



Systemic Lupus Erythematosus and Overlap Syndromes: A Review

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ARTICLE INFO	ABSTRACT
Published Online: 30 May 2025	Systemic lupus erythematosus (SLE) is a long-term autoimmune disease that can affect multiple organs and produce various autoantibodies. Its symptoms can range from mild skin issues to serious organ complications. In some cases, people with SLE may also show signs of other autoimmune conditions like systemic sclerosis, polymyositis, or rheumatoid arthritis—this is known as an overlap syndrome. These conditions can be difficult to diagnose and treat because their symptoms and test results often overlap. Managing these syndromes usually requires a personalized approach, using medications that suppress the immune system and target the most affected organs. Recognizing overlap syndromes early and tailoring treatment to each patient's specific needs can lead to better outcomes. Ongoing studies into how these diseases work may help identify common pathways and lead to more effective treatments in the future.
Corresponding Author: T. Rama Rao	Systemic lupus erythematosus (SLE) is a multifaceted autoimmune disease noted by ubiquitous inflammation and tissue destruction. Overlap syndromes refer to cases where SLE occurs along with other autoimmune disease, including rheumatoid arthritis or Sjögren's syndrome, which can present a special set of clinical manifestations and treatment considerations. Learning these overlaps are key to good management and better patient outcomes.
KEYWORDS: systemic lupus erythematosus, autoimmune, polymyositis, rheumatoid arthritis, overlap, diagnosis.	

OVERVIEW OF SYSTEMIC LUPUS ERYTHEMATOSUS (SLE):

Systemic lupus erythematosus (SLE) is a chronic autoimmune disease that can involve multiple organ systems, including skin, joints, kidneys, and heart. It is characterized by the generation of autoantibodies, with antinuclear antibodies (ANAs) being an important class, against the body's own tissues. Symptoms can vary greatly between patients, including fatigue, joint pain, skin rashes and organ dysfunction.[1]

Overlap Syndromes in SLE:

Overlap syndromes, a condition in which SLE occurs in concert with other autoimmune diseases, can also result in an ambiguous clinical picture.

Overlap syndromes, in other words, coexistence of SLE with other autoimmune diseases, add further complexity to the clinical spectrum.

Some common conditions of overlap are:

SLE and Sjögren's syndrome: Sjögren's syndrome (SS) is an autoimmune disorder affecting exocrine glands mostly leading to dry eyes (keratoconjunctivitis sicca) and dry

mouth (xerostomia), SS can either be a primary condition occurring in isolation or a secondary disorder that occurs alongside other autoimmune diseases like Systemic Lupus Erythematosus (SLE).

SS associated with SLE is called secondary Sjögren's syndrome. This relationship makes diagnosis and management more difficult in patients with both autoimmune diseases.[2]

Pathophysiology:

SLE and SS have similar immunological characteristics; both are characterized by aberrant immune homeostasis, in which the immune system of the body destroys its own tissues. For secondary SS due to SLE, immune cells particularly B lymphocytes, infiltrate the exocrine glands, such as the salivary and lacrimal glands, causing inflammation, damage, and fibrosis. This leads to diminished function of these glands, which presents as the classic symptoms of dry eyes and dry mouth.

Both conditions share another notable characteristic: the production of autoantibodies. In SLE, Common autoantibodies including anti-nuclear antibodies (ANA) and

anti-double-stranded DNA antibodies (anti-dsDNA) are detected. The presence of specific autoantibodies such as anti-Ro (SS-A) and anti-La (SS-B) is common in SS Patients positive for anti-Ro and anti-La antibodies.[3]

Symptoms:

In the context of SLE, SS is characterized by dryness-related symptoms primarily. Dry eyes cause irritation, gritty feelings, burning, and trouble with prolonged reading or exposure to wind. Dry mouth causes problems swallowing, talking and eating, often with a sore or swollen tongue. [4] Patients may also suffer from increased dental caries, oral infections and difficulties wearing dentures.

Apart from those common features, systemic manifestations are also shown due to secondary SS in SLE like arthralgia, malaise or fatigue, and lymphadenopathy. These manifestations overlap with the general symptoms of SLE, which makes diagnosis tricky. Additionally, people with both diseases may also have an increased risk of developing lymphoma, particularly mucosa-associated lymphoid tissue (MALT) lymphoma.[5]

Diagnosis:

Diagnosis of SLE with secondary Sjögren's syndrome includes clinical features, serological tests, and biopsy.

Key diagnostic tests include:

Central to diagnosis are the symptoms of dry eyes and mouth and signs of inflammation in the affected glands.

Serological tests: Anti-Ro (SS-A) and anti-La (SS-B) antibodies are highly suggestive of SS, especially in patients with SLE.

Schirmer's test: This test is used to measure tear secretion and the severity of dry eyes.

Minor salivary gland biopsy: Biopsy of minor salivary gland can be done to confirm lymphocytic infiltration, which is hallmark of SS.

