CLINICAL AND LABORATORY MANIFESTATIONS OF THROMBOCYTOPENIA IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Abstract — In systemic lupus erythematosus (SLE) various antibodies are produced against cells including platelets and result in thrombocytopenia. In the literature, the incidence of thrombocytopenia varied from 7% to 52%, in seven series of SLE patients with a mean cumulative percentage of 14.5% (1-5). SLE patients referred to the Lupus Unit of the Rheumatology Research Center, Tehran University for Medical Sciences (Shariati Hospital) during the period of 1975 to 1977 were included in this study. Thrombocytopenic patients were selected and 72 items were studied. The incidence of thrombocytopenia in Iranian SLE patients was 16.6%, which is similar to the mean cumulative percentage mentioned above. There was no difference in sex ratio between thrombocytopenic and nonthrombocytopenic patients. The same was true for the mean age at the onset of the disease. In 70% of patients there was mild to moderate thrombocytopenia (platelet from 50000 to 150000/mm3). The remaining (30%) had severe to very severe thrombocytopenia. In 1.9% of patients had a previous diagnosis of idiopathic thrombocytopenic purpura (ITP). The following symptoms were seen more often in thrombocytopenic patients than in others: Hemolytic anemia ($p<0.001$), leukopenia ($p<0.001$), lymphopenia ($p<0.001$), splenomegaly ($p<0.00007$), and abortion ($p<0.0006$). For the followings the p value was less than 0.05: ESR $\geq$ 100, positive FANA, positive Anti-dsDNA antibodies, positive VDRL, and positive anticardiolipin antibodies. All thrombocytopenic patients except one (previously splenectomized) were controlled by the medical treatment. Severe and very severe thrombocytopenia were controlled in 86% of cases by moderate to high dose steroids, with or without cytotoxic drugs. In 10% of cases, thrombocytopenia was controlled by a combination of chloroquine and low dose steroid ($\leq$ 15 mg prednisolone daily). In 4%, other medical treatments (Danazol, etc.) were needed.

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Key words: SLE; thrombocytopenia

INTRODUCTION

In systemic lupus erythematosus (SLE) various antibodies are produced against cells including platelets resulting in thrombocytopenia. In seven series of SLE patients the prevalence of thrombocytopenia varied from 7% to 52% with a mean cumulative percentage of 14.5 (1-5). Thrombocytopenia is used as an activity and severity index (6-8).

The aim of this study was to demonstrate: (1) The characteristic of thrombocytopenia in Iranian SLE patients. (2) The characteristics of thrombocytopenic SLE patients compared to non-thrombocytopenic patients. (3) To evaluate the treatment of these patients.

MATERIALS AND METHODS

Patients Selection

All SLE patients visited during the priod of 1975 to 1997 in our Center (RRC), were included in this study.

Diagnosis Method

Diagnosis was based on the clinical and laboratory picture of the disease and not on the ACR diagnosis criteria which had a sensitivity of 90% in Iran (9), to not miss the other 10% of patients that have SLE disease but have not ACR diagnosis criteria.

Statistical Methods

The RRC database for SLE comprises 266 items on the clinical and laboratory manifestations. Seventy-two items were compared in thrombocytopenic and non-thrombocytopenic patients. A percentage and a confidence interval (CI) at 95% were calculated for each item. The comparison between items was done by the chi square test. The Yates correction formula was applied when necessary.

Definitions

The following definitions were used (10). Mild thrombocytopenia: platelet from 100,000 to 150,000/mm^3. Moderate thrombocytopenia: 50,000 to 100,000. Severe thrombocytopenia: 20,000 to 50,000. Very severe thrombocytopenia: platelet count < 20,000/mm^3. Mild Leukopenia: WBC between 3000 to 4500/mm^3. Moderate leukopenia: WBC between 2000 to 3000/mm^3. Severe leukopenia: WBC less than 2000/mm^3. Mild lymphopenia: lymphocyte counts from 1000 to 1500/mm^3. Moderate lymphopenia: 500 to 1000/mm^3. Severe lymphopenia: Lymphocyte counts < 500 / mm^3. Anemia: Hb<12gr/dl in female and <14gr/dl in male. Mild anemia: Hb between 12 and 10 gr/dl.

Moderate anemia: Hb between 9.9 to 8 g/dl. Severe anemia: Hb between 7.9 to 6 g/dl. Very severe anemia: Hb<6g/dl. Hemolytic anemia: Anemia with reticulo - cytosis.

