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CASE REPORT

Oral Lesion Management in Juvenile SLE with Hepatosplenomegaly

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Background: Systemic Lupus Erythematosus (SLE) is an autoimmune disease with unknown etiology resulting in chronic multi-organ inflammation. Juvenile Systemic Lupus Erythematosus (JSLE) is a specific diagnosis of SLE in juvenile, characterized by oral ulceration.

Purpose: This case report attempts to provide information for oral medicine specialists in managing JSLE patients with hepatosplenomegaly.

Case Presentation: A 17-year-old female patient was referred from the Pediatrics Department with mouth ulcers accompanied by dry lips and a tendency to bleed. The most concerning lesion was located on the left buccal mucosa, a single ulceration measuring 5x6mm. Multiple ulcerations spread over the upper and lower labial mucosa, with haemorrhagic crusts on the lips. Painful ulceration can lead to difficulties in mouth opening and impaired function in eating and drinking. Central erythema was seen on the palate. Pseudomembranous candidiasis was also seen on the patient's tongue. The hepatosplenomegaly was confirmed by CT scan, with enzyme values of SGPT (386 U/L) and SGOT (504 U/L).

Case Management: Administration of 0.9% NaCl was instructed to the patient to maintain oral hygiene and help moisturize lips in order to remove haemorrhagic crusts. Administration of 0.025% hyaluronic acid mouthwash and topical steroid ointment mixture for ulcerated and inflammatory conditions. Drug adjustments were made based on laboratory tests and the patient's clinical condition was improving.

Conclusion: Managing oral symptoms helps reduce morbidity in JSLE patients. Topical corticosteroids are considered the first line in controlling oral inflammation. Dentists play a role in improving patients' oral hygiene with the aim of reducing the risk of other opportunistic infections.

Keywords: hepatosplenomegaly, juvenile SLE, SLE, oral ulcer

Introduction

Systemic lupus erythematous (SLE) is an autoimmune disease with unknown etiology. The condition causes multi-organ inflammation and resulting tissue damage, by producing and secreting autoantibodies and pathogenic immune complexes, in tissues and cells.[1,2] Adaptive and innate immune systems including B cells and T cells are involved in this condition. Exposure to sunlight, drugs, chemical compounds and hormones are important environmental factors associated with the severity and recurrence of SLE.[2] The clinical manifestations of these patients vary widely, in general musculoskeletal involvement, especially joint inflammation and pain, rash, and fever are common. These symptoms may develop slowly or appear suddenly.[3]

The global incidence and new patient rate of SLE is estimated to be 5.14 (1.4 to 15.13) per 100000 person-years. In terms of overall population prevalence, the estimate is 43.7 (15.87 to 108.92) per 100000 person-years.[2,4] Specifically, in Indonesia, the prevalence of SLE itself has not been documented optimally, but there are data from rheumatology clinics from several hospitals in Indonesia, which show an increase in data on patients with SLE in 2015, 2016, and 2017 as much as 17.9–27.2%, 18.7–31.5%, 30.3–58%, respectively.[5] The ratio of females to males is 2:1 to 15:1,[6] and commonly

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occurs in the age range of 9–58 years, with the highest incidence in 21–30 years old.[5] Prospective studies in Indonesia from 2015 to 2021 show the peak incidence in children is 13 years of age, with a female-to-male ratio of 9.5:1.[7]

Oral lesions are one of the clinical manifestations that occur in patients with SLE. The American College of Rheumatology has made oral manifestations one of the assessment criteria for the diagnosis of SLE.[8] The prevalence of oral lesions can be differentiated according to the type of lupus itself: oral manifestations in systemic lupus are 8–45%, 3–20% in cutaneous chronic lupus and 4–25% in discoid erythematous.[9,10] Manifestations on the oral mucosa that have been frequently reported include ulceration, which occurs in more than 40% of the patients,[11] xerostomia, salivary gland disorders, temporomandibular disorders (TMDS TMJ), gum lesions such as bleeding and oedema.[10] Kuhn et al said that oral lesions are more common in women, 2.7 times greater than in men.[12]

Ulceration is the most common oral lesion in juvenile SLE (JSLE). They usually occur unnoticed or without complaint and do not necessarily indicate the severity of the disease. The most commonly reported types of lesions are palatal erythema and aphthous ulcers, which signify an active SLE condition. As for systemic conditions, JSLE patients usually have complaints of mucocutaneous lesions, renal involvement, central nervous system disorders, and hematological abnormalities. This case report describes the role of dentist, especially oral medicine, in managing oral lesions in a juvenile patient with SLE from hospitalization to post-treatment control.

Case Presentation

A 17-year-old female inpatient was referred from the Pediatrics Department to the Oral Medicine Department at Hasan Sadikin Hospital with complaints of painful mouth ulcers, dryness of the lips and difficulties in swallowing. This condition made it difficult for the patient to eat and drink, resulting in the patient's physical condition becoming weak and debilitated. The ulcer has been present for 3 days, has not improved and tends to bleed. However, the bleeding has stopped since the previous day. The Pediatrics Department administered Kenalog in Orabase® in response to this patient's oral condition.

