Available online: https://e-journal.unair.ac.id/jps

Case Report

Neuropsychiatric Symptoms in Corticosteroid Induced Systemic Lupus Erythematosus (Sle) Patients: a Case Report

Tri Ratnawati[1]

[1]General practitioner, Adjidarmo Hospital Lebak, Banten, Indonesia

Received: July 24, 2023
Accepted : September 15, 2023
Published Online : November 1, 2024

Correspondence Author:
Email: abipoenya@gmail.com

Abstracts

Introduction: Systemic lupus erythematosus (SLE) is a chronic autoimmune inflammatory disease with an unknown etiology and various clinical manifestations, course, and prognosis. Classes of medication used in the management of SLE include non-biological immunosuppressives, corticosteroids, biologic therapy, and immunoglobulins. The effect of using corticosteroids in the management of SLE still evokes debate regarding the emergence of mental health disorders. **Case**: A 24-year-old female patient was admitted to the hospital with an initial diagnosis of acute confusional stage, anemia, chronic disease, and systemic lupus erythematosus (SLE). Anticonvulsants, corticosteroids, and packed red blood transfusions had been given to the patient. The course of the disease during the hospitalization the next days, the patient experienced slurred speech, giggling, place and time disorientation, and visual hallucinations. The patient was consulted to a psychiatrist, got atypical antipsychotics and benzodiazepines, and then experienced improvement. **Discussion**: Patients with moderate SLE, in this case characterized by lupus nephritis, were given corticosteroids. Administration of corticosteroids to SLE patients will increase the risk of developing neuropsychiatric symptoms such as acute confusional state, anxiety, mood disorders, cognitive disorders, and seizures. This can occur due to increased permeability of the blood-brain barrier mediated by pro-inflammatory cytokines, resulting in the formation of autoantibodies against neural antigens, in which phospholipid proteins appear intracranially. **Conclusion**: Corticosteroid administration in SLE will cause neuropsychiatric symptoms such as slurred speech, giggling to herself, delirium, and visual hallucinations. Further design studies are needed to address the neuropsychiatric effects of corticosteroids in SLE.

Keywords: Systemic Lupus Erythematosus, Corticosteroids, Mental Health Disorder

Cite this as: Ratnawati. T.. "Neuropsychiatric Symptoms in Corticosteroid Induced Systemic Lupus Erythematosus (Sle) Patients: a Case Report". Jurnal Psikiatri Surabaya, vol. 13, no. 2, pp.206-213, 2024. doi: 10.20473/jps.v13i2.47788

INTRODUCTION

Systemic lupus erythematosus (SLE) is a chronic autoimmune inflammatory disease with an unknown etiology and diverse clinical manifestations, course, and prognosis [1]. Often referred to as a disease of a thousand faces because its manifestations are very wide and can be fatal [2]. Manifestations range from mild, affecting the skin or joints, to severe life-threatening, for example neuropsychiatric systemic lupus erythematosus (NPSLE), lupus nephritis, pneumonitis, carditis, and other organs [3]. In general, it is often found in young women with high hormonal activity [4].

Neuropsychiatric Systemic Lupus Erythematosus (NPSLE) is a group of neurological, psychiatric, and cognitive disorders that can be experienced by up to 40% of SLE patients [5]. Cognitive dysfunction is one of the most common forms of neuropsychiatric systemic lupus erythematosus (NPSLE). Such cognitive dysfunction can be found in 20–60% of SLE patients [6]. Cohort studies of SLE patients show that nearly half will develop NPSLE during the course of their disease. It affects 14% to more than 80% of adults and 22% to 95% of children. NPSLE is the least understood but responsible subcategory of SLE for significant morbidity and mortality [7].

SLE patients need proper and correct treatment and care when undergoing therapy. Treatment of SLE patients generally aims to treat symptoms that induce remission and maintain remission for as long as possible as the disease progresses [3]. Classes of drugs used in the management of SLE include non-biological immunosuppressants, corticosteroids, non-steroid anti-inflammatory drugs, antimalarial drugs, biological therapy, and immunoglobulin [8]. The use of these drugs depends on the patient's condition, severity of the disease, and manifestations that appear in these patients, including severe or life-threatening SLE, for example manifestations of NPSLE, Lupus Nephritis, and severe thrombopenia [9].

