DOI 10.26724/2079-8334-2025-1-91-253-258
UDC 616.5-002.52-071

V.V. Talash
Poltava State Medical University, Poltava

PROBLEMS OF SYSTEMIC LUPUS ERYTHEMATOSUS DIAGNOSTICS

e-mail: viktorya.talash@gmail.com

Systemic lupus erythematosus is a chronic systemic connective tissue disease of unknown etiology, which is often accompanied by multiorgan involvement with the development of complications. Given the heterogeneity of the clinical picture, the high probability of developing serological abnormalities, establishing the diagnosis is a multidisciplinary problem. The low rates of morbidity and prevalence of this disease in Ukraine, compared to the global rates, indicate insufficient and untimely detection of systemic lupus erythematosus in patients. The purpose of the study was to analyze information on the features of systemic lupus erythematosus diagnosis, diagnostic criteria to develop further prospects for developing an algorithm for its diagnosis. On the basis of literary data, the article presents modern concepts of etiology and pathogenesis, clinical manifestations of systemic lupus erythematosus, highlights the main difficulties in diagnosis. The article presents a brief analysis of systemic lupus erythematosus study history, an overview of modern possibilities of its laboratory diagnosis, and clinical criteria for establishing a diagnosis, which will allow doctors to establish a timely diagnosis and prescribe adequate therapy, thereby improving the detection rates of systemic lupus erythematosus and increasing the quality and life expectancy of patients.

Key words: systemic lupus erythematosus, juvenile systemic lupus erythematosus, lupus nephritis, antinuclear antibodies, antibodies to double-stranded DNA, nephrobiopsy.

В.В. Талаш

ПРОБЛЕМИ ДІАГНОСТИКИ СИСТЕМНОГО ЧЕРВОНОГО ВОВЧАКА

Системний червоний вовчак – хронічне системне захворювання сполучної тканини достеменно невідомої етіології, яке часто супроводжується поліорганними ураженнями з розвитком ускладнень. Ураховуючи гетерогенність клінічної картини, велику ймовірність розвитку серологічних аномалій встановлення діагнозу становить мультидисциплінарну проблему. Низькі показники захворюваності та поширеності цієї недуги в Україні, порівняно з світовими, вказують на недостатнє і несвоєчасне виявлення системного червоного вовчака у хворих. Метою даної роботи було проаналізувати відомості щодо особливостей діагностики системного червоного вовчака, критерії встановлення діагнозу для напрацювання подальших перспектив розробки алгоритму його діагностики. На підставі літературних даних у статті наведені сучасні уявлення щодо етіології та патогенезу, клінічних проявів системного червоного вовчака, висвітлені основні труднощі в діагностиці. Представлений в статті короткий аналіз історії вивчення системного червоного вовчака, огляд сучасних можливостей його лабораторної діагностики, клінічних критеріїв установлення діагнозу дозволять лікарям своєчасно встановити діагноз та призначити адекватну терапію і, тим самим, покращити показники виявлення системного червоного вовчака та підвищити якість і тривалість життя пацієнтів.

Ключові слова: системний червоний вовчак, ювенільний системний червоний вовчак, вовчаковий нефрит, антинуклеарні антитіла, антитіла до двоспіральної ДНК, нефробіопсія.

The study is a fragment of the research project "Justification of the use of traditional and non-traditional methods of prevention and rehabilitation therapy in patients with cardiovascular pathology with high cardiovascular risk", state registration No. 0124U000095.

Systemic lupus erythematosus is a chronic autoimmune relapsing-remitting CSCTD of unknown etiology, which develops under the influence of numerous endogenous and exogenous factors against the background of genetic predisposition [22]. According to many authors, the conditions that increase the likelihood of SLE developing are: insolation, exposure to other electromagnetic waves, infections, in particular, infection with the Epstein-Barr virus, smoking, obesity, sleep disorders and reproductive age in women [5, 6].

The pathogenesis of SLE is not fully known. There are several pathophysiological mechanisms that lead to impaired reactivity of the immune system, first of all – hyperactivation of B and T cells with hyperproduction of autoantibodies (autoAB) to nuclear antigens (AG), loss of immunological tolerance and defective clearance of apoptotic cells and/or immune complexes (IC) with their deposition in glomeruli, tubules, basement membranes of peritubular and other capillaries of target organs with the development of immunoinflammatory damage to internal organs and vessels [16, 26].