The patient complained of body aches, rashes and hair loss 2 months ago. This condition was examined at Kebon Jati Hospital, and the diagnosis of SLE was confirmed. Approximately 2 weeks ago, the patient complained of the same condition and finally decided to be treated at Hasan Sadikin Hospital. Comprehensive and multidisciplinary examinations established that, in addition to SLE, the patient was also diagnosed with hepatosplenomegaly, during the third week of hospitalisation. Enlargement of the liver and spleen were found during abdominal CT scan. Blood tests performed during treatment are shown in Table 1.

During this two-week period, the patient took a diverse drug regimen that administered by the Pediatrics Department, which includes Levofloxacin, Amikacin, Ampicillin-Sulbactam and Ethambutol for the antibiotics. Fluconazole was given intravenously. Steroidal anti-inflammatory drugs were given IV Methylprednisolone and Triamcinolone Acetonide topically. Omeprazole and Ca. Carbonate as antacid and PPI. Vitamin D and Curcuma as dietary supplements and Paracetamol were also given.

Table 1 Hematology Examination Result

Date/Hematology Parameters	November 18, 2022	November 24, 2022	December 24, 2022
Haemoglobin	9.3 g/dL ^{L}	7.8 g/dL ^{L}	12.1 g/dL
Hematocrit	27.7% ^{L}	23.4% ^{L}	37.4%
Erythrocyte	3.47 mil/uL ^{L}	2.94 mil/uL ^{L}	4.38 mil/uL
Leucocyte	2.17 x 103/uL ^{L}	7.80 x 103/uL	11.81 x 103/uL
SGPT	99 U/L ^{H}	386 U/L ^{H}	116 U/L ^{H}
SGOT	246 U/L ^{H}	504 U/L ^{H}	28 U/L

Abbreviations: L, low; H, high; SGPT, Serum glutamic pyruvic transaminase; SGOT, Serum glutamic oxaloacetic transaminase.

On extraoral examination, the patient's conjunctiva was anemic, and there was dryness and exfoliation of the lips that tends to bleed along with hemorrhagic crusts with serous sanguinolenta. During intraoral examination, there were lesions covering on almost all areas of the oral mucosa. Multiple ulceration on the upper and lower labial mucosa. A painful ulceration on the left buccal mucosa measuring 5 × 6 mm with erythema border. Central palatal erythema was seen on the palatum durum. Candidiasis pseudomembrane was also seen on the dorsum of the tongue, accompanied by papillae elongation (Figure 1).

Case Management

NaCl 0.9% was administered and used to perform several instructions related to the patient's oral condition. Cleaning the teeth using a saline-moistened gauze was the most important thing because during the 2 weeks of hospitalisation, the patient neglected her oral hygiene. Hemorrhagic crusts on the lips and labial mucosa were also instructed to be dressed using moist gauze (NaCl 0.9%) as often as possible. This was done five times a day, with the aim of moistening lips and removing the crusts.

The condition of multiple and widespread ulcerations on the upper and lower labial mucosa, a topical steroid ointment mixture, was administered to the patient. A mixture containing Dexamethasone 0.5 mg mixed with Lanolin 2.5 mg and petroleum jelly added up to 25 mg was instructed for the patient to use it three times a day, after applying saline dressing. Considering other ulcerations, one of which was on the left buccal mucosa and also other ulcers that were difficult to reach by hand, 0.025% hyaluronic acid was administered to relieve inflammation locally.

During the second visit, on 22 November 2022 (Figure 2), it was seen that the general condition of the patient's oral cavity had improved. The patient's tongue still showed whitish plaque, which was finally given Nystatin® oral suspension, but had to be stopped after 2 days of administration regarding the hepatosplenomegaly condition. The ointment was stopped and replaced with petroleum jelly. The other medication was continued until the next evaluation,