Neuropsychiatric lupus is a symptom of lupus that involves the central and peripheral nervous systems with clinical manifestations that vary from less obvious symptoms such as mood and cognitive disorders to more obvious symptoms such as stroke, seizures, and myelopathy [8]. Management of therapy in neuropsychiatric lupus is currently lacking due to limited research on therapeutic approaches in neuropsychiatry lupus [10]. The study at Hasan Sadikin General Hospital Bandung found common psychiatric, central nervous, and peripheral nervous manifestations were mood disorder, headache, and mononeuropathy, respectively [11]. Use of corticosteroids in the management of SLE can cause neuropsychiatric disorders such as depression, mania, agitation, mood instability, anxiety, insomnia, catatonia, depersonalization, excessive feelings of happiness or delirium, dementia, and psychosis [12]. The incidence of steroid-induced psychotics is approximately 2% in adults. Steroid psychosis is a syndrome with symptoms such as depression, hypomania, irritability, anxiety, insomnia, restlessness, fatigue, impaired memory, and decreased concentration and focus [12].

Coronavirus disease 2019 (COVID-19) is caused by the severe acute respiratory syndrome coronavirus 2 (SARS CoV-2), a member of the Coronaviridae family of viruses, which is responsible for the pneumonia outbreak in late December 2019, later officially announced as a pandemic. Mental health issues became interesting during pandemic COVID-19 [13]. Mental health is a state of wellbeing that includes emotional, psychological, and social. Mental health during a pandemic includes parallel processes at two different levels for the concepts of insanity and outbreak or contagion. One of the processes is the reflection of the epidemiological process of the pandemic in the realm of psychology, reflecting thoughts, behavior, and emotional responses [14]. This is just as a physical disease has a pathogen, spreads via a vector, follows a mode of transmission,

ferments during incubation, and explodes to defeat the host. The psychological aspects of outbreaks have a core of misinformation, accepting uncertainty, growing in doubt as they incubate in the limbic system, and then, through media and communication vectors, exploding in the form of individual or mass panic, threatening to overwhelm the coping resources of an individual or the whole community [15]. The purpose of writing this case report is to review the possibility of neuropsychiatry-induced corticosteroids.

CASE

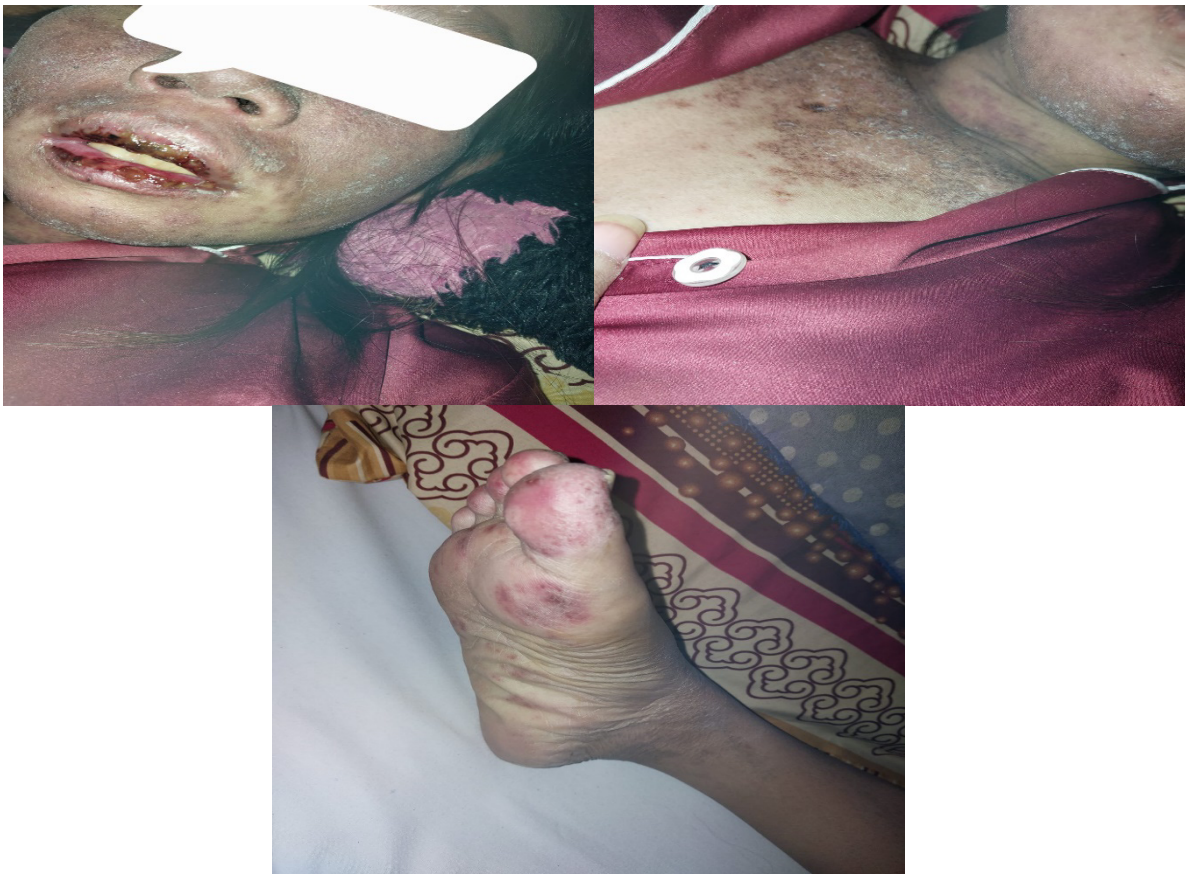
A 24-year-old woman was brought to the emergency room at Lebak Banten Hospital with complaints of seizures since 3 hours before entering the emergency room. According to the patient's family, seizures lasted 5 minutes with eyes rolling upwards and hands and feet twitching. Patient tends to be unable to calm down and rage continuously so that patient's family is forced to tie patient to her bed so she doesn't injure herself. Besides seizure, family said patient experienced severe headaches, accompanied by spinning dizziness.