Lip biopsy: A lip biopsy may be done in some cases to look for characteristic changes in the salivary glands.[6]

Treatment:

Management of secondary Sjögren's syndrome associated with SLE is primarily symptomatic, addressing dryness and inflammation. Dry eyes can be treated with lubricating eye drops, punctal plugs, and corticosteroids. Salivary stimulants (including pilocarpine) and artificial saliva can help relieve dry mouth. Dental care is also a part of regular checkup to protect your teeth from decay and infections.

Because SLE is an autoimmune disease, patients with secondary SS may require immunosuppressive therapy to control systemic symptoms and prevent exacerbations of disease. Depending on the severity of the SLE and other SS symptoms, medications such as hydroxychloroquine, corticosteroids, and immunosuppressants like methotrexate or mycophenolate mofetil are used.[7][8]

Rheumatoid Arthritis in Systemic Lupus Erythematosus:

Both rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE) are chronic autoimmune diseases with extensive shared features, especially regarding their

musculoskeletal manifestations. RA is predominantly a disease in which synovial joints have a ubiquitous expression of the synuclein and synovial identity1, while SLE is a multisystem autoimmune disease that affects other organs such as skin, kidneys, heart, and joints. In SLE patients with RA kinds of features, the diagnosis and treatment of the disease may be difficult, and this coexistence is called 'rheumatoid arthritis in SLE' or 'rheumatoid-like arthritis in SLE'.[9]

Pathophysiology:

Both HLADRB1 alleles and antiphospholipid antibodies are associated with increased risk of RA in SLE; the pathogenesis is multifactorial involving both genetic predisposition and immune dysregulation. Both diseases are caused by the body's immune system attacking its own tissues, but they have somewhat different underlying mechanisms. Various immune cells, especially T lymphocytes and B lymphocytes are able to infiltrate the synovium (lining of the joints) where inflammatory cell infiltrates result in chronic inflammation, pannus development and progressive joint destruction. In SLE, the immune dysfunction is more global, with multiples autoantibodies such as anti-nuclear (ANA), anti-dsDNA, and anti-Smith (Sm) antibodies produced. Anti-CCP (cyclic citrullinated peptides) and rheumatoid factor (RF) may also be present in such cases where patients demonstrate overlap features for both diseases. In patients presenting with both SLE and RA, the immune system attacks the joints in much the same way as it does in RA, with synovial inflammation resulting in pain, swelling, and stiffness.[10][11]

Symptoms:

The symptoms of rheumatoid arthritis in SLE typically involve the joints and may mimic those of RA. Common symptoms include:

Joint pain and stiffness: Like in RA, SLE-associated arthritis would lead to pain, swelling, joint tenderness, morning stiffness, especially at the small joints of the knee, the hands, wrists.

Non-deforming arthritis: Joint deformities typical of RA (e.g., ulnar deviation, swan-neck deformities) are infrequent in SLE-associated arthritis. But functional continuity is nevertheless all too possible. Pain - associated disability with multi-joint involvement.[12]

Symmetric involvement: The arthritis is symmetric in both RA and SLE (e.g., wrists, knees, and fingers).

Systemic symptoms: Patients with SLE and RA may also have nonspecific systemic findings, such as fatigue, fever, weight loss, and malaise. These are overlapping manifestations of SLE.[13] [14]

Diagnosis:

Diagnosis of rheumatoid arthritis in SLE requires a careful clinical assessment and may be made based on several diagnostic steps:

Clinical history and examination: The initial important step in differentiating SLE-related arthritis from primary RA is through clinical history taking and a detailed clinical examination. Joint involvement, the presence of extra-

articular symptoms, and patterns of disease progression can aid the clinician in diagnosis.

Serological tests:

Rheumatoid factor (RF) and anti-CCP antibodies are specific to RA but can also be seen in a few SLE patients (relatively rare) Identification of the systemic autoimmune component can be aided by the presence of anti-nuclear antibodies (ANA) and anti-dsDNA antibodies in SLE.[15]

Imaging — X-rays and ultrasound can help assess the degree of joint inflammation and damage. Although degenerative joint erosions and deformities are hallmark features of RA, However, in SLE related arthritis there is a complete absence of this. Exclusion of other etiologies: infection or drug induced arthritis should be excluded.[16]

Treatment:

Managing the underlying SLE is generally the same approach used in treating rheumatoid arthritis. The strategy depends on the degree of symptoms and organ involvement:

Nonsteroidal anti-inflammatory drugs (NSAIDs):

NSAIDs can be used to relieve joint pain and inflammation. Caution must be exercised while prescribing these to the patients having renal involvement as well as gastrointestinal problems, as these are prevalent in SLE.

Corticosteroids: Oral or injectable corticosteroids are commonly used to manage inflammation. Prednisone is commonly used to manage systemic lupus and arthritis symptoms in SLE, but long term use requires monitoring for its side effects.