The incidence and prevalence of SLE depends on gender, age, race and ethnicity and vary significantly in different regions of the Earth. Thus, in North America, SLE is diagnosed quite often (23.2 and 241 cases per 100,000 people per year, respectively), in different states of the USA, the incidence ranges from 1.0 to 7.6 cases per 100,000 population per year, and the prevalence ranges from 53.3 to 149.5 (average – 81.1), in the UK these figures are 4.9 and 65.0, respectively [23]. Very low incidence and prevalence rates have been recorded in Ukraine – from 0.3 to 0.7 cases per 100,000 people per year and –

17.1, respectively, which is significantly lower than global figures [13] and indicates an insufficient level of SLE detection. Publications in recent years demonstrate a trend of steady growth in the incidence of SLE, especially in the post-COVID period [6, 26].

At the same time, there are reports of juvenile systemic lupus erythematosus (JSLE), which occurs when symptoms of SLE appear in people under 18 years of age. Among patients with SLE, they account for 15–20 %. The incidence of JSLE is variable and is 0.36–2.5 per 100,000, and the prevalence is 1.89–34.1 per 100,000 population, respectively [1].

It is reported that in all age and ethnic groups, SLE is more common in women (from 5 to 15:1) [5, 11]. Currently, 3.4 million cases of SLE have been registered in the world, of which 90 % are women [2]. It is noteworthy that the peak incidence in women falls on the age of 15 to 44 years, while in men SLE usually manifests later [9]. The peak age of onset of symptoms of JSLE is 12.6 years, mainly girls are affected, in the ratio: 4.7–5.6:1.0, however, the gender predominance of females among children is less pronounced compared to adults. Thus, by the age of 5, JSLE occurs in approximately the same ratio in boys and girls. It is noteworthy that the frequency of arthritis, nephritis, neurological manifestations in JSLE is negatively correlated with the age at the onset of the disease [1]. In addition, there are gender differences in the course of SLE [23]. Thus, women more often develop dermatitis, arthritis and lesions of the central nervous system (CNS), while men develop kidney damage [2].

Systemic lupus erythematosus is a clinically heterogeneous disease that has several phenotypes with different clinical manifestations: from mucocutaneous [13] to multiorgan [4, 5, 9, 16, 22, 33] with the development of typical [15, 18, 19, 30, 34] and unpredictable complications [36].

For JSLE, kidney and central nervous system involvement with the development of various neuropsychiatric manifestations are typical: headache, psychosis, cognitive dysfunction, and cerebrovascular disorders. Lupus nephritis occurs in 80 % of these patients. Under this condition, in 19 % it rapidly progresses to end-stage renal failure. Other manifestations of JSLE are: hematological disorders (hemolytic anemia, lymphopenia and thrombocytopenia), skin and mucous membrane lesions (cheekbone rash, photosensitivity, oral mucosal ulcers, skin vasculitis), gastrointestinal tract (hepatosplenomegaly, autoimmune hepatitis, pancreatitis, serositis, esophageal motility disorders and nonspecific abdominal pain), joints. It is noteworthy that the frequency of nephritis, neurological manifestations, arthritis in JSLE is negatively correlated with age at disease onset [1].

In recent years, the diagnosis of the disease is clinical and based on the definition of the classification criteria of the American College of Rheumatology and the European League Against Rheumatism (EULAR/ACR) 2019 and/or on the basis of the classification criteria for lupus nephritis (LN) of the International Society of Nephrology/Renal Pathology Society (ISN/RPS) 2003 [8, 25]. However, the multiorganism of the clinical picture, the high probability of the development of serological abnormalities is a multidisciplinary problem at the time of diagnosis [12].

Despite the optimization of specific medical care for patients with SLE, they still have a very high risk of progressive organ damage, the development of complications, which leads to disability and mortality of these patients [27].

Timely diagnosis and adequate pathogenetic therapy (PGT) can reduce the activity of immune damage to organs, and thereby reduce the risk of complications and increase the quality and duration of life of patients [5, 33], which makes it urgent to highlight the problem of SLE diagnosis.

