Original Research Article

A study of clinical profile and assessment of disease activity in systemic lupus erythematosus patients

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Abstract

Introduction: Systemic Lupus Erythematosus (SLE) is an autoimmune disease in which organs, tissues, and cells undergo damage mediated by tissue-binding autoantibodies and immune complexes. SLE primarily occurs in young women in their twenties. The disease expression is greatly influenced by the combined effect of genetic, environmental, demographic and geographical factors. Genetic factor superimposed on certain environmental factors plays a very pivotal role in manifesting abnormal immunological response. There is a wide variation in the natural history of systemic lupus erythematosus among different ethnic and geographical groups. Severity ranges from a mild disease with rash and arthritis to a devastating illness with renal failure and central nervous system involvement. The purpose of this study is to delineate the clinical pattern and disease course in patients with SLE at our centre and to compare it with National data on lupus patients.

Aim and objectives: To describe the clinical profile in systemic lupus erythematosus patients and to assess the disease activity of SLE with SLEDAI criteria in SLE patients.

Materials and methods: This study was an observational study conducted in 50 patients of Systemic Lupus Erythematosus who were admitted in Department Of Medicine, Gandhi Hospital, Telangana during the period from January 2017 – June 2018.

Results: The age of the patients ranged from 16 to 48 years with a mean of 26.52 years. Diagnosis was based on the SLICC criteria for the diagnosis of SLE. All the patients satisfied at least 4 criteria needed for diagnosis of SLE as per the recommendations.
Conclusion:

Key words

Neurosonogram, Cranial, Abnormalities, Neonates.

Introduction

The first known medical use of the term lupus appeared in the description of the healing of Eraclius, Bishop of Liege, at the shrine of St Martin in Tours, 916AD, by Herbernus of Tours [1, 2]. The term lupus, Latin for wolf, was used in the 18th century to describe a variety of skin conditions [2]. Systemic Lupus Erythematosus (SLE) is a chronic, usually life-long, potentially fatal autoimmune disease characterized by unpredictable exacerbations and remissions with protean clinical manifestations. In SLE there is a predilection for clinical involvement of the joints, skin, kidney, brain, serosa, lung, heart and gastrointestinal tract. It is an autoimmune disease characterized by immune [3] dysregulation resulting in the production of antinuclear antibodies (ANA) and other autoantibodies, generation of circulating immune complexes, and activation of the complement system. The first case of systemic lupus erythematosus (SLE) was reported from India in 1965 followed by two more case reports and further, a series of eight cases, till 1969. Prevalence of systemic lupus erythematosus (SLE) was studied in the northern Indian population. The reported prevalence of SLE ranges from 14 to 60 per 100,000 9. The main causes of death were irreversible renal damage, infections and neurological involvement. The incidence of lupus is dramatically higher in women than men. The peak incidence is between the ages of 15- 45 years, the childbearing years, when the female – to – male ratio is about 12: 1. In pediatric and older patients the female- to – male ratio is closer to 2:1.

Pathogenesis

SLE is the prototypic immune complex disease, characterized by excessive autoantibody production, immune complex formation, complement activation and immunologically mediated tissue injury. B cell and T cell abnormalities, including defects in B cell tolerance, autoantigen specific T helper cells and intrinsic T cell functional and biochemical irregularities, result in the production of autoantibodies [4]. Production of at least some of these autoantibodies is driven by increased levels of nucleosomes, perhaps reflecting accelerated apoptosis of lymphocytes, and the consequent abnormal cytokine concentrations. The result of these abnormalities is an array of autoantibodies and circulating immune complexes along with deficient phagocytic mononuclear function. Genetic susceptibility to lupus is strongly supported by studies showing linkage, association to familial aggregation, and twin concordance. The known genetic associations implicate HLA-DR and DQ Loci in the class II MHC. The concordance rate in monozygotic twins is between 30 to 50% [12]. SLE is characterized by the presence of high titre auto antibodies to a diverse group of autoantigens. Recently it was shown that 88% of patients had autoantibodies for an average of 3.3 years prior to the diagnosis [5, 6]. Of the characteristic panel of autoantibodies, antinuclear, anti- Ro, anti- La, and anti-phospholipid appear first followed by anti-Sm and anti-RNP. These autoantibodies are a feature of antigen- driven T cell- dependent immune response [7, 8].

