Systemic Lupus Erythematosus – A Review


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ABSTRACT

Systemic lupus erythematosus (SLE) is an autoimmune disease. It is distinguished by the presence of autoantibodies that are directed against nuclear antigens. Because it affects multiple systems, patients might appear in a wide variety of ways. The complicated aetiology of this illness is reflected in the clinical variability of the condition, which emphasises the significance of genetic determinants and individual vulnerability to environmental influences. Every organ in the body is susceptible to SLE. Rash, arthritis, and exhaustion are the most typical symptoms. SLE can induce nephritis, neurological issues, anaemia, and thrombocytopenia at the more severe end of the spectrum. Substantial titres are acknowledged to be of 1:80 or greater. Relapsing and remitting SLE has three therapeutic goals: managing acute episodes of potentially fatal illness, reducing the likelihood of flares during times of relative stability, and managing the less serious but frequently incapacitating day-to-day symptoms. Corticosteroids and immunosuppressive therapies are typically reserved for major organ involvement; anti-CD20 monoclonal antibody is now used in patients with severe disease who have not responded to conventional treatments. Despite major advancements in prognosis brought about by the use of corticosteroids and immunosuppressive medications, SLE still has a sizable effect on the mortality and morbidity of people affected.

Key words: Systemic lupus erythematosus, lupus.

DEFINITION

Autoimmune in origin, systemic lupus erythematosus (SLE) is a clinically heterogeneous disease characterised by the development of autoantibodies against nuclear antigens. It is a multi-system disease by definition, and patients can present in a wide variety of ways. As a part of the effort to maintain the patient population as homogeneous as feasible for research reasons, classification criteria have been devised. The American College of Rheumatology (ACR) publishes these criteria (Table 1), which combine clinical signs and symptoms with abnormalities found in blood tests like a positive anti-nuclear antibody or thrombocytopenia. These criteria were revised in 1982 [1]. They were modified once more in 1997 [2] to reflect a better understanding of the role of antiphospholipid antibodies in patients with SLE.

Table 1: Diagnostic criteria of SLE. Adapted from Tan et al, 1982 [1]. A person is said to have SLE if he/she meets any 4 of these 11 Criteria simultaneously or in succession.

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<th>CRITERION</th>
<th>DEFINITION/EXAMPLES</th>
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<tr>
<td>1. Malar rash</td>
<td>Fixed erythema over the malar eminences, tending to spare the nasolabial folds</td>
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<td>2. Discoid rash</td>
<td>Erythematous raised patches, may scar</td>
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<td>3. Photosensitivity</td>
<td>Skin rash as a result of unusual reaction to sunlight</td>
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<td>4. Oral ulcers</td>
<td>Usually painless</td>
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<td>5. Arthritis</td>
<td>Non-erosive: Jaccoud’s arthropathy</td>
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<tr>
<td>6. Serositis</td>
<td>a) Pleuritis – pleuritic pain, pleural rub, pleural effusion</td>
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<tr>
<td></td>
<td>b) Pericarditis – ECG changes, rub, pericardial effusion</td>
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<tr>
<td>7. Renal disorder</td>
<td>a) Proteinuria (&gt; 3+ or 0.5 g/day) b) Cellular casts in urine</td>
</tr>
<tr>
<td>8. Anti-nuclear antibody</td>
<td>Exclude drug causes</td>
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EPIDEMIOLOGY
Women are up to 10 times more likely than men to have SLE, and women in childbearing years are disproportionately affected [3]. Reliable statistics on the frequency of SLE are few in the world. This issue is exacerbated by inconsistent case definitions and data gathering techniques, however it is obvious that ethnicity has an impact on the numbers. An estimate of the general prevalence puts it at roughly 1 per 1000. In the overall population, the prevalence was reported to be 27.7/100,000 in a research from Birmingham, UK, but it was approximately 9 times higher in Afro-Caribbean females [4]. According to data from a nationwide health survey in the USA, the prevalence of SLE, which is defined as having received a diagnosis of SLE from a doctor, was found to be 241/100,000 [5]. Considering that this may be an exaggeration, combining self-reporting with proof of a current prescription for anti-malarial, corticosteroids or more immunosuppressive drugs decreased this number to 53.6/100,000 [5].

AETIOLOGY
The complicated aetiopathogenesis of this disease mirrors the clinical variability of the condition. First twin studies suggested the significance of genetic variables. Comprehensive genome screening has revealed a number of intriguing candidate locations [7]. Disease may develop in those who are vulnerable as a result of a range of environmental factors, such as exposure to sunlight, medications, and infections, particularly those caused by the Epstein-Barr virus. Lupus flares can happen in different ways and at different periods, even within the same patient. The particular pathogenic mechanisms underlying SLE remain poorly known despite substantial research. It is generally believed that at least some of these autoantibodies, which are mostly directed against nuclear elements such nucleosomes, DNA, and histones, are raised in the majority of patients, either by precipitating as immune complexes in target organs or by cross-reacting with other functionally relevant substances, have a direct pathogenic role. These autoantibodies are present and persistent, indicating abnormalities in tolerance brought on by aberrant processing of autoantigens after apoptosis and aberrant T and B lymphocyte function.

