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Small Vessel Vasculitis, an Uncommon Presentation of Systemic Lupus Erythematosus: A Case Report

Vasculitis de pequeño vaso, presentación infrecuente de lupus eritematoso sistémico: reporte de un caso

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SUMMARY

Introduction: *Systemic lupus erythematosus (SLE) has diverse clinical manifestations. Vasculitis is one of the clinical manifestations found in SLE. Vasculitis is present in different clinical forms, with purpura lesions seeming to be uncommon.*
Case Presentation: *We report a case of a 20-year-old male SLE patient who developed purpura on his extremities. Histologically, the lesions were suggestive of leukocytoclastic vasculitis.*
Conclusion: *Leukocytoclastic vasculitis is an uncommon manifestation of SLE. Physicians need to be aware that purpura can occur as a result of secondary vasculitis in SLE, even if the patient does not exhibit high disease activity.*

Keywords: *SLE, leukocytoclastic vasculitis, palpable purpura.*

RESUMEN

Introducción: *El lupus eritematoso sistémico (LES) tiene diversas manifestaciones clínicas. La vasculitis es una de las manifestaciones clínicas que se encuentran en el LES. La vasculitis se presenta en diferentes formas clínicas, pareciendo infrecuentes las lesiones de púrpura.*
Presentación del caso: *Presentamos el caso de un paciente masculino de 20 años con LES que desarrolló púrpura en las extremidades. Histológicamente, las lesiones eran sugestivas de vasculitis leucocitoclástica.*
Conclusión: *La vasculitis leucocitoclástica es una manifestación poco frecuente del LES. Los médicos deben ser conscientes de que la púrpura puede ocurrir como resultado de una vasculitis secundaria en el LES, incluso si el paciente no muestra una alta actividad de la enfermedad.*

Palabras clave: *LES, vasculitis leucocitoclástica, púrpura palpable.*

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INTRODUCTION

Systemic lupus erythematosus is a multisystem chronic autoimmune disease with an estimated 3.7 million cases globally. The incidence of

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SLE in the Asia-Pacific region is between 0.9 and 8.4 cases per 100 000 people per year, and the prevalence is between 3.7 and 127 cases per 100 000 people (1). SLE attacks women more than men (2). The annual incidence ratio of male and female SLE patients per 100 000 population is 0.7-1.5:7.9-9.3. Men with SLE often have aggressive clinical presentations, faster organ damage, and a worse prognosis than women with SLE (3).

SLE has diverse clinical manifestations, ranging from skin rashes to significant organ damage. Vasculitis is one of the clinical manifestations found in patients with SLE (4). Cutaneous vasculitis is not a rare manifestation of SLE, and SLE-related vasculitis can indicate a different clinical course. The spectrum of symptoms of vasculitis in SLE ranging from mild to severe is only limited to skin blood vessels, and the severe spectrum can attack other organs (5). A wide variety of antibodies are found in the serum of patients with SLE, and anti-nuclear antibodies (ANA) is one of the diagnostic characteristics in patients with SLE. Still, a positive ANA is not an absolute requirement for an SLE diagnosis (6).

This case showed that SLE can occur in men with manifestations of vasculitis and a negative ANA. Immediate therapy is paramount to reducing morbidity and mortality.

CASE PRESENTATION

The patient is a 20-year-old male, from Surabaya, unmarried, with a high school education, working as a self-employed employee, referred from Gotong Royong Hospital with a diagnosis of Henoch-Schönlein purpura and SLE. The patient complained of reddish patches on their hands and feet for two weeks (Figure 1), in addition to knee and ankle joint pain. The pain seemed to fade, improve with movement, and stiffen when at rest. For reddish patches and joint pain, the patient attended an internist and was prescribed ibuprofen 400 mg three times a day and methylprednisolone 8 mg three times daily. There was no improvement in the patient's complaints, therefore the dosages of ibuprofen and methylprednisolone were increased to 800 mg three times per day and 16 mg three times per day, respectively. Patients complained of nausea and vomiting for one day, and they threw up every food and liquid they consumed. No fever, cough, chest tightness, or throat pain was present.