RESULTS

Thrombocytopenia was detected in 218 cases (16.6%, CI = 4.9), of 1310 SLE patients. The mean age was 23.7 years (SD: 9.7, CI=1.3); The 200 cases were female (91.7%, CI=3.8) and 18 cases were male (8.3%, CI=6.1). There was very severe thrombocytopenia in 11% (CI=6.1), severe thrombocytopenia in 20% (CI=13.8), moderate thrombocytopenia in 46% (CI=11.2), and mild thrombocytopenia in 23% (CI=13.5) of patients. There was a previous diagnosis of idiopathic thrombocytopenic purpura in 25 cases; 1.9% (CI=5.3) of the total SLE patients and 11.5% (CI=12.5) of the thrombocytopenic SLE patients.

In 4 cases there was a combination of hemolytic anemia and thrombocytopenia at the onset of the disease; 0.3% (CI=5.3) of the total SLE patients and 1.8% (CI=13) of the thrombocytopenic SLE patients.

Leukopenia was detected in 132 cases of thrombocytopenic patients (60%, CI=8.3). Mild leukopenia was seen in 50% (CI=13.4) of them, moderate leukopenia in 33% (CI=15.5), and severe leukopenia in 17% (CI=17.3) of patients.

Lymphopenia was seen in 139 cases (64%, CI=7.9). Severe lymphopenia was seen in 26.5% (CI=16.3), moderate lymphopenia in 43% (CI=14.4), and mild lymphopenia in 30.5% (CI=15.9) of them.

Anemia was found in 165 cases (75.7%, CI=6.5). Very severe anemia was found in 16% (CI=16), severe anemia in 22% (CI=15.6), moderate anemia in 29% (CI=14.6), and mild anemia in 33% (CI=14.2) of them. Hemolytic anemia was detected in 33 cases (18%, CI=13).

FANA was done in 200 cases, it was positive in 175 cases (87.5%, CI=4.9). RF was checked in 159 cases, it was positive in 59 cases (37%, CI=12.3). Anti-dsDNA antibodies were checked in 190 cases, it was positive in 167 cases (88%, CI=4.9). In 145 cases, one or more of the complement components (C3,C4, CH50) were found to be below (76%, CI=6.9). VDRL was done in 181 patients, it was positive in 39 cases (22%, CI=13). CRP was done in 174 cases, it was positive in 94 cases (54%, CI=10). Anticardiolipin antibodies (aCL) was checked in 37 patients, it was positive in 13 cases (35%, CI = 25.9). ESR was checked in 198 cases, it was higher than 100 mm/h in 95 cases (48%, CI=10), between 50 and 99 mm/h in 79 cases (40%, CI=10.8), between 20 and 49 mm/h in 15 cases (7.5%, CI=13.3), and it was normal in 9 cases (4.5%, CI=13.5).

In 63 cases (29%, CI=11.2) the spleen was palpable (Splenomegaly). Thrombophlebitis was reported in 7 cases (3.2%, CI=13). Spontaneous abortion was reported in 23 cases (10.5%, CI=12.5)

Petechia, purpura, echymosis were seen in 42% (CI=21.1) of severe and very severe thrombocytopenic cases; Hematuria in 42% (CI=21.1); GI bleeding in 14% (CI=25.7); Epistaxis in 6% (CI=26). These problems did not occured due to mild to moderate thrombocytopenia.

Within the SLE patients with thrombocytopenia 11 patients died; non of them were died due to thrombocytopenia.

All thrombocytopenic patiens, except one (previously splenectomized), were controlled by medical treatment (corticosteroids, cytotoxic drugs, Danazol, etc.). Severe and very severe thrombocytopenia were 65 cases. In 23 of them (36%, CI=10) thrombocytopenia was controlled by moderate to high doses of corticosteroids (0.5-1 mg/kg/day of prednisolone). In 32 cases (50%, CI=14.1), thrombocytopenia was controlled by a combination of cytotoxic and moderate to high doses of corticosteroids. In 7 cases (10%, CI=22.2), thrombocytopenia was controlled by a combination of chloroquine and low dose of corticosteroids (< 15 mg prednisolone daily). In 3 cases (4%, CI=22.1), thrombocytopenia was controlled by other medical treatments (Danazol, etc.).