The purpose of the study was to analyze information on the features of the clinical course of systemic lupus erythematosus, diagnostic criteria for developing an algorithm for its diagnosis.

Materials and methods. Based on a review of the medical literature, analysis of articles obtained from a search of the PubMed, SCOPUS, Web of Science, MedScape databases for the period from 2020 to 2024, using a combination of terms: “systemic lupus erythematosus, juvenile lupus erythematosus, lupus nephritis, antinuclear antibodies, antibodies to double-stranded DNA, nephrobiopsy”, 38 sources with documented cases of SLE were selected, of which 23 were published in English.

Results of the study and their discussion. The heterogeneity of clinical manifestations and course of SLE causes difficulties in developing diagnostic criteria. The problem of diagnosing SLE is one of the multidisciplinary problems, taking into account its comorbid, often complicated course.

The study of SLE clinical manifestations began with the research of the French dermatologist Cazenave Pierre-Louis as early as 1851. Systemic lupus erythematosus was initially considered a skin disease. In 1872, the Austrian doctor Gebra Ferdinand Ritter divided this disease into cutaneous and systemic forms, and in 1878 he first called the lupus rash on the nose and cheeks a “butterfly”. According to the German doctor Paul Gottlieb Werlhof, in 1878, thrombocytopenic purpura was found in patients with SLE. Data from the Canadian physician William Osler, 1894, also indicated kidney damage in these patients. In addition, he noted that damage to the joints, muscles, and internal organs in this disease is

possible without skin manifestations. In 1904, the German dermatovenereologist Josef Jadasson first used an immunological approach to diagnose SLE. In 1924, the American doctors E. Liebman and B. Sachs described endocarditis as a manifestation of SLE. Since 1948, thanks to the work of American doctors Malcolm Hargreaves and Mac Cullen, the diagnosis of SLE has been based on the determination of LE cells (from "Lupus Erythematosus"), which they found in bone marrow aspirates. Then they were found in peripheral blood, synovial and cerebrospinal fluid, pleural and pericardial exudates of patients with SLE [14].

In 1976, I.E. Tareeva developed a clinical classification of lupus nephritis (LN) based on the identified histological changes in renal tissue in NB [33]. The diagnostic criteria for SLE were first proposed in 1971 by the American College of Rheumatology. In 1982, the European League Against Rheumatism (EULAR) developed the first classification approaches for the diagnosis of SLE. Since then, the criteria for the diagnosis of SLE have been continuously improved. In 1997, the American College of Rheumatology (ACR) updated these criteria. Since 2003, the diagnosis of SLE has also been verified based on the ISN/RPS criteria for LN. According to this classification, 6 morphological classes of LN are distinguished, which serve not only as markers of LN, but also as necessary for predicting the course of the disease and a differential approach to the tactics of PGT. In 2012, the international cooperation of clinics for systemic lupus erythematosus – Systemic Lupus International Collaborating Clinics (SLICC) proposed new diagnostic criteria, according to which patients must meet at least four criteria, including one clinical and one immunological: an increased level of antinuclear antibodies (ANA) or – NB results confirming the presence of LN. They allow classifying patients with LN based on nephrobiopsy data in the presence of elevated ANA titer or ANA dsDNA levels in the absence of other clinical criteria. These are the criteria currently recommended for verifying the diagnosis in the population of patients with JSLE. In 2019, EULAR/ACR proposed updated clinical criteria that are superior in sensitivity and specificity to those of previous years [8, 25]. The entry criterion is the determination of the ANA titer on cells of the transplanted human laryngeal adenocarcinoma epithelioid line HEp-2 by indirect immunofluorescence [8, 25]. This method is recommended by leading experts, including European (EASI group, 2010) and American expert groups (ACR ANA Taskforce, 2008) as the gold standard, since it allows the detection of nuclear autoantibodies to nucleic acids (dsDNA, ssDNA, RNA), ribonucleoproteins, as well as to most conformational and insoluble antigens already at the onset of the disease [2].