According to the patient's family, a week earlier the patient looked weak, tired, lethargic, had no appetite because the oral mucosa was blistered, and had dry and scaly skin over the face and whole body. Patient also did not want to take medicines from an internal medicine specialist who was controlled for 2 months before emergency room admission. Patients sometimes cry hysterically during menstruation and sometimes talk, rambling to their husbands and parents. Patient has been married since 2 years ago but has not had children. According to family, the patient had no menstrual disturbances before or during her illness.

From the history of the patient's course, initially 10 months ago the patient had complaints of weakness, fatigue, lethargy, and pain in all joints, a reddish rash on both cheeks, and hair loss. Then she was being treated by an internal medicine specialist, received a packed red cell transfusion, and examined with an ANA test and anti-dsDNA profiles. According to the patient's husband, the patient was diagnosed with systemic lupus erythematosus (SLE) and received therapy with 3x16 mg methylprednisolone, 1x5 mg folic acid, and 2x5000 ui vitamin D. Patient had a routine control schedule with an internal medicine specialist after the previous hospitalization, but she did not want to take the medicine since last month.

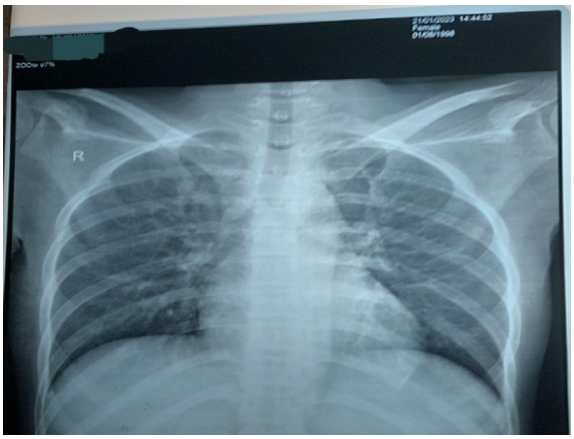
History of heart disease, hypertension, drug allergies, diabetes, or joint disease was denied. History of disease related to the structure of the brain was denied. History of alcohol or psychoactive substance consumption was denied.

