



## Hepatitis Lupus in Systemic Lupus Erythematosus in Male Patients

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### ABSTRACT

Systemic Lupus Erythematosus (SLE) is a complex autoimmune disease characterized by autoantibodies against the cell nucleus and involves many organ systems in the body with unknown etiologies and various clinical manifestations, disease course and prognosis. SLE can be found at all ages, generally appearing at age 9-58 years with a peak at age 28 years. It is more common in women with a ratio of women to men 15: 1 to 22: 1. The highest incidence and prevalence of SLE was found in North America 23.2 / 100.000 population / year and 241 / 100.000 population. In Indonesia, there has been an increase in visits to SLE patients from 17.9-27.2% in 2015 to 30.3-58% in 2017. One of the manifestations of SLE is hepatitis lupus, which is inflammation of the liver tissue. Lupus hepatitis can occur in 20-50% of patients with SLE. It was reported that a 20-year-old man presented with complaints of pain in the joints of the right and left hands which increased since 1 week. The patient also complained of reddish patches on the face, hair loss and mouth sores. Physical examination revealed anemic eye conjunctiva, malar rash, oral ulcer. During the joint examination, there was tenderness in bilateral MCP and PIP. The abdominal examination revealed hepatomegaly. Investigations revealed anemia, thrombocytopenia, increased liver function. Abdominal ultrasound revealed hepatomegaly. ANA profile examination was positive for anti RNP, anti-sm, and anti-ribosomal protein antibodies. The patient was diagnosed with Systemic Lupus Erythematosus with lupus hepatitis according to the ACR (American College of Rheumatology) criteria in which the patient had 6 criteria. The patient was given therapy with 2x125 mg of intravenous methyl prednisolone for 3 days and hydroxychloroquine 1x200 mg orally and other symptomatic drugs.

### 1. Introduction

Systemic Lupus Erythematosus (LES) is a complex autoimmune disease that attacks various body systems. Genetic and environmental factors are known to play a role in the pathogenesis of this disease. LES has clinical manifestations, immunological and laboratory abnormalities in the course of the disease, as well as a variety of disease consequences. Clinical manifestations in the skin, joints, kidneys, and other organ systems do not always coincide, and may develop over the course of the disease.<sup>1,6</sup>

The highest incidence and prevalence of LES was found in North America with 23.2 / 100.000 population / year and 241 / 100.000 population. Polyclinic data in several hospitals in Indonesia shows an increase in

LES patient visits, namely 17.9 - 27.2% (2015), 18.7 - 31.5% (2016), and 30.3-58% (years 2017). The ratio of girls to boys is 15: 1 to 22: 1. The highest age range was 21-30 years.<sup>1</sup> The incidence of LES was also found to be higher among African, Asian and Hispanic races than for Caucasians, Canadians and Spanish.<sup>2,5</sup>

Systemic lupus erythematosus is a complex autoimmune disease characterized by autoantibodies against the cell nucleus and involves many organ systems in the body. One of the manifestations is lupus hepatitis, which occurs in 20-50% of LES patients.<sup>3</sup>

Liver dysfunction is common in LES patients. This may reflect liver disease as a component of LES, liver disorders associated with other autoimmune diseases such as primary biliary cirrhosis, drug poisoning, or

other unrelated diagnoses, such as viral infection.<sup>13</sup>

The anti-ribosomal P antibody is a useful serological marker for lupus hepatitis and was positive in 44% of lupus hepatitis patients. Anti-Smith antibodies are another useful marker for lupus hepatitis. Approximately 99% of patients who are anti-SM positive meet the diagnostic criteria for LES.<sup>13</sup>

### **Clinical Findings**

A male patient 20 year old was treated with complaints of pain in the joints of the right and left hands which increased since 1 week before admission to the hospital. Pain has been felt since 2 months ago and was felt in the wrists and feet, elbows, knees and shoulders. Pain is felt intermittently. There was no history of joint stiffness.

The patient also complained of reddish patches on the face since 2 months before being admitted to the hospital, reddish spots increased when exposed to sunlight, no pain, no itching. Hair loss experienced since 2 months before entering the hospital, canker sores since 3 weeks before entering the hospital. Weakness and fatigue that have increased since 1 week, decreased appetite since 1 week before admission to hospital. There is no fever.

