# A Case of Neuropsychiatric Systemic Lupus Erythematosus as A Sequela of Kikuchi's Disease

Theo Audi Yanto[1,2], Nathania Raphaeli Mulia[1], Abraham Fatah[1]

[1]*Faculty of Medicine, Pelita Harapan University, Tangerang, Indonesia*
[2]*Department of Internal Medicine, Siloam Hospital Lippo Village, Tangerang, Indonesia*

Nanthania Raphaeli, Fatah Abraham. A Case of Neuropsychiatric Systemic Lupus Erythematosus as a Sequela of Kikuchi's Disease**.** Medicinus. 2022 June; 10(2):87-95.
**Keywords:** Kikuchi's disease; Systemic lupus erythematosus; Neuropsychiatric systemic lupus erythematosus; Case report
**Correspondance:** Nathania Raphaeli Mulia. Faculty of Medicine Univ. Pelita Harapan
**E-mail:** nathaniarm@yahoo.com
Telephone: 0816 140 1065
**Online First: June 2022**

**Abstract**

The aetiology of Kikuchi's Disease (KD), a benign condition associated with multiple lymph node enlargements, remains unknown but several reported cases associate it with systemic lupus erythematosus (SLE). A 34-year-old Indonesian woman presented with multiple painless lymph node enlargements around the neck with three weeks of fever, myalgia, arthralgia, night sweats, and weight loss. Laboratory examination showed pancytopenia and elevated ESR. HIV and tuberculin skin testing were negative. Lymph node biopsy confirmed the diagnosis of KD. One week later, despite improvement in lymphadenopathy, she developed fever. Her ANA, anti-Smith antibodies, and anti-Ribosomal-P protein antibodies were positive. She was diagnosed with SLE and managed as an inpatient with high dose methylprednisolone. One week later, the patient developed psychotic symptoms and fever. The results of Laboratory examinations with lumbar puncture were unremarkable. She was diagnosed with neuropsychiatric SLE (NPSLE) and managed with methylprednisolone, paracetamol, folic acid, alprazolam, and amitriptyline. One month later, the patient returned with three days of fever and dyspnea. Despite improvement in neuropsychiatric symptoms, pneumonia and tonsillopharyngitis were diagnosed based on physical examination and chest X- rays. Her condition deteriorated into septic shock. She suffered cardiac arrest and was pronounced dead, despite attempted resuscitation.While KD is a benign condition, diagnosis is challenging due to its rarity and similarity to other lymphadenopathy diseases. Its association with SLE and NPSLE carries poor prognosis with higher mortality rate from the disease progression and adverse medication effects. Thus, early intervention and prevention of complications are crucial in managing patientswith KD.

## Introduction

Kikuchi's disease (KD), also known as necrotizing histiocytic lymphadenitis, is a benign and self-limiting condition with multiple lymph node enlargements along with a history of 2 – 3 weeks of fever. The disease's aetiology remains unknown; yet it is frequently associated with the onset of an autoimmunological process, such as systemic lupus erythematosus (SLE). Diagnosing KD clinically remains a huge challenge due to its similarities to other diseases, such as tuberculosis lymphadenopathy and malignant lymphoma. Hence, we present a case of neuropsychiatric systemic lupus erythematosus (NPSLE) in a 34-year - old woman which manifested one month after she had experienced the early manifestations of KD.

## Case Illustration

A 34-year-old Indonesian woman came with multiple painless swellings around the neck, along with fever of 3 weeks duration. She also experienced myalgia, arthralgia, and night sweat, and had lost 5 kilograms from her body weight. There was no past history of previous chronic diseases or contact with tuberculosis. On physical examination, she appeared to be fully alert, oriented, and

febrile. She had multiple, enlarged, painless, mobile, bilateral, cervical lymph nodes of varying sizes, with the biggest lymph node palpated at the right posterior triangle of her neck and measuring around 1.5 cm x 1.5 cm x 1.5 cm. No lymph node enlargement was identified in other body regions. Routine hematological panel results were hemoglobin (Hb) 9.4 g/dL, white blood cells (WBC) 3,020 /µL, platelet count 92,000 /µL, and erythrocyte sedimentation rate (ESR) 68 mm/hour. Blood smear samples were taken and showed the appearance of microcytic hypochromic anemia with markers of viral infection. Tests for anti-HIV and tuberculosis showed negative results. She underwent an incisional biopsy procedure to her right cervical lymph node. Histopathological examination presented the appearance of a large area of necrosis filled with lymphoid cells, abundant karyorrhexis debris, and histiocytes, which suggested the diagnosis of Kikuchi's disease. (Figures 1, 2, 3, and 4)

