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CASE REPORT

Hepatitis-like onset of systemic lupus erythematosus in a 9-year-old female patient

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ABSTRACT

Systemic lupus erythematosus (SLE) is a multisystem autoimmune disease the etiology and pathomechanism of which remain unclear. This case report presents the diagnostic difficulties caused by the atypical manifestation of SLE in a nine-year-old girl. The finding of an isolated increase in liver enzymes initiated the differential diagnosis of liver disease. The occurrence of additional symptoms in the following months, such as recurrent episodes of urticaria, followed by joint pains, formed the basis for further search for the cause of the presenting complaints. Finally, a diagnosis of SLE was established on the basis of clinical symptoms and laboratory results, including the detection of a lupus anticoagulant. The treatment was initiated with good outcome. This case illustrates how diverse and atypical clinical manifestations with uncharacteristic laboratory results SLE can present with, which can cause diagnostic difficulties and contribute to delays in making a correct diagnosis and starting effective treatment.

KEY WORDS:

systemic lupus erythematosus, autoimmune hepatitis, liver enzyme elevation.

INTRODUCTION

Systemic lupus erythematosus (SLE) is a multisystem autoimmune disease. Despite intensive research, fully understood etiology and pathomechanism remain unknown. The disease is characterized by a variable course with periods of exacerbations and remissions, involving multiple organs and systems. Systemic lupus erythematosus is characterized by a high expression of autoantibodies. Due to the potential involvement of many tissues and organs, the clinical presentation can be highly diverse, ambiguous and individualized, posing a diagnostic challenge.

The total prevalence of SLE is estimated at 40–50 out of 100 000 cases and 10–15% of all cases occur in childhood. The frequency of onset increases with age and is peaking between 16 and 55 years of age. Women are affected 6–10 times more frequently than men. The characteristic predisposition to SLE in females is less pronounced in the first decade of life [1–3]. Unlike adults, children often have a more aggressive form of SLE from the onset, with a significantly higher risk of active lupus nephritis and experiencing more organ damage. In spite of that, often making the definitive diagnosis in children is difficult and prolonged due to a considerable diversity of symptoms [4, 5].

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The aim of this report is to present an atypical case of juvenile SLE with a severe course and very uncharacteristic initial symptoms manifested mainly by fluctuations in liver test activity. The patient we present is an excellent example of the variety of symptoms and diagnostic challenges associated with this disease.

CASE REPORT

In a healthy female patient, at the age of 9 years, during routine primary care evaluation, isolated elevated liver aspartate aminotransferase (AST) and alanine aminotransferase (ALT) activities were found, in the absence of any other biochemical abnormalities, including other liver function tests. Serum protein and albumin concentrations, indicators of the coagulation system (prothrombin time – PT, and activated partial thromboplastin time – APTT), C-reactive protein (CRP) and complete blood counts were normal. The patient was in good general condition, active according to her age, and her family history of chronic diseases was unremarkable. She was referred to the Infectious Diseases Outpatient Clinic, where viral infections caused by: cytomegalovirus (CMV), Epstein-Barr virus (EBV), hepatitis A, B and C viruses (HAV, HBV and HCV) were ruled out. Serological tests for toxocariasis and toxoplasmosis were negative. Stool examination did not reveal the presence of parasite eggs or cysts and both *Helicobacter pylori* and *Giardia lamblia* antigens in stool were negative. A thyroid dysfunction as well as α-1 antitrypsin deficiency, cystic fibrosis, coeliac and Wilson's disease were excluded. The abdominal ultrasound evaluation was normal. Phospholipids and timonacic were initiated as a symptomatic and hepatoprotective treatment.

