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SEX AND AGE AS PROGNOSTIC FACTORS IN ESSENTIAL THROMBOCYTHEMIA

MARIA LUIGIA RANDI, FABRIZIO FABRIS, CARLA ROSSI, TIZIANA TISON, ERSILIA BARBONE, ANTONIO GIROLAMI

Background. **The major causes of morbidity and mortality in essential thrombocythemia (ET) are bleeding and thrombotic accidents, but a prognostic pattern for these complications has not yet been discovered.**

Materials and methods. **In this study we report data from a large cohort of patients with thrombocytosis, distinguished for sex and age, in order to define their thrombotic risk. The prevalence of vascular complications recognized in 86 patients with essential thrombocythemia was studied. In addition, 91 patients with polycythemia vera (PV), 20 with myelofibrosis (MF) and 63 with secondary thrombocytosis (ST) were evaluated.**

Results. **6.3% of ET subjects younger than 40 (4.6% of males and 7.0% of females), 11.8% of patients between 40 and 65 years old (14.9% of males and 9% of females), and 16.8% of subjects over 65 (14.6% of males and 17.8% of females) showed thrombotic accidents. In the PV and MF groups thromboses occurred more frequently than in the ET groups for all ages and for both sexes. On the contrary, ST subjects showed fewer thromboses than ET patients, but their incidence rose with patient age; moreover the prevalence of males in this group was limited. In ET patients, particularly in females, the incidence of thrombosis was low under 40 years of age, but rapidly increased later.**

Conclusions. **ET females over 40 must be followed with particular attention in order to prevent thrombotic complications.**

KEY WORDS: Essential thrombocythemia, myeloproliferative diseases, thrombocytosis.

Essential thrombocythemia (ET) has always been considered the least common of the chronic myeloproliferative disorders (MPD). However, the advent of automated platelet counting has revealed an increasing number of asymptomatic patients in whom this diagnosis is made casually.

The major causes of morbidity and mortality in ET are bleeding and thrombotic accidents. Therefore, a number of studies have been performed with the aim of recognizing a prognostic pattern for thromboses and hemorrhages in ET patients [1]. Unfortunately, this pattern has not been discovered and, at present, we still have no sure way of predicting vascular complications in these patients [2].

In this study we report data from a large cohort of patients in order to define their thrombotic risk.

PATIENTS AND METHODS

We considered 260 patients with thrombocytosis, diagnosed in our Department during the last 13 years, and with an individual follow-up of no less than 3 years. Sixty-three other patients were excluded from the study because their follow-up was not long enough. Eighty-six subjects (33 males and 53 females) were affected by ET according to the diagnostic criteria proposed by the Polycythemia Vera Study Group (PVSG) [3]; 91 patients showed polycythemia vera (PV) (47 males and 44 females) [4], 20 were affected by myelofibrosis (MF) (5 males and 15 females), and 63 showed a secondary or reactive thrombocytosis (ST) (26 males and 37 females). Platelet counting was carried out by a Hemalogcell Coulter and by a direct method in every instance. All thrombotic incidents (coronary artery disease, cerebro-vascular accidents, peripheral vascular disease, deep vein thrombosis, thrombosis of the mesenteric and/or portal district) that occurred when platelet counts were higher than 500 x 10^9/L platelets were considered. All patients were distributed in 3 groups according to their age: group A = under 40, group B = 41-65 years old, and group C = over 65, and were also distinguished according to sex.

RESULTS

Group A contained 18 subjects (5 males and 13 females) with ET whose mean platelet count was 1184.1 ± 678.7 x 10^9/L; 42 patients (18 males and 24 females) in group B showed a mean platelet count of 1070.4 ± 411.5 x 10^9/L and the 26 (10 males and 16 females) in group C had a mean platelet count

From the Istituto di Semeiotica Medica, via Ospedale 105, 35100 Padova, Italy.