From general physical examination, patient looked seriously ill; level of consciousness was delirium with GCS E4V3M5 = 12. Vital signs obtained: blood pressure 110/70 mmHg, pulse rate 98 x/min, respiratory 28 x/min, axillary temperature 37.8 °C. Height 145 cm, weight 35 kg, body mass index (BMI) 16.64 kg/m2, and nutrition status was malnutrition. Conjunctival pallor was seen, ears and nose examination within normal limits. The pharyngeal throat is not hyperemic, the tonsils are T1-T1, and the and the neck lymph nodes are not enlarged. Lung and heart examinations within normal limits. On auscultation of the lungs, vesicular breath sounds were obtained, as was regular auscultation of heart sounds I and II. Superior and inferior extremities within normal limits. Neurologic status: physiological reflexes (+), pathological reflexes (-). Localized status at face showed scaly brownish rash on both cheeks, front chest wall, and erythema in the right and left dorsum pedis areas.



Picture 1. Patient's Skin Clinical Manifestation

On complete blood count, results showed WBC 5.2 x 103 /µL, RBC 2.87 x 106 /µL, hemoglobin 7.7 g/dL, hematocrit 23.1%, MCV 80.5 fL, MCH 26.8 Pg, MCHC 33.3 g/d, and platelet 167 x 103 / µL. From blood chemistry results, obtained SGOT 57 U/L, SGPT 21U/L, urea 59.06 mg/dl, creatinine 1.1 mg/dL, sodium 141mmol/L, potassium 4.1 mmol/L, random blood glucose 64 mg/dL, and albumin 3.3 gr/dL. Complete urinalysis results showed proteinuria +4 (1000 mg/dl), blood +2 (50 RBC/ul), urine leukocytes 40-50, and urine color slightly cloudy. Immunological examination revealed non-reactive anti-HCV and HBSAG. On immunoserological examination, a positive ANA titer of 1/3200 was found, and a positive anti-ds-DNA titer of 723 in the patient. Supporting x-ray results of the patient's chest showed lung and heart within normal limits.



Picture 2. Patient's Chest X-ray

Patient was treated in the internal medicine ward by an internal medicine specialist as doctor in charge, co-treated with neurologists and dermatologists. Initially, the patient was diagnosed with acute confusional stage patient, anemia et causa chronic disease, systemic lupus erythematosus (SLE). Patients received therapy during hospitalization: infusion of normal saline 500 ml within 8 hours, intravenous injection of omeprazole 1x40 mg, phenytoin 2x100 mg, Vitamin D 2x5000 ui, folic acid 2x1 mg, CaCO3 3x50 mg, 2x125 mg methylprednisolone and SB1 white, and packed-red cell transfusion 2 bags.

During treatment at hospital, patient was consulted by neurology department, but it was stated that there were no neurological disorders in the patient. As three days of treatment, the patient began to talk, slurred, giggle herself, had place and time disorientation, and claimed that she saw a monkey figure in the inpatient ward that other people could not see. Before hospitalization, patients had not experienced similar complaints. On the 4th day of treatment, the patient was then consulted by a psychiatrist, and psychiatric status' results were obtained. Patient's thought processes showed the impression of non-realistic, non-logical thoughts, incoherent thought flows, and no bizarre delusions found in thought content. Patient has visual hallucinations and insight with score 3, with stressor that patient feels tired because continually go back and forth to hospital for treatment. Patient's clinical diagnosis leads to acute psychotic disorder, with differential diagnosis being organic mental disorder. Patient received additional therapy with risperidone 2x1 mg and fluoxetin 1x20 mg.

On the 5th day of treatment, the patient was admitted to the hospital in calmer condition and did not ramble on. Results of the complete blood count showed hemoglobin was 10.2 g/dl. Patient's outpatient therapy includes lansoprazole 1x30mg, folic acid 2x1mg, CaCO3 3x50mg, methylprednisolone 3x16mg, phenytoin 2x100mg, Vitamin D 2x5000ui, risperidone 2x1mg, and fluoxetin 1x20mg. Patients are advised to go to internal specialists and psychiatrists for control.

DISCUSSION

Systemic lupus erythematosus (SLE) is a systemic disease with various clinical picture with multifactorial causes including genetic, environmental, and hormonal exposure to the environment (ultraviolet rays, drug-induced), and infectious agents that are also thought to have a relationship with the development [16]. Clinical manifestations can be mild, only affecting the skin or joints, to severe manifestations that are life-threatening, such as neuropsychiatric systemic lupus erythematosus (NPSLE), lupus nephritis, pneumonitis, carditis, and other organs. In general, it is often found in young women with high hormonal activity [9] .