Criteria

SLE involves all the organ systems. Influenced by the Jones criteria for acute rheumatic Fever the American College of Rheumatology published the preliminary criteria for the diagnosis of SLE in 1971. The criteria were revised in 1982 and 11 were listed. The 8 presence of 4 criteria is required for making a diagnosis of SLE, a disease with such protean manifestations and variable course. The 1997 modification of the 1982 revised ACR criteria for SLE help distinguish patients with SLE from patients with other connective tissue diseases.

The 1997 revised ACR criteria for the classification of SLE:

1. Malar rash - Fixed erythema, flat or raised, over the malar eminences, sparing the nasolabial folds
2. Discoid rash - Erythematous raised patches with adherent keratotic scaling and follicular plugging: atrophic scarring may occur in older lesions.
3. Photosensitivity - Skin rash as a results of unusual reaction to sunlight, by patient history or physician observation.
4. Oral ulcers – Oral or nasopharyngeal ulceration, usually painless, observed by a physician
5. Non-erosive arthritis - Involving two or more peripheral joints, characterized tenderness, swelling or effusion
6. Pleuritis or pericarditis - Pleuritis - convincing history of pleuritic pain or rub heard by a physician or evidence of pleural effusion. Pericarditis - documented by electrocardiogram or rub or evidence of pericardial effusion.
7. Renal disorder: (a) Persistent proteinuria >0.5g/day or >3+ if not performed or (b) Cellular casts - may be red cell, hemoglobin, granular, tubular or mixed.
8. Seizures or psychosis - Seizures - in the absence of offending drugs or known metabolic derangement: e.g. uremia, ketoacidosis or electrolyte imbalance.
9. Psychosis - in the absence of offending drugs or Known metabolic derangement: e.g. uremia, ketoacidosis or electrolyte imbalance.
10. Hematologic disorder - (a) Hemolytic anemia with reticulocytosis or (b) Leukopenia - less than 4000/mm^3 on two occasions or (c) Lymphopenia - less than 1500/mm^3 on two occasions or (d) Thrombocytopenia - less than 100 000/mm^3 in the absence of offending drugs.
11. Immunologic disorder - (a) Anti-DNA: antibody to native DNA in abnormal titer or (b) Anti-Sm: presence of antibody to Sm nuclear antigen or (c) Positive finding of anti-phospholipid antibodies based on: (1) an abnormal serum concentration of lgG or lgM anti-cardiolipin antibodies (2) a positive test for lupus anticoagulant using a standard method or (3) a false-positive test for at least 6 months and confirmed by Treponema pallidum immobilization or fluorescent treponomal antibody absorption test.
12. Positive ANA - An abnormal titer of ANA by immunofluorescence or an equivalent assay.

Assessment of disease activity

Because no single measure can describe status in all SLE patients, standardized indices for assessing SLE disease activity have been created. In addition to the Physicians "Global Assessment (an estimate of activity rated on a 0 to 3 visual analog scale), the most common measures used include the SLE Disease Activity Index (SLEDAI), the British Isles Lupus Assessment Group (BILAG), the Systemic Lupus Activity Measure (SLAM), the Lupus Activity Index (LAI) 29,30 , and the European Consensus Lupus Activity Measurement (ECLAM). All of these indices are valid, reliable, and comparable. The SLEDAI is the easiest assessment tool to use [9].