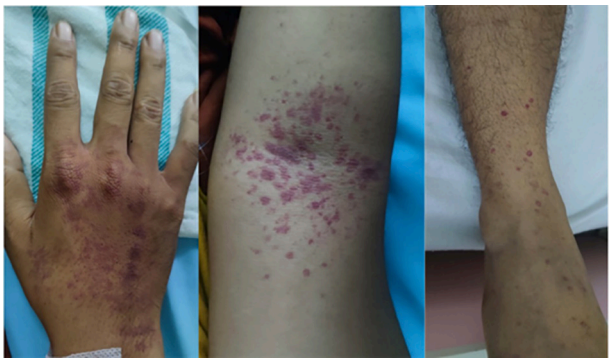

Figure 1. Reddish patches on the hands and feet.

The patient was then hospitalized at Gotong Royong Hospital and given intravenous fluids (NaCl 0.9 %), antibiotics (cefoperazone (1 gram twice daily intravenously), methylprednisolone (125 mg three times daily intravenously), pantoprazole (40 mg twice daily intravenously), ondansetron (4 mg three times daily intravenously), and paracetamol (500 mg three times daily) (1 gram three times a day). The patient experienced black feces up to one time after two days of treatment—a significant amount but not black vomit. Before 1.5 months ago, the patient had surgery to remove a cyst from behind the right ear. The patient presented with red eyes one month ago and was examined by an ophthalmologist, who diagnosed elevated eyeball pressure. The patient is receiving acetazolamide 500 mg twice a day, polyvinylpyrrolidone eye drops, and tobramycin 1 drop six times daily. At the 2-week follow-up, eyeball pressure was normal, and the dosage was reduced to acetazolamide 500 mg once per day, polyvinylpyrrolidone eye drops, and tobramycin 1 drop four times daily. The history of hair loss and facial flushing upon exposure to sunshine was denied. The patient's family history of diabetes, hypertension, cardiovascular disease, autoimmune disease, and cancer was denied. In the last five years, the patient has smoked one to

two cigarettes per day and used around one to two glasses of alcohol each week.

On examination, the patient's general condition was weak and moderately ill, with a GCS of 456, Body Mass Index (BMI) of 25.05, blood pressure of 130/70 mmHg, pulse rate of 100 beats per minute, respiratory rate of 24 beats per minute, an axillary temperature of 38 degrees Celsius, and a pain scale of 4. An examination of the head and neck revealed anemic conjunctiva without icteric sclera, cyanosis, and dyspnea. No retraction was observed throughout the thoracic examination, which was symmetrical. The cardiac examination revealed normal S1/S2 and no murmur or gallop. Both lungs were reported to have basic vesicular sounds and no wheezing, but rales. Examining the abdomen revealed normal bowel sounds, no pain, and no enlargement of the liver and spleen. Examining the patient's extremities revealed edema and purpura in both the superior and inferior extremities, which were warm with capillary refill time (CRT) less than 2 seconds.

The laboratory tests are listed in Table 1. On May 31, 2021, a chest x-ray (CXR) revealed a reticulogranular pattern in the right perihilar-paracardial and left paracardial regions, with interstitial lung edema and interstitial pneumonia serving as differential diagnoses.

The patient was diagnosed with Henoch-Schönlein Purpura (HSP), with vasculitis as a differential diagnosis, et causa systemic lupus erythematosus (SLE), post melena et causa suspect gastropathy and nonsteroidal anti-inflammatory drugs (NSAID), normochromic normocytic anemia, et causa gastrointestinal bleeding, and acute kidney injury (AKI). The patient has been administered a high-calorie, high-protein soft diet of 2 100 kcal with additional egg whites; an infusion of Ringer Dextrose 5 % (RD5) 1 000 mL every 24 h; ceftriaxone 1 g intravenously every 12 h; omeprazole 40 mg intravenously bolus every 6 h; tranexamic acid 500 mg.