Diagnosis of NPSLE can be made if the patient's clinical manifestation meets SLE diagnostic criteria. Currently, there are the latest clinical criteria for diagnosing SLE issued by Systemic Lupus International Collaborating Clinics (SLICC) in 2012 [5]. Diagnosis can be made if more than 4 criteria are found (at least 1 clinical criteria and 1 immunological criteria) (Table 1).

Tabel 1. Systemic Lupus International Collaborating Clinics (SLICC) Criteria

Clinical Criteria	Kriteria imunologi
Acute subcutaneous lupus (malar rash, bullous lupus, TEN)	ANA
Chronic subcutaneous lupus (discoid rash, verrucous lupus)	Anti-Dsdna
Oral atau nasal ulceration	Anti sm
Arthtritis	Antifosfolipid AB
Serositis	Low complement
Renal problems	Direct Coomb's test
Neurologic problems	
Anemia	
Trombositopenia	

In this case, the diagnosis of SLE in this patient was made using SLICC criteria; there are 4 clinical criteria, including anemia, chronic cutaneous lupus, arthritis, and neurological disorders in the form of seizures. As well as 2 immunological criteria, including ANA test (+) and anti-DNA test (+) (minimum 4 criteria with at least 1 clinical criterion and 1 immunological criteria) [5].

SLE is an autoimmune chronic inflammatory disease that has widespread impacts on other organs and can be life-threatening. The female population who suffers from this disease is generally of productive age, namely in the age range of 15-44 years [2]. The case presented is a case of a 24-year-old woman with SLE with hematological, neuropsychiatric, and skin involvement and lupus nephritis. A Retrospective Study of Drug Used and Potential Drug Interactions in Patients with Systemic Lupus Erythematosus found 210 SLE people consisted of 12.86% males and 87.14% women. 29.05% of the patients aged 17-25 years [17].

The FDA-approved drugs used for the treatment of SLE in the United States are glucocorticoids, aspirin, and hydroxychloroquine. Glucocorticoids are one of the main therapies in the management of NPSLE. In America alone, glucocorticoids are the most often used medication for the management of SLE. Glucocorticoids are used in patients with clinical manifestations of seizures, refractory headaches, chorea, transverse myelitis, etc. The oral dose of glucocorticoids used is 1-2 mg/kg/day or 1 gram/day for 3 days, followed by high-dose oral glucocorticoids [4].

The therapy used in this case included infusion of normal saline 500 ml within 8 hours, intravenous injection of omeprazole 1x40 mg, phenytoin 2x100 mg, Vitamin D 2x5000 ui, folic acid 2x1 mg, CaCO3 3x50 mg, 2x125 mg methylprednisolone and SB1 white, and packed-red cell transfusion 2 bags. The patient was given corticosteroids because of moderate SLE with clinical signs of lupus nephritis. A few days after administration of corticosteroids, the patient experienced psychotic symptoms such as slurred speech and the feeling of seeing a monkey figure in the inpatient ward that other people could not see and giggling to herself.

According to a case report in Nepal, administration of corticosteroids to SLE patients will induce neuropsychiatric symptoms such as acute confusional state, anxiety, mood disturbances, cognitive disturbances, and seizures. This occurs due to increased permeability of the blood-brain barrier, which is mediated by proinflammatory cytokines, so that autoantibodies are formed against neural antigens, in which phospholipid proteins appear in intracranial [18]. Based on the previous 10-year prospective study, different results showed that there was a tendency to improve cognitive function in patients receiving glucocorticoid therapy with azathioprine and mycophenolate. Women with SLE who received long-term corticosteroid therapy had worse executive function than those who did not receive the therapy. Thus, a neuropsychological evaluation is recommended before starting corticosteroid therapy to control for cognitive effects [12].