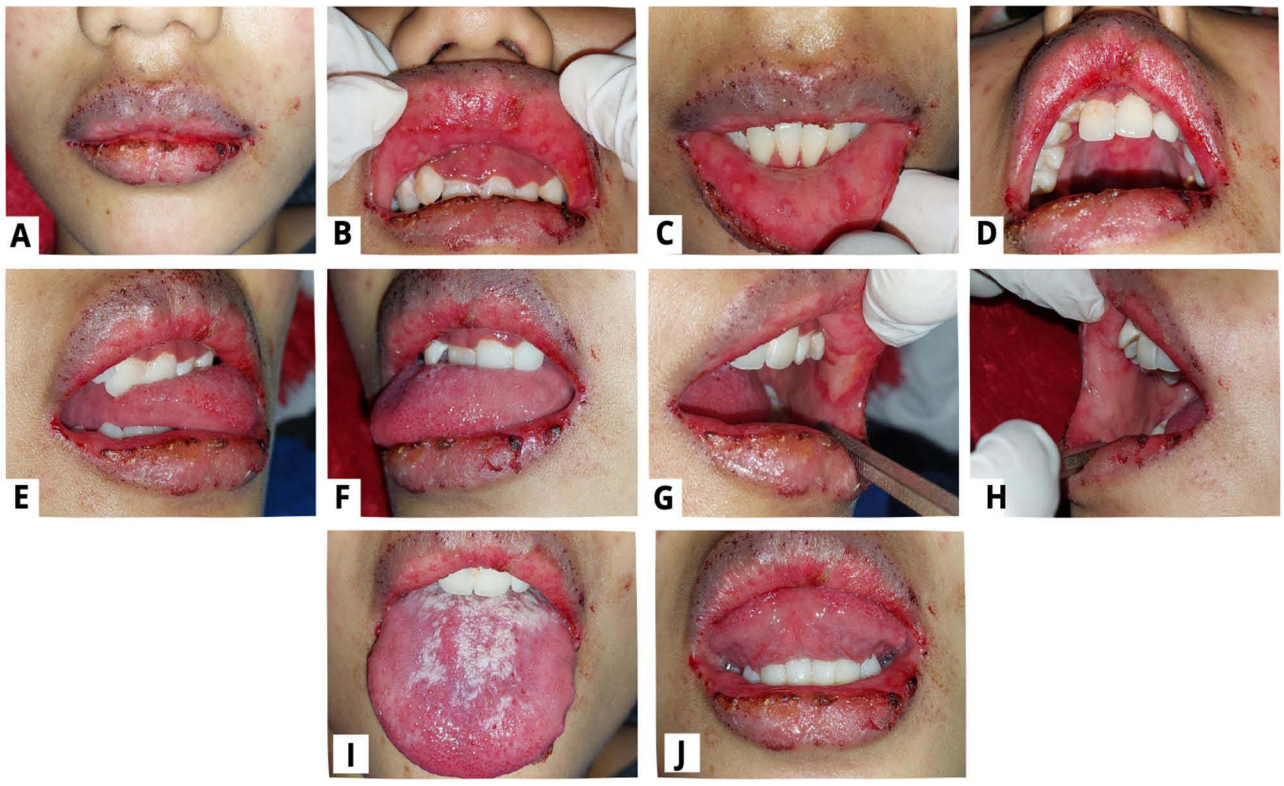

Figure 1 Haemorrhagic crusts on the lips, along with multiple ulcerations on the oral mucosa (**A–C, E-H and J**); Palatal erythema (**D**); Pseudomembranous candidiasis can be seen on the patient's tongue (**I**).