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Correspondence: Dr.ssa M.L. Randi, Istituto di Semeiotica Medica, via Ospedale 105, 35100 Padova, Italy.

of 898 ± 341 x 10^9/L. There was no significant difference between the platelet numbers of the three groups. The main data of our ET patients and the other patients with thrombocytosis are reported in Table 1. A vascular complication was the presenting disease feature in 15 patients with ET (17.4%), in 30 with PV (30.9%), in 4 with MF (2%) and in 3 with ST (4%).

Table 1. - *General data from our patients with thrombocytosis. group A:* <40; group B: 40-65; group C: ·65 years old

Groups	Patients (N°)	Sex M/F	Platelets x 10^9/L
ET A	18	5/13	1184.1 ± 678.9
B	42	18/24	1070.4 ± 411.5
C	26	11/15	898 ± 341
PV A	10	7/3	795.1 ± 235.3
B	46	25/21	833.2 ± 335.9
C	35	15/20	937.4 ± 386.4
MF A	5	0/5	802 ± 130
B	6	3/3	961 ± 403
C	9	2/7	817.3 ± 530
ST A	23	11/12	775.2 ± 223.3
B	25	13/12	710.7 ± 171.9
C	15	2/13	623.5 ± 134.4

PV = polycythemia vera, ET = essential thrombocythemia, MF = myelofibrosis, ST = reactive thrombocytosis

Thrombotic episodes occurred in 6.3% of ET patients in group A, 11.8% from group B and 16.8% in group C. Figure 1 shows the distribution of the percentage of thrombotic accidents in patients with thrombocytosis related to age and to the years of follow-up. An apparently progressive increase in the incidence of thrombotic manifestations was noted as age increased. Fig. 2 shows the breakdown according to sex. In group A thrombotic episodes developed in 4.6% of males and 7% of females; in group B thrombosis occurred in 14.9% of males and 9% of females, in group C in 14.6% of males and 17.8% of females.

Thrombotic accidents were recognized in 13.5% of the PV patients in group A (13.1% of males and 15.2% of females), in 11.7% of those in group B (12.8% males and 10.4% females), and in 17.2% of those in group C (10.9% males and 21.8% females). Thrombosis occurred in 6% of the MF patients in group A (0% males and 4.2% females), in 12.6% of those in group B (13.5% males and 11.9% females) and in 11.3% from group C (12.8% males and 10.7% females). Of the ST subjects, 5.7% from group A (3% males and 8.2% females), 7.3% from group B (6% males and 8.7% females) and 14.5% (31.2% males and 12% females) from group C suffered thromboses.

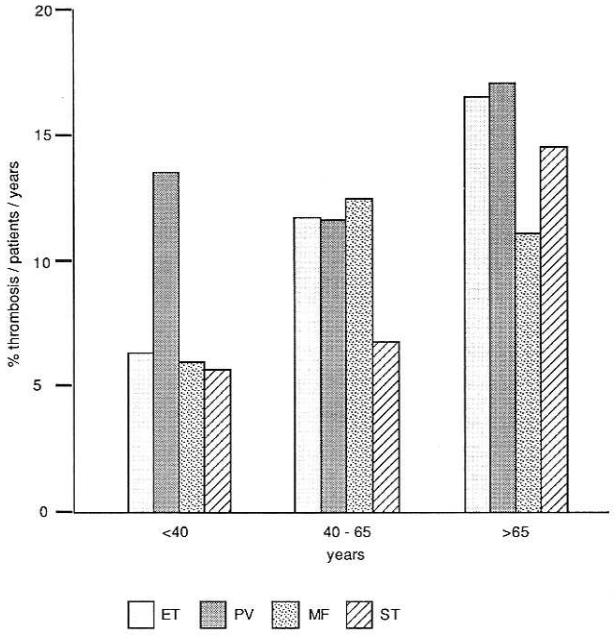

Fig. 1. - Prevalence of thrombotic accidents seen in our thrombocytosis patients, distributed according to age groups. PV = polycythemia vera, ET = essential thrombocythemia, MF = myelofibrosis, ST = secondary thrombocytosis. It is interesting to note that the incidence of thrombosis in ET and ST patients increases with age.