The release of endogenous glucocorticoids can provide a physical and physiological stress response. The release of glucocorticoid compounds will increase levels of corticotrophin-releasing hormone (CRH) and Arginine Vasopressin (AVP). These two hormones activate the sympathetic nervous system and the hypothalamic-pituitary-adrenal (HPA) axis. In addition, the hippocampus and amygdala, which specifically regulate stress responses, also have glucocorticoids receptors. Translocation of the steroid receptor complex to the nucleus of neurons with glucocorticoid receptors will change gene transcription, and these changes will produce neurotransmitters including dopamine and serotonin as well as neuropeptides, namely somatostatin and beta-endorphins. Increased serotonin levels in the synaptic cleft will affect the mood of patients treated with corticosteroid agents [19].

After experiencing neuropsychiatric complaints, the patient was consulted by the mental health department and given 2x1 mg of risperidone and 1x20 mg of fluoxetin. In this case, atypical antipsychotics and antidepressants were given to suppress positive symptoms in patients. The patient received risperidone therapy because it is an atypical antipsychotic drug that functions to inhibit Dopamine D2 receptors, which will reduce the negative symptoms of psychosis. It also inhibits Serotonin 2A receptors (serotonin-dopamine antagonists) by increasing the release of dopamine in the central region of the brain, thereby reducing motor side effects and improving cognitive and affective symptoms [20]. Flouxetin is a benzodiazepine. It works by: 1. binding to the benzodiazepine receptor on the GABA-A ligand, which is the gate of the chloride channel complex; 2. Increase the effect of GABA inhibitors; 3. Inhibits neuronal activity in the amygdala, which is beneficial for anxiety disorders [21].

CONCLUSION

A 24-year-old female patient was diagnosed with SLE, lupus nephritis, and when she was given corticosteroid treatment, she developed neuropsychiatric symptoms such as slurred speech, giggling to herself, disorientation of place and time, and visual hallucinations, so the patient was consulted by a psychiatrist for treatment. The need for multidisciplinary collaboration in the management of moderate and severe SLE so that neuropsychiatric symptoms can be prevented and further research with different research designs.

ACKNOWLEDGEMENTS

Acknowledgments can be given to those involved with this research.

CONFLICT OF INTEREST

Authors need to include in the Conflict of Interest regarding the consequences that may arise in the future due to the exposure of scientific data with the interests of related institutions.

REFERENCES

[1] A. Naziha, G. A. Maharatih, and Bulan Kakanita Hermasari, "Hubungan Dukungan Sosial dengan Tingkat Depresi Pasien Systemic Lupus Erythematosus (SLE)," Plex. Med. J., vol. 1, no. 6, pp. 234–241, 2023, doi: 10.20961/plexus.v1i6.498.

[2] A. Narani, "Systemic Lupus Erythematosus (SLE) - a review of clinical approach for diagnosis and current treatment strategies," Jaffna Med. J., vol. 31, no. 2, pp. 9–13, Dec. 2019, doi: 10.4038/jmj.v31i2.73.

[3] An'nurihza Zidhan Azhara, I Gusti Bagus Indro Nugroho, and Bulan Kakanita Hermasari, "Hubungan Resiliensi Diri dengan Tingkat Kecemasan Pasien Systemic Lupus Erythematosus (SLE)," Plex. Med. J., vol. 2, no. 1, pp. 26–31, 2023, doi: 10.20961/plexus.v2i1.456.

[4] Yuliasih, "Perkembangan Patogenesis dan Tata Laksana Systemic Lupus Erythematosus," J. Univ. Airlangga, vol. 4, no. 2020, pp. 38–54, 2020.

[5] D. Nurlita, A. Bachtera Barus, D. I. Anggraini, and R. Wahyudo, "Neuropsychiatric Systemic Lupus Erythematosus Neuropskiatrik Sistemik Lupus Eritematosus," Lampung, Feb. 2019.

[6] E. Manca, "Autoantibodies in Neuropsychiatric Systemic Lupus Erythematosus (NPSLE): Can They Be Used as Biomarkers for the Differential Diagnosis of This Disease?," Clin. Rev. Allergy Immunol., vol. 63, no. 2, pp. 194–209, 2022, doi: 10.1007/s12016-021-08865-2.

[7] Y. Nie et al., "The influence of intrathecal injection of methotrexate and dexamethasone on neuropsychiatric systemic lupus erythematosus (NPSLE): a retrospective cohort study of 386 patients with NPSLE," Arthritis Res. Ther., vol. 25, no. 1, Dec. 2023, doi: 10.1186/s13075-023-03030-w.