Table 1. Comparison of thrombocytopenic and non-thrombocytopenic patients

Findings	Non-thrombocytopenic	Thrombocytopenia	P.value
Female/male	1172/138	200/18	NS
Mean age	23.9	23.75	NS
Leukopenia	31%	60%	0.00038
Lymphopenia	39.2%	64%	0.00045
Anemia	48.5%	75.7%	0.000073
Hemolytic anemia	4.3%	17.9%	0.001014
ESR ≥ 100	32.9%	48%	0.029592
CRP (+)	55.5%	54%	NS
FANA (+)	81.2%	87.5%	0.033886
Anti-dsDNA(+)	79.75%	87.9%	0.008478
VDRL (+)	15.4%	21.5%	0.040832
RF (+)	33.3%	37.1%	NS
aCL	25.9%	35.1%	0.028
Splenomegaly	17.5%	28.9%	0.000071
PPE*	11.9%	42%	0.000002
Hematuria*	43.5%	42%	NS
GI bleeding*	3.1%	14%	0.000008
Abortion	4.8%	10.5%	0.000660
Thrombophebitis	3.2%	3.2%	NS
Death	8%	5%	NS

PPE: Petechia, Purpura, and Ecchymosis

* Cases of very severe and severe thrombocytopenia

DISCUSSION

The prevalence of thrombocytopenia in Iranian SLE patients (16.6%) is similar to the mean cumulative percentage (14.5%) of other countries (1-5).

There was no difference in sex ratio between thrombocytopenic SLE patients and the others (Table 1). The same was found for the mean age at the onset of the sisease (Table 1). In 70% there was a mild to moderate thrombocytopenia. The remaining (30%) had severe to very severe thrombocytopenia. In 1.9% of the patients, there was a previous diagnosis of ITP. The comparison of clinical and laboratory manifestations of thrombocytopenic and non-thrombocytopenic patients showed the following differences (Table 1):

(1) Anemia, hemolytic anemia, leukopenia, and lymphopenia were more common in thrombocytopenic patients ($p<0.001$).

(2) Splenomegaly was more common in thrombocytopenic than in non-thrombocytopenic patients ($p<0.00007$).

(3) Abortion was more common in thrombocytopenic than in non-thrombocytopenic patients ($p<0.0006$).

(4) ESR>100, positive FANA, positive Anti-dsDNA antibodies, positive VDRL, and positive aCL were more common in thrombocytopenic than in non-thrombocytopenic patients ($p<0.04$).

Thrombocytopenia was not the direct cause of death in SLE patients.

REFERENCES

1. Dubois E.l., Tuffanelli D.L., Clinical manifestations of systemic lupus erythematosus. Computer analysis of 520 cases. JAMA Oct 12; 190: 104-111; 1964.

2. Estes D., Christian C.L., The natural history of systemic Lupus erythematosus by prospective analysis. Medicine Mar; 50: 85-95; 1971.

3. Gladman D., Urowitz M., Tozman E., Glynn M., Hemostatic abnormalities in systemic lupus erythematosus. Q.J., Med summer; 52: 424-433; 1983.

4. Ropes M.W., Systemic Lupus Erythematosus. Cambridge MA: Harvard University press, 1976.

5. Mc Gehee, Harvey A., Shulman LE, Tumulty AP, Lockard conley C., Schoenrich EH, Systemic Lupus Erythematosus: Review of the literature and clinical analysis of 138 cases. Medicine Dec; 33 (4): 291-437; 1954.

6. Clark WF, Linton AL, Cordy PE, Keown PE, Lohmann RC, Lindsay RM. Immunologic findings, thrombocytopenia and disease activity in Lupus nephritis. Can Med J: 118: 1191-1195; 1978.

7. Bombardier C, Gladman DD, Urowitz MB, Karon O. Chang CH, Committee on Prognosis Studies in SLE. Development and validation of the SLEDAI: a disease activity index for Lupus patients. Submitted.

8. Committtee on Prognosis Studies in SLE. Prognosis Studies in SLE: an activity index [abstract]. Arthritis Rheum.: 29 Suppl: S93; 1986.

9. Davatchi F, Chams C, Akbarian M, Evaluation of the 1982 American Rheumatism Association revised criteria for the classification of systemic lupus erythematosus. Arthritis Rheum; 28: 715; 1985.

10. Francisco P., Quismorio, JR, Hemic and lymphatic abnormalities in SLE. In: Daniel J. Wallace., Bevara Hannahs Hahn, editors. Dubois' Lupus Erythematosus. Philadelphia, London: Lea & Febiger, 1993; 418-430.