These classification criteria include clinical and immunological domains. The clinical domains include: constitutional (fever ≥38.3 °C), hematological (leukopenia, thrombocytopenia, autoimmune hemolysis), neuropsychiatric, mucocutaneous (non-scarring alopecia, oral ulcers, acute, active skin lesions, subacute cutaneous lupus or chronic cutaneous lupus), serous (pleural or pericardial effusion, acute pericarditis), renal (proteinuria >0.5 g/24 h, LN morphological classes according to results of NB. Classification of SLE based on the EULAR/ACR 2019 criteria requires one clinical criterion and ≥10 points from additional criteria. Under this condition, only one criterion with the highest score in each domain is counted [18]. Although the diagnosis of SLE remains clinical, it requires mandatory laboratory confirmation by increasing the titer of ANA and the levels of highly specific biomarkers – anti-double-stranded deoxyribonucleic acid (anti-dsDNA) and/or Smith antigen (anti-Sm), decreased complement levels (C3 and/or C4). In addition, the list of immunological domains of these criteria includes determination of the level of antiphospholipid (APS) antibodies, anti-beta-2-glycoprotein (IgG) (Anti-β2GP1) and lupus anticoagulant (LA) [27, 34]. If the latter is exceeded, the risk of developing arterial and venous thrombosis increases to 60–70 % [15, 34]. Along with them, the frequency of adverse pregnancy outcomes also increases [31]. It should be noted that the level of anti-dsDNA correlates with disease activity and increases several months before relapse of SLE on the background of decreased complement indices [32]. At the same time, it is reported that there is a possibility of the development an overlap syndrome between SLE and antineutrophil cytoplasmic (ANCA)-associated systemic vasculitis (SV), which potentiate each other, worsening the prognosis of the disease. Under these conditions, it is advisable to include in the examination plan the determination of ANCA to myeloperoxidase and to proteinase-3 [19, 20].

According to many researchers, the clinical symptoms of SLE do not always occur simultaneously and can develop at any stage of the disease. In the debut of SLE, nonspecific general symptoms usually prevail. Fever, fatigue and arthralgia are the most frequent manifestations [11, 12]. Many researchers report the manifestation of SLE with aplastic anemia [10, 36]. In addition, cases of the debut of SLE with isolated kidney damage [30, 35] are described in the scientific literature, in 60–80 % of patients LN and nephropathy associated with antiphospholipid syndrome (APS) [34] – thrombotic microangiopathy are detected already in the early stages of the disease [15]. Many of them develop secondary arterial

hypertension [21] and chronic kidney disease, leading to renal failure [18, 38]. Currently, 28 types of skin manifestations of SLE are known, which can occur at different stages of the disease. They are divided into specific and non-specific [3, 13], which occur in other diseases and require careful differentiation from "mimics" [12]. M.B Jus et al. report the development of an extremely rare case of soft tissue calcification in patients with SLE [3]. W Gilcrease et al. indicate the development of polymorbidity in SLE [22]. Thus, SLE is characterized by the development of interstitial lung disease, aspiration pneumonia [24], gastrointestinal pathology [16], cognitive impairment and symptoms of CNS damage [9, 14], atherosclerosis and symptoms of cardiovascular system damage [21]. V.M. Zhdan and co-authors in their study showed that 24 % of SLE patients have insulin resistance in the absence of diabetes mellitus (DM) [4]. This confirms the heterogeneity of clinical symptoms and the complexity of SLE diagnosis. SLE is suspected when clinical manifestations from two or more body systems are present and have no clear explanation [12, 31].