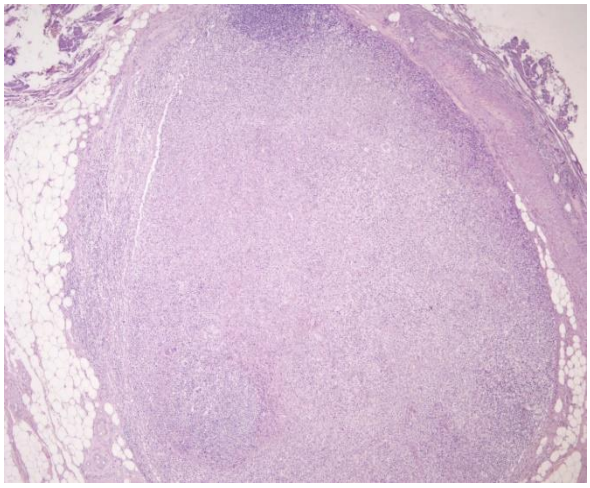

**Figure 1.** H&E 4x, cervical lymph node biopsy section showing a large necrotic area filled with abundant lymphoid cells.

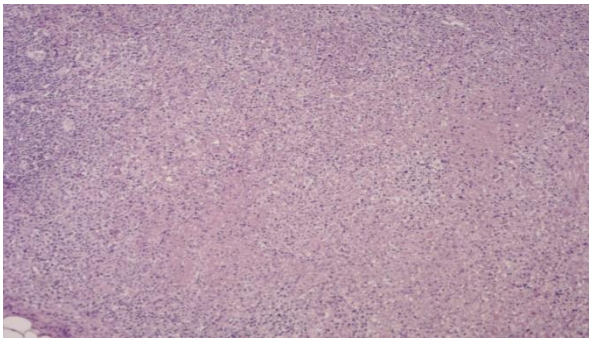

**Figure 2.** H&E 10x, cervical lymph node biopsy section showing debris without the appearance of any intact neutrophils around the necrotic area.

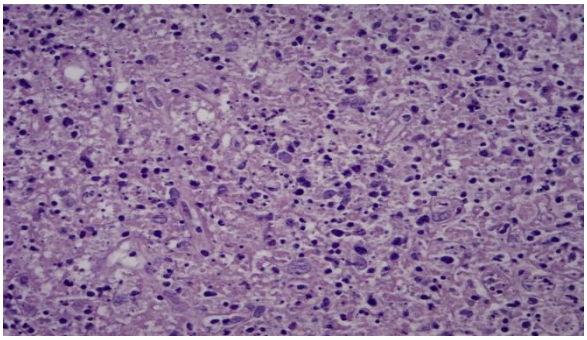

**Figure 3.** H&E 40x, cervical lymph node biopsy section showing abundant histiocytes with karryohexis debris. Some histiocytes appeared to have crescent-shaped nuclei.

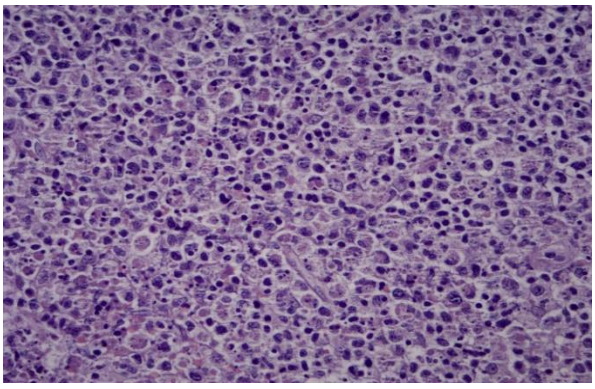

**Figure 4.** H&E 100x, cervical lymph node biopsy section showing the appearance of immunoblastic cells around the necrotic area.