Variable, moderately increased AST and ALT activities, not exceeding 10 times the upper normal limit, were observed over the following year and a half until the age of 11 years. At that time, the laboratory tests revealed a significant increase in ALT (334 U/I [N: 10–35 U/l]) and AST (208 U/I [N: 10–60 U/l]) activity. The patient also started to report occasional sensations of weakness and fatigue, bone and migrating joint pain of mild intensity. She also had a brief, uncharacteristic episode of cheek erythema. Infections caused by primary and secondary hepatotropic viruses were excluded again. Serological tests revealed presence of SARS-CoV-2 antibodies and low positive (1 : 320) antinuclear antibodies (ANA) with negative: anti-mitochondrial antibody (AMA), anti-smooth muscle antibodies, liver-kidney microsomal antibody, soluble liver/liver-pancreas antibodies. Total IgG concentration (20.4 g/l [N: 6.38–17.00 g/l]) and IgG4 subset were slightly elevated (2.66 g/l [N: 0.012–1.699 g/l]). A suspicion of autoimmune hepatitis (AIH) was raised and the patient was referred to the Department of Pediatrics, Gastroenterology and Nutrition. However, the result of liver biopsy did not support diagnosis of AIH, revealing only minimal inflammatory-necrotic changes in small groups of hepatocytes with accompanying mononuclear inflammatory infiltrates and a minimal collagen fiber proliferation around central veins. Also, liver elastography and magnetic resonance cholangiopancreatography did not show any abnormalities. Regularly controlled liver function tests showed fluctuation with occasional tendency to decrease, but never reaching the normal range (Figure 1). After the next four months, during the summer holidays, the patient developed the first episode of urticaria, followed by periodic further episodes affecting different areas of the body, with variable severity pruritus, but without angioedema (Figure 2). The patient was consulted by an allergologist; *Mycoplasma pneumoniae*, EBV and SARS-CoV-2 infection were excluded. The urticaria activity score 7 was 18 points (mainly due to the present urticaria and slight itching). The family history confirmed sun allergy reaction in the patient's mother. Finally idiopathic urticaria was diagnosed followed by treatment with a double dose of type 1 antihistamine drugs.

Due to recurrent episodes of urticaria, increasing frequency of reported osteoarticular pain and a rising tendency to bruise, the diagnostics for immunological and coagulation disorders has been expanded. Von Willebrand factor deficiency was ruled out and vitamin K was included in the treatment due to prolonged prothrombin time. Subsequent serological tests revealed positive ANA with positive line HEp-2 antibodies and dsDNA-NCX (210.09 IU/ml [N: < 100 IU/ml]), borderline AMA-M2, and decreased values of C-3c (0.8 g/l [N: 0.9–1.8 g/l]) and C-4 (0.0 g/l [N: 0.1–0.4 g/l]) complement component. Lupus anticoagulant (LAC) and rheumatoid factor (RF) were obtained, but before the results became available, the patient had to be admitted to the hospital due to the appearance of concurrent non-traumatic massive soft tissue hemorrhage of the right cheek, hard and soft palate, numerous small hemorrhages of the skin of the lower extremities (Figure 3). She also reported breathing difficulties, right hypogastric pain and a soft tissue inflammation of the left ulnar fossa at the site of the venipuncture, which took place on the previous day. In the following days, pain symptoms in the large joints of the shoulder girdle and upper limbs with restricted mobility arose. Laboratory tests revealed: prolonged PT (16.5 sec [N: 10.4–13 sec]) and APTT (40.5 sec [N: 25.9–36.6 sec]), with normal activity of the other blood clotting factors (V, VII, VIII, IX, XI, XII). In addition, biochemical tests have shown a markedly elevated erythrocyte sedimentation rate (ESR) (51 mm [N: 5–10 mm]) with negative CRP [N: < 10]. Concurrently, there has been a full normalization of activity of AST and ALT. At this time antibodies against HSV were present in IgM and IgG classes without clinical symptoms of infection. A smear of the upper respiratory tract showed presence of HCOV-NL63 antigen. Lung ultrasound revealed anechoic fluid in the right pleural cavity extending to the lower edge of the scapula in the sitting position. Peripheral vascular Doppler ex-