The patient came with a moderate general condition and awareness composmentis cooperative, blood pressure 120/80 mmHg, pulse 87 x/minute, breath 18 x/minute, temperature 36.8 °C. On general physical examination, head examination revealed anemic conjunctival, malar rash and oral ulcer, lung and heart examination, within normal limits. On examination of the abdomen, the liver was palpable, 2 lower fingers of the archus costarum, 3 lower digits of the xyphoideus

process, flat surface, sharp edges, solid consistency. On examination of the joints, there was swelling in the MCP and PIP joints bilaterally with pain.

Examination of liver function obtained SGPT 158 u / L, SGOT 73 u / L. The HBsAg and anti-HCV hepatitis markers were non-reactive. Kidney function and electrolytes are within normal limits. The results of routine urine examination showed +1 proteinuria, no erythrocytes and sediment were found in the patient's urinalysis. Routine feces within normal limits.

Disease activity was assessed with a MEX-SLEDAI score with a score of 10 or a severe LES. The patient was then given methyl prednisolone injection therapy at a dose of 125 mg 2 times a day for 3 days, hydroxychloroquine 1x200 mg orally, osteocal 1x1000 mg orally, lansoprazole 1x30 mg orally and other symptomatic drugs.

In the patient, an ultrasound examination of the abdomen showed an enlarged liver, flat surface, homogeneous and smooth parenchyma, sharp edges, not widened veins, not widened bile duct, normal portal vein, 0.96 cm diameter, absent ascites, gall bladder, pancreas, spleen and kidneys within normal limits.

The patient also performed a renal ultrasound examination because the routine urine examination found +1 proteinuria. Kidney ultrasound results were obtained with sonographic impressions of both kidneys according to normal kidney images. Patient education was conducted to trace lupus nephritis in patients with kidney biopsy, but the patient refused.

After 6 days of treatment the patient had improved and was planned to be outpatient. The dose of methyl prednisolone was reduced on day 4 to 2 x 62.5 mg and the patient was discharged with 3x8 mg of methyl prednisolone.



Figure 1. Malar rash and oral ulcer in patient





Figure 2. Abdominal ultrasound results





Figure 3. Kidney ultrasound results

## 2. Discussion

It has been reported that a 20-year-old male patient who was admitted to the Internal Medicine Ward at Dr M Djamil General Hospital was diagnosed with active systemic lupus erythematosus, lupus hepatitis, lupus nephritis and normocytic normochromic mild anemia.

Diagnosis of Systemic Lupus Erythematosus is enforced from history, physical examination and investigation. From the history, this patient found complaints of joint pain, pain in the joints since 2 months ago which were felt in the ankles, elbows, knees and shoulders. Pain is felt intermittently. Red patches on the face that increase when exposed to sunlight, and hair loss easily. Physical examination found red spots on both cheeks that were not raised and raised on the

skin without pain, as well as mouth ulcers and hepatomegaly. On laboratory investigations, mild normocytic normochromic anemia, lymphopenia, proteinuria, and positive ANA profile results on anti-RNP, anti-sm, and anti-ribosomal protein antibodies.<sup>2,3,4</sup>

According to the American College of Rheumatology, this patient found 6 criteria so that this patient was established and treated as Systemic Lupus Erythematosus. According to the Indonesian Rheumatology Association, if there are 4 or more of these criteria, the LES diagnosis has a sensitivity of 85% and a specificity of 95%.<sup>2</sup>

This patient was also diagnosed with lupus nephritis. Lupus nephritis is a risk factor for morbidity

and mortality in SLE and 10% of lupus nephritis patients will progress to end stage renal disease. The presence of hematuria, proteinuria, or pathologic urine sediment on urinalysis indicates that there is lupus nephritis (NL). The diagnosis of NL is confirmed when there is proteinuria > 500 mg / 24 hours with or the presence of hematuria (> 8 erythrocytes / TBSA) with or without decreased renal function.<sup>2</sup> However, this patient only found proteinuria (+1) which is equivalent to 30 mg / 24 hours proteinuria. Nor were there any erythrocytes or sediment in the urinalysis of this patient. The renal ultrasound image was also found to be normal. However, the diagnosis of lupus nephritis cannot yet be ruled out because the gold standard for examining lupus nephritis is kidney biopsy, but it was not performed in this patient because the patient refused.<sup>7,8,11</sup>