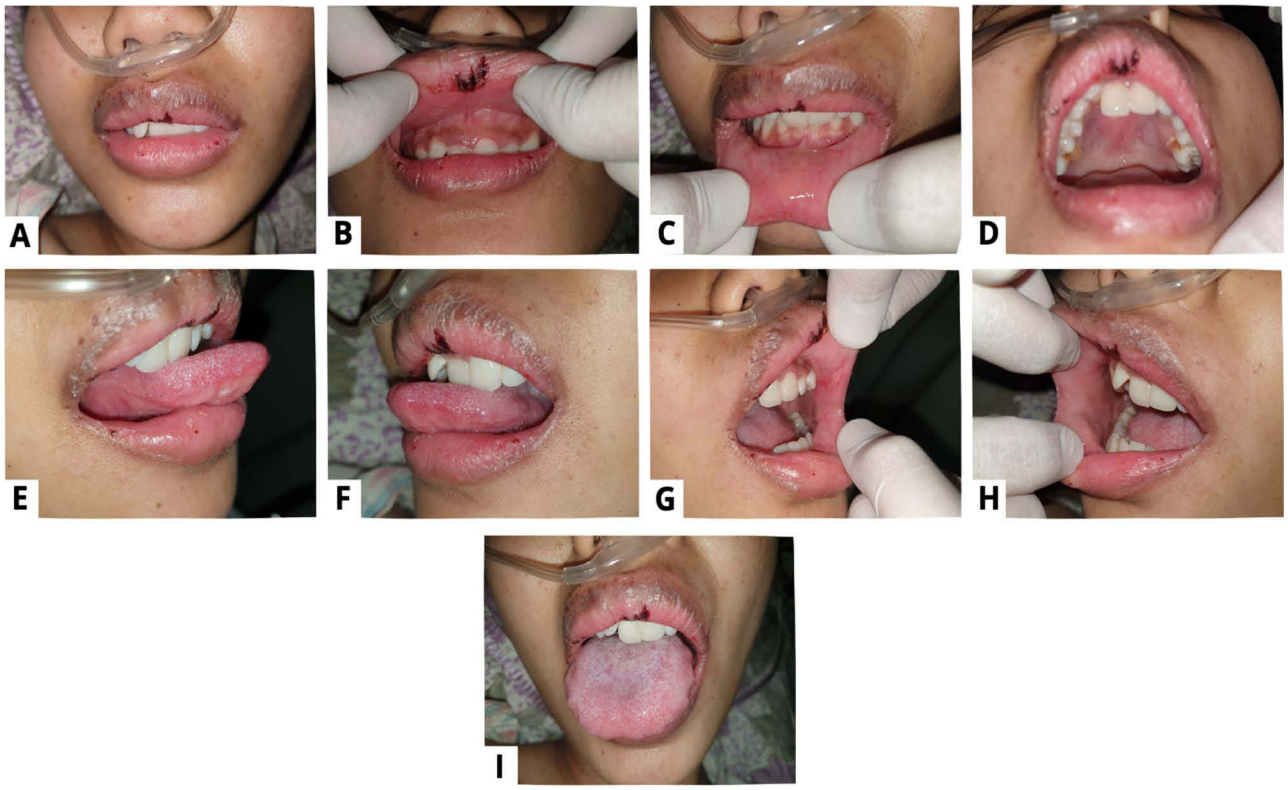

Figure 2 Overall improvements in the patient's oral condition on the second visit (**A**–**I**).

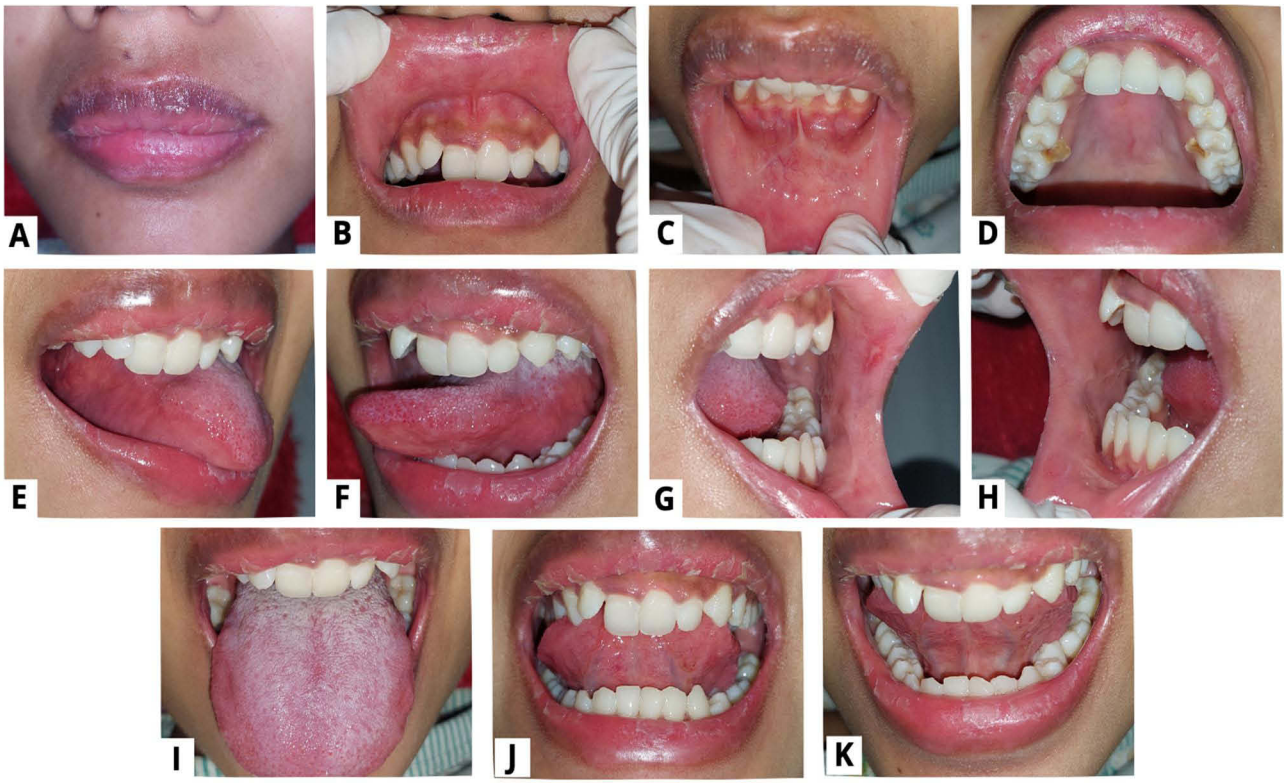

Figure 3 Improvement of the oral lesion on the 10th day (**A**–**K**).

