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Laboratory assessment of systemic lupus erythematosus: Review article

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***Abstract*---Background:** Systemic lupus erythematosus (SLE) is a multifaceted autoimmune disorder characterized by the production of autoantibodies and immune complexes, which play essential roles in its pathogenesis, diagnosis, and classification. Recent classification criteria emphasize the inflammatory nature of SLE, which is critical for assessing disease activity. **Aim:** This review article aims to evaluate the laboratory assessments utilized in diagnosing and monitoring SLE, with a specific focus on serological markers and their relation to inflammatory processes. **Methods:** A comprehensive review of current literature on SLE laboratory assessments, including serological markers such as autoantibodies, erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP), was conducted. Additionally, recent classification criteria from EULAR and ACR were analyzed to determine their implications for understanding SLE activity and inflammation. **Results:** The review found that inflammatory markers, particularly ESR, correlate with disease activity in SLE, while CRP levels may indicate bacterial infection rather than SLE activity. Furthermore, pro-inflammatory cytokines significantly contribute to the inflammatory manifestations seen in SLE. **Conclusion:** Laboratory assessments for SLE should emphasize inflammatory markers to enhance disease management. Integrating

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these markers with clinical features will improve diagnostic accuracy and provide a better understanding of SLE's inflammatory underpinnings.

***Keywords*---**Systemic lupus erythematosus, autoantibodies, inflammation, laboratory assessment, EULAR, ACR, erythrocyte sedimentation rate, C-reactive protein.

Introduction

Systemic lupus erythematosus (SLE) is a well-known autoimmune disorder that affects multiple systems. Central to its pathogenesis are the production of autoantibodies and the formation of immune complexes, which are pivotal in both the diagnosis and classification of the disease [1, 2]. Serological features, such as these, play a significant role in diagnostic criteria. Notably, recent classification guidelines, including the 2019 criteria set by the European League Against Rheumatism (EULAR) and the American College of Rheumatology (ACR) [3, 4], as well as earlier standards like the Systemic Lupus International Collaborating Clinics (SLICC) 2012 [5], ACR 1997 [6], and ACR 1982 [7], do not incorporate inflammation markers. Although C-reactive protein (CRP), a typical inflammatory marker in clinical labs, is generally not markedly elevated in SLE cases, a significant rise in CRP levels may indicate bacterial infection rather than SLE-related activity. Nevertheless, immune complexes in SLE almost always result in inflammatory processes, with the majority of clinical manifestations being driven by inflammation.

The clinical features of SLE, particularly those outlined in the EULAR/ACR 2019 criteria, emphasize the inflammatory nature of the disease. For example, renal involvement, joint issues, serosal inflammation, and mucocutaneous manifestations are predominantly inflammatory. Renal features such as class III or IV nephritis carry a weight of 10 in the criteria and are inflammatory in nature, while other renal conditions like class II or V nephritis, proteinuria exceeding 0.5 g/day, and musculoskeletal involvement (e.g., joint issues) are also classified as inflammatory, with varying degrees of importance. Similarly, mucocutaneous symptoms, including malar rash and subacute cutaneous lupus erythematosus (LE), have distinct inflammatory characteristics, whereas hematologic and certain neuropsychiatric symptoms (e.g., seizures) show partial or no inflammatory involvement. Moreover, with the exception of some hematological and neuropsychiatric symptoms, most organ involvement in SLE is associated with inflammatory mechanisms. Understanding how immune complex deposition triggers inflammation across various organs is crucial. The location and formation of immune complexes are influenced by factors like their size, charge, and specificity. While the autoantibodies involved in this process are not fully identified, some measurable examples include anti-double-stranded DNA (dsDNA) antibodies, which play a role in proliferative lupus nephritis by depositing on charged basement membranes, and anti-RNA-binding Ro-60 antibodies, which are involved in subacute cutaneous lupus erythematosus.

Once deposited, immune complexes activate the immune system through both complement activation and Fc receptor engagement. In mouse models of SLE, Fc receptors are necessary for the development of renal disease [8]. Cell death in affected tissues is mediated by cytotoxic T cells and the complement system, while inflammation is primarily driven by monocytes and macrophages. These cells produce a variety of pro-inflammatory cytokines upon binding immune complexes, including tumor necrosis factor (TNF), interleukin-1 (IL-1), IL-6, IL-15, and IL-18 [9]. These cytokines, particularly TNF, IL-1, IL-6, and IL-18, are also highly expressed in lupus nephritis, linking them directly to inflammation [10]. Additionally, immune complex detection triggers the production of type I interferons and immunoregulatory cytokines such as IL-10, IL-15, and B-cell activating factor (BAFF/BLyS), which are essential for disease regulation [11, 12, 13].