On day two, the patient complained of coughing up mucus and continued skin redness. Normal vital signs were present. Still, a physical examination revealed purpura in both the upper and lower extremities. The laboratory tests are listed in Table 1. Examination of the urine reveals dysmorphic erythrocytes. Both hyperuricemia and hypocalcemia were added to the patient's evaluation. A pulse dose of methylprednisolone IV, 500 mg every 24 h; preemptive lamivudine, 100 mg orally once a day; allopurinol, 100 mg orally every 24 h; calcium carbonate ($CaCO_3$), 500 mg orally every 8 h, and packed red cell (PRC) transfusions, two bags per day, were added to the treatment until Hb was 10 mg/dL.

The redness of the skin diminished on day five (Figure 2). Laboratory analysis of procalcitonin at 0.52 ng/mL. The Chest X Ray (CXR) revealed pneumonia, a partially organized right pleural effusion, and pulmonary edema. Microbiological analysis of sputum revealed the presence of yeast. Fluconazole, 200 mg IV every 24 h, was added to the treatment regimen, and methylprednisolone was reduced to 62.5 mg IV every 24 h.

The redness of the skin diminished on the eighth day. Laboratory testing can be found in Table 1. CXR was unremarkable. The patient receives 16 mg orally every 8 h of methylprednisolone treatment.

The redness of the skin continued to improve on day 14. The sputum microbiology test revealed *Enterobacter cloacae* and *Klebsiella ozaena* (ESBL) which were sensitive to amikacin and meropenem, as well as *Candida tropicalis* was sensitive to fluconazole. Hospital-associated pneumonia (HAP) was added to the assessment, and amikacin was administered intravenously (IV) every 12 h.

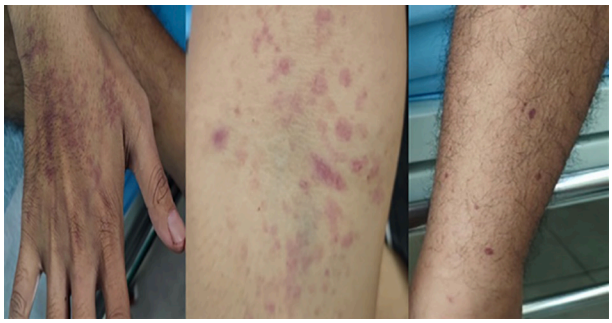

Figure 2. After a pulse dose of Methylprednisolone, the redness of the hands and feet improved.

On the sixteenth day, the patient had no symptoms and a normal physical exam. ANA profiles PM Scl100 (+) and Anti-neutrophil cytoplasmic antibody (ANCA) titers of 1:10 were detected in laboratory tests. Leukocytoclastic vasculitis was added to the patient's diagnosis after a skin biopsy revealed them. The patient was released on oral methylprednisolone 16 mg every 8 hours, oral allopurinol 100 mg every 24 h, oral $CaCO_3$ 500 mg every 8 h, and oral lamivudine 100 mg every 24 h.

Table 1. Laboratory test summary

Laboratory parameter	Day 1	Day 2	Day 5	Day 8
Hemoglobin (g/dL)	8.4	-	-	10.4
Leukocytes (/mm^3)	11 000	-	-	8 450
Neutrophils (/mm^3)	9, 55	-	-	6 125
Lymphocytes (/mm^3)	1 474	-	-	1 653
Platelets (/mm^3)	305 000	-	-	395 000
Sodium (mEq/L)	138	-	-	-
Potassium (mEq/L)	4.5	-	-	-
Chloride (mEq/L)	104	-	-	-
Blood sugar (mg/dL)	98	-	-	-
BUN (mg/dL)	86	-	-	31
Creatinine (mg/dL)	6	-	-	1.3
Total bilirubin (mg/dL)	0.87	-	-	-
Direct bilirubin (mg/dL)	0.3	-	-	-
AST (U/L)	20	-	-	-
ALT (U/L)	56	-	-	-
Albumin (g/dL)	2.86	-	-	-
Uric Acid (mg/dL)	-	12.3	-	-
Calcium (mg/dL)	-	7.5	-	-
Phosphate (mg/dL)	-	6.5	-	-
HBsAg	reactive	-	-	-
IgA (mg/dL)	184	-	-	-
ANA test (AU/mL)	-	12.7	-	-
C3 (mg/dL)	-	47	-	-
C4 (mg/dL)	-	4.7	-	-
Procalcitonin (ng/mL)	-	-	0.52	-
Urinalysis				
Color	Yellow with clear clarity			Yellow with clear clarity
pH	5.5			5.5
Specific gravity	1 006			1 006
Blood	+3			+2
Leukocytes	+2			Negative
Protein	+2			Negative
Bilirubin	Negative			Negative
Glucose	Negative			Negative
Ketone	Negative			Negative
Protein creatinine ratio (g/gCr)	≥ 0.5			<0.15
Albumin creatinine ratio (mg/gCr)	≥300			≥300