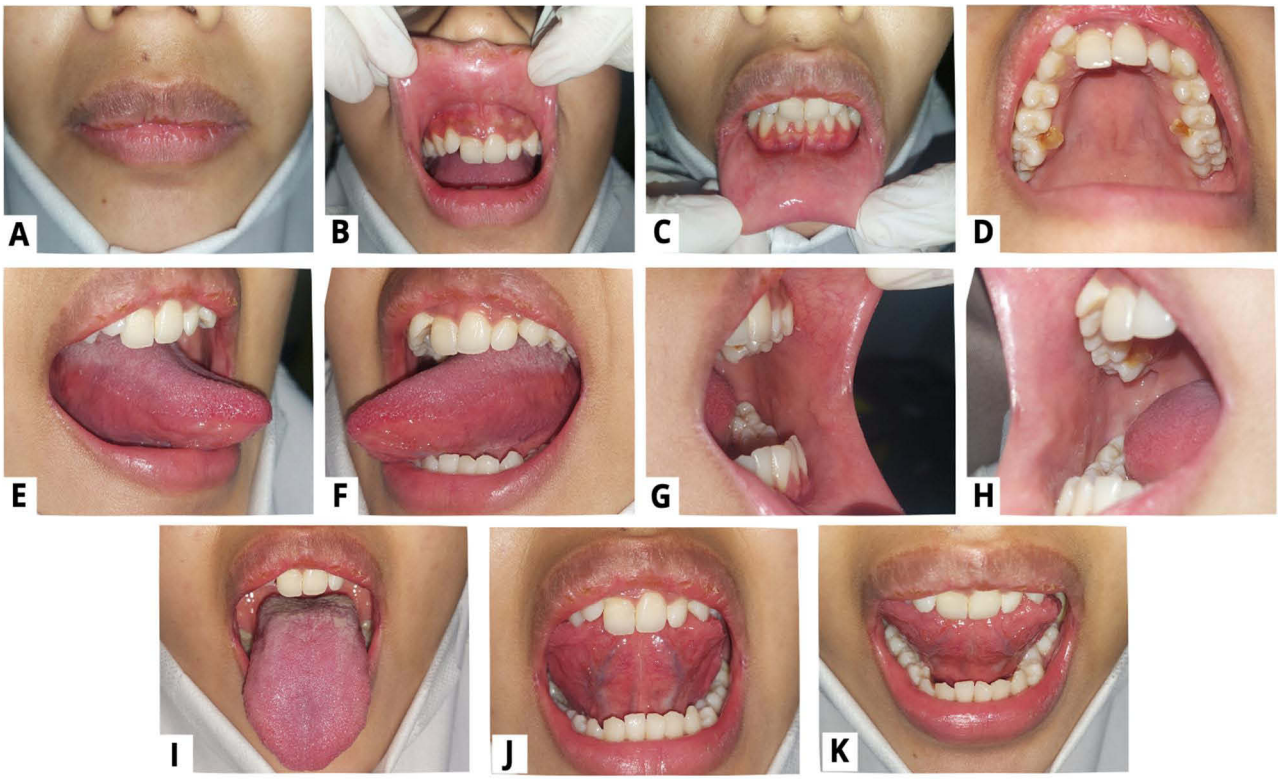

Figure 4 Patient has no complaints in the oral cavity (**A**–**K**).

for the next 6 days. On 28 November 2022, the patient had no complaints about his oral cavity, but clinically there was still a presence of exfoliative cheilitis, coated tongue and ulcer in the left buccal mucosa, which had subsided. (Figure 3)

The patient was discharged 2 days later and continued outpatient care. The last visit was conducted on 16 December 2022. The patient had no complaints, could follow oral hygiene instructions and gave advice to the patient to extract radix of deciduous teeth 55 and 65. (Figure 4)

Discussion

Systemic Lupus Erythematosus is an autoimmune disease that has heterogeneous clinical characteristics, coupled with unclear knowledge of its etiology and prevalence, making it a complicating factor in diagnosis and treatment plans.[13] Complex interactions between impaired or incomplete apoptosis, dysregulation of the innate and adaptive immune systems, complement activation, immune complexes, and tissue inflammation lead to sustained autoimmune processes. These conditions result in chronic inflammation that affects almost all organs and tissues in the body.[14,15] In this case, the patient had already been diagnosed with SLE, so our Department focused on treating the patient's oral lesions, and the subsequent systemic condition was handled by the Pediatrics Department.

Lesions were seen on almost every surface of the patient's oral mucosa during the intraoral clinical examination (lips, upper and lower labial mucosa, right and left buccal mucosa, tongue dorsum, palate). Du et al, conclude that oral mucosal lesion such as chelitis or lupus cheilitis, central erythema on palatal area, and candidiasis are several lesions that are strongly associated with SLE,[16] which also can be seen in this case. Oral manifestations are one of the criteria in ACR used to establish the diagnosis.[17] Khatibi et al, stated that oral lesions found in patients are estimated at 7–52%.[18] Mucocutaneous manifestations are estimated at 70–75% in the juvenile-onset systemic lupus erythematous population.[19] According to the ACR criteria, the terminology for oral ulceration is "ulceration of the oral or nasopharynx, which is painless and found by the clinician".[20] Pongsawat et al stated that this condition is usually more common in JSLE than in adults, and indicates that the disease is in an active state.[20,21]