The activity of systemic lupus erythematosus (SLE) is predominantly characterized by inflammatory processes. Pro-inflammatory cytokines and effector immune cells contribute significantly to inflammatory diseases affecting various organs. An examination of established SLE disease activity scores, including the British Isles Lupus Activity Group (BILAG) score, European Consensus Lupus Activity Measure (ECLAM), SLE Index Score (SIS), SLE Disease Activity Index (SLEDAI), and Systemic Lupus Activity Measure (SLAM) [14, 15], reveals that a majority of organ activities are indicative of inflammatory responses. Many organ manifestations explicitly reflect inflammation, as evidenced by terms ending in "-itis" or the use of the descriptor "inflammatory." However, some symptoms, such as lupus-related skin rashes and mucosal ulcers, do not carry these specific nomenclatures. Consequently, most organ-related symptoms can be attributed to immune complex deposition and the resulting inflammation. Noteworthy exceptions to this inflammatory phenotype in SLE manifestations include cytopenias (such as leukopenia, thrombocytopenia, and hemolytic anemia), thrombotic events associated with secondary anti-phospholipid syndrome (APS), and certain neuropsychiatric symptoms, which are directly mediated by autoantibodies.

In the context of SLE activity scores, various inflammatory organ manifestations are recognized, including active rashes, mucosal ulcers, vasculitis, arthritis, and pleuritis, among others. Additionally, certain laboratory parameters indicative of inflammation, such as increased erythrocyte sedimentation rate (ESR) and the presence of urinary casts, are also incorporated into these validated activity indices. While complement consumption serves as a marker of immune complex deposition, it does not directly reflect inflammation; the ESR, however, relates to both autoimmunity and inflammation. Therefore, lupus activity, as assessed by these validated instruments, integrates the direct effects of autoantibodies along with indicators of autoimmunity, immune complex deposition, and clinical signs of organ inflammation. Ultimately, the substantial inflammatory component associated with SLE activity means that scores derived from these indices generally correlate closely with inflammatory activity.

Erythrocyte Sedimentation Rate (ESR) and Its Contributors

The erythrocyte sedimentation rate (ESR) is a well-established indicator that is frequently elevated in cases of active systemic lupus erythematosus (SLE). Consequently, it is logical that an increased ESR is incorporated into three out of five validated SLE activity scores [16]. In general, the factors contributing to elevated ESR can be attributed to alterations in serum proteins or erythrocyte characteristics. The former category typically encompasses conditions such as hypergammaglobulinemia, monoclonal gammopathy, and heightened fibrinogen levels, while the latter primarily reflects reductions in erythrocyte count and size. Notably, some of the factors accelerating the ESR are inflammatory in nature, while others are not. Therefore, to fully understand the inflammatory contribution to increased ESR, it is essential to examine all relevant components.

Protein Contributions to Increased ESR

Although oligoclonal and monoclonal gammopathies can occur, they are not prevalent among SLE patients and are not directly associated with the disease. In contrast, polyclonal hypergammaglobulinemia is frequently observed in SLE [16], aligning with the autoimmune characteristics of the disorder. This hypergammaglobulinemia indicates heightened activity of B cells and plasma cells, reflecting autoimmunity rather than inflammation. While interleukin-6 (IL-6) is an exception, stimulating B cell activity, most pro-inflammatory cytokines tend to limit rather than enhance the production of polyclonal antibodies. Fibrinogen serves as another protein of interest in the context of inflammatory disease, as it is often elevated during inflammation as part of the acute phase response. However, unlike in other inflammatory disorders, elevations of fibrinogen in SLE are generally mild [17]. Furthermore, fibrinogen levels do not appear to correlate with IL-6 levels in lupus-related inflammation [18]. Although low fibrinogen levels can arise from intravascular activation of the coagulation cascade, this phenomenon does not contribute to an increased ESR. Thus, fibrinogen is unlikely to be a significant contributor to elevated ESR levels in active SLE.