A week after the patient underwent the incisional biopsy procedure, she presented with multiple discoid lesions around the nose, fever, arthralgia, headache, and bilateral palpebral edema. These symptoms started to show as her cervical lymph nodes regressed in size compared with her previous admission. On examination, she appeared to be alert, hypotensive, and febrile. Routine hematological panel results were Hb 8.20 g/dL, WBC 2,360 /µL, platelet count 45,000/µL and ESR 71 mm/hour. Another blood smear sample was taken and showed the appearance of microcytic hypochromic anemia along with fragmentocytes. Both liver and kidney function panels were within the normal range. Her ANA profile was positive for anti-nRNP/Smith and anti-Ribosomal-P protein antibodies. The patient was then diagnosed with systemic lupus erythematosus (SLE). She was admitted and given methylprednisolone injection 1 x 500 mg i.v for five days, and the dose was tapered off every two days. She went home with a maintenance dose of oral methylprednisolone 3 x 16 mg per day.

On a follow up examination one week later, the patient presented with anxiety and psychotic symptoms, including persecutory ideas and fluctuating disorientation, along with high fever of around 38-39$^{o}$C. The previously noted discoid lesions around her nose and bilateral palpebral edema had regressed after she received corticosteroid from her previous admission. Vital signs were within normal limits except for her fever. She was delirious and disoriented towards persons. Orientation towards time and place were intact. No neurological deficit was identified. Hematological panel only showed microcytic hypochromic anemia; WBC and platelet count were within the normal range. Head CT scan and lumbar puncture did not show any abnormalities. The patient was diagnosed with neuropsychiatric systemic lupus erythematosus (NPSLE) and admitted. She received methylprednisolone injection 1 x 125 mg i.v, paracetamol 3 x 1000 mg i.v, folic acid 1 x 400 µg p.o, alprazolam 2 x 1 mg p.o, and amitriptyline 2 x 10 mg p.o. After five days, she became fully alert and nonfebrile. Hence, she was discharged with a maintenance medication dose of oral methylprednisolone 3 x 16 mg, haloperidol 2 x 2.5 mg, and clobazam 2 x 10 mg.

One month later, the patient returned to the emergency department with a three day-onset of dyspnoea and fever. She appeared to be restless yet did not present any psychotic symptoms. She was hypotensive, tachycardic, tachypneic, febrile, and her oxygen saturation was 90%. Physical examination showed hyperemic pharynx and tonsils with the presence of pus, along with rhonchi and crackles heard all over both of her lungs. Chest X-ray showed nodular infiltrations on both of her lungs. Routine hematological panel showed Hb 10.10 g/dL, WBC 1,980/µL with neutrophilia, platelet count 71,000/µL, and ESR 67 mm/hour. Blood gas analysis panel showed respiratory acidosis. The patient was diagnosed with septic shock and respiratory failure caused by hospital-acquired pneumonia and suppurative tonsillopharyngitis. The patient received 15 lpm of oxygen through a non-rebreathing mask and a total of 1000 cc NaCl 0.9% fluid loading. She was given ceftazidime 3 x 2 grams i.v, levofloxacin 1 x 750 mg i.v, fluconazole 1x200mg p.o, dexamethasone 2x5mg i.v, and paracetamol 3 x 1,000 mg i.v. On the third day, she was found to be comatose ($E_1M_1V_1$) and her vital signs deteriorated. Two days later, she had cardiorespiratory arrest. Cardiopulmonary resuscitation was performed but unsuccessful. She was then pronounced dead.

Before her condition deteriorated, the patient had given consent to this case report for publication in a scientific journal without revealing her identity. The hospital's review board institution approved for publication this case report with undisclosed patient's identity for educational purposes.

Kikuchi's disease (KD), also known as necrotizing histiocytic lymphadenitis, is a rare, self-limiting, and benign condition of multiple lymphadenopathies that has a site of predilection at the cervical region. Most cases of KD are identified in a young population of about 20-30 years old, with a female to male ratio of 4:1. Higher

prevalence is found among Asian individuals.[1–4] Although exact aetiology and pathogenesis remain unclear, clinical findings in KD are similar to characteristics of viral infections, where it shows prodromal flu-like symptoms, unresponsiveness to antibiotics, and the same morphological features on lymph nodes, namely necrosis in the T-cell area, infiltrations of immunoblasts, and immunologic evidence of T-cell predominance (Figure 4). Numerous viruses, including Epstein-Barr virus, human herpes virus family, herpes simplex virus, parvovirus B19, HIV, HTLV-1 and dengue viruses have been proposed as implicated with the incidence of KD. Nonetheless, no studies have confirmed a causal relationship between viral infections and KD.[5–7]

