systemic involvement in SLE patient,which may result from both the physical effect of autoimmunity on the nervous system and the suffering due to pain and disability. (Figueiredo-Braga et al., 2018) Therefore, it is crucial to be aware of any early signs and symptoms of systemic involvement and consult with the corresponding department. Multidiscipline approach might result in less severe complications, better quality of life and higher therapy success rate in CLE and SLE patients.

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