According to Charras et al, juvenile SLE (under 18 years of age) has more aggressive symptoms, higher disease activity, and medication burden (considering the use of corticosteroid drugs). More severe manifestations and organ damage have also been reported, including an increased incidence of renal, cardiovascular and neuropsychiatric involvement.[22] The organ involvement in this patient was pleural effusion (occurs in 45–60% of the patients with SLE),[23] hepatosplenomegaly (incidence of 39% hepatomegaly and 6% splenomegaly),[24] and extrapulmonary TB (abdominal TB was diagnosed in this patient). A cohort study in 2022 by Hamijoyo et al, stated that there were 61 out of 113 SLE patients (44.2%) with extrapulmonary TB.[25]

Liver involvement, such as hepatomegaly in SLE, can be established by observing the level of enzyme values in the liver and looking at CT scan images (Figure 5). Elevated SGOT and SGPT results as consequences of medication toxicity, fatty liver diseases, and HBV and HCV viral infections are indicators of liver inflammation. High doses of glucocorticoids drugs are responsible for the fatty liver condition. In addition, a study by Shaik et al, stated that fatty liver in juvenile SLE can occur, even without the involvement of drug use.[26] The patient's hepatomegaly was also confirmed from the CT scan by the Radiology Department.

Splenomegaly also appears on CT scan images. Splenomegaly occurs due to vascular pressure from an inflamed liver.[27] Swollen spleen leads to the destruction of erythrocytes, and hepatomegaly itself causes a reduction in the production of iron, vitamin b12, and folic acid,[28] resulting in anemia. These conditions result in disruption of oral mucosal integrity and result in the formation of oral ulcerations.[28] Patients with chronic liver conditions are reported to have a wide variety of oral conditions, such as xerostomia, lichen planus, ulceration and erosion. The presenting complaint in this patient was ulceration.[28]

Abnormal blood counts occur in 50% of the patients with chronic diseases. The American College of Rheumatology has SLE criteria that state the presence of conditions with involvement in the hematological condition. While lymphopenia is a common condition, anemia may also occur.[29] In this case, the patient was not only anemic but also had leucopenia. Carli et al, in 2015 stated that leucopenia occurred in 22–41, 8% of the cases. It appears that this condition occurs purely due to the SLE condition without the effects of drugs that can lower leucocyte levels. However, researchers are still unable to explain specifically, why this happens.[30,31]

In order to discontinuing medications, clinicians must have the appropriate knowledge such as understanding the indications and determining which medication(s) that should be stopped within the proper sequence. Besides that, proper planning along with communicating, and coordinating with patients and other clinicians involved are another important matter. Finally, evaluating the patient for positive or negative outcomes after discontinuation.[32] When steroids are

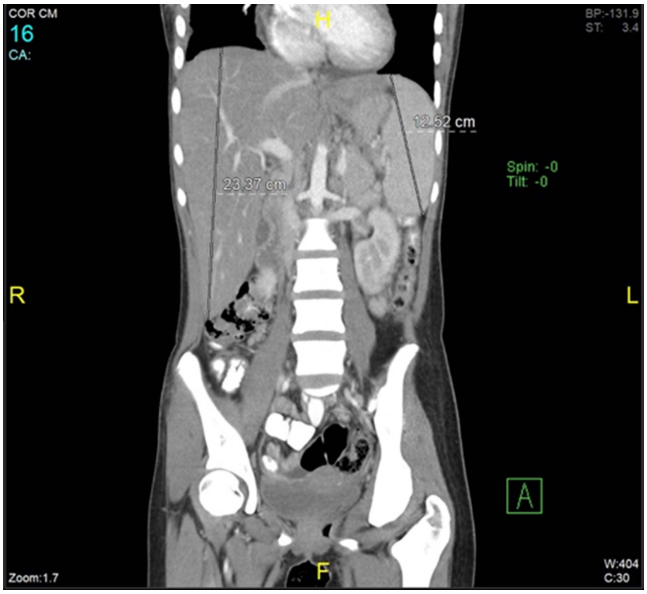

Figure 5 The hepatosplenomegaly condition can be seen on CT scan image.

administered for a few days or, at most, 2 or 3 weeks, serious adverse effects seem unlikely. Nonetheless, it is crucial to choose the lowest effective dosage and avoid prolonging treatment beyond what is required. The likelihood of adverse consequences rises with prolonged or frequent use.[33]

The first-line therapy for ulceration in the oral cavity is topical steroid.[19] Considering the patient's systemic condition and laboratory examination, it is necessary to discontinue and adjust some of the drugs taken.[32] Discontinuing the steroid-based topical medication and Nystatin® oral suspension was done immediately after observing the SGOT and SGPT values associated with hepatomegaly and clinical improvement. However, the use of physiological fluids, in this case NaCl 0.9%, was still used to improve oral hygiene, as well as maintaining moisture on the lips using petroleum jelly.[34]