Many KD cases have been reported to be associated with SLE. Hence, an underlying autoimmunity process in KD is postulated to have an association with other autoimmune diseases.[8–10] Due to similar aetiologies, signs and symptoms, and pathophysiology mechanisms, KD has also been described with association in Wegener granulomatosis, Sjogren syndrome, Graves' disease, and Still disease.[11] In SLE, the molecular pathogenesis is explained by aberrant innate immune responses that lead to tissue injury via release of pro-inflammatory cytokines, activation of T and B cells, and production of autoantibodies.[12] Changes in immune response are also associated with genetic and environmental factors, such as infections, that trigger the dysregulation of immune systems.[6,12] Even though the histopathology characteristic of KD simulates SLE, KD itself does not show seropositivity in markers like ANA, anti-dsDNA, etc.[6] A genetic factor that may play a role in KD that contributes to autoimmunity is the presence of particular human leukocyte antigens (HLA), particularly HLA-DPA1 and HLA-DPB1, which have been found in several autoimmune diseases including SLE. In addition to that, HLA-DPA1 has also been found in several immune-associated diseases, namely inflammatory bowel disease, post-streptococcal acute glomerulonephritis, ankylosing spondylitis, SLE, and other systemic vasculitis.[13] HLA-DP is also associated with SLE, even though the presence of HLA-DR in SLE with a higher immunostimulatory effect than HLA-DP.[14] These shared genetic predilections may explain the complexity of comorbidities between KD aSLE, and possibly other autoimmune diseases. Although several factors may link KD with the development of SLE, further studies are needed to confirm the exact mechanisms.

Sixty to ninety percent cases of KD show bilateral lymph node enlargements, with a 2-3 weeks history of fever in 30-50% cases.[7,11] Other symptoms such as weight loss, night sweats, myalgia, and arthralgia have also been reported.[15] Compared with SLE, most lymph node enlargements in KD have a predilected site at the cervical region, but lymph node involvement can happen in any body region.[16,17] 40% cases of KD show skin rashes, which can overlap with the manifestation of SLE. Rashes due to KD and SLE share the same histological findings.[18] Routine haematology profile in KD can show low haemoglobin, white blood cells, and platelet count, with a high ESR, even though there are also cases in which the haematological panels stay within normal limits. 30% cases show the appearance of atypical lymphocytes from the blood smear examination.[5] In this case, a blood smear sample was taken and showed the appearance of microcytic hypochromic anemia with markers of viral infection. This finding might relate to viral infection which started the development of KD. However, further serological examination was not performed to justify this theory.

The gold standard to diagnose KD is through histopathological examination, which shows the appearance of irregular paracortical necrotic areas that are surrounded with karyorrhexis debris and histiocytes with crescentic-shaped nuclei. Immunohistology samples show dominant presence of CD8+ T cells compared with CD4+ and minimum count of B cells, and express histiocytes antigens such as lysozyme, myeloperoxidase, and CD68.[6,19] Histopathological examination also excludes other causes of lymphadenopathies, especially to more

serious cases, such as lymphoma or malignancy.[2] KD has also been reported as an incomplete phase of lupus lymphadenopathy, which showed with a minimum count of cytotoxic T cells immunohistologically.[17]

KD is typically self-limited within 1 to 4 months. With the probability of an underlying autoimmunological process happening previously, a follow up examination is recommended for every patient diagnosed with KD. In this case, the patient showed discoid lesions as the presenting symptom of SLE one month apart from when she first experienced early manifestations of KD. According to LILACS reports in 2004, only 35 cases of KD correlate with the incidence of SLE.[19] This patient has fulfilled EULAR/ACR criteria for SLE with a total of 20 points: fever (2 points), low platelet count (4 points), discoid lesions (4 points), arthritis (6 points), and positive anti-Smith antibody (6 points).[20]

Early treatment for severe cases of SLE includes pulse therapy of high dose of intravenous methylprednisolone 1,000 mg for three days, followed by tapering off dosages, and cyclophosphamide once a month for the first six months. Hashimoto reported 535 cases of SLE had a better outcome after being treated with both steroid and immunosuppressive agents. However, there are also findings that report a similar outcome after being treated with steroid alone. In this case, the patient received 5 days of intravenous methylprednisolone without cyclophosphamide.[19] The steroid dosage was tapered off, and she went home with a maintenance oral dose of methylprednisolone 3 x 16 mg.