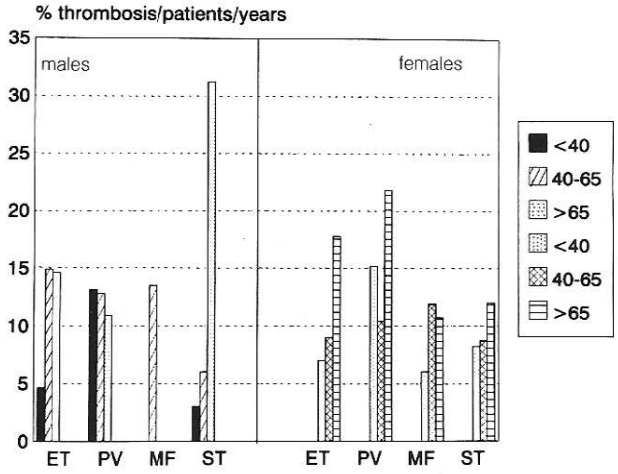

Fig. 2. - Prevalence of thrombosis in patients with thrombocytosis as related to age and sex. PV = polycythemia vera, ET = essential thrombocythemia, MF = myelofibrosis, ST = secondary thrombocytosis.

Discussion

Thrombotic and hemorrhagic complications have been widely described during the course of primary thrombocytosis [2].

Moreover, it is well known that only patients with thrombocytosis in MPD are prone to vascular complications, while reactive thrombocytosis does not increase the risk of thrombosis. In some MPD patients with active bleeding or thrombosis, a reduction of the platelet count may result in symptomatic improvement [5]. But the contribution of a high platelet count to bleeding and thrombosis in primary thrombocytosis and, in particular in ET, remains unclear. Bleeding time [2], in vivo platelet aggregation studies [6], abnormal platelet glycoprotein composition [7], acquired storage pool disease [8] have all been correlated to ET, but no test has been recognized as prognostic for hemostatic complications [5]. Our data indicate that thrombotic accidents among ET patients are less frequent than those in PV patients only for subjects under 40. Although the group of young ET patients is small, this observation is in agreement with previous data [9 10]. Increasing age in ET patients seems to induce more thromboses. In the past, we reported a low incidence of thrombosis in patients over 70 [11], but these present data do not distinguish very old patients from the others. In MF the gap in the prevalence of thrombotic episodes is between young and middle-aged subjects. In our PV patients, age does not modify the incidence of thrombosis. These data, in contrast to previous findings [9], are probably due to the small number of PV patients in group A. On the contrary, the risk of thrombosis appears to rise continuously with passing age in both ET and ST patients. This might be due more to the development of atherosclerosis risk factors than to thrombocytosis «per se» [12]. These observations are more significant in females. It is probable that a high platelet count becomes a thrombotic risk factor only when the natural protection of estrogens disappears. In other primary thrombocytoses we could not recognize a similar situation. In PV patients the main thrombotic risk factors are rheological alterations [13]. On the contrary, the cause of the high incidence of thrombosis in MF patients is not clear. The diagnosis of MF is not always a prompt one, due to the lack of systemic symptoms. Moreover, in the first stages of the disease, MF resembles ET. In ET and ST patients the progressive increase in the thrombotic incidence with age is astonishing. It would seem that thrombocytosis in middle-aged and older people is not of trifling importance. In ST this is probably related to the high incidence of neoplastic patients. These data seem to recommend particular attention for females over 40 affected by ET, since they are particularly prone to thrombotic accidents. In the future, this group of patients must be subject to special consideration in an attempt to evaluate whether therapeutic measures are indicated.

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