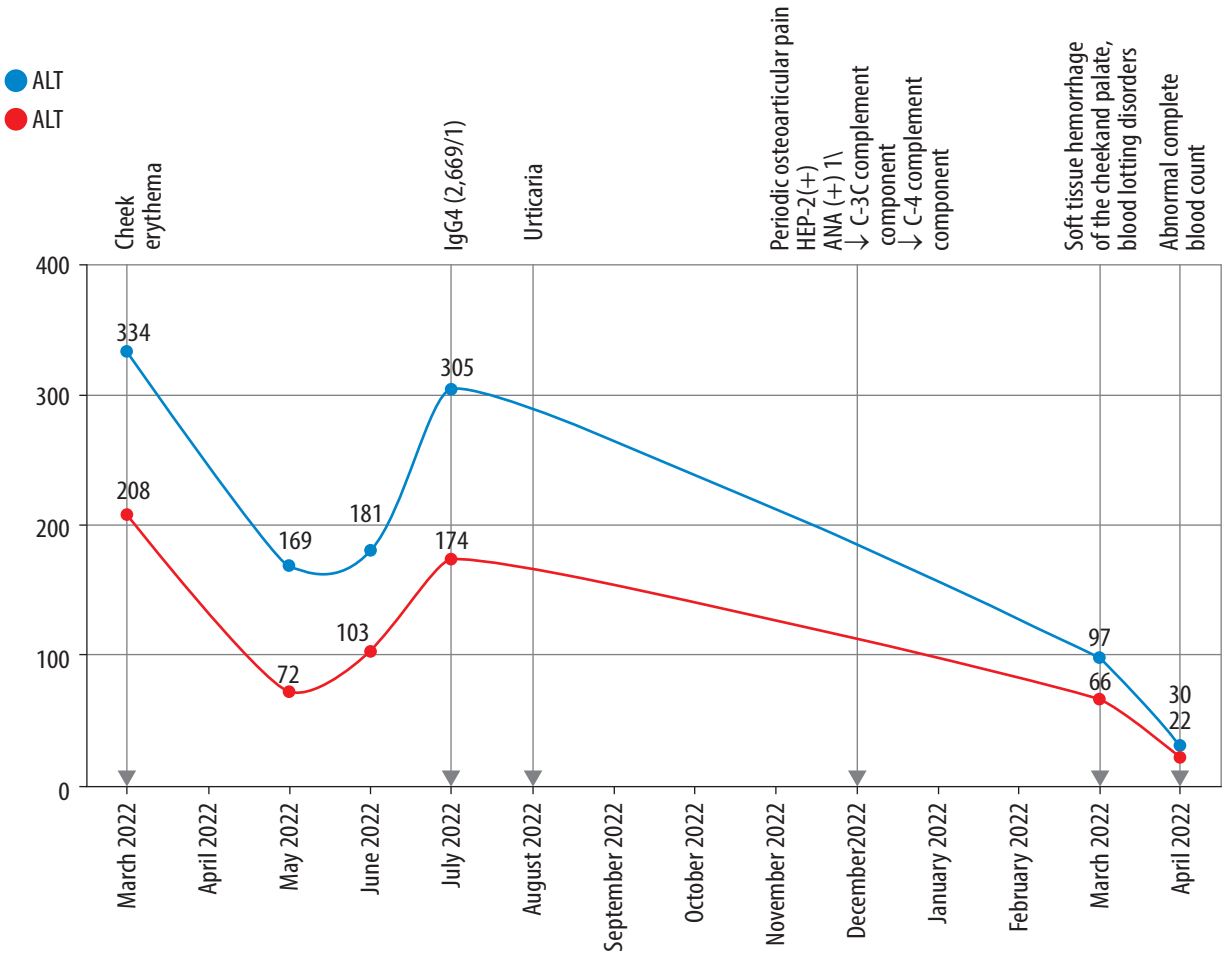


FIGURE 1. Fluctuation of liver enzyme levels and onset of symptoms of the patient (own elaboration)

amination excluded thrombosis. The results of previously sampled tests showed high LAC (LA1 140.6 s [N: 31–44], LA2 48.1 s [N: 30–38], LA1/LA2 2.92 [N: 0.8–1.2]), positive ANA (1 : 5000) [N: < 1 : 100], slightly elevated IgG (20.10 g/l) with normal IgA and IgM levels, significantly elevated IgG4 levels (11.05 g/l), decreased complement components, C1 inhibitor levels at the lower limit of normal (0.2 g/l [N: 0.18–0.32]), elevated IL-6 values of 15.79 pg/ml [N: < 7.0 pg/ml]. A suspicion of systemic disease was raised and the patient was transferred to the Department of Rheumatology for further evaluation and treatment. Based on the clinical picture, results of laboratory tests and very high systemic lupus erythematosus disease activity index (SLEDAI) score [6] of 22 points, juvenile SLE was diagnosed. Consequently, the intravenous infusion of methylprednisolone at a dose of 10 mg/kg b.w. for 5 days was introduced in the treatment, followed by continued treatment with an oral preparation at a dose of 2 mg/kg b.w., monitoring the patient's condition, levels of complement system components and coagulation parameters (APTT, LAC) successively decreasing the dose. Mycophenolate mofetil, hydroxychloroquine and salicylic acid in an anticoagulant dose were added. The treatment resulted in an improvement of the general condition (well-being, pain), regression of pleural fluid, slow regression of vascular lesions (hemorrhages, subluxations). The patient remains in continuous outpatient care in the outpatient setting, normalization of tests has been achieved (complement components, LAC, reduction of autoantibodies levels). Positive cardiolipin and anti-β-2 glycoprotein IgG antibodies persist