One week later, the patient developed flare from her SLE and showed neuropsychiatric symptoms. She fulfilled SLEDAI score of 9 points: psychosis (8 points) and fever (1 point).[21] Early assessments on SLE patients who develop neuropsychiatric manifestations should also consider risk factors for cardiovascular or cerebrovascular diseases. The diagnosis of neuropsychiatry systemic lupus erythematosus (NPSLE) is made per exclusion with the aid of CT scan, MRI, EEG, and lumbar puncture. A study in India shows 26.6% cases of SLE with positive anti-Ribosomal-P protein antibodies had psychotic manifestations.[22,23] The blood-brain barrier (BBB), antibodies, cytokines, such as tumour necrosis factor (TNF), interleukin-6 (IL-6), IL-1, and interferon alpha (IFN-α); and N-methyl-D-aspartate (NMDA) receptors are involved in the pathogenesis of NPSLE. It is disruption of BBB and binding of antibodies to their receptors responsible for the release of cytokines and toxic reactions that lead to damage to central nervous systems.[24]

Even though SLE itself is associated with a higher risk of infection that leads to a higher mortality rate, long-term use of corticosteroid can increase the burden in fighting the infections in patients with SLE.[25,26] The risk factors for infections are associated with anti-dsDNA titre, low complement levels, presence of nephritis, and long-term use of steroid and/or cyclophosphamide.[26] This patient with NPSLE was indicated for corticosteroid use and cyclophosphamide. Adjunctive treatment with short-term cyclophosphamide, in addition to steroid, carries more benefit in controlling seizures, peripheral and cranial neuropathy, and optic neuritis with no increased risk of infection compared to steroid alone.[27] 33% of SLE patients who received an equivalent dose of 7.5 mg prednisone daily suffer from E. coli, Staphylococcus pneumoniae and Streptococcus pneumoniae infections.[28] Another cohort study found an increased risk of nosocomial infection about 136 times in SLE patients who received steroid in the first three months compared with patients who did not receive steroid in their therapy regimen. A similar finding from a cohort study also reported a high prevalence of opportunistic infections caused by herpes zoster, Mycobacterium, Cytomegalovirus, and fungal infections.[29] With the high risk of infection, alternative immunomodulator agents with better side effect profiles, such as mycophenolate mofetil or IV immunoglobulin (IVIG), can be used for longer duration in patients with NPSLE.[27] In addition to that, a well-known therapy for SLE with hydroxychloroquine may be beneficial as a preventive approach in central nervous system (CNS) Lupus

associated with cerebrovascular disease; yet its role on NPSLE is still unknown.[22,30] SLE patients are also recommended to receive vaccination against influenza and Streptococcus pneumoniae, and prophylaxis therapy against possible opportunistic infection with anti-mycobacterials, antifungals, and antivirals.[31] Due to limitations in patient management in our country, patients with socioeconomic problems, such as in this case, may not eligible for optimal treatment. Therefore, in this case, an adjusted management with preventative and palliative approach is the last alternative option in addition to patient education about disease progression, complications, and associated worse prognosis. However, further studies are needed to determine the role in maximizing palliative treatment in patients with KD and NPSLE who are ineligible for other immunomodulators due to socioeconomic problems.

## Conclusion

Kikuchi's disease is a rare, benign enlargement of lymph nodes with unknown aetiology and can be misdiagnosed as tuberculosis lymphadenopathy or malignant lymphoma. KD may be a benign and self-limiting disorder, but the presence of SLE in this patient carried poor prognosis. A comprehensive, multidisciplinary approach in managing NPSLE with its complications is a must due to a higher risk of infections, putting the patient at a higher risk of mortality. Thus, a follow-up plan in KD cases is crucial to assess any potential autoimmune sequelae with an appropriate investigation, prevention of complications, and treatment plan.

## Acknowledgments

We thank Siloam General Hospital in Tangerang, Indonesia for all of the facilities that it provided to support the diagnosis and management of this patient; and for the doctors and nurses who contributed in taking care of this patient.