Conversely, plasma albumin has an inverse effect on ESR levels. Adequate albumin levels typically lower the ESR, while diminished production results in an elevated rate. Research has demonstrated that plasma albumin levels are significantly lower in individuals with SLE compared to healthy individuals, and in those with active SLE versus inactive disease [19]. Inflammation can negatively impact albumin synthesis in the liver during the acute phase response. Additionally, decreased appetite, influenced by elevated tumor necrosis factor (TNF) levels, may also contribute to reduced albumin production. These mechanisms may be relevant in the context of active SLE. However, renal loss of albumin due to damaged glomeruli likely represents the most critical factor leading to decreased serum albumin levels, particularly in patients with lupus nephritis [19]. Thus, the impact of reduced albumin on ESR serves as a notable inflammatory component.

Anemia

Anemia constitutes another significant inflammatory contributor to the ESR. Low hemoglobin and erythrocyte levels are commonly observed in patients with active lupus [20]. While hemolytic anemia is a hallmark of SLE, accounting for 4 points in the new EULAR/ACR 2019 criteria [3], its prevalence in SLE is relatively low [5]. As previously mentioned, hemolytic anemia is classified as a direct autoimmune manifestation resulting from antibodies targeting erythrocytes, rather than as an indicator of inflammation. In fact, the anemia often observed in SLE patients is primarily due to chronic disease processes [20]. This condition is typically linked to elevated interleukin-6 (IL-6) levels, which in turn increase hepcidin levels [21, 22, 23]. Although a direct correlation based on serum levels has not been established in SLE [24], a larger study in rheumatoid arthritis (RA) suggested a clear relationship in that context [25, 26, 27]. Nevertheless, an association between increased ferritin levels—another component of the acute phase response—and disease activity has been documented in SLE [28]. Additionally, it is plausible that elevated interferon levels, observed in active SLE, contribute to the development of anemia [29, 30]. Collectively, these factors may explain the association between anemia and SLE disease activity [31]. Low hemoglobin levels are also predictive of renal flares [24], likely reflecting disease activity as previously discussed. However, renal involvement may additionally result in decreased erythropoietin levels, which is almost certainly an independent contributor to anemia in SLE patients with renal damage and is primarily linked to tissue damage rather than disease activity. Given that many SLE patients are young females, hypochromic anemia due to iron deficiency is expected to be prevalent, which has been substantiated in research [20]. Iron deficiency has been shown to significantly reduce hepcidin levels [25], potentially complicating its relationship with IL-6.

Routine Serum/Plasma Markers of Inflammation
C-Reactive Protein:

C-reactive protein (CRP) serves as the primary biomarker for inflammation; however, in patients with systemic lupus erythematosus (SLE), CRP is more indicative of severe infections. Consequently, it is pertinent to examine the specific role of CRP in SLE. CRP is primarily influenced by interleukin-6 (IL-6) [32], which is elevated in individuals with active SLE [33, 34]. Notably, CRP levels are frequently not entirely within the normal range in active SLE cases [35, 36]. Elevated CRP concentrations are commonly associated with active serositis [37], arthritis [38], or myositis [39]. In contrast, in most other clinical scenarios, CRP levels in active SLE typically remain below 60 mg/L (6 mg/dL) [35]. When levels exceed these thresholds, the likelihood of severe infections increases significantly. For instance, CRP levels of 150 mg/L (15 mg/dL) suggest a high probability of infection, while levels at or below 20 mg/L (2 mg/dL) render infection unlikely [39]. This distinction is clinically significant, given that severe infections represent a major mortality risk for individuals with SLE [40, 41, 42].

Interestingly, while CRP levels tend to be elevated in active SLE compared to inactive cases, the reverse is observed during infections in SLE patients [36]. Specifically, those with severe infections tend to exhibit lower CRP levels when

their SLE is active, as opposed to when it is inactive [36]. This trend could be attributed to immunosuppression; however, such a phenomenon appears to be specific to SLE and potentially other connective tissue diseases, rather than observed in conditions such as ANCA-associated vasculitis or giant cell arteritis. Therefore, it is more plausible that SLE activity influences CRP production. One hypothesis suggests that type I interferons may have an inhibitory effect on IL-6 signaling [43, 44], consistent with findings that a significant proportion of patients with active SLE present an interferon signature [45, 46]. Given the increase in erythrocyte sedimentation rate (ESR) in active SLE, while CRP levels do not reach the same degree, it is not surprising that the ESR-to-CRP ratio is considerably higher in active SLE than in SLE with concurrent infections [47]. Conversely, the CRP-to-ESR ratio serves as an even more reliable predictor of severe infection than CRP levels alone [39].