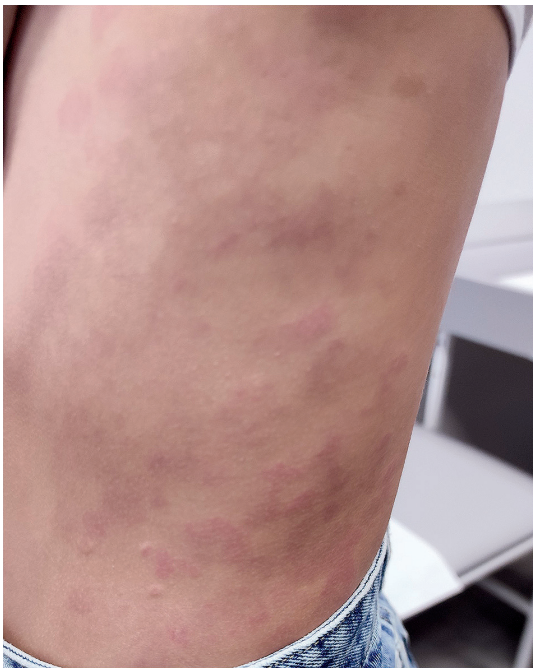
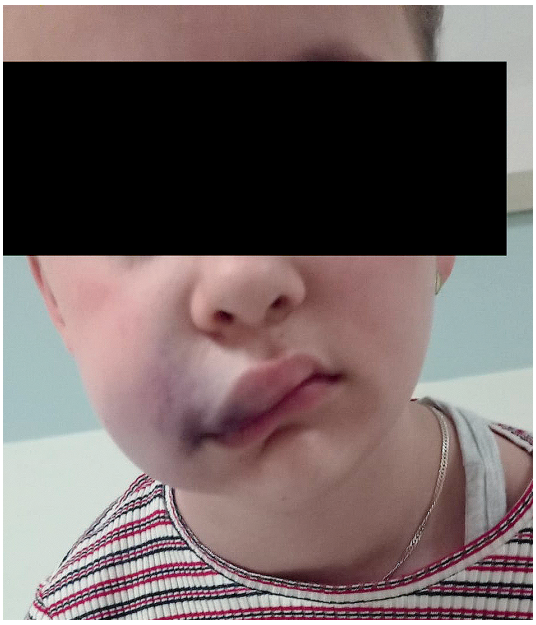


FIGURE 2. Skin lesions of the nature/characteristic of urticaria on the trunk



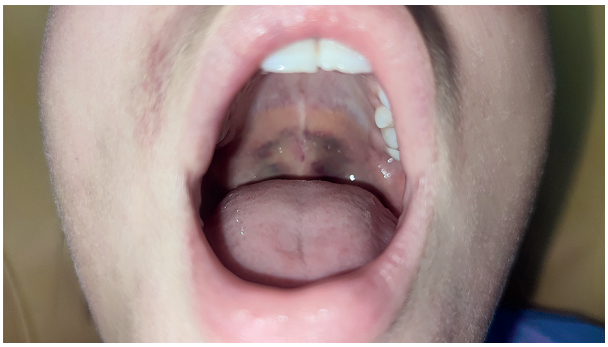


FIGURE 3. Massive soft tissue hemorrhage of the right cheek, hard and soft palate

TABLE 1. Characteristics of systemic lupus erythematosus forms [3, 7]

Form of SLE	Characteristics
Cutaneous	a. Acute type: photosensitisation, butterfly-shaped facial erythema, full-body erythema, bullous rash b. Subacute type: **annular erythema**, psoriasis-like, does not leave scars c. Chronic type: discoid lupus erythematous Some unspecific skin symptoms of SLE: urticaria, Raynaud's symptom, hand erythema, periungual erythema, non-painful ulcerations of mouth and nasal mucosa, teleangiectasia of nail walls, subungual petechiae, livedo reticularis
Renal	Glomerulonephritis, nephrotic syndrome, renal tubular acidosis
Haematological	Lymphadenopathy, splenomegaly, hepatomegaly, symptoms of thrombocytopenia, anemia. Macrophage activtion syndrome may occur
With changes in the circulatory system	Symptoms of hypertension, heart failure, myocarditis, endocarditis, coronary artery disease, arteriosclerosis. Pericarditis, tachycardia, heart murmurs and precordial pain may occur
Neuropsychiatric	Transient ischemic attack, stroke, headache, behavioral changes, depression
With changes in the musculoskeletal system	Arthritis (often painful), muscle pains, osteopenia
With changes in respiratory system	**Pleural effusion**, alveolar bleeding, pulmonary hypertension
With changes in alimentary system	**Abdominal pain,** nausea, vomitus, which may coexist with SLE-related exudative peritonitis, pancreatitis or **hepatitis**