## Authorship

Theo Audi Yanto evaluated and treated the patient. Nathania Raphaeli Mulia performed data collection from the patient and her medical files. Theo Audi Yanto, Nathania Raphaeli Mulia, and Abraham Fatah drafted the manuscript. Nathania Raphaeli Mulia and Abraham Fatah performed data analysis and interpretation. Theo Audi Yanto supervised and gave expert advice regarding the manuscript. Theo Audi Yanto, Nathania Raphaeli Mulia, and Abraham Fatah gave the final approval of the version to be published. All authors declared that all the images and figures in this manuscript is/are author's own work and/or has obtained necessary permission to re-use the content from the authors and publisher of respective materials.

## Conflicts of interest

None

## Funding

Not applicable

## References

1. Bosch X, Guilabert A. Kikuchi-Fujimoto disease. Orphanet J Rare Dis. 2006;3:3–5

2. Humphreys S, Oikonomou KG, Ward N, Aye M. Kikuchi Disease : The Great Masquerador - A Case Report and Review of the Literature. Med Case Rep. 2018; 62:1–4. http://dx.doi.org/10.21767/2471-8041.100097

3. Rahman MSU, Muktadir G, Ahmed SAM. Case Report Kikuchi's Disease : A Case Report. Faridpur Med Coll J. 2013;8:96–8. https://doi.org/10.3329/fmcj.v8i2.20395

4. Bosch X, Guilabert A, Miquel R, Campo E. Enigmatic Kikuchi-Fujimoto Disease A Comprehensive Review. Am J Clin Pathol. 2004;122:141–52. https://doi.org/10.1309/yf08-1l4t-kywv-yvpq

5. Soedibyo S. Kikuchi-Fujimoto Disease. Med J Indones. 2005;14:107–13. https://doi.org/10.13181/mji.v14i2.178

6. Deaver D, Horna P, Cualing H, Sokol L. Pathogenesis , Diagnosis , and Management of Kikuchi – Fujimoto Disease. Cancer Control. 2014;313–21. https://doi.org/10.1177/107327481402100407

7. Pepe F, Disma S, Teodoro C, Pepe P, Magro G. Kikuchi-Fujimoto disease: A clinicopathologic update. Pathologica. 2015;107:120–9.

8. Baenas DF, Diehl FA, Salinas MJH, Riva V, Diller A, Lemos PA. Kikuchi – Fujimoto disease and systemic lupus erythematosus. Int Med Case Rep J. 2016;9:163–7. https://doi.org/10.2147%2FIMCRJ.S106396

9. Vithoosan S, Karunarathna T, Shanjeeban P, Piranavan P, Matthias T, Gamlaksha D, et al. Kikuchi-Fujimoto disease associated with systemic lupus erythematosus complicated with hemophagocytic lymphohistiocytosis: A case report. J Med Case Rep. 2019;13:1–7. https://doi.org/10.1186%2Fs13256-019-2100-1

10. Rojas-Villarraga A, Amaya-Amaya J, Rodriguez-Rodriguez A, Mantilla RD, Anaya JM. Introducing polyautoimmunity: Secondary autoimmune diseases no longer exist. Autoimmune Dis. 2012;1. https://doi.org/10.1155%2F2012%2F254319

11. Perry AM, Choi SM. Kikuchi-Fujimoto Disease: A Review. Arch Pathol Lab Med. 2018;142: 1341-6. https://doi.org/10.5858/arpa.2018-0219-ra

12. Choi J, Kim ST, Craft J. The pathogenesis of systemic lupus erythematosus-an update. Curr Opin Immunol [Internet]. 2012;24:651–7. Available from: http://dx.doi.org/10.1016/j.coi.2012.10.004

13. Haddad J, Shammaa D, Abbas F, Mahfouz RAR. First report on HLA-DPA1 gene allelic distribution in the general Lebanese population. Meta Gene [Internet]. 2016;8:11–3. Available from: http://dx.doi.org/10.1016/j.mgene.2016.01.004

14. Furukawa H, Kawasaki A, Oka S, Ito I, Shimada K, Sugii S, et al. Human leukocyte antigens and systemic lupus erythematosus: A protective role for the HLA-DR6 alleles DRB1*13:02 and *14:03. PLoS One. 2014;9:1–7. https://doi.org/10.1371%2Fjournal.pone.0087792

15. Padhan P, Tripathy KP, Sahoo SR, Maikup D, Mahapatra N. Kikuchi – Fujimoto Disease Presenting as Pyrexia of Unknown Origin. Indian J Rheumatol 2018;13:56-9. http://dx.doi.org/10.4103/injr.injr_101_17

16. López-villegas VJ, Medina-morales DA, Alzate-piedrahita JA, Aguirre AM, Rivera LMS. Kikuchi-Fujimoto disease in a patient with systemic lupus erythematosus and generalized lymphadenopathy. Rev Colomb Reumatol. 2018; 25: 216-20.