DISCUSSION

SLE is a chronic, systemic autoimmune disease with variable severity and the potential for flares. Damage to the kidneys, heart, blood vessels, central nervous system, skin, lungs, muscles, and joints can lead to morbidity and an increase in mortality. SLE has clinical symptoms, immunological and laboratory abnormalities,

disease progressions, and illness sequelae. The clinical symptoms of the skin, joints, kidneys, and other organ systems may not necessarily occur simultaneously. A T-cell imbalance is characteristic of SLE, an autoimmune disease. Disease activity is associated favorably with the Th17/Treg ratio. In the early phases of the disease, when clinical manifestations are minor, as in cases of ANA negativity or specific dominant organs, or in sporadic clinical presentations that can be lethal and necessitate prompt action, the diagnosis of SLE can be extremely difficult. A negative ANA test cannot eliminate the SLE diagnosis, as 20 % of patients have an ANA test (true or false negative) at different disease phases. However, lupus without ANA antibodies is less common. The diagnosis of SLE involves clinical symptoms backed by laboratory tests that reveal an immunological or inflammatory response in several organs (7,8).

The diagnosis of SLE is based on clinical symptoms and subsequently corroborated by laboratory tests that reveal immunological reactivation or inflammation in many organs. To guarantee that patient groups do not overlap, the most recent criterion categorization integrates the ACR-1997, SLICC-2012, and EULAR/ACR 2019 classifications. ANA or other positive immunological markers (autoantibodies or hypo-complements) are necessary to classify SLE according to SLICC-2012 and EULAR/ACR-2019, but not ACR-1997. SLE diagnosis does not require meeting categorization criteria. The SLICC-2012 and EULAR/ACR-2019 criteria are more sensitive than the ACR-1997 criteria in patients with early disease stages; however, some patients with potentially severe disease may still be missed (9). Modifying categorization criteria (Figure 4) can improve sensitivity, impose earlier diagnosis, and expedite treatment for patients with a high illness burden (7).

In this instance, the patient had an ANA-negative and hypo-complement test, along with arthritis as a clinical complaint. The 2019 EULAR/ACR criteria awarded this patient a total of 10 points (6 for arthritis and 4 for hypocomplementemia). This patient met the criteria for clinical SLE based on the diagnostic technique utilized for patients with SLE suspicion.

The incidence of vasculitis in SLE ranges between 11 and 36 percent. Vasculitis is characterized by inflammatory cell infiltration and necrosis of the blood vessel walls (Figure 3). Vasculitis can affect blood vessels of all sizes and organs, with prognoses ranging from mild to fatal. Lesions of the skin are more frequently associated with the involvement of tiny blood vessels (10). Purpura, urticaria, and lesions on the extremities might manifest as cutaneous vasculitis in SLE. The most prevalent kind of vasculitis is small-vessel vasculitis. Clinical symptoms of this leukocytoclastic vasculitis include hematuria and hemoptysis. The most prevalent lesions of cutaneous vasculitis are punctuated vasculitis lesions, which typically develop on the hands but can also manifest on the lower extremities. Purpura is the second most prevalent form of vasculitis of the skin. This purpura appears most frequently on the hands. HSP as cutaneous small vessel vasculitis with deposition of IgA and other immune components within the vessel walls is a possible differential diagnosis for skin vasculitis (10-12). SLE patients with renal vasculitis have glomerular lesions, hypertension, anemia, hematuria, and renal insufficiency, which progresses to kidney failure and high SLEDAI scores (13,14).