Materials and methods

This study was an observational study conducted in 50 patients of Systemic Lupus Erythematosis

who were admitted in Department of Medicine, Gandhi Hospital, Telangana during the period from January 2017 – June 2018. All the patients of Systemic Lupus Erythematosus who presented with varying signs and symptoms were included in this study and analyzed clinically and laboratory wise. A detailed history was taken with particular emphasis on various organ systems Involvement. This was followed by detailed clinical examination. An elaborate laboratory examination was done which include complete hemogram, blood urea, serum creatinine, serum electrolytes, complete urine examination, 24 hours urinary protein, ESR, liver function tests, C3, C4 levels, Antinuclear antibody, anti-ds DNA, anti-sm, anti-cardiolipin antibody, X-ray chest, ECG, Echocardiogram, USG Abdomen, Renal biopsy, CT and MRI when required. Disease activity was calculated for each patient according to SLEDAI criteria [10].

Results

The age of the patients ranged from 16 to 48 years with mean of 26.52 years and median age of patients 24 years.

The most common presenting complaint was fever (68%) followed by arthritis (56%), oral ulcers (56%), alopecia (50%), malar rash (44%), photosensitivity (28%), myalgias (20%). 12% of the patients presented with seizures, 8% had psychosis and 6% presented with stroke. Out of 50 patients, 36 (72%) patients were married and 14 (28%) unmarried. 3 (6%) of them had history of recurrent abortions. Diagnosis was based on the SLICC criteria for the diagnosis of SLE. All the patients satisfied at least 4 criteria needed for diagnosis of SLE as per the recommendations. Acute cutaneous lupus 44%, chronic cutaneous lupus 36%, oral ulcers 56%, non-scarring alopecia 50%, Synovitis 56%, Serositis 30%, Renal 42%, Neurological 26%, hemolytic anemia 4%, leucopenia/ lymphopenia 30%, Thrombocytopenia 34%, ANA 100%, Anti-dsDNA 96%, Anti-Sm 14%, Anti-Phospholipid antibody 18%, low complement 40%. ANA was positive in all patients studied. The pattern of immunoflourescence test was Homogenous 66%, Speckled 28%, Rim pattern 4%, Nucleolar 2%. Hematological abnormalities were detected in 34 (68%) of the patients. The various abnormalities included are anemia, leucopenia, lymphopenia, thrombocytopenia and AIHA. Arthritis was the commonest initial manifestation and was seen in 28 (56%) patients. Symmetrical, non-erosive, non-deforming polyarthritis was present in 21 (42%) patients. Oligoarthritis was present in 6 (12%) patients and monoarthritis in 1 (2%) patients. Generalized myalgia and myositis were present in 10 (20%) each respectively. Manifestations noted were photosensitivity, malar rash, discoid rash, alopecia, oral ulcers, vasculitic rash, Raynaud's phenomenon. 3(6%) patients had gangrene of toes.

Renal involvement was seen in 21(42%) patients. Renal biopsy was done in 10 patients. Diffuse proliferative glomerulonephritis (WHO class IV) was the most commonly seen histological pattern, seen in 8(16%) patients. One patient had focal and segmental glomerulonephritis (WHO class III) and one had membranous glomerulonephritis (WHO class V). Neuropsychiatric manifestations like seizures, psychosis, neuropathy and CVA were seen in 13 (26%) patients.

Pleuro-pulmonary involvement was seen in 6 (12%) patients. All of them had pleural effusion. Out of 50, 3(6%) patients had pulmonary tuberculosis. Out of 50, 9(18%) patients had pericardial effusion without any signs of tamponade. One patient had both mitral and aortic regurgitation.

Two patients had pancreatitis, two had upper gastro intestinal bleed due to gastritis which was probably steroid induced. All patients were ANA positive. Anti -dsDNA was positive in 48 patients (**Table – 1**).

Out of 50 patients, low C3 was found in 20 (40%) patients, low C4 in 16 (32%) patients. Both C3 and C4 were low in 18(36%) patients.

Table – 1: Immunological profile.