Procalcitonin

Unlike CRP, procalcitonin (PCT) is primarily utilized as a marker for severe bacterial infections, including septicemia or pneumonia [48]. Although PCT lacks complete specificity and may be elevated in certain hematological conditions absent of infection, patients with active SLE can also exhibit increased PCT levels [36]. However, such elevations are typically mild, with levels exceeding 0.5 ng/mL indicating a likely infection [49]. Thus, PCT is not an effective biomarker for assessing SLE disease activity but can indicate a significant infection when CRP levels are also notably elevated. PCT may be particularly useful for differentiating between SLE with active pleuritis and concurrent infection, as PCT does not usually rise in SLE serositis, contrasting with CRP levels [49].

Complement Proteins

The evaluation of complement system components is a well-established practice in assessing disease activity [14]. Indeed, diminished complement levels are characteristic of SLE and have been incorporated into the SLICC classification criteria [50] as well as the more recent EULAR/ACR classification criteria [3, 4]. While the total (lytic) complement test, measured by CH50 (or CH100), was one of the first established tests, the direct assessment of complement proteins C3 and C4 is now the most commonly employed method. Genetic deficiencies in the upper complement components, such as C1q, C1r, C1s, or C4, predispose individuals to SLE [2, 51]. This predisposition likely stems from impaired clearance of apoptotic cells, leading to a scenario where these non-inflammatory dead cells begin to resemble other dead cells, inciting an immune response over time [52, 53]. Recent studies suggest that C1q also downregulates CD8 positive T cells through effects on mitochondrial metabolism [54]. C4 deficiency is relatively common in SLE, and routine measurements of C4 are often not beneficial in these patients. However, in the majority of SLE patients, both C3 and C4 complement levels can be monitored to evaluate immune complex disease. The classical pathway of complement activation begins with the binding of immune complexes to C1q, which subsequently recruits C1r and C1s. During this process, complement components C4, C2, and C3 are sequentially cleaved, with the larger C4b and C3b (as well as C2a) components remaining in the active complex, while

the smaller C4a and C3a, termed anaphylatoxins (alongside C5a), exhibit chemotactic properties.

Current assays predominantly measure total levels of C3 and C4. As these proteins are cleaved throughout the complement cascade, their overall levels tend to decline. However, since complement proteins are also part of the acute phase response, their levels can increase during inflammation. In the context of infection, maintaining sufficient complement protein levels is essential for pathogen clearance. Consequently, while inflammation elevates these proteins, immune complex disease can deplete complement levels [55], resulting in C3 and C4 levels (and CH50) being influenced by both processes. In active SLE, C3 and C4 levels are often reduced [56], indicating that the direct effects of immune complex-mediated complement activation, reflective of the autoimmune component, overshadow the inflammatory response. Novel tests detecting split products may provide even greater specificity for the autoimmune aspect, removing the influence of the acute phase response. Hence, while complement activity exists at the intersection of autoimmunity and inflammation, the assessment of complement components is fundamentally linked to immunological factors rather than solely inflammatory activity.

S100 Proteins:

S100 proteins, classified as alarmins, are primarily derived from monocytes, macrophages, or neutrophils and are recognized by Toll-like receptor 4 (TLR4) [57]. This interaction induces inflammatory responses in immune cells. In rheumatology, S100 proteins have gained attention, particularly concerning autoinflammatory diseases in pediatric populations [58]. The calcium-binding proteins S100A8 and S100A9 are the most prevalent among this family and have been observed to be elevated in patients with active systemic lupus erythematosus (SLE) compared to those with inactive disease, with levels decreasing following immunomodulatory therapy [59][60][61]. Notably, while S100A8/A9 proteins correlate with clinical disease activity, as well as anti-dsDNA antibodies and active nephritis, they exhibit a negative correlation with skin manifestations of the disease [60]. Given that type I interferons are likely pivotal in SLE-related skin conditions [62], it can be posited that the response of S100A8/A9 may be downregulated by interferons, akin to the relationship observed with C-reactive protein (CRP) [57]. Furthermore, S100A8/A9 have been associated with active disease and cardiovascular risks [63]. Despite their pathophysiological relevance, these proteins may not serve as ideal markers for assessing overall inflammatory disease activity. Conversely, S100A12 shows promise as a more reliable marker. It displays one of the most significant disparities between SLE patients and healthy individuals [64], and demonstrates a stronger correlation with disease activity compared to S100A8/A9 [65][66]. These findings position S100A12 as a compelling candidate for evaluating inflammatory disease activity in SLE.