The principle of treating lupus nephritis is to suppress the inflammatory reaction of lupus, improve kidney function, or at least maintain kidney function so that it does not decrease. In patients with highly active lupus, a methyl pulse dose of 500-1000mg / iv / day may be given to induce rapid anti-inflammatory action. After 3 days of administration continued with the administration of oral methylprednisolone 0.5-1 mg / day. In this patient the indication for being given a methyl pulse dose of 250 mg / iv / day was because based on the criteria for assessing SLE activity, namely the MEX-SLEDAI criteria, a score of 10 was obtained so that the patient was treated with a methyl pulse dose. According to Saleem et al, after the use of immunosuppressive therapy for 6-8 months, 20-50% of kidney histological examination will provide a picture of the active inflammatory process with positive proteinuria. In fact, after several years of immunosuppressive treatment, the inflammatory activity of the kidneys is still ongoing even though remission has been achieved.<sup>7,8,12</sup>

The patient also had hepatomegaly with HBsAg and anti-HCV tests, both non-reactive and elevated SGOT / SGPT. Based on this examination, the patient was diagnosed as hepatitis lupus because of a sudden

increase in liver function and the discovery of hepatomegaly with a flat surface and sharp edges on abdominal ultrasound examination, although other causes of viral hepatitis have not been excluded because other hepatitis markers have not been examined.<sup>9,13</sup>

The ANA profile examination results were positive for anti-ribosomal P antibodies, whereas 44% of the anti-ribosomal P antibodies were positive in patients with lupus hepatitis, and negative in autoimmune hepatitis. In addition, anti-Smith antibodies can also be used as markers for lupus hepatitis. A liver biopsy is also required to diagnose lupus hepatitis. Common histopathologic findings in lupus hepatitis include mild portal infiltration with lymphocytes, neutrophils, and plasma cells and hydropic degeneration of liver cells; steatosis, mild cholestasis, focal necrosis, and nodular cirrhosis may also be present. The discovery of 1q complement deposits seen by immunohistochemical examination of the liver very strongly points to lupus hepatitis.<sup>9,13</sup>

Anemia in SLE patients varies between chronic disease anemia, hemolytic anemia, blood loss, renal insufficiency, infection and myelodysplasia and aplastic anemia. Anemia in SLE is caused by suppression of erythropoiesis due to chronic inflammation. It is very possible that there is anemia due to an autoimmune process or not, anemia acquired in the form of anemia of chronic disease, iron deficiency followed by autoimmune hemolytic anemia.<sup>10</sup>

Education provided to patients in the form of recommendations for regular follow-up to monitor the course of the disease and side effects of treatment. Corticosteroids should be tapered off carefully. In addition, it is also necessary to carry out routine blood checks and blood chemistry every 3 months and anti-dsDNA tests every 3-6 months as well as monitoring the side effects of the treatment given due to the relatively long time of therapy.

### 3. Conclusion

Systemic lupus erythematosus is an autoimmune

disease that attacks various systems in the body including liver tissue, inflammation of the liver or hepatitis. Lupus can occur in about 20-50% of LES. Where a liver biopsy is needed to diagnose lupus hepatitis. Liver biopsy features in lupus hepatitis are mild portal infiltration with lymphocytes, neutrophils, and plasma cells and hydropic degeneration of liver cells; steatosis, mild cholestasis, focal necrosis, and nodular cirrhosis may also be present. If a biopsy cannot be performed, the diagnosis of lupus hepatitis can be made based on the results of the ANA profile examination where the anti-ribosomal P is 44% positive in patients with lupus hepatitis, and negative in autoimmune hepatitis. In addition, anti-Smith antibodies can also be used as markers for lupus hepatitis.

Another thing that needs to be considered in managing LES-related lesions is reducing risk factors. Sun protection is important because LES-related lesions are very easily triggered and exacerbate due to UV rays. Patients are required to use sunscreen when outside the house and wear clothes that protect themselves from the sun.

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