SLE – systemic lupus erythematosus
Symptoms present in the patient are highlighted.

(no thrombotic incidents were observed). The patient remains on a maintenance dose of methylprednisolone of 2 mg daily. She continues the remaining medications with good tolerance. She has returned to school activities, feels well, reports no complaints and is physically active.

DISCUSSION

Systemic lupus erythematous is an autoimmune disease characterized by an unpredictable, varying course and uncertain prognosis. Childhood-onset SLE appears on average between 11 and 12 years of age and represents around 10–20% of all SLE cases. Systemic lupus erythematosus presents either in a multisystemic form or affects just one or few organs. Due to this fact it may pose a significant issue when it comes to its diagnosis. General symptoms that are presented in patients with SLE are fatigue, weakness, headache, decrease of body mass, hair loss, subfebrile states and nose bleeds. Systemic lupus erythematosus may appear in various forms which are summarized in Table 1.

In order to make a diagnosis, serological criteria must be met, as well as one should exclude other potential causes of unspecific symptoms. Highly specific anti-

TABLE 2. Classification criteria for systemic lupus erythematosus [8]

Entry criterion Antinuclear antibodies at a titer of ≥ 1 : 80 on HEp-2 cells or an equivalent positive test (ever)			
Present-apply additive criteria		**Absent-do not classify as SLE**	
Additive criteria*			
Clinical domains and criteria	**Weight**	**Immunology domains and criteria**	**Weight**
Constitutional		Antiphospholipid antibodies	
Fever	2	Anti-cardiolipin antibodies or Anti-β2GP1 antibodies or Lupus anticoagulant	2
Hematologic		Complement proteins	
Leukopenia	3	Low C3 or low C4	3
Thrombocytopenia	4	Low C3 and low C4	4
Autoimmune hemolysis	4		
Neuropsychiatric		SLE-specific antibodies	
Delirium	2	Anti-dsDNA antibody** or	
Psychosis	3	Anti-Smith antibody	6
Seizure	5		
Mucocutaneous			
Non-scarring alopecia	2		
Oral ulcers	2		
Subacute cutaneous or discoid lupus	4		
Acute cutaneous lupus	6		
Serosal			
Pleural or pericardial effusion	5		
Acute pericarditis	6		
Musculoskeletal			
Joint involvement	6		
Renal			
Proteinuria > 0.5 g/24 h	4		
Renal biopsy class II or V lupus	8		
nephritis			
Renal biopsy class II or V lupus	10		
nephritis			

Anti-β2GPI – anti-β2-glycoprotein I, anti-dsDNA – anti-double-stranded DNA, SLE – systemic lupus erythematosus
** Do not count a criterion if there is a more likely explanation than SLE.*
Occurrence of a criterion on at least one occasion is sufficient.
SLE classification requires at least one clinical criterion and ≥ 10 points.
Criteria need not occur simultaneously.
Within each domain, only the highest weighted criterion is counted toward the total score (additional criteria within the same domain will not be counted).
*** In an assay with 90% specificity against relevant disease controls.*

bodies for SLE are ANA type anti-Sm and anti-dsDNA. Other coexistent antibodies might be ANCA, anti-SS-A, anti-SSB, anti-RNP, anti-RibP, anti-Ku, anti-PCNA, anti-histone and antiphospholipid. In presence of the elevated titer of ANA, the additional criteria must be fulfilled for SLE diagnosis (Table 2) [8].

Clinically significant score for SLE activity assessment is SLEDAI [6]. Among comorbidities of SLE may be antiphospholipid syndrome and recurrent infections including common viral and bacterial with typical or atypical presentation and opportunistic infections. Infections among patients with SLE are a major source of morbidity, mortality, hospitalization and death [9].

