ORIGINAL RESEARCH PAPER
Volume - 11 | Issue - 11 | November - 2022 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

HEMATOLOGIC MANIFESTATIONS OF SYSTEMIC LUPUS ERYTHEMATOSUS IN A TERTIARY CARE CENTRE

Pathology

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ABSTRACT

Background: Systemic lupus erythematosus (SLE) can present with hematologic manifestations alone or with features of systemic involvement. Diagnosis may be delayed or missed at presentation time, especially in those with hematologic abnormalities as the initial manifestation, with low index of clinical suspicion or inadequate follow-up. **Aim And Objectives:** To study the prevalence and the type of hematologic manifestations in SLE from pathologist's perspective. **Setting And Design:** Retrospective observational study. **Material And Methods:** Study was done in 63 SLE patients in a tertiary care hospital in Secunderabad for duration of one and half years, from January 2018 to June 2019. Hematological parameters of the same were retrieved. **Results :** It was observed that anemia was the most common hematologic finding with iron deficiency anemia (IDA) being the commonest cause followed by hemolytic anemia. Leucopenia with predominant lymphopenia was the most common WBC abnormality and thrombocytopenia was seen in majority of the patients. Bi and pancytopenia was also observed. Raised erythrocyte sedimentation rate (ESR) was a common finding. Deranged coagulation profile was seen due to secondary anti-phospholipid antibody (APLA) syndrome, hemolysis and sepsis on anticoagulant. Bone marrow studies showed varied findings including hypocellularity, dyspoiesis in the erythroid, myeloid and megakaryocytic series and abnormal localisation of immature precursors (ALIP) aggregates. **Conclusion:** This study was conducted to estimate the proportion of patients with hematological abnormalities as the manifestation of SLE and to study the nature of hematological problems, so that the empirical treatment can be started.

KEYWORDS

Anemia, SLE, Thrombocytopenia.

INTRODUCTION

SLE is an autoimmune disease in which organs and cells undergo damage initially mediated by tissue-binding autoantibodies and immune complexes.[1] Active disease is associated with raised anti ds DNA antibodies and reduced levels of complement C3 and/or C4 levels.[2]

Hematologic manifestations of SLE are diverse and often are the presenting manifestations of the disease. In SLE auto antibodies are known to develop against any antigen in all tissues. Therefore hematologic manifestations are more frequent, since blood and blood vessels together contain more diverse number of antigens than any other organ in the body. Sometimes SLE present with hematologic abnormalities alone, without features of musculoskeletal, skin, or other systemic involvement .Sometimes the diagnosis may be delayed or initially missed if the index of suspicion is low or if there is improper and inadequate follow up.[3]

MATERIALAND METHODS

It was a retrospective observational study done in 63 cases of SLE in a tertiary care hospital in Secunderabad for a total duration of one and half years, during the period of January 2018 to June 2019. Complete blood picture evaluation including hemoglobin, total and differential WBC count, platelet count, ESR and iron studies done in all the patients admitted to the department of Rheumatology with a clinical diagnosis of SLE (as per Systemic Lupus International Collaborating Clinic Criteria for classification of SLE) were included along with the demographic details of the patients keeping the anonymity of the identity. Bone marrow examination and coagulation profile results (if done) were also retrieved. Institutional ethical committee clearance was taken for the above study.

Patients of all age groups and both sexes are included in the study. However we had no cases younger than 12 years in our study period. Inadequate and unsatisfactory blood samples (insufficient quantity, improper collection, clotted samples), pregnant women (who may have anemia due to pregnancy) and patients of ACTD coming in out patient department in Rheumatology clinic were all excluded.

After confirming homogenous distribution of data, it was entered using Microsoft Excel 2010 version and analysed. Data was summarized in percentages and proportions.

RESULTS

A total data of 63 SLE patients were collected out of which 54 were female (85.71%) and 9 were male (14.28%), the female to male ratio being 6:1.

(I) RBC FINDINGS:

Anemia was the most common hematologic abnormality detected in 45 of the 63 cases (71.42%). The most common cause of anemia was iron deficiency seen in 31/ 45 (68.88%) patients followed by haemolytic anemia (AIHA) in 8/45 (17.77%) patients and anemia of chronic disease (ACD) in 6/45 (13.33%) patients. None of the patients had any recorded evidence of renal disease. No significant abnormality was noted in other RBC indices like MCV, MCH, MCHC and RDW.

(ii) WBC FINDINGS:

Leucopenia was seen in 23/63 (36.50%) patients, leucocytosis was seen in 8/63 (12.69%) patients while in 32/63 (50.79%) patients WBC counts were normal. The most common abnormality was lymphopenia seen in 39/63 (61.90%) patients, followed by neutrophilia in 16/63 (25.39%) patients. 12/63 (19.04%) patients had neutropenia while the least common abnormality was lymphocytosis which is seen in 5/63 (7.93%) patients.

(iii) PLATELET FINDINGS:

Platelet abnormalities were seen in 20 (31.74%) patients of which thrombocytopenia was seen in 19/20 patients and thrombocytosis was seen in 1/ 20 patients.

TABLE SHOWING HEMATOLOGICAL FINDINGS IN SLE

SR. NO.	PARAMETERS	LOW	NORMAL	HIGH	TOTAL
1	HEMOGLOBIN	45 (71.42%)	18 (28.58%)	00	63
2	TOTAL WBC	23 (36.50%)	32 (50.79%)	08 (12.69%)	63
3	LYMPHOCYTE	39 (61.90%)	19 (30.17%)	05 (7.93%)	63
4	NEUTROPHIL	12 (19.04%)	35 (55.57%)	16 (25.39%)	63
5	PLATELET	19 (30.15%)	43 (68.25%)	01 (1.58%)	63

(iv) BICYTOPENIA/ PANCYTOPENIA:
17 patients presented with bicytopenia of whom 9 patients had anemia with leucopenia, and the remaining 8 patients had anemia with thrombocytopenia. 12 patients presented with pancytopenia.