An elevated ANA titer is a hallmark laboratory sign of SLE and should be investigated first. A positive ANA test with a titer ≥1:80 on HEp-2 cells and/or antinuclear factor (ANF) are the main screening indicators for the diagnosis of SLE [17]. Although they are specific in only 20% of cases, positive results are noted in more than 97 % of SLE cases. L.N.Efremenkova and co-authors note that an increase in ANA titer can be observed from several months to several years before the clinical manifestation of SLE [6]. At the same time, in addition to SLE, they can be increased in other CSCSD, SV, autoimmune hepatitis and thyroiditis, diabetes, viral infections, and also in a significant part of healthy people, due to low specificity [7, 19, 20, 28, 37]. The diagnosis is verified by the presence of true, nuclear ANAs to DNA. They are divided into two main types: antibodies that react with double-stranded (native) DNA (a-DNAn, dsDNA) and antibodies that react with single-stranded (a-ssDNA). Antibodies to DNA are a serological marker of SLE. Antibodies to dsDNA are more specific for the diagnosis of SLE than antibodies to a-ssDNA, which are found in the serum of patients with other rheumatoid diseases and have no significant diagnostic value [1, 27]. In addition, there are reports of cases when several years before the appearance of clinical manifestations of SLE in patients, serological abnormalities can be detected. That is, an increase in specific for SLE immunological indicators on the background of clinical signs that do not meet the established criteria for the disease. This phenomenon is described in the professional medical literature as preclinical lupus [17, 33]. Under these conditions, elevated ANA levels are detected 10 years before diagnosis verification in 47 % of patients with SLE, anti-dsDNA antibodies are detected in 55 % of cases 2.5 years before SLE manifestation, anti-Sm antibodies are detected in less than 30 % of patients with SLE several months before its diagnosis and are always associated with anti-histone antibodies (aRNP), APS antibodies are detected in 18 % of patients, on average, 3 years before the appearance of specific signs of SLE [17, 30]. In addition, for the diagnosis of SLE, assessment of the inflammatory activity of the disease, the effectiveness of PGT and the prognosis of the disease, generally accepted clinical, biochemical, and coagulological methods of blood testing, general urinalysis, determination of the ratio of albumin and creatinine in the urine, acute phase blood parameters, Wasserman reaction, assessment of proteinogram, daily proteinuria, screening for concomitant diseases and comorbidities is carried out, and the glomerular filtration rate is calculated using the online CKD-EPI calculator [29].

Thus, when SLE is suspected, laboratory tests can confirm or refute the diagnosis. Initially, it is recommended to perform a screening laboratory test for ANA titer and screening laboratory tests: ESR. Complete blood count, biochemical blood test, complete urine test.

Blood test results in the presence of SLE may reveal cytopenia (thrombocytopenia ($<100x10^9$/L) and/or leukopenia ($<4x10^9$/L), lymphopenia), signs of autoimmune hemolysis (positive Coombs test, hemolytic anemia, reticulocytosis, decreased haptoglobin levels, increased indirect bilirubin, lactate dehydrogenase) [38].

In case of positive screening (especially in case of positive ANA), further differentiation of ANA is determined (anti-Sm, -Ro/SSA, -La/SSB, -U1RNP, dsDNA antibodies, levels of C3, C4 complement components, antiphospholipid antibodies, lupus anticoagulant, eGFR, daily protein excretion (if proteinuria is detected in a general urine analysis), albumin/creatinine ratio in one urine sample; urine examination for dysmorphic erythrocytes in the sediment [32]. It is noteworthy that the presence of antibodies to dsDNA is a mandatory diagnostic criterion for SLE. The recommended frequency of their determination is 1 time in 3 months.

Further laboratory and instrumental studies should be performed depending on clinical symptoms. Other laboratory biomarkers (cytokines, endothelial activation markers, immunoglobulins, IC, cryoglobulins, lymphocyte subpopulations, genetic markers, bone and cartilage metabolism indicators,

apoptosis markers, etc.) have less clinical significance compared to acute phase inflammation and autoantibodies and can be used to monitor disease activity and response to treatment [32].

Conclusions

1. The diagnosis of systemic lupus erythematosus is clinical, but requires laboratory confirmation.

2. SLE is suspected when clinical manifestations from two or more body systems are present and have no clear explanation.

3. A positive test for antinuclear antibodies in a titer ≥1:80 on HEp-2 cells and/or antinuclear factor are the main screening indicators for establishing the diagnosis of systemic lupus erythematosus.

4. The presence of antibodies to double-stranded DNA is a mandatory diagnostic criterion for systemic lupus erythematosus and correlates with disease activity.

5. The combined use of ELISA methods and the detection of ANF on HEp2 cell lines by indirect immunofluorescence, as well as the determination of antibodies to double-stranded DNA and complement levels (C3, C4 or CH50), allow to avoid false-negative test results in systemic lupus erythematosus.