[8] S. Sarwar et al., "Neuropsychiatric Systemic Lupus Erythematosus: A 2021 Update on Diagnosis, Management, and Current Challenges," Cureus, Sep. 2021, doi: 10.7759/cureus.17969.

[9] I. Halimah Bharata, L. Gde Sri Adnyani

Suari, and D. Puji Lestari, "GANGGUAN KOGNITIF TERKAIT SLE: SEBUAH TINJAUAN PUSTAKA," 2021.
[10] S. M. Ragab and A. M. Ibrahim, "Neuropsychiatric lupus erythematosus in a cohort of Egyptian patients," Egypt. J. Neurol. Psychiatry Neurosurg., vol. 58, no. 1, Dec. 2022, doi: 10.1186/s41983-022-00464-y.
[11] S. D. Putra, M. Nurmansyah Ardisasmita, and L. Hamijoyo, "Neuropsychiatric Manifestation Screening among Systemic Lupus Erythematosus Patients in Hasan Sadikin General Hospital Bandung," 2017.
[12] M. Janes, S. Kuster, T. M. Goldson, and S. N. Forjuoh, "Steroid-induced psychosis," Baylor Univ. Med. Cent. Proc., vol. 32, no. 4, pp. 614–615, Oct. 2019, doi: 10.1080/08998280.2019.1629223.
[13] S. S. Hejazian, S. M. Hejazian, F. Farnood, and S. Abedi Azar, "Dysregulation of immunity in COVID-19 and SLE," Inflammopharmacology, vol. 30, no. 5. Springer Science and Business Media Deutschland GmbH, pp. 1517–1531, Oct. 01, 2022. doi: 10.1007/s10787-022-01047-2.
[14] M. Izzatika, R. A. Syakurah, and I. Bonita, "Indonesia's mental health status during the Covid-19 pandemic.," Indig. J. Ilm. Psikol., vol. 6, no. 2, pp. 78–92, Nov. 2021, doi: 10.23917/indigenous.v6i2.14024.
[15] E. Purnawati, L. D. Saraswati, M. A. Wurjanto, and S. Yuliawati, "The Effect of the Covid-19 Pandemic on Mental Health (Children, Adolescents, Young Adults) and Mental Health Service: Systematic Review," Unnes J. Public Heal., vol. 11, no. 2, pp. 179–197, Jul. 2022, doi: 10.15294/ujph.v11i2.53472.
[16] L. Kwee, "Systemic Lupus Erythematosus dengan Manifestasi Tidak Biasa," J. Med. Heal., vol. 3, no. 1, pp. 73–82, 2021.
[17] S. P. Astini, N. N. W. Udayani, and H. Meriyani, "Studi Retrospektif Penggunaan Obat dan Potensi Interaksi Obat Pasien Systemic Lupus Erythematosus," J. Ilm. Medicam., vol. 7, no. 2, pp. 77–83, 2021, doi: 10.36733/medicamento.v7i2.2271.
[18] B. D. Pathak et al., "Psychotic symptoms in a patient with Systemic Lupus Erythematosus: A diagnostic dilemma between lupus psychosis and steroid induced psychosis," Ann. Med. Surg., vol. 84, no. November, p. 104843, 2022, doi: 10.1016/j.amsu.2022.104843.
[19] J. Deng, N. E. Chalhoub, C. M. Sherwin, C. Li, H. I. Brunner, and S. L. City, "HHS Public Access," vol. 49, no. 56, pp. 251–259, 2020, doi: 10.1016/j.semarthrit.2019.03.010.Glucocorticoids.
[20] X. He, X. L. Duan, and J. S. Liu, "A Case of Neuropsychiatric Systemic Lupus Erythematosus With Hair Loss as the First Diagnostic Symptom," Front. Psychiatry, vol. 13, no. May, pp. 1–5, 2022, doi: 10.3389/fpsyt.2022.839566.
[21] E. Abrol et al., "Psychosis in systemic lupus erythematosus (SLE): 40-year experience of a specialist centre," Rheumatol. (United Kingdom), vol. 60, no. 12, pp. 5620–5629, 2021, doi: 10.1093/rheumatology/keab160.