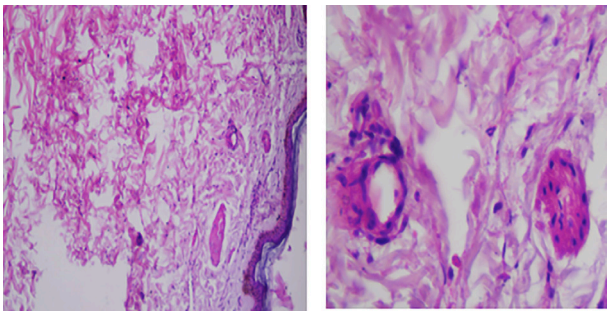

Figure 3. Leukocytoclastic vasculitis affecting superficial vessels from a skin biopsy patient.

Vasculitis treatment in lupus erythematosus is extremely restrictive, and time-consuming diagnostics restrict life-threatening clinical outcomes. Inflammation-related clinical indicators, such as the size of afflicted blood

vessels and organs, are associated with treatment. The treatment of cutaneous vasculitis with antimalarials is effective. The use of 200-400 mg of hydroxychloroquine per day is effective, particularly in patients with vasculitis, urticaria, and hypocomplementemia. Patients with minimal vasculitis of the skin react to the administration of colchicine (0.6 mg twice daily); however, relapses are possible following medication cessation. If there are contraindications to the use of earlier medications, then thalidomide and dapsone (50-200 mg per day) are effective alternatives (13). Long-term corticosteroids and immunosuppressants, such as cyclophosphamide, azathioprine, and mycophenolate mofetil, are used to treat visceral organ-afflicting vasculitis. Other effective treatments include intravenous immunoglobulins and biological medicines such as rituximab (10). Various types of vasculitis, including severe lupus cutaneous vasculitis that is resistant to conventional therapy, have been successfully treated with azathioprine (2 mg per kg body weight per day), despite its side effects, which include leukopenia, liver disorders, hypersensitivity reactions, and infections. In refractory, severe lupus vasculitis, immunoglobulin at a dose of 1 g per kg of body weight for 2 days followed by 400 mg per kg of body weight every month until the resolution of the disease — or pulse steroid therapy — is widely recognized. Methylprednisolone is administered intravenously at 10-30 mg per kg of body weight (maximum 1 g) once daily for three days, followed by an injection of 1 mg per kg of body weight per day for one week, and then tapered for one month until the least maintenance dose is reached. The gold standard of providing 1 mg of methylprednisolone per day for three days is associated with considerable infection-related consequences. 1.5 mg of methylprednisolone per day for three days is also useful for minimizing infection complications (11) for six months (13).

This patient had cutaneous purpura, kidney hematuria, and dysmorphic erythrocytes in urine sediments as signs of vasculitis. Patients with skin and visceral organs are administered a 500 mg methylprednisolone pulse daily. The patient's skin lesions improved after the use of steroids. The maintenance dosage of 62.5 mg of methylprednisolone per day was continued. The patient's skin biopsy revealed the presence of leukocytoclastic vasculitis, indicating that these patients have vasculitis due to SLE.

Reactivation of the hepatitis B virus is an immunosuppressive therapy adverse effect associated with higher mortality and morbidity in rheumatic disease patients. Reactivation of hepatitis B can be avoided through thorough screening and surveillance. Reactivation occurs in people with chronic hepatitis B infection (HBsAg-positive), but it can also occur in those who have recovered from hepatitis B infection (HBsAg-negative or anti-HBc-positive). The use of glucocorticoids is associated with an incidence of hepatitis B reactivation between 4 % and 50 % in patients with hepatitis B infection. Glucocorticoid administration with a dose of >20 mg of prednisolone and a period of >4 weeks poses a moderate risk of hepatitis B reactivation, and antiviral prophylaxis should be used. Prior to measuring immunosuppression, hepatitis B screening was required to prevent the reactivation of this disease. 1-2 weeks before beginning immunosuppressive medication is the optimal time to begin antiviral prophylaxis, particularly in individuals with a high viral load. Prophylactic therapy continues for up to 6 months following completion of antirheumatic therapy, or 12 months if rituximab is used (15,16). This patient's HBsAg was reactive. Before the pulse dose of Methylprednisolone (500 mg daily for three days), antiviral prophylaxis with Lamivudine, 100 mg once daily, was administered to the patient.