6. The simultaneous use of the 2012 SLICC and 2019 EULAR/ACR criteria minimizes diagnostic errors.

7. The gold standard for detecting lupus nephritis and verifying systemic lupus erythematosus is nephrobiopsy.

8. Determination of antineutrophil cytoplasmic antibodies to myeloperoxidase and proteinase-3 will help to exclude overlap syndrome with ANCA-associated systemic vasculitides.

9. Elevated levels of antiphospholipid antibodies in the setting of lupus nephritis indicate nephropathy associated with antiphospholipid syndrome and a high risk of developing thrombotic complications and pregnancy pathology.

Prospects for further research include identifying an optimal combination of methods for examining patients with suspected SLE to develop an algorithm for its diagnosis, thereby establishing a timely diagnosis.

References

1. Biliavska IuV, Oshlyanska OA, Shevchenko NS. Yuvenilnyi systemnyi chervonyi vovchak. Shcho varto pamiataty revmatolohu dorosloi sluzhby? Ukr J Rheumatol. 2021;2(84):19-28. doi: 10.32471/rheumatology.2707-6970.84.16287. [in Ukrainian].

2. Viunitska LV, Gavrilenko TI, Pidgaina OA, Ryzhkova NO, Protsenko GO. Osoblyvosti laboratornoi diahnostyky kolahenoziv. Ukr J Rheumatol. 2022;2(88):25-33. doi: 10.32471/rheumatology.2707-6970.88.17072. [in Ukrainian].

3. Dzhus MB, Ivashkivskyi OI, Karasevska TA, Potomka RA, Novytska AL, Mikuksts VYa, et al. Kaltsynaty miakykh tkanyn pry systemnomu chervonomu vovchaku. klinichnyi vypadok ta ohliad literatury. Ukr J Rheumatol. 2021;1(83):64-73. doi: 10.32471/rheumatology.2707-6970.83.16006. [in Ukrainian].

4. Zhdan VM, Tkachenko MV, Babanina MYu, Volchenko HV, Kitura YeM, Ivanytskyi IV. Insulinorezystentnist pry systemnomu chervonomu vovchaku. CM. 2024;2:49-54. doi: 10.30841/2786-720X.2.2024.307530. [in Ukrainian].

5. Yehudina YeD, Trypilka SA. Diahnostyka ta likuvannia systemnoho chervonoho vovchaka. Health Ukr 21st Cent [Internet]. 2023 [tsytovano 2024 Hrud 12];20(557):43. Dostupno: https://health-ua.com/revmatologia/sistemni-zaxvoriuvannia-spolucnoyi-tkanini/75402-dagnostika-talkuvannya-sistemnogo-chervonogo-vovchaka. [in Ukrainian].

6. Yefremenkova LN, Kovalevska LA, Vrublevska CV, Hrytsyk VP, Kachurova IM, Syvyi SM, et al. Debiut systemnoho chervonoho vovchaka pislia perenesenoho COVID-19. Herald Maritime Med. 2023;1(98):86-91. doi: 10.5281/zenodo.7806274. [in Ukrainian].

7. Katerenchuk IP, Tkachenko LA, Yarmola TI. Urazhennia nyrok pry revmatychnykh zakhvoriuvanniakh [Internet]. Kyiv; 2017 [tsytovano 2024 Lystop 22]. 144 p. Dostupno: https://repository.pdmu.edu.ua/handle/123456789/19607. [in Ukrainian].

8. Kovalenko VM, Rekalov DH, Yatsyshchyn RI, Holovach IYu, Stanislavchuk MA, Ter-Vartanian SKh, et al. Systemnyi chervonyi vovchak. Klinichni rekomendatsii. Kyiv, 2020. 76 p. [in Ukrainian].

9. Koliadenko DI, Yaremenko OB, Nahirna MI. Neiropsykhiatrychni proiavy u khvorykh na systemnyi chervonyi vovchak: poshyrenist, klinichni ta laboratorni asotsiatsii. Ukr J Rheumatol. 2023;1(91):1-7. doi: 10.32471/rheumatology.2707-6970.91.17688. [in Ukrainian].