The systemic condition of the patient becomes a challenge for the Oral Medicine Department in managing the patient's oral complaints. Involvement of other organs and blood pathology in patients, if left untreated, will increase patient morbidity. Adjustments in medication are based on the patient's clinical condition and the results of the supporting examination.[32] In addition, oral hygiene is also an important factor that needs to be improved in this patient, with the goal of reducing the risk of other opportunistic infections.[34] Multidisciplinary management of this patient is considered optimal, based on the clinical condition of the patient on 16 December 2022, with a good condition, no pain, and good oral hygiene and free of oral lesions. Oral hygiene is an important factor that needs to be addressed to prevent secondary infections in patients with immunocompromised condition. Symptomatic therapy allows patients to achieve optimal food intake and therefore accelerates recovery of systemic conditions.

Conclusion

Oral manifestations such as oral DLE and aphthous ulcer on the oral mucosa (such as buccal, labial, and palate) are common in juvenile SLE patients) and usually without pain. Laboratory examination and CT scans are essential in diagnosing and managing JSLE patients along with multidisciplinary management is required. Topical corticosteroids are still the first line in controlling oral inflammation; however, the drug regimen should be adjusted in juvenile SLE especially when hepatosplenomegaly is present.

Consent Statements

The patient has approved and written informed consent for the publication of this case report including the images. The institution has also approved the publication of this article.

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Disclosure

The authors report no conflicts of interest in this work.

References

1. Sebastiani GD, Prevete I, Iuliano A, Minisola G. The importance of an early diagnosis in systemic lupus erythematosus. *Isr Med Assoc J*. 2016;18(3–4):212–215.
2. Stojan G, Petri M. Epidemiology of systemic lupus erythematosus: an update. *Curr Opin Rheumatol*. 2018;30(2):144–150. doi:10.1097/BOR.0000000000000480
3. Berrsias GK, Loannidis JP, Aringer M, et al. EULAR recommendations for the management of systemic lupus erythematosus with neuropsychiatric manifestations: report of a task force of the EULAR standing committee for clinical affairs. *Ann Rheum Dis*. 2010;69(12):2074–2082. doi:10.1136/ard.2010.130476
4. Tian J, Zhang D, Yao X, Huang Y, Lu Q. Global epidemiology of systemic lupus erythematosus: a comprehensive systematic analysis and modelling study. *Epidemiol Sci*. 2023;82:351–356. doi:10.1136/ard-2022-223035
5. Perhimpunan Reumatologi Indonesia. Diagnosis dan pengelolaan lupus eritematosus sistemik. Perhimpunan Reumatologi Indonesia; 2019.
6. Pons-Estel GJ, Ugarte-Gil MF, Alarcón GS. Epidemiology of systemic lupus erythematosus. *Expert Rev Clin Immunol*. 2017;13(8):799–814. doi:10.1080/1744666X.2017.1327352
7. Setabudiawan B, Grahani R. Indonesian epidemiologic data of paediatric systemic lupus erythematosus. *Lupus*. 2017;4(suppl 1):A201.1.