Immunological profile	No. of patients	%
ANA	50	100
Anti-ds DNA Ab	48	96
Anti-sm Ab	7	14
APLA	9	18
Anti Ro Ab	1	2

Treatment

Low dose glucocorticoids were initiated in all patients who presented with constitutional symptoms with minor systemic involvement. Hydroxychloroquin/ chloroquine was given to all patients with skin and musculoskeletal involvement High dose glucocorticoids were initiated in 10 (20%) patients. 4 patients with vasculitis, 3 patients with lupus nephritis, 2 patients with severe arthritis and 1 patient with mononeuritis multiplex received high dose steroids. Cyclophosphamide was administered in 4(8%) patients. All of them had renal involvement. One had mononeuritis multiplex. 52 Azathioprine was given to 4 (8%) patients. Two of them had autoimmune hemolytic anemia and the other two had myositis and neuropathy. Methotrexate was given to 7 (14%) patients. 5 of them had lupus nephritis, one patient had rhupus and one patient had myositis. Mycophenolate mofetil was administered in two patients. Both of them had lupus nephritis.

Discussion

This was an observational study on 50 patients with systemic lupus erythematosus admitted in the Department of Medicine at Gandhi Hospital. There was a female preponderance with all the patients being females in this study. This finding has been similar to most of the studies which have shown a predominance of females in studies of SLE. Binoy, et al. reported an average female to male ratio of 19:1. Another Indian series by Malaviya, et al. [13] had a female to male ratio of 8:1. The increased frequency of SLE among females is thought to be due to hormonal effects. The mean age of the patients in this study was 26.52 years.

Mean duration of illness at diagnosis in 50 patients in this study was 10 months. In the study of Malaviya, et al. [13], median duration was 17 months and in study of R Saigal, et al. the median duration was 24 months.

Clinical features

The most common presenting symptom was fever, found in (68%) of the patients. This finding was similar to that documented by other studies. Paul BJ [12] has described an incidence of 50.6% for fever in a series of SLE patients. Wallace DJ [11, 14] has described an incidence of 84% in his series. In most of the patients, fever is related to the disease activity. The second most common clinical feature was arthritis and arthralgias, which was present in 56% of the patients in this study. In an analysis of 520 cases by Wallace DJ, 92% of patients had arthritis and arthralgias [14].

Analysing different series of patients from North India, South India, Eastern India and Western India describes an incidence of 57%, 68%, 75% and 76% respectively. Oral ulcers were present in 56% of the patients in this study. In a series of studies described by Wallace DJ [14], oral ulcers were present in 36% of cases. This study documented a higher incidence compared to western studies but the incidence is similar to that documented in studies from India. Malar rash was observed in 44% of the patients. This was similar to the series described by Wallace DJ [14], where an incidence of 10-61% was documented.

Photosensitivity was observed in 28% of the patients. Wallace described an incidence of 37% incidence among 464 patients in his study. Overall, the relative frequency of each of the major clinical features at presentation.

Diagnostic criteria

The commonest criterion satisfied was ANA positivity. It was seen in all the patients in this study. ANA positivity is reported to be positive in 90-95% of cases.

The most common pattern of immunoflourescence for ANA observed in this study was a homogenous pattern which was the most common pattern reported in literature.

Conclusion

This was an observational study done on 50 patients of SLE. Mean age of SLE in cases was 26.52 years. Highest incidence was found in age group of 21-30 years of age. The most common presenting complaint in this study was fever seen in 68%. The mean duration of illness prior to diagnosis was 10 months. Next most common presentation was arthritis and oral ulcers seen in 56%. Hematological manifestations were documented in 68%. Renal involvement was present in 42% of patients, proteinuria being the most common urinary abnormality. Lupus nephritis was the most common indication for high dose glucocorticoids and immunosuppressants. Neuropsychiatric manifestations were seen in 26% GIT involvement was seen in 16% ANA was positive in all patients. Anti-ds DNA were positive in 96%. Low complement levels were present in 40%. The SLEDAI score was above 5 in 98% of the patients and more than 10 in 62% of the patients and thus shows high disease activity. Two patients had a fatal outcome. Both of them had lupus nephritis.

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