17. Neto NSR, Bonfiglioli KR, Milanez FM, Macêdo PA, Levy-Neto M. Lymphadenopathy and systemic lupus erythematosus. Bras J Rheumatol. 2010;50:96-101.

18. Dalton J, Shaw R, Democratis J. Case Report Kikuchi-Fujimoto disease. Lancet [Internet]. 2014;383:1098. Available from: http://dx.doi.org/10.1016/S0140-6736(14)60262-2

19. Santana A, Lessa B, Galrão L, Lima I, Santiago M. Kikuchi-Fujimoto's disease associated with systemic lupus erythematosus : case report and review of the literature. Clin Rheumatol. 2005;24:60-3. https://doi.org/10.1007/s10067-004-0923-6

20. Aringer M, Costenbader K, Daikh D, Brinks R, Mosca M, Ramsey-Goldman R, et al. 2019 European League Against Rheumatism / American College of Rheumatology Classification Criteria for Systemic Lupus Erythematosus. Arthritis & Rheumatology. 2019;0:1–13. https://doi.org/10.1136/annrheumdis-2018-214819

21. Bichile LS, Chewoolkar VC. Lupus Flare : How to Diagnose and Treat. Med Updat 2011;281–6. https://doi.org/10.31138%2Fmjr.28.1.4

22. Magro-Checa C, Zirkzee EJ, Huizinga TW, Steup-Beekman GM. Management of Neuropsychiatric Systemic Lupus Erythematosus: Current Approaches and Future Perspectives. Drugs. 2016;76:459–83. https://doi.org/10.1007/s40265-015-0534-3

23. Pradhan V, Patwardhan M. Neuropsychiatric manifestations and associated autoantibodies. Rheumatol Int. 2015;541–5. https://doi.org/10.1007/s00296-014-3114-z

24. Zhang Y, Han H, Chu L. Neuropsychiatric lupus erythematosus: Future directions and challenges; a systematic review and survey. Clinics. 2020;75:1–7. https://doi.org/10.6061%2Fclinics%2F2020%2Fe1515

25. Jung JY, Yoon D, Choi Y, Kim HA, Suh CH. Associated clinical factors for serious infections in patients with systemic lupus erythematosus. Sci Rep [Internet]. 2019;9:1–8. https://doi.org/10.1038/s41598-019-46039-5

26. Jung JY, Suh CH. Infection in systemic lupus erythematosus, similarities, and differences with lupus flare. Korean J Intern Med. 2019;9:9704. https://doi.org/10.3904/kjim.2016.234

27. Garcia-Cavazos R, Brey R. Neuropsychiatric systemic lupus erythematosus. Systemic Lupus Erythematosus. 4th Ed. 2004;757–83.

28. Ruiz-irastorza G, Olivares N, Ruiz-arruza I, Martinez-Berriotxoa A, Egurbide MV, Aguirre C. Predictors of major infections in systemic lupus erythematosus. Arthritis Res Ther. 2009;11:1–8. https://doi.org/10.1186/ar2764

29. Yang SC, Lai YY, Huang MC, Tsai CS, Wang JL. Corticosteroid dose and the risk of opportunistic infection in a national systemic lupus erythematosus cohort. Lupus. 2018;1819–27. https://doi.org/10.1177/0961203318792352

30. Kang D, Mok CC. Management of Psychosis in Neuropsychiatric Lupus. J Clin Rheumatol Immunol. 2019;19:9–17. https://doi.org/10.1142/S2661341719300015

31. Fanouriakis A, Bertsias G. Changing paradigms in the treatment of systemic lupus erythematosus. Lupus Sci Med. 2019;6:1–10. https://doi.org/10.1136/lupus-2018-000310

**Author's Statement**

The authors declared that all the images and figures in this manuscript is/are author's own work and/or has obtained necessary permission to re-use the content from the authors and publisher of respective materials.

**Theo Audi Yanto**