A Current Perspective of Systemic Lupus Erythematosus: A Literature Review

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Abstract

Background. Systemic lupus erythematosus (SLE), is a chronic autoimmune disease that affects various organ systems in the body. This disease is characterized by an abnormal immune reaction, in which the body's immune system attacks the body's own tissues, resulting in inflammation and damage. Symptoms of lupus vary greatly, ranging from fatigue, joint pain, skin rashes, to serious complications such as kidney and heart damage. Systemic lupus erythematosus (SLE) is characterized by dysfunction of the immune system and is clinically heterogeneous, presenting with renal, dermatological, neuropsychiatric, and cardiovascular.

Methods. The research method used was literature review using electronic databases through national and international journals such as Google scholar and ScienceDirect as well as health articles such as Cleveland Clinic. The inclusion criteria used by the authors were to limit articles or journals published in the last five years starting from 2019 to 2024.

Disscusion. Systemic lupus erythematosus (SLE) classification criteria are often chosen based on tradition, consensus and statistics, without considering deeper etiological and pathogenetic aspects. This process can result in a lack of scientific objectivity, as it does not explore causal relationships between criteria and disease mechanisms.

Conclusion. Systemic Lupus Erythematosus (SLE) is a systemic autoimmune disease characterized by aberrant immune system reactions, affecting various organs in the body. Genetic, environmental and hormonal factors contribute significantly to the development of this disease, which is more common in women of reproductive age.

Keywords: Systemic Lupus Erythematosus (SLE), Autoimmune, Symptoms, Diagnosis

Introduction

Systemic Lupus Erythematosus (SLE) is a systemic autoimmune disease characterized by aberrant immune system activity.¹ Widely affecting various organs, genetic factors, environmental factors and hormonal factors are believed to contribute to the occurrence of SLE.² This disease is more common in women, especially those of reproductive age, with genetic and environmental factors playing a role in its pathogenesis. The diagnosis of lupus is often challenging, requiring a combination of clinical history, physical examination, and a series of laboratory tests. This disease is a complex autoimmune disease entity with heterogeneous skin and systemic manifestations that can progress over the course of the disease.³

Methods.

The research method used was literature review using electronic databases through national and international journals such as Google scholar and ScienceDirect as well as health articles such as Cleveland Clinic. The inclusion criteria used by the authors were to limit articles or journals published in the last five years starting from 2019 to 2024.

Discussion

Clinical Symptoms

Manifestations of clinical symptoms of Lupus disease are usually found on the skin, because the skin is the second most frequently affected organ system in systemic lupus erythematosus (SLE), with skin manifestations occurring in 70-85% of individuals during the course of the disease and as symptoms that appear in up to 25% of patients^{1.} In the 1960s before autoimmune serology was generally available, skin changes were said to be the second most common clinical manifestation of SLE³.

Clinical symptoms of lupus vary widely, but some common ones include:

- 1. Fatigue: Unusual feeling of tiredness.
- 2. Joint Pain: Pain, swelling, or stiffness in the joints.
- 3. Skin Rash: Butterfly-shaped rash on the face.
- 4. Fever: Recurrent mild fever.
- 5. Kidney Problems: Inflammation or damage to the kidneys.

- 6. Chest Pain: Pain when breathing deeply (pleuritis).
- Headache: Headache or other neurological symptoms.
 Symptoms may come and go, making diagnosis challenging.

Pathophysiology

The pathophysiology of systemic lupus erythematosus (SLE) involves complex interactions between genetic, environmental, and immune system factors. The following is an explanation of the pathophysiology of this disease²:

- 1. Immune Dysregulation: In individuals with lupus, there is a disturbance in the regulation of the immune system. Immune cells, such as lymphocytes found in the body, produce antibodies against the body's own antigens, known as autoantibodies.
- Formation of Immune Complexes: These autoantibodies can bind antigens and form immune complexes. These complexes can deposit in tissues and organs, causing inflammation and damage.
- 3. Inflammation: Accumulated immune complexes trigger an inflammatory response, involving immune cells such as neutrophils, macrophages, and T cells. This causes extensive tissue damage, especially in the skin, joints, kidneys, and nervous system.
- 4. Environmental Factors: Exposure to environmental factors, such as ultraviolet light, infections, and certain medications, can trigger or precipitate lupus in genetically susceptible individuals.
- 5. Genetic Factors: There is a genetic predisposition in lupus, where certain gene variations contribute to the development of this disease.

Overall, lupus is an example of a complex immune dysfunction, in which autoimmune mechanisms cause an overreaction against the body's own tissues, resulting in variable clinical manifestations. Further research continues to be carried out to understand more deeply the pathophysiological mechanisms and find more effective therapies.

Laboratory findings and Lupus classification criteria.

Systemic lupus erythematosus (SLE) classification criteria are often chosen based on tradition, consensus and statistics, without considering deeper etiological and pathogenetic aspects. This process can result in a lack of scientific objectivity, as it does not explore causal relationships between criteria and disease mechanisms. Classifications that are not based on an understanding of etiology can confound the definition of SLE, including whether the disease should be viewed as a single entity or a variation of several pathological processes. To improve

understanding, a more evidence-based and integrated approach between classification and biological mechanisms is expected to provide a clearer picture of SLE⁷.