Full remission of the disease is defined as no symptoms with no steroid or immunosuppressant use and is very rare. Low disease activity means achieving ≤ 3 points in SLEDAI [8] with the use of antimalarial drugs or ≤ 4 points with ≤ 7.5 mg of prednisolone use and good tolerance of immunosuppressants [3, 10].

The aim of SLE treatment is achieving, as far as possible, full remission or low activity of the disease and preventing its relapse. Treatment needs to be adjusted in

order to minimize organ injury, prevent adverse effects and improve quality of patients' life. It is recommended to constantly monitor the disease course as well as antiphospholipid antibody levels, infections and cardiovascular diseases [10, 11].

Pharmacotherapy used in SLE treatment includes antimalarial drugs, corticosteroids, immunosuppressants (such as methotrexate, azathioprine, mycophenolate mofetil) and biological drugs.

CONCLUSIONS

The patient's symptoms initially pointed to the diagnosis towards hepatological diseases. The changing constellation of symptoms over time prompted a continuous search for the cause of the abnormality, which eventually led to a correct diagnosis.

Infectious, gastroenterological, allergological, hematological, immunological and rheumatological reasons were considered in the differential diagnosis, indicating the difficulty in diagnosing this complex disease. Therefore, in case of non-specific symptoms that do not point to a clear diagnosis, it is worth considering SLE [9, 12–14].

DISCLOSURES

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2. Assistance with the article: None.
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4. Conflicts of interest: None.

REFERENCES

1. Filipowicz-Sosnowska A, Zimmermann-Górska I, Hruby Z, et al. Choroby układowe tkanki łącznej. In: Interna Szczeklika 2023. Gajewski P (ed.), Medycyna Praktyczna, Kraków 2023, 2065-2142.
2. Gietka P. Toczeń rumieniowaty układowy. In: Pediatria II. Kawalec W, Grenda R, Kulus M (eds.). T. 2. Wydawnictwo Medyczne PZWL, Warszawa 2018, 1046-1052.
3. Kania U. Układowy toczeń rumieniowaty. In: Pediatria, Pietrzyk JJ, Kwinta P (eds.). T. 3. Wydawnictwo Uniwersytetu Jagiellońskiego, Kraków 2018, 355-361.
4. Weller-Heinemann F. Toczeń rumieniowaty układowy (SLE). In: Poradnik kliniczny pediatria. Claßen M, Sommerburg O. Wyd. 2. Forum Media, Poznań 2021, 608-610.
5. Tian J, Zhang D, Yao X, et al . Global epidemiology of systemic lupus erythematosus: a comprehenswive systematic analysis and modelling study. Ann Rheuma Dis 2023; 82: 351-356.
6. Available from: https://www.researchgate.net/figure/Systemic-lupus-erythematosus-disease-activity-index-SLEDAI_tbl1_7485133.
7. Fanouriakis A, Tziolos N, Bertsias G, et al. Update on the diagnosis and management of systemic lupus erythematosus. Ann Rheum Dis 2021; 80: 14-25.
8. Aringer M, Costenbader K, Daikh D, et al. 2019 European League Against Rheumatism/American College of Rheumatology Classification Criteria for systemic lupus erythematosus. Arthritis Rheumatol 2019; 71: 1400-1412.
9. Singh BK, Singh S. Systemic lupus erythematosus and infections. Reumatismo 2020; 72: 154-169.
10. Fanouriakis A, Kostopoulou M, Alunno A, et al. 2019 update of the EULAR recommendations for the management of systemic lupus erythematosus. Ann Rheum Dis 2019; 78: 736-745.
11. Trindade VC, Carneiro-Sampaio M, Bonfa E, et al. An update on the management of childhood-onset systemic lupus erythematosus. Paediatr Drugs 2021; 23: 331-347.
12. Zhang L, Yin L, Lv W, et al. Clinical analysis of patients with systemic lupus erythematosus complicated with liver failure. Clin Rheumatol 2023; 42: 1545-1553.
13. Utama AA, Kisworini P, Raihan R. Liver involvement during flare-ups in pediatric SLE: lupus hepatitis vs. other causes. Indonesian J Case Rep 2023; 1: 5-9.
14. Tahernia L, Alimadadi H, Tahghighi F, et al. Frequency and type of hepatic and gastrointestinal involvement in juvenile systemic lupus erythematosus. Autoimmune Dis 2017; 2017: 8097273.