Cytokines and Chemokines:

Beyond the aforementioned routine markers, various cytokines are closely linked to SLE activity, including type I interferons, particularly IFNα, IL-6, IL-10, IL-15,

IL-18, BAFF/BLyS, and TNF [12][19][33][46][67][68][69][70][71][72]. While IFNα is predominantly secreted by plasmacytoid dendritic cells (pDC) [73], the other cytokines primarily arise from monocytes and macrophages. In contrast to these, T-cell cytokines, such as IFNγ, typically act locally and are often present in insufficient quantities for measurement. Among the cytokines elevated in SLE, IL-10, IL-15, and BAFF/BLyS predominantly fulfill immunoregulatory roles rather than purely inflammatory functions.

IL-18 and IL-18 Binding Protein (IL-18BP):

IL-18 is a pro-inflammatory cytokine that signals through NFκB and MAP kinases, known for inducing IFNγ production, which is elevated in various autoimmune diseases [88][89][90]. Its levels are significantly increased in active systemic lupus erythematosus (SLE) [67][70][89][91][92] and in patients with lupus nephritis [93][94][95]. IL-18 correlates directly with SLE disease activity [67][70][91][96], making it a potential inflammatory marker. Alongside IL-18, IL-18BP is also upregulated in SLE [91][92][95], particularly associated with active nephritis [92][95]. Interestingly, both bound IL-18BP and free IL-18 are increased [91]. While IL-18BP serves to bind IL-18, the transcription of IL-18BP is influenced by IFNγ, which is downstream of IL-18, thus forming a negative feedback loop. This interplay suggests that both could function as interdependent markers of inflammatory disease activity, although this remains more of a theoretical concept than a clinically established parameter at present.

TNF and Soluble TNF Receptor 2 (sTNFR2):

TNF is a potent pro-inflammatory cytokine that is notably elevated in active SLE and shows a strong correlation with disease activity [12][33]. Thus, it may still represent the most reliable inflammatory marker in this category [19]. TNF is induced by immune complexes [9] and is highly expressed in inflammatory organ diseases associated with SLE, such as lupus nephritis. Despite its possible negative immunoregulatory effects [98][99], TNF blockade using therapies like infliximab [100][101] and etanercept [102] has demonstrated efficacy. Although TNF measurement can be performed using various assays, there is considerable variability between these assays, and their reliability for routine use is questionable, likely due to the complexities of TNF kinetics. Notably, sTNFR2 levels, which correlate with both TNF and disease activity [33][103][104][105], might provide a more stable and feasible parameter for monitoring. While not yet established for routine assessment, measuring sTNFR2 could be a promising candidate based on existing scientific data.

Chemokines:

Serum or plasma chemokines, like many cytokines, can be easily quantified using ELISA technology. While chemokines are typically produced in response to cytokines and serve as indirect markers of inflammation, studies have shown associations with disease activity. Notably, CCL2/MCP-1, CXCL10/IP-10, and CCL19 are recognized as interferon-inducible genes, which has led to a composite score for estimating interferon activity linked to SLE disease activity [106][107]. Previous research has identified increased levels of CCL2 [96][108][109] and

CXCL10 [96][110] in patients with active SLE, illustrating the role of these chemokines in reflecting the interferon influence within the disease. Additionally, chemokines such as CCL-11 [109], CXCL13 [111], and CXCL16 [112] have also been associated with disease activity, while serum levels of IL-8 [96], CCL17 [113], CXCL16 [114], and CX3CL1 [109] correlate with active lupus nephritis.

Urinary Markers of Inflammation:

Monitoring renal involvement is crucial in SLE, as lupus nephritis is the most frequent and dangerous manifestation of the disease. Moreover, lupus glomerulonephritis often presents asymptomatically, making laboratory monitoring essential for detecting new renal involvement and assessing nephritis activity during therapy.

