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Original Research Article

Study of hematological profile of systemic lupus erythematosus

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ABSTRACT

Background: Hematological abnormalities are prevalent in systemic lupus erythematosus (SLE), with approximately 72% of patients experiencing anemia, primarily in the form of autoimmune hemolytic anemia. Other manifestations include leukopenia (32%), lymphopenia (54%), and thrombocytopenia (23%). This study aimed to further investigate these hematological manifestations, which may serve as presentations of SLE and might be overlooked if suspicion levels are low.
Methods: A descriptive observational study was conducted over 18 months at a Sir Ganga Ram hospital, a tertiary care centre. One hundred thirteen SLE cases, comprising newly diagnosed patients and previously diagnosed patients' records, were reviewed, with 13 cases excluded based on exclusion criteria. One hundred patients with hematological abnormalities and fulfilling ≥4 SLICC criteria for SLE diagnosis were included in the study.
Results: One hundred cases of SLE with hematological abnormalities (88 women, 12 men) were analyzed. At presentation, 83% (n=84) of patients displayed hematological manifestations. The most prevalent abnormality was anemia, present in 72% of the study group, with a mean hemoglobin level of 10.073 gm/dl. Additionally, leukopenia, lymphopenia, thrombocytopenia, and pancytopenia were observed in 32%, 54%, 23%, and 14% of cases, respectively. Neutropenia was detected in only 5% of cases.
Conclusions: Hematological manifestations are the most common presenting signs of SLE in North India. Anemia, with a multifactorial basis, is the most frequent hematological abnormality throughout the disease course. A high index of suspicion is crucial when evaluating cases of anemia in daily clinical practice.

Keywords: Anemia of chronic disease, Autoimmune hemolytic anemia, Iron deficiency anemia, Leukopenia, Systemic lupus erythematosus, Thrombocytopenia

INTRODUCTION

Systemic lupus erythematosus (SLE) is a chronic autoimmune inflammatory disease that has protean manifestations and follows a relapsing and remitting course. Over 80 percent of cases occur in women during their childbearing age.[1] SLE can affect almost any organ system; thus, its presentation and course are highly variable, ranging from indolent to fulminant. The classical presentation of a triad of fever, joint pain and rash in a woman of childbearing age should prompt investigation into the diagnosis of SLE.[2,3] Patients with SLE may initially present with constitutional, musculoskeletal, dermatologic, renal, neuropsychiatric, pulmonary, gastrointestinal, cardiac or hematological features.[4]

Patients may present with any of the following manifestations: constitutional (e.g., fatigue, fever, arthralgia, weight change; musculoskeletal (e.g., arthralgia, arthropathy, myalgia, frank arthritis, avascular necrosis); dermatologic (e.g., malar rash,

photosensitivity, discoid lupus); renal (e.g., acute or chronic renal failure, acute nephritic disease); neuropsychiatric (e.g., seizure, psychosis); pulmonary (e.g., pleurisy, pleural effusion, pneumonitis, pulmonary hypertension, interstitial lung disease); gastrointestinal (e.g., nausea, dyspepsia, abdominal pain); cardiac (e.g., pericarditis, myocarditis); hematologic (e.g., cytopenias such as leukopenia, lymphopenia, anemia, or thrombocytopenia).[4]

Hematologic manifestations in SLE

All the cellular elements of the blood and coagulation pathway can be affected in SLE patients. SLE is immunological disease, so hematological manifestations are expected to be more common than the other features, since antigens are more often present in blood and blood vessels than any other organ and in SLE auto antibodies are developed against any antigens and tissues.[5]

Sometimes, hematological abnormalities can be caused by the pathophysiology of SLE itself, but times they can be present in SLE due to some other etiology found in patients with SLE but not be a manifestation of SLE. It is important to distinguish hematological abnormalities as either manifestations of SLE, consequence of SLE treatment or as part of another blood cell dyscrasias.

Anemia is a common hematological abnormality in SLE. The most frequent cause of anemia in SLE is suppressed erythropoiesis from chronic inflammation (anemia of chronic disease) which is the most common form (60-80%).[6] Other causes are iron deficiency anemia, autoimmune haemolytic anemia and anemia due to blood loss.

Leukopenia in SLE may occur as a result of lymphopenia, neutropenia or a combination of both. The prevalence of lymphopenia in SLE ranges from 20 to 81% and its degree may correlate with disease activity. Both T and B lymphocytes are reduced, while natural killer cells are typically increased.[7] Leukopenia patients with SLE are found to have reduced surface expression of complement regulatory proteins CD55 and CD59.[8,9] Deficiency of these proteins may make these cells susceptible to complement-mediated lysis. There is increasing evidence that endogenous production of type 1 interferons (IFNs) is implicated in the pathogenesis of neutropenia and lymphopenia in SLE. Elevated serum levels of IFN-a in SLE correlate inversely with leucocyte numbers.[10,11]

Thrombocytopenia with platelet count of <100000/mm^3 may appear in 10-25% of SLE patients. It has a reported prevalence ranging from 7 to 30% in large series of patients with SLE.[11] Thrombocytopenia may, like anemia, result from a number of immune (antiplatelet antibodies, anti-thrombopoietin antibodies, antiphospholipid antibodies, etc.) and non-immune (drug-induced bone marrow suppression, infection, etc.) causes.[12,13]

Objective

The objective of this study was to investigate further, the hematological manifestations which may be the presentation of SLE and may be missed if the index of suspicion is low.

METHODS

The study was conducted in the department of internal medicine at Sir Ganga Ram Hospital in New Delhi, India, from December 2015-July 2017, following approval from the hospital's Ethics Committee. It was a descriptive study including 100 patients, who were either newly diagnosed case of SLE (using SLICC criteria) or previously diagnosed cases obtained from the hospital records. Patients under 18 years of age, pregnant women, patients who were on treatment were excluded from the study.