10. Mormol I, Borzykh O, Gerasymenko N, Esanu C, Ozarchuk L. Urazhennia krovotvornoi systemy u khvoroi na systemnyi chervonyi vovchak ta efektyvnist likuvannia mikofenolatom mofetilom. Med and Ecol Probl. 2022;26(5-6):7-10. doi: 10.31718/mep.2022.26.5-6.02. [in Ukrainian].

11. Protsenko HO, Dubas VV. Systemnyy chervonyy vovchak: stan problemy v Ukrayini ta sviti. Ukr J Rheumatol. 2020;4(82):25-34. Ukrainian. doi: https://doi.org/10.32471/rheumatology.2707-6970.82.15749. [in Ukrainian].

12. Protsenko HO, Dubas VV. Analiz vidterminuvannia vstanovlennia diahnozu pry systemnomu chervonomu vovchaku. Ukr J Rheumatol. 2022;1(87):1-6. doi: 10.32471/rheumatology.2707-6970.87.16747. [in Ukrainian].

13. Protsenko HO, Dubas VV, Uzun SV, Tsokalo YaV, Zbarashchenko-Hasan MI. Shkirni proiavy pry systemnomu chervonomu vovchaku (vypadok z klinichnoi praktyky). Ukr J Rheumatol. 2023;1(91):1-6. doi: 10.32471/rheumatology.2707-6970.91.17654. [in Ukrainian].

14. Synyachenko OV, Kovalenko VM, Bortkevych OP, Gnylorybov AM, Golovach IY, Yermolaieva MV, et al. Istoriia rozvytku systemnykh zakhvoriuvan spoluchnoi tkanyny ta systemnykh vaskulitiv u dzerkali numizmatyky. Ukr J Rheumatol. 2020;3(81):4-11. doi: 10.32471/rheumatology.2707-6970.81.15423. [in Ukrainian].