Disease-modifying antirheumatic drugs (DMARDs):

Hydroxychloroquine (commonly used in SLE) and methotrexate can be used to help manage symptoms from an arthritis perspective. If symptoms are not controlled adequately by DMARDs, biologics, such as tumor necrosis factor (TNF) inhibitors, may be used.

Immunosuppressive therapy: In more severe cases of SLE with underlying RA - like manifestations, the use of more potent immunosuppressive agents like mycophenolate mofetil or azathioprine can be considered as a part of treatment for systemic disease and inflammation.

Joint protection: Working with a rehabilitation specialist to identify joint-protection strategies may help protect joints and prevent further damage. [17]

SLE and Systemic Sclerosis (SSc): The classic trifecta of skin thickening and pulmonary involvement.

Clinical Features of Overlap Syndromes:

Overlap syndromes are characterized by the presence of a mixture of symptoms from both SLE and the overlapping disease.

For example:

Dermatomyositis: Has muscle weakness and skin rashes in addition to the usual manifestations of SLE.

Polymyositis: Muscle inflammation can predominate, further complicating diagnosis and treatment.[18][19]

Distinctive autoantibodies can tease out the conditions where autoantibodies are present, such as anti-Scl-70 in SSC or anti-Ro/SSA in Sjögren's syndrome.

Diagnosis and Management:

Diagnosis requires a comprehensive clinical assessment, autoantibody lab testing and imaging studies as appropriate. Possible management strategies may include: Immunosuppressive therapies: Include corticosteroids and disease-modifying antirheumatic drugs (DMARDs) to suppress inflammation. Symptomatic: Relief of symptoms such as pain or fatigue.

Collaborative care: Working with various specialists, such as rheumatologists and dermatologists, to ensure holistic treatment.[6][15]

Prognosis and Challenges:

The outcome of patients with SLE and overlap syndromes ranges from mild symptomatology associated with good survival to severe multi-organ involvement associated with a poorer prognosis.

Challenges include:

Higher risk for complications: Renal involvement or pulmonary hypertension.

Why treatment can be challenging: It can be a lot balancing any treatment for competing maladies.

CONCLUSION

Knowledge about the relationship of SLE with overlapping syndromes is important for diagnosis and management. Further studies are necessary to fully elucidate these complex interactions and optimise management of affected patients. Moving Forward - Exploring Research and Clinical Applications. Uncovering the "biomarkers" behind the condition could predict which SLE patients may go on to develop overlap syndromes and a more personalized approach to intervention and therapy could be used. Improvements in personalized medicine could show promise if treatment could be individualized using an autoantibody profile specific to the patient. Novel therapeutic agents targeting specific pathways common to SLE and overlapping conditions are enroute in clinical trial, with a wide therapeutic window and their potential to improve outcomes and avoid side effects.[20]

Patient Education and Support:

Providing patients with information about SLE and its possible co-occurrence with other autoimmune diseases is important for self-management and treatment adherence. They are trained in the unique challenges of managing multiple autoimmune diseases and can offer not just emotional support but practical advice for dealing with the burdens of living with these conditions. This initiative encourages patients to practice a healthy lifestyle to control symptoms and improve overall health by regularly exercising and having a balanced diet.

This therefore gives rise to a need to comprehensively cater for the physical and emotional care of patients as they should be holistic in their approach due to the complexities of this disease and its overlap syndromes.

Ongoing collaboration between healthcare providers, researchers, and patients will be paramount to improving our understanding and management of these complex disorders.

Novel Therapies and Updates:

Therapies: New biologic therapies are in development that directly target the immune pathways activated in SLE and its overlapped syndromes, holding the promise of more specific and effective management. Research on stomach microbiome and auto immune diseases is reaching prominence with studies suggesting that gut health might play a role in the disease activity and response of treatment. Telemedicine has played an increasingly important role in this, allowing important access to care and follow-up for patients with complex illnesses.[21][22]

Holistic Options and Lifestyle Changes

Complementary and alternative medicine (CAM), including acupuncture and mindfulness-based practices, may also play a role in symptom management and quality of life for people with SLE and overlap syndromes. This will enable regular follow-up and tracking of disease activity and treatment optimization in a timely manner. Your skills will propel you to re-establish a disciplined routine and a supportive network of family and friends as immediate, mobility-deprived access offers the perfect opportunity to bolster emotional resilience while securing the practical supports to manage what is to come.

Advocacy and Awareness

Part of the SLE awareness campaign and its overlap syndromes need to educate the community for better diagnostic criteria and increased treatment options. Such advocacy activities can ensure patients receive some of the most innovative therapies and supportive services, in addition to enabling research dollars for these intricate conditions. Community education programs could also help in educating the public and health care professionals on the complexities of autoimmune disease, and foster an informed and supportive environment for people with autoimmune disease.[23][24]

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