Hematological profile of both the group of patients were obtained and recorded. Descriptive statistics were analysed with SPSS version 17.0 software. Continuous variables were presented as mean±SD. Categorical variables were expressed as frequencies and percentages. Association between two or more variables were compared using chi squared test. P<0.05 was considered statistically significant.

RESULTS

Out of 100 patients that were found to have SLE during the study period 88% were females and 12% were males thus clearly indicating preponderance for females (Table 1).

Table 1: Gender distribution.

Sex	Frequency	Percentage	Cumulative
Female	88	88.0	88.0
Male	12	12.0	100.0
Total	100	100.0	

Table 2: Age distribution.

Age	Frequency	%	Cumulative %
≤20 years	3	3.0	3.0
21-30 years	26	26.0	29.0
31-40 years	26	26.0	55.0
41-50 years	21	21.0	76.0
51-60 years	18	18.0	94.0
>60 years	6	6.0	100.0
Total	100	100.0	

The patient's age at the time of presentation varied from 18 years to 60 years with a mean of 39.85 years (SD

12.832 years). Out of 100 patients, 56 (56%) patients were under the age of 40 years. In male patients 9 out of twelve (75%) were >40 years indicating that SLE occur in males in later part of year (Table 2).

Table 3: Percentage of hematological manifestation in SLE.

Hematological manifestation	Frequency	Percentage
Anemia	72	72
Leukopenia	32	32
Neutropenia	5	5
Lymphopenia	54	54
Thrombocytopenia	23	23
Pancytopenia	14	14

Majority of the participants 12 (18%) and 13 (20%) had mild to moderate anemia respectively while 2 (3%) had life threatening anemia. While, majority of the participants had mild leukopenia 12 (18%) while only 4 (6%) had moderate leukopenia. Whereas, majority of the participants 11 (17%) had mild thrombocytopenia. Only 1 (1.5%) of the participant had severe thrombocytopenia (Table 3).

Table 4: Percentage of patients with anemia.

Anemia	Frequency	%	Cumulative %
ACD	9	9.0	9.0
AIHA	26	26.0	35.0
IDA	10	10.0	45.0
IDA/ACD	14	14.0	59.0
No	26	26.0	85.0
Other	15	15.0	100.0
Total	100	100.0	

Of the 72% of the patients who had anemia majority were autoimmune hemolytic anemia with 26%, IDA were 10%, ACD was 9% and mixed IDA/ACD were 14%. (Table 4).

DISCUSSION

Systemic lupus erythematosus (SLE) is a prototypic systemic autoimmune disease with variable multisystem involvement and heterogeneous clinical features, ranging from mild to life threatening.

In a study conducted in a tertiary care centre in North Kerala it was found that hematological manifestations were the most common initial manifestation of SLE and it was one of the presenting manifestations in 82% of the subjects.[5]

A series of studies reviewed by BudMan showed that anemia occurred in 57-78% of patients with SLE.[14] ACD was the most common type of anemia. Anemia with positive coombs test was seen in 10% of the cases.

One study by Nossent et al of 126 patients with SLE showed that 47% had neutropenia, 27% had thrombocytopenia, 20% had lymphopenia and 13% had haemolytic anemia.[15]

Hematological abnormalities (anemia, leukopenia, lymphopenia and thrombocytopenia were found to be the most common presentation of SLE and it was the presenting manifestation in 83% of the subjects. This observation is contradictory to the description of the disease in most western and Indian textbook and majority of previously conducted studies.[16,17] However a multicentre French study and a study conducted in India had shown that the most common initial presentation was hematological.[5,18] The prevalence of hematological findings in SLE in these studies were similar to that seen in our patients.

The most prevalent hematological abnormality was anemia present in 72% of the patient in the study group with a mean haemoglobin value of 10.073 gm/dl. This also validates in different studies where the most common presentation was anemia.[15,6,19]

The most common type was AIHA which was seen in 26% of patient. This was followed by ACD and IDA which were seen in 10% and 9% of patients respectively. This is in contrast to western literature according to which the most common type of anemia was ACD. According to a study done in Europe by Swaak et al, ACD was the most prevalent and seen in 27% of the cases and hemolytic anemia in 5% of the cases.[20] A similar study done in Athens had shown that ACD was present in 37.1%, IDA in 35.6%, AIHA in 14.4% of cases.[21] Another study conducted in India had shown that AIHA was seen in 27.9% of cases.[5]

Other hematological abnormalities included were leukopenia present in 32% of patients. This comprised of lymphopenia in 54%, neutropenia in 5%. Thrombocytopenia was seen in 23% and pancytopenia in 14% of patients. Presence of leukopenia has been associated in some studies with anti-ds-DNA positivity, a component of the SLE diagnostic criteria and prognostic indicator.[22] Similarly, our patients with cytopenia at diagnosis were significantly found to be positive for anti-dsDNA in 34% patients. This also suggests that in patients presenting with leukopenia and lymphopenia, other signs and symptoms of SLE should be carefully looked into and anti-dsDNA can be ordered to confirm the suspicion.

The observational study lacked patient follow-up, hindering assessment of the persistence of hematological abnormalities and complications. Disease activity correlation was not explored, and coexisting manifestations were disregarded. Exclusion of paediatric patients limited generalization, and the small sample size may have affected statistical power.

CONCLUSION

Studies over a long period have demonstrated that hematological involvement is common in SLE, however in our study we concluded that hematological involvement as early as at the time of presentation is commonly seen in SLE patients. The most common abnormality being anemia whose etiology is multifactorial. Thus, all cases of anemia should be carefully evaluated and managed.

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