(v) COAGULATION FINDINGS:
Coagulation parameters were available in 39 (61.90%) patients. Prothrombin time (PT) was done in 17/39 (43.58%) patients while activated partial thromboplastin time (aPTT) was done in 32/39 (82.05%) patients. PT was prolonged in 3 patients, aPTT was prolonged in 2 patients, both PT and aPTT was prolonged in 2 cases.

(vi) ESR: 54 (85.71%) patients had raised ESR while normal ESR was seen in 9 (14%) patients.

(vii) BONE MARROW FINIDINGS:
Bone marrow was done in 10 patients, which had the following findings

- Three patients had focal abnormal localisation of immature precursors (ALIP).
- Four patients had hypocellular marrow with significant dyspoiesis in erythroid series.
- Two patients had megakaryocytic hyperplasia with peripheral blood thrombocytopenia, proving immune mediated thrombocytopenia.
- One patient had normal marrow with no significant findings.

DISCUSSION

In our study anemia was the most common hematologic manifestation detected in 45/63 (71.42%) patients. The most common cause of anemia was IDA seen in 31 (68.88%) patients followed by hemolytic anemia in 8 (17.77%) patients and ACD in 6 (13.33%) patients. Fozya Bashal et al (2013) [4] found ACD (37.1%) as the most common abnormality followed by IDA (35%) and AIHA(14.4%) . Sufian A et al (2017) [5] in his study of 89 SLE patients also found anemia as the most frequent hematologic manifestation present in 77.5% patients. ACD was seen in 34.8%, IDA was seen in 32.6% and AIHA was diagnosed in 10.1% patients. Beyan et al (2006) [6] in their study of 115 SLE patients found ACD as the most common encountered picture (seen in 46%). All these studies showed ACD as the most common cause of anemia. Our study showed IDA as the most common cause. This correlated with the decreased serum iron levels and elevated TIBC. All our patients were in-patients requiring NSAIDs for treatment and IDA is a known complication due to the drugs.

Leucopenia was seen in 23 (36.50%) patients and leucocytosis was seen in 8 (12.69%) patients. The most common abnormality was lymphopenia seen in 39 (61.90%) patients , followed by neutrophilia in 16 (25.39%) patients. 12 (19.04%) patients had neutropenia while lymphocytosis was seen in 5 (7.93%) patients. Sasidharan et al (2012) [3] found 17 (16%) patients with leucopenia in their study of 108 SLE patients which is much less than the present study. Sufian A et al (2017) [5] in his study of 89 SLE patients found neutropenia in 19.1% and lymphopenia in 17.9% . The finding of neutropenia in their study is comparable with our study. However, lymphopenia was a significant finding (61%) in our study. Overall marked lymphopenia is strongly correlated with higher disease activity. All our patients were in-patients with significant disease activity. Therefore the significant lymphopenia is well correlated.

Thrombocytopenia was found in 43 (40%) patients in the study conducted by Sasidharan et al (2012) [3] while in the study conducted by Ziakas et al (2004) [6] thrombocytopenia was seen in 29/50 (58%) patients. However in our study thrombocytopenia was seen in 19/20 (95%) patients. This increased percentage of thrombocytopenia may be explained by the disease activity flare and concomitant sepsis.

We found 17 patients (26.98%) of bicytopenia of whom 9 patients had anemia with leucopenia, and the remaining 8 patients had anemia with thrombocytopenia. 12 patients (19.04%) were of pancytopenia. However McGhee A (2015) [7] reported pancytopenia during lupus flare in their case report of a single patient.

Coagulation abnormalities were observed in 7/63 patients of whom 2 with prolonged PT were found to have neutrophilia with thrombocytopenia , which was an evidence of sepsis and were on anticoagulants; 2 cases had evidence of hemolysis, of which one had a positive Coomb's test –diagnosed as AIHA, and the other case had pancytopenia with evidence of sepsis which explains the prolonged PT and aPTT. Cases with prolonged aPTT and a normal CBP were worked up for APLA which is a known complication of lupus [1] and 4 APLA cases were reported in this study.

Bone marrow aspiration and biopsy data is limited as was done in only 10 SLE patients. They had variable findings including hypocellularity, dyspoiesis in the erythroid, myeloid and megakaryocytic series and ALIP aggregates on biopsy. These findings were similar to the findings of study done by M. Vougarelis et al (2006). [8]

To the best of our knowledge there is very limited literature stating hematologic manifestations in SLE patients in Indian population from a pathologist's perspective.

However, our study had only in-patients who had disease with significant activity. Therefore the hematologic manifestations in quiescent phase may be missed. Also, all the parameters for a complete hematologic workup such as serum ferritin, LDH, serum bilirubin and stool for occult blood were not included in the study due to non availability of the same in records.

CONCLUSION

Anemia is the most common hematologic finding seen in SLE. Iron deficiency is the commonest cause of anemia followed by hemolytic anemia. Leucopenia with predominant lymphopenia was seen in SLE. Majority of the patients had thrombocytopenia. Bi and pancytopenia was observed. Raised ESR was a common finding. Deranged coagulation profile is observed due to secondary APLA, hemolysis and sepsis on anticoagulant. Bone marrow studies had variety of findings including hypocellularity, dyspoiesis in the erythroid, myeloid and megakaryocytic series and ALIP aggregates on biopsy.

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