15. Taran OI. Trombotychna trombotsytopenichna mikroanhiopatiia. Kidneys. 2022;2(4):66-69. doi: 10.22141/2307-1257.0.2.04.2013.85358. [in Ukrainian].
16. Abrahamovych U, Abrahamovych O, Nadashkevich O, Farmaha M, Kobak L. Pathogenetic Association of Digestive System Lesions with Systemic Lupus Erythematosus: Characteristics and Prevalence. PMGP. 2020;5(1):e0501225. doi: 10.26766/pmgp.v5i1.225.
17. Ameer MA, Chaudhry H, Mushtaq J, Khan OS, Babar M, Hashim T, et al. Overview of Systemic Lupus Erythematosus (SLE) Pathogenesis, Classification, and Management. Cureus. 2022;14(10):e30330. doi: 10.7759/cureus.30330.
18. Anders HJ, Saxena R, Zhao MH, Parodis I, Salmon JE, Mohan C. Lupus nephritis. Nat Rev Dis Primers. 2020;6(1):7. doi: 10.1038/s41572-019-0141-9.
19. Banos A, Thomas K, Garantziotis P, Filia A, Malissovas N, Pieta A, et al. The genomic landscape of ANCA-associated vasculitis: Distinct transcriptional signatures, molecular endotypes and comparison with systemic lupus erythematosus. Front Immunol. 2023;14:1072598. doi: 10.3389/fimmu.2023.1072598.
20. Botero B JD, Bernal-Macías S, Celis P CA, Lasso A JI, Rodríguez J, Arias Álvarez L, et al. Systemic lupus erythematosus/ANCA-associated vasculitis overlap: An explanation for atypical lupus manifestation. Lupus. 2022;31(4):495-499. doi: 10.1177/09612033221084519.
21. Cheung AK, Chang TI, Cushman WC, Furth SL, Hou FF, Ix JH, et al. Executive summary of the KDIGO 2021 Clinical Practice Guideline for the Management of Blood Pressure in Chronic Kidney Disease. Kidney Int. 2021;99(3):559-569. doi: 10.1016/j.kint.2020.10.026.
22. Gilcrease W, Manfredi L, Sciascia S, Ricceri F. From Multimorbidity to Network Medicine in Patients with Rheumatic Diseases. Rheumatol Ther. 2024. doi: 10.1007/s40744-024-00724-8.
23. Hoi A, Igel T, Mok CC, Arnaud L. Systemic lupus erythematosus. Lancet. 2024;403(10441):2326-2338. doi: 10.1016/S0140-6736(24)00398-2.
24. Joy GM, Arbiv OA, Wong CK, Lok SD, Adderley NA, Dobosz KM, et al. Prevalence, imaging patterns and risk factors of interstitial lung disease in connective tissue disease: a systematic review and meta-analysis. Eur Respir Rev. 2023;32(167):220210. doi: 10.1183/16000617.0210-2022.
25. Julkunen H. Guideline 00446. Systemic lupus erythematosus (SLE) [Internet]. Kyiv: MOZ; 2017 [updated 2017 Jul 31; cited 2024 Dec 13]. Available from: https://guidelines.moz.gov.ua/documents/3299.
26. Kaidashev I, Shlykova O, Izmailova O, Torubara O, Yushchenko Y, Tyshkovska T, et al. Host gene variability and SARS-CoV-2 infection: A review article. Heliyon. 2021;7(8):e07863. doi: 10.1016/j.heliyon.2021.e07863.
27. Kant S, Kronbichler A, Sharma P, Geetha D. Advances in Understanding of Pathogenesis and Treatment of Immune-Mediated Kidney Disease: A Review. Am J Kidney Dis. 2022;79(4):582-600. doi: 10.1053/j.ajkd.2021.07.019.
28. Katerenchuk IP, Tkachenko LA, Yarmola TI, Talash VV. Microscopic polyangiitis – a view of the problem through the lens of a nephrologist. Wiad Lek. 2021;74(4):1024-1031. doi: 10.36740/WLek202104140.
29. National Kidney Foundation. KDOQI Clinical Practice Guideline for Diabetes and CKD: 2012 Update. Am J Kidney Dis. 2012;60(5):850-886. doi: 10.1053/j.ajkd.2012.07.005.
30. Piga M, Arnaud L. The Main Challenges in Systemic Lupus Erythematosus: Where Do We Stand? J Clin Medi. 2021;10(2):243. doi: 10.3390/jcm10020243.
31. Putra RS, Najirman. Treatment of Systemic Lupus Erythematosus with Anti SSA and SSB Positive Pregnancies. Biosmed. 2022;6(3):1523-1529. doi: 10.37275/bsm.v6i3.470.
32. Rana RS, Naik B, Yadav M, Singh U, Singh A, Singh S. Serum complements and immunoglobulin profiles in systemic lupus erythematosus patients: An observational study at a teaching hospital. J Family Med Prim Care. 2022;11(2):608-613. doi: 10.4103/jfmpc.jfmpc_960_21.
33. Siegel CH, Sammaritano LR. Systemic Lupus Erythematosus: A Review. JAMA. 2024;331(17):1480-1491. doi: 10.1001/jama.2024.2315.
34. Siniscalchi C, Rossetti P, Carolla G, Micco P, Stella A, Riva M. A review on management of antiphospholipid syndrome in clinical practice. Ital J Med. 2023;17(2):1649. doi: 10.4081/itjm.2023.1649.
35. Solhjoo M, Goyal A, Chauhan K. Drug-Induced Lupus Erythematosus. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 [updated 2023 Apr 3; cited 2024 Nov 14]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK441889.
36. Wibowo T, Kawada S, Ishida Y, Yoshimine Y, Ishikawa N, Kawamoto K, et al. Autoimmune myelofibrosis associated with systemic lupus erythematosus: a case report. Mod Rheumatol Case Rep. 2020;4(1):28-33. doi: 10.1080/24725625.2019.1650697.
37. Yarmola TI, Gutsalenko OO, Katerenchuk IP, Tkachenko LA, KostrikovaYA, Talash VV. Microscopic polyangiitis hiding behind the mask of COVID-19: A case series and minireview. Ukr J Nephrol Dial. 2023;2(78):5-21. doi: 10.31450/ukrjnd.2(78).2023.02.
38. Yu C, Li P, Dang X, Zhang X, Mao Y, Chen X. Lupus nephritis: new progress in diagnosis and treatment. J Autoimmun. 2022;132:102871. doi: 10.1016/j.jaut.2022.102871.

Стаття надійшла 17.03.2024 р.