Treatment

Treatment of non-renal systemic lupus erythematosus. Top-to bottom sequence does not imply order of preference (eg, MTX, AZA and MMF are equal options for second-line therapy in mild disease or first-line therapy in moderate disease).

Mild disease: constitutional symptoms; mild arthritis; rash \leq 9% body surface area; platelet count (PLTs) 50–100× 109 /L; SLEDAI \leq 6; BILAG C or \leq 1 BILAG B manifestation.

Moderate disease: moderate-severe arthritis ('RA-like'; rash 9%–18%BSA; PLTs 20– 50×109 /L; serositis; SLEDAI 7–12; \geq 2 BILAG B manifestations). Severe disease: major organ threatening disease (cerebritis, myelitis, pneumonitis, mesenteric vasculitis); thrombocytopenia with platelets18%BSA SLEDAI>12; \geq 1 BILAG A manifestations.

Recommendation of belimumab and anifrolumab as first-line therapy in severe disease refers to cases of extrarenal SLE with non-major organ involvement, but extensive disease from skin, joints, and so on.

The use of anifrolumab as add-on therapy in severe disease refers mainly to severe skin disease. For patients with severe neuropsychiatric disease, anifrolumab and belimumab are not recommended. ANI, anifrolumab; aPL, antiphospholipid antbodies; APS, antiphospholipid syndrome; AZA, azathioprine; BEL, belimumab; BILAG, British Isles Lupus Assessment Group; CNI, calcineurin inhibitor; CYC, cyclophosphamide; GC, glucocortocoids; HCQ, hydroxychloroquine; IV, intravenous; MMF, mycophenolate mofetil; MTX, methotrexate; PO, per os; RTX, rituximab; SLEDAI, SLE Disease Activity Index; VKA, vitamin K antagonists⁶.

Prognosis

The prognosis for lupus, or systemic lupus erythematosus (SLE), varies depending on many factors, including the severity of the disease, the organs involved, and the response to treatment. Many people with lupus can live productive lives with proper management. With proper treatment, many patients experience long periods of remission. However, lupus can cause serious complications if left untreated, so it is important to see a doctor regularly and follow a treatment plan⁴.

Conclusion

Systemic Lupus Erythematosus (SLE) is a systemic autoimmune disease characterized by aberrant immune system reactions, affecting various organs in the body. Genetic, environmental and hormonal factors contribute significantly to the development of this disease, which is more common in women of reproductive age. Lupus diagnosis is often challenging and requires a multidisciplinary approach, including clinical history, physical examination, and laboratory tests.

Clinical manifestations of systemic lupus erythematosus (SLE) are most commonly seen on the skin, with approximately 70-85% of patients experiencing skin symptoms during the course of the disease. Other common symptoms include fatigue, joint pain, butterfly-shaped rash, fever, kidney problems, chest pain, and headaches. The wide variety of symptoms and its episodic nature make diagnosing lupus a challenge. A good understanding of these clinical manifestations is important for early detection and effective management. Patients with low C3 and C4 levels are more easily diagnosed with systemic lupus erythematosus (SLE) than patients with higher levels.

References

- 1. Yu H, Nagafuchi Y, Fujio K. Clinical and immunological biomarkers for systemic lupus erythematosus. Biomolecules. 2021;11(7):1–16.
- 2. Pan L, Lu MP, Wang JH, Xu M, Yang SR. Immunological pathogenesis and treatment of systemic lupus erythematosus. World J Pediatr. 2020;16(1):19–30.
- 3. Stull C, Sprow G, Werth VP. Cutaneous Involvement in Systemic Lupus Erythematosus: A Review for the Rheumatologist. J Rheumatol. 2023;50(1):27–35.
- Parodis I, Tamirou F, Houssiau FA. Prediction of prognosis and renal outcome in lupus nephritis. Lupus Sci Med. 2020;7(1):1–6.
- 5. Fanouriakis A, Tziolos N, Bertsias G, Boumpas DT. Update in the diagnosis and management of systemic lupus erythematosus. Ann Rheum Dis. 2021;80(1):14–25.
- Fanouriakis A, Kostopoulou M, Andersen J, Aringer M, Arnaud L, Bae SC, et al. EULAR recommendations for the management of systemic lupus erythematosus: 2023 update. Ann Rheum Dis
- Rekvig OP. SLE classification criteria: Is "The causality principle" integrated and operative – and do the molecular and genetical network, on which criteria depend on, support the definition of SLE as "a one disease entity" – A theoretical discussion. Autoimmun Rev. 2023;22(12):103470.
- 8. Furie, Joan P. M., and Kathleen C. Stohl. 2020. "Advances in the Management of

Systemic Lupus Erythematosus: 2020 Update." Nature Reviews Rheumatology 16 (9): 527–538.

- Fan Y, Hao YJ, Zhang ZL. Systemic lupus erythematosus: year in review 2019. Chin Med J. 2020;133(18):2189–96.
- 10. Basta F, Fasola F, Triantafyllias K, Schwarting A. Systemic lupus erythematosus (SLE) therapy: the old and the new. Rheumatol Ther. 2020;7(3):433–46.
- Yuan Z, Zhang W, Jin Z, Wang Y, Lin Z, Xie Z, et al. Global research trends in precision-targeted therapies for systemic lupus erythematosus (2003–2023): A bibliographic study. Heliyon. 2024