SYSTEMIC LUPUS ERYTHEMATOSUS DAN EDEMA EKSTREMITAS PADA WANITA 50 TAHUN DENGAN PROFIL *ANTINUCLEAR-ANTIBODY* NEGATIF

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ABSTRAK

Systemic lupus erythematosus (SLE) adalah penyakit autoimun dengan 90 persen penderitanya wanita.Penyakit ini dapat menyerang berbagai organ seperti persendian, kulit, saraf, jantung dan ginjal.Diagnosis ditegakkan dengan terpenuhinya minimal empat dari sebelas kriteria *American College of Rheumatology* (ACR).Pasien wanita 50 tahun datang dengan keluhan nyeri persendian kaki dan tangan sejak enam tahun lalu, keluhan diikuti munculnya bercak kemerahan pada muka empat tahun berikutnya.Pasien juga mengaku sering mengalami demam dan rambut rontok dua tahun terakhir.Pemeriksaan fisik menunjukkan adanya malar rash, poliarthritis, stomatitis, nodul subkutan pada tangan, pitting edema pada tangan dan kaki. Pemeriksaan laboratorium didapatkan hemoglobin 11.9 g/dL, leukosit 8.70 x 10^3/ul, trombosit 494 x 10^3/ul, ureum 22.0 mg/dL, kreatinin 1.10 mg/dL, glukosa sewaktu 86.3 mg/dL, SGOT 28 U/L, dan SGPT 15 U/L. Pemeriksaan elektrokardiogram (EKG) menunjukkan irama sinus takikardi. Foto *X-Ray* pedis menunjukkan adanya lesi porotik multipel bilateral.Foto *X-Ray* thoraks dalam batas normal.Tes *Antinuclear Antibody* (ANA) didapatkan titer 1:320, dengan ANA *profile* negatif.Pemeriksaan Anti-dsDNA menunjukkan hasil negatif.Diagnosis SLE ditegakkan dengan manifestasi klinis pada pasien yang telah memenuhi empat dari sebelas kriteria ACR, walaupun pemeriksaan ANA dan anti-dsDNA menunjukkan hasil negatif.

Kata Kunci :*Systemic lupus erythematosus*, *antinuclear antibody*, edema

Systemic lupus erythematosus and extremity oedema in 50 years old woman with negative antinuclear-antibody

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Systemic lupus erythematosus (SLE) is an autoimmune disease which can affect almost any organ in body. The diagnosis is based on eleven criteria made by the American College of Rheumatology (ACR). We present a woman aged 50 years old with multiple joint pain for 6 years. It followed by skin rash appears on the face 4 years after. She also had experience fever and hair fall for the last 2 years. Vital signs were in normal range except for pulse rate 105/minute. Physical examinations showed malar rash, polyarthritis, oral ulcers, subcutaneous nodules and pitting oedema on all extremities. Laboratory test findings hemoglobin 11.9 g/dL, leucocytes 8.70 x 10^3/ul, thrombocytes 494 x 10^3/ul, ureum 22.0 mg/dL, creatinine 1.10 mg/dL, random glucose 86.3 mg/dL, SGOT 28 U/L, and SGPT 15 U/L. Electrocardiogram (ECG) record showing sinus tachycardia. Thorax x-ray was in normal while x-ray of pedis described bilateral multiple porotic lesion. Antinuclear-antibody (ANA) and Anti-dsDNA examination get the negative result. The patient gets methylprednisolone and most of her symptoms relieved. This case gives understanding that oedema of extremities can happens in SLE without any proved of organ damage. More, physicians should not used ANA and anti-dsDNA as main benchmark in diagnosing SLE.

Keywords: Systemic lupus erythematosus, antinuclear antibody, oedema

Introduction

Systemic lupus erythematosus (SLE) is an autoimmune disease which affect almost any organ system in body. More than 90% of cases occur in women, frequently starting at childbearing age. Polyarthritis, malar rash, fever, stomatitis and oedema are common manifestations of SLE. However, extremity oedema without any proved of renal and heart involvement are considered a rare condition. The diagnosis of this disease is based on the presence of 4 of the 11 ACR criteria including ANA and anti-dsDNA test. On the other hand, a small subset of SLE patients with typical clinical findings of SLE was reported to have persistently negative ANA tests. This study, we present the case of SLE patient with extremities oedema and ANA profile-negative test.