Urinary Protein and Urinary Albumin:

Proteinuria is a classical marker of SLE kidney disease, as damage to the glomeruli leads to varying degrees of protein loss, characteristic of immune complex nephritis. SLE activity scores rely heavily on proteinuria to evaluate nephritis activity. A reduction of proteinuria to less than 700–800 mg per day is linked to a favorable renal prognosis [115]. Consequently, quantifying urinary protein is vital for monitoring lupus nephritis [116]. To simplify monitoring, spot urine protein/creatinine ratios have largely replaced 24-hour urine measurements [117]. In lupus nephritis, proteinuria primarily consists of albuminuria, making it a straightforward yet effective marker for detecting nephritis activity [118][119]. Despite its clinical significance, proteinuria and albuminuria have a notable limitation: they cannot reliably differentiate between ongoing inflammation and damage. Renal injury can also produce substantial amounts of urinary protein. Consequently, residual inflammatory activity and treatable proteinuria may be underestimated [100]. Moreover, indirect methods of estimating lupus nephritis activity, such as serum complement and autoantibody levels, lack reliability. Therefore, there is a need for additional, more precise urinary markers.

Urinary Cytokines and Chemokines:

Examining further urinary proteins directly associated with inflammation may provide advantages over measuring total proteinuria or albuminuria. Candidates include cytokines and chemokines, easily measurable via ELISA. The pro-inflammatory cytokine IL-6 has been found elevated in the urine of patients with active lupus nephritis [120], alongside IL-10 [121], which may have a more autoimmune role than a purely immunoregulatory function in human SLE. Increased urinary levels of IL-18 have also been observed in lupus nephritis patients [92]. However, the evidence surrounding urinary cytokines is only partially convincing, potentially due to issues of stability and dilution. Urinary chemokines, however, may present a more promising option. For instance, CC chemokine ligands CCL2, CCL4, CCL5, and CCL8 are increased in the urine of patients with active lupus nephritis compared to those with inactive disease, as are CXC chemokine ligands CXCL9/MIG, CXCL10, and CXCL16 [120][122].

Cells in the Urine:

Analyzing urinary sediment has long been a critical aspect of diagnosing lupus nephritis and estimating its activity. Indeed, lupus activity scores incorporate leukocyturia, hematuria, and casts as indicators of renal activity. Dysmorphic erythrocytes, damaged as they pass through capillaries, and cellular casts are specific markers of active nephritis. However, accurate analysis of urinary sediment requires significant expertise, and glucocorticoids can quickly obscure abnormalities. Additionally, leukocyturia can occur in cases of simple cystitis. Consequently, there is a trend to exclude sediment analysis from definitions of complete renal remission in scientific studies [123]. While this does not eliminate the utility of urinary erythrocytes for early detection of new lupus nephritis, it limits the use of urinary sediment for ongoing monitoring during treatment.

Innovative approaches utilizing flow cytometry have been employed for analyzing urinary leukocytes as well as those in peripheral blood. Urinary leukocytes can partially reflect the glomerular leukocyte population. Specifically, urinary T cells have been demonstrated to assist in differentiating between active and inactive lupus nephritis [124][125][126][127] and evaluating these cells may serve as a routine parameter in monitoring lupus nephritis. Such lymphocytes would offer more direct evidence of active nephritis compared to merely measuring increased chemokines that promote their influx into the kidneys.

Conclusion

In conclusion, the laboratory assessment of systemic lupus erythematosus (SLE) plays a crucial role in diagnosing and managing this complex autoimmune disorder. The pathogenesis of SLE is characterized by the production of autoantibodies and immune complexes, leading to a range of inflammatory processes that affect various organs. Recent classification criteria, including those set forth by the European League Against Rheumatism (EULAR) and the American College of Rheumatology (ACR), have highlighted the importance of recognizing inflammatory manifestations as central to the disease's activity. The review illustrates that serological markers, particularly the erythrocyte sedimentation rate (ESR) and pro-inflammatory cytokines, serve as reliable indicators of SLE activity. The elevation of ESR reflects the inflammatory status and correlates with various organ involvements, emphasizing the need for continuous monitoring. Although C-reactive protein (CRP) is a standard marker for inflammation, its utility in SLE is nuanced, as elevated levels often signify infections rather than disease activity. Moreover, the complex interplay between immune complexes, autoantibodies, and inflammatory pathways underpins the diverse clinical manifestations of SLE. By understanding how immune complex deposition triggers inflammation, healthcare providers can better anticipate potential flares and complications associated with the disease. Overall, integrating laboratory assessments that prioritize inflammatory markers with clinical evaluations will enhance the diagnosis and management of SLE. As ongoing research elucidates the intricate mechanisms involved in SLE's pathophysiology, future diagnostic criteria may evolve to further refine the identification and classification of the disease, ultimately leading to improved patient outcomes.

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