8. Fanouriakis A, Tziolos N, Bertsias G, Boumpas DT. Update on the diagnosis and management of systemic lupus erythematosus. *Am Rheum Dis*. 2020;80(1):14–25. doi:10.1136/annrheumdis-2020-218272
9. Wardhani R, Sufiawati I. Oral manifestations of systemic lupus erythematous and its comprehensive management: two case reports. *Maj Kedokt Bandung*. 2018;50(1):62–68. doi:10.15395/mkb.v50n1.1234
10. Kudsi M, Nahas LD, Alsawah R, Hamsho A, Omar A. The prevalence of oral mucosal lesions and related factors in systemic lupus erythematosus patients. *Arthritis Res Ther*. 2021;23(229). doi:10.1186/s13075-021-02614-8
11. Nico M, Romiti R, Lourenço S. Oral lesions in four cases of subacute cutaneous lupus erythematosus. *Acta Derm Venereol*. 2011;91(4):436–439. doi:10.2340/00015555-1103
12. Kuhn A, Bonsmann G, Anders H-J, Herzer P, Tenbrock K, Schneider M. The diagnosis and treatment of systemic lupus erythematosus. *Dtsch Arztebl Int*. 2015;112(25):423–432. doi:10.3238/arztebl.2015.0423
13. Narváez J. Lupus eritematoso sistémico 2020. *Med Clin*. 2020;155(11):494–501. doi:10.1016/j.medcli.2020.05.009
14. Fava A, Petri M. Systemic lupus erythematosus: diagnosis and clinical management. *J Autoimmun*. 2019;96:1–3. doi:10.1016/j.jaut.2018.11.001
15. Kang S, Amagai M, Bruckner AL, et al. *Fitzpatrick's Dermatology*. Mc Graw Hill; 2019.
16. Du F, Qian W, Zhang Z, Zhang L, Shang J. Prevalence of oral mucosal lesions in patients with systemic lupus erythematosus: a systematic review and meta-analysis. *BMC Oral Health*. 2023;23(1030):1–10. doi:10.1186/s12903-023-03783-5
17. Aringer M, Costenbader KH, Daikh DI, et al. European league against rheumatism/American college of rheumatology classification criteria for systemic lupus erythematosus. *Arthritis Rheumatol*. 2019;71(9):1400–1412. doi:10.1002/art.40930
18. Khatibi M, Shakoorpour AH, Jahromi ZM, Ahmadzadeh A. The prevalence of oral mucosal lesions and related factors in 188 patients with systemic lupus erythematosus. *Lupus*. 2012;21(12):1312–1315. doi:10.1177/0961203312454589
19. Chiewchengchol D, Murphy R, Edwards SW, Beresford MW. Mucocutaneous manifestations in juvenile-onset systemic lupus erythematosus: a review of literature. *Pediatr Rheumatol Online J*. 2015;13(1):1. doi:10.1186/1546-0096-13-1
20. Rodsaward P, Prueksrisakul T, Deekajorndech T, Edwards SW, Beresford MW, Chiewchengchol D. Oral ulcers in juvenile onset systemic lupus erythematosus a review of the literature. *Am J Clin Dermatol*. 2017;18(6):755–762. doi:10.1007/s40257-017-0286-9
21. Kristina E, Sufiawati I. Oral lesions as a clinical sign of systemic lupus erythematosus. *Dent J*. 2018;51(3):147–152. doi:10.20473/j.djmkg.v51.i3.p147-152
22. Charras A, Smith A, Hendich CM. Systemic lupus erythematosus in children and young people. *Curr Rheumatol Rep*. 2021;23(20):15. doi:10.1007/s11926-021-00985-0
23. Kim S, Park HB, Cho YK, Yi S. Refractory pleural effusion in systemic lupus erythematosus treated by pleurectomy. *J Rheum Dis*. 2017;24(1):43–48. doi:10.4078/jrd.2017.24.1.43
24. Vaisllant AA, Goyal A, Varacallo M. Systemic lupus erythematosus.In *StatPearls*. StatPearls Publishing;2023. Available from: https://www.ncbi.nlm.nih.gov/books/NBK535405/. Accessed July 18, 2024.
25. Hamijoyo L, Sahiratmadja E, Ghassani NG, et al. Tuberculosis among patients with systemic lupus erythematosus in Indonesia: a cohort study. *Open Forum Infect Dis*. 2022;9(7). doi:10.1093/ofid/ofac201
26. Imran S, Thabah MM, Azharudeen M, Ramesh A, Bobby Z, Negi VS. Liver abnormalities in systemic lupus erythematosus: a prospective observational study. *Cureus*. 2021;13(6). doi:10.7759/cureus.15691
27. Chapman J, Goyal A, Azevedo AM. Splenomegaly. *StatPearls*. StatPearls Publishing;2023. Available from: https://www.ncbi.nlm.nih.gov/books/NBK430907/. Accessed July 18, 2024.
28. Aberg F, Helenius-Hietala J. Oral health and liver disease: bidirectional associations—A narrative review. *Dent J*. 2022;10(2):16. doi:10.3390/dj10020016
29. Giannouli S, Voulgarelis M, Ziakas PD, Tzioufas AG. Anaemia in systemic lupus erythematosus: from pathophysiology to clinical assessment. *Ann Rheum Dis*. 2006;65(2):144–148. doi:10.1136/ard.2005.041673
30. Fayyaz A, Igoe A, Kurien BT, et al. Haematological manifestations of lupus. *Lupus Sci Med*. 2015;2(1):e000078. doi:10.1136/lupus-2014-000078
31. Linda C, Chiara T, Sabrina V, Viola S, Mosca M. Leukopenia, lymphopenia, and neutropenia in systemic lupus erythematosus: prevalence and clinical impact—A systematic literature review. *Semin Arthritis Rheum*. 2015;45(2):190–194. doi:10.1016/j.semarthrit.2015.05.009
32. Bain KT, Holmes HM, Beers MH, Maio V, Handler SM, Pauker SG. Discontinuing medications: a novel approach for revising the prescribing stage of the medication-use process. *J Am Geriatr Soc*. 2008;56(10):1946–1952. doi:10.1111/j.1532-5415.2008.01916.x
33. Institute for Quality and Effeciency in Health Care. Using steroids correctly and avoiding side effects. National Library of Medicine; 2018. Available from: https://www.ncbi.nlm.nih.gov/books/NBK563106/#:~:text=Serioussideeffectsarebelievedtheriskofsideeffects. Accessed November 3, 2023.
34. Agustina N. Oral hygiene menggunakan NaCl 0.9%. KEMENKES RI; 2022. Available from: https://yankes.kemkes.go.id/view_artikel/592/oral-hygiene-menggunakannacl-09. Accessed July 18, 2024.