Case presentation

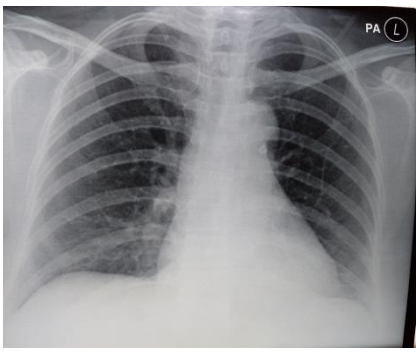
A fifty-year-old javanese woman with no previous relevant medical problems presented to the PKU Muhammadiyah Hospital in Surakarta, Indonesia, in January 2019 with main symptom of multiple joint pain for the past six

years. The pain was greatly felt on ankles and knees of both legs, even the patient felt it on all part of her joints. Four years later the patient experienced painless rash on her face. Two years after, the rash spreading on skin around the body with round-scale formed, and it was painful. She also felt fever and hair fall. All of these symptoms relapsed and disappear simultaneously in the same time. The patient didn't know what trigger her symptoms. She had no history of allergies or previous autoimmune disease in family history.

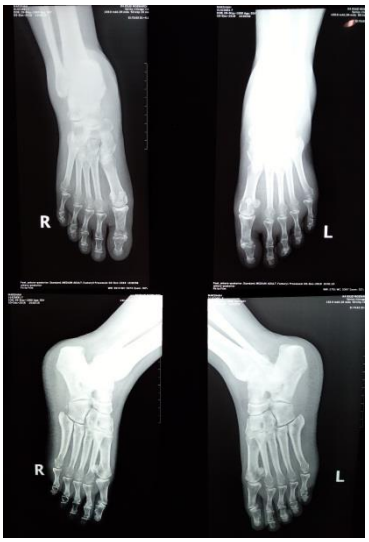
Physical examination revealed malar rash on the face and discoid rash all over the skin around the body. There were many scars on the oral mucosa indicating ulcers ever happened before. The patient admitted that she often experienced mouth ulcers but denied any pain. There were no indicators of pallor, jaundice, or lymphadenopathy. Thorax and abdominal examination showed no abnormality.

Upper extremities showed less oedema in comparison with lower extremities which revealed pitting oedema extending up to the knees. All of her vital signs were within the normal range (blood pressure 130/80 mmHg, temperature 36,7^{o}C, respiration rate 20/ minute) except for pulse rate 105/minute. Her weight was 54 kg with 156 cm tall.

Patients laboratory investigations showed white blood cell count of 8.70 x 10^3/ul, hemoglobin 11.9 g/dL, hematocrit 37.3%, thrombocytes 494 x 10^3/ul, ureum 22.0 mg/dL, creatinine 1.10 mg/dL, random glucose 86.3 mg/dL, SGOT 28 U/L, and SGPT 15 U/L. and the erythrocyte sedimentation rate (ESR) 45 mm/h. She had no proteinuria on urinalysis but had slight hematuria (4-5) and bacteriuria. Electrocardiogram (ECG) record showing sinus tachycardia. Thorax x-ray showed no cardiomegaly and normal formed of lungs without any pleural effusion or oedema. However, x-ray of pedis described bilateral multiple porotic lesion in multiple bones starting from calcaneus, talus, and cuneiform. Antinuclear-antibody (ANA) and Anti-dsDNA examination get the negative result even with repetition in 3 times. The patient also had ANA profile negative in all antigen test.



Picture 1. Thorax imaging of patient was normal without any effusion or cardiomegaly



Picture 2. x-ray of pedis described bilateral multiple porotic lesion in multiple bones starting from calcaneus, talus, and cuneiform.