A male with SLE and vasculitis was discovered in this instance. 2019 ACR/EULAR criteria were used to identify patients with SLE (Figure 4). Men have a more aggressive clinical presentation and a poorer prognosis if diagnosed with SLE (3). Vasculitis occurs in just 11 %-36 % of SLE patients, and its symptoms range from moderate to life-threatening (10). Patient's urine was also found to have dysmorphic erythrocytes, indicating the presence of vasculitis that had progressed to the kidney and necessitated more intensive treatment.

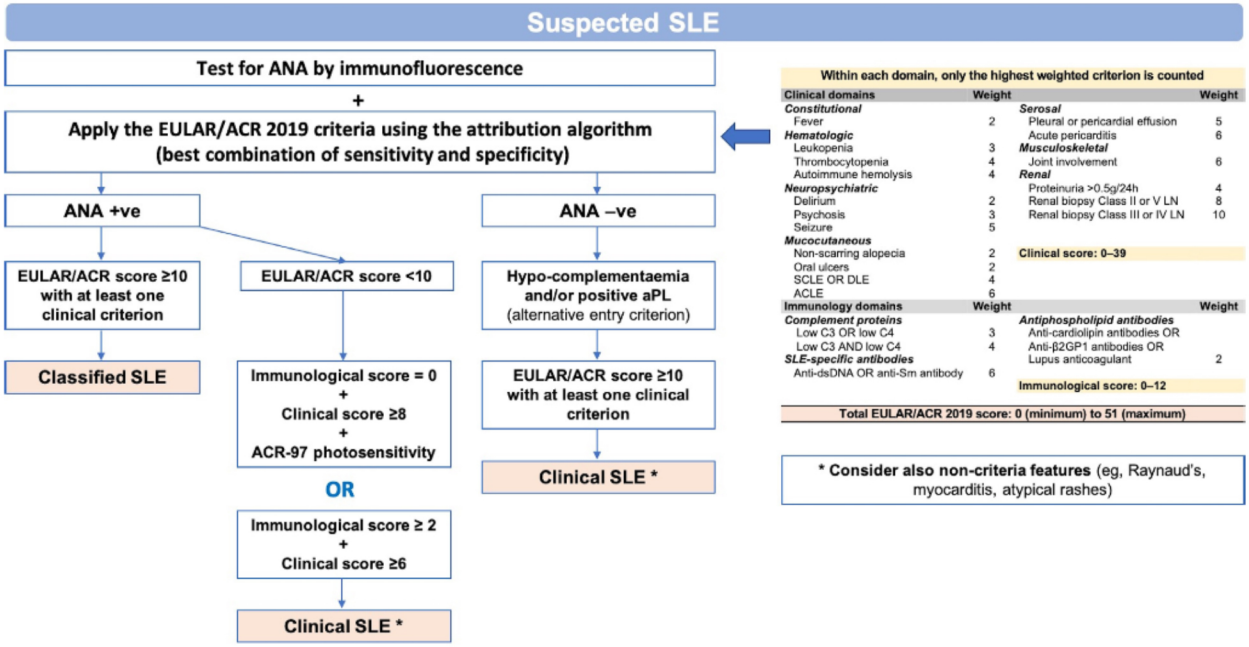

Figure 4. Approach to diagnosis in patients with suspected SLE (7).

CONCLUSION

The vasculitis of a 20-year-old male has been described as a symptom of SLE. Reddish patches on the patient's hands and feet led to a two-week hospitalization. A sample of the skin revealed leukocytoclastic vasculitis upon histopathological investigation. The patient's skin lesions improved following treatment with a pulse dose of methylprednisolone. This patient had chronic hepatitis B, and antiviral prophylaxis was used to avoid hepatitis B reactivation.

Conflicting Interest(s)

The authors declare no conflict of interest.

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