DIFFERENTIAL DIAGNOSIS
The range of potential differential diagnoses varies depending on how each case is presented. The general clinical characteristics of widespread pain and exhaustion signify that fibromyalgia and other chronic pain syndromes may occasionally be suitable differential diagnoses. It is significant to remember that a patient may have both fibromyalgia and SLE.

A cluster of features will be present in several patients. Suggesting an autoimmune rheumatic disease, even when the precise diagnosis is not yet obvious from the initial presentation. A percentage of these “undifferentiated” people would later develop systemic sclerosis or other illnesses like full-blown SLE.

Several cancers that are pertinent to this age group, like lymphoma and leukaemia, can appear with a similar clinical presentation. Likewise, there are important overlap with how some illnesses, including bacterial endocarditis, HIV/AIDS, and tuberculosis, appear. Before beginning treatment for SLE, it is unquestionably essential to rule out an underlying infection given the immunosuppressive nature of the needed medications.

ORAL MANIFESTATION
SLE frequently involves the cardiovascular and haematological systems. SLE patients with positive anti-phospholipid antibodies were found in a meta-analysis published last year. Compared to individuals who did not have antiphospholipid antibodies, patients with antibodies had a greater probability of having thrombocytopenia (odd ratio 2.48, 95% confidence interval [CI] 2.10-2.93).

According to data from hospitalised US patients, SLE was linked to a higher prevalence of atherosclerotic cardiovascular disease than non-SLE patients (25.6% vs. 19.2%, respectively).

As the third most common cause of death in SLE, pulmonary arterial hypertension (PAH), a fatal cardiac consequence of the disease, has been identified. According to a nationwide cohort research, PAH was diagnosed in 2.13% of the 15,783 incident SLE patients, primarily (about 70%) in the first five years following the onset of the disease.

Overall 1-, 3-, and 5-year survival rates following PAH diagnosis were 87.7%, 76.8%, and 70.1%, respectively. Last year, many different risk factors for differentiating PAH from SLE were studied. Also, due to the systemic symptoms and disease activity, several researchers proposed an unique classification of SLE-PAH, the vasculitic subtype and vasculopathic subtype. The hope of precision medicine in SLE-PAH was highlighted by the potential treatment differences between the two separate clusters of patients.

LABORATORY DIAGNOSIS
More than 90% of SLE patients have anti-nuclear antibodies that are active (ANA). Substantial titres are considered to be ones that are at least 1:80. Even if it is sensitive, ANA is not very specific for SLE. Several additional conditions, such as systemic sclerosis, polymyositis, and other chronic infections, are also associated with a positive ANA test. Obtainable nuclear antigens should be checked in all cases (ENA). Various ENAs are connected to various clinical presentations, such as secondary Sjogren’s syndrome and renal involvement for anti-Sm and anti-Ro, respectively.

Although this test is not frequently accessible in most regular labs, antibodies to double-stranded DNA (dsDNA) and more recently nucleosomes are more specific. Anti-dsDNA titres and SLE are also indicators of renal involvement. Serial testing is a good monitoring tool because the titres of these antibodies also fluctuate with disease activity. Generally, a disease flare is accompanied by a drop in complement and lymphocyte count, as well as an increase in dsDNA antibody titre and erythrocyte
sodium and intramuscular injections of depot corticosteroids are the main contributing factor. Today's patients with less than five years of disease, while reducing others' likelihood of flare-ups during times of comparatively stable conditions and managing the less serious but frequently incapacitating day-to-day symptoms. The majority of medications are still broadly immunosuppressive in action due to our inadequate knowledge of the particular pathogenesis of SLE, which increases the risk of side effects.

Hydroxychloroquine, at the milder end of the spectrum, is frequently utilised. This works well for weariness, joint discomfort, and skin conditions. For arthralgia and arthritis, non-steroidal anti-inflammatory medications are also helpful, while methotrexate may be needed for more aggressive treatment. Although immunosuppressive treatments and high dose intravenous steroids are sometimes used for moderate illness, low dose oral steroids and intramuscular injections of depot Steroids are typically only used when major organs are involved.

Similar to this, immunosuppressive medications like azathioprine and cyclophosphamide are occasionally used for serositis and haemorrhagic Illness of the womb. Moreover, immunoglobulin may be needed in cases of persistent autoimmune thrombocytopenia.

PROGNOSIS

Despite major improvements in treatment over the past ten years, there is still a high risk of mortality and long-term morbidity associated with SLE. One thousand patients in a European research, those who presented with nephropathy had a lower year survival probability of 88% than those with SLE (92% overall) [3]. While ranging significantly from 18 to 81 years, the average age at death was 44.

The length of the disease influences the death’s cause. In one cohort [22], renal lupus caused the majority of mortality in patients with less than five years of disease, while the group that passed away later in the disease’s course had vascular disease as the main contributing factor.

References

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