She diagnosed as having ANA-negative SLE on the basis of malar rash, polyarthritis, painless oral ulcers, subcutaneous nodules, fever, and hair fall. The patient gets methylprednisolone and most of her symptoms were controlled.

On anamnesis the patient said that her leg and arm started swelling in period of the last two years. Over that period, she felt that her weight tend to higher than before. She denied experiencing any of tingling sensation at the extremities.

Discussion

Systemic lupus erythematosus is a chronic inflammatory autoimmune disease that involves many different organ systems, and this illness exhibits a wide spectrum of clinical manifestations. The diagnosis of SLE depends on the patient's clinical and laboratory abnormalities. Various kinds of autoantibodies are present in SLE patients, and ANA is one of diagnostic criteria for SLE, having a frequency of 95% or greater in SLE patients[1]. However, several investigators have reported that small groups of patients with the clinical features of SLE have negative tests for ANA. These patients appear to represent 1 -5% of the SLE population. The age of onset and the female predominance are the same for ANA-negative SLE as for ANA-positive SLE[2,3].

One explanation for the ANA-negative finding is technical inaccuracy. The description of ANA-negative lupus was first raised by Koller *et al.* in 1976. They described five patients who were ANA-negative but had clinical features consistent with SLE. Reports of ANA-negative SLE have decreased markedly in recent years probably because of the use of better substrates in ANA testing. Previously a variety of less efficient substrates were used like rat liver, mouse liver, human spleen, human prostate cell, and human granulocytes. The introduction of Hep-2 cells (a rapidly dividing human epithelial cell line) as a routine substrate for ANA determination has led to a well standardized assay with a marked increase in sensitivity[2]. McHardy *et al.* identified 38 adults who had a high DNA-binding capacity, but negative fluorescent ANA testing

(with a rat liver substrate), and the clinical diagnosis of SLE was established for these patients. In another study, the previously ANA negative finding, with using mouse liver substrate, in the sera of patients with SLE or subacute cutaneous lupus erythematosus was found to be anti-Ro antibody positive by performing enzyme-linked immunosorbent assays[4].

Another cause of ANA-negative findings is that ANA is present, but its bound in the form of immune complexes. However, most ANA-negative patients have persistently negative tests for ANA after a long follow-up period. Technical factors or prozone effects have been described as the possible reason for this[5].

Oedema has been reported in the literature as a symptom of SLE[6]. There are reports of periorbital oedema, lower limb pitting oedema, facial oedema, remitting asymmetrical pitting oedema and angioedema. All as presentations of SLE[7]. There are several cases of SLE presenting with generalised oedema due to either protein-losing enteropathy (PLE), an association with nephrotic syndrome, or polyserositis in the form of massive bilateral pleural and pericardial effusions. The underlying cause of generalised oedema in SLE patients without systemic manifestations is not yet clear. Günaydin *et al*. postulated that the localised oedema observed in his reported case was most likely due to vasculitis, which had led to an obstruction of the lymphatic vessels[8]. Pittau *et al*. believed that oedema may be due to a transient impairment in lymphatic drainage or pre-existing increased capillary permeability, as demonstrated in patients with connective tissue disorders[9]. Marks *et al*. proposed that there was an increase in vascular permeability in patients with connective tissue diseases. In yet another patient with periorbital oedema, increased dermal mucin deposits were observed during a biopsy[10].

The patient in this case said that her leg and arm started swelling in period of the last two years before taking any medication. Nephrotic syndrome as a cause of oedema in this patient was excluded by the absence of urinary protein. However, PLE cannot be excluded since the protein serum level was not measured in this patient

The findings of this case report are limited as albumin serum level of the patient were not measured.

Conclusions

This case described a 50-years old woman with typical clinical manifestations of SLE including extremities oedema. There were no proved of renal or heart failure. ANA and anti-dsdna test were negative in this patient even with

repetition. The diagnosis of SLE was made based on the minimal four out of eleven criteria made by ACR. This case gives understanding that edema of extremities can happens in SLE without any proved of organ damage. More, physicians should not used ANA and anti-dsDNA as main benchmark in diagnosing SLE.

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