Polycythemia Vera and Idiopathic Erythrocytosis: Comparison of Clinical and Laboratory Parameters

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Abstract

Objective: To evaluate the various clinical and laboratory parameters of Polycythemia vera and idiopathic erythrocytosis in order to differentiate between two entities at the Aga Khan University Hospital.

Methods: Twenty six patients of polycythemia vera and 34 patients of idiopathic erythrocytosis were analyzed with respect to clinical features and laboratory findings.

Results: Patients with idiopathic erythrocytosis were males with a mean age of 41 years and no splenomegaly. Patients with polycythemia were older males and females with splenomegaly, red cell count of mor than 6.5 million/cmm, haematocrit 55%, leucocytosis, thrombocytosis and low erythropoietin level.

Conclusion: Based on the above-mentioned findings, we suggest that polycythemia vera and idiopathic erythrocytosis are separate entities and the diagnosis of these can be made on the basis of clinical and laboratory parameters (JPMA 54:249;2004).

Introduction

Polycythemia is defined as an increase in hematocrit or packed red cell volume caused by different pathological conditions and factors that may or may not be associated with an increase in total quantity of red cells or increase in red cell mass.[1] On the basis of red cell mass the polycythemia is further sub classified into relative and absolute polycythemia. The patients with absolute polycythemia can be placed in one of the three diagnostic groups a) Polycythemia vera b) Secondary polycythemia c) Idiopathic erythrocytosis.

Polycythemia vera is a myeloproliferative disorder characterized by excessive proliferation of erythroid, myeloid and megakaryocytic elements in the marrow, increase cell count on peripheral blood and increased erythroid mass.[2] The diagnostic criteria proposed by Polycythemia Vera Study Group are well established.[3] Secondary polycythemia is a group of disorder with an increase in red cell mass due to a rise in erythropoietin production.[4]

A significant proportion of patients who cannot be assigned to either polycythemia vera and secondary polycythemia are grouped together under the category of idiopathic erythrocytosis, which is a diagnosis of exclusion.[1,2] It is a heterogeneous, relatively new but well recognized disorder and a substantial number of patients with absolute polycythemia belong to this category. Newer diagnostic techniques such as in vitro culture of erythroid colonies, karyotyping, erythropoietin assay and supine oximetry have some influence on the established criteria to differentiate idiopathic erythrocytosis from polycythemia vera and secondary polycythemia[5] but these tests are only available in the specialized centers.

In this study, we have compared the various clinical and laboratory parameters of patients with polycythemia vera and idiopathic erythrocytosis and have tried to evaluate the statistically significant variables to distinguish between these two conditions.

Patients and Methods

This is a retrospective cross-sectional study conducted at the Aga Khan University Hospital on patients who presented to the clinic or were directly admitted in the hospital during the period between July 1994 to June 2001. Medical records of all patients were retrieved for detailed analysis of clinical and laboratory data.

Demographic features including age, sex, month and year of presentation were noted. Clinical symptoms, signs and laboratory data including hemoglobin, hematocrit red blood cell count, white blood cell count, platelet count and erythropoietin level of all these patients at the time of presentation were noted on a questionnaire.

The inclusion criteria were hematocrit of more than or equal to 45 on two occasions in females and hematocrit of more than or equal to 48 on two occasions in males. These patients then underwent red cell mass estimation and those who had an increased red cell mass were included. The following established diagnostic criteria proposed by Polycythemia Vera Study Group[6] were then applied with slight modifications:

1. Major criteria: a) red cell mass 32ml/kg or more in females and 36ml/kg or more in males, b) Oxygen saturation more than or equal to 92%, c) Splenomegaly.

2. Minor criteria: a) white cell count more than or equal to 12.0×10^9E/L, b) Platelet counts more than or equal

to 400x10^{9}E/L.

Three major or first two major and two minor criteria were used for the diagnosis of polycythemia vera. Those patients who did not fit in polycythemia vera and secondary polycythemia were assigned the diagnosis of idiopathic erythrocytosis.

The patients of secondary polycythemia were excluded. The data were collected on a computerized database and were analyzed on SPSS version 10.0. Means of different variables were determined. Comparison of variables of polycythemia vera and idiopathic erythrocytosis was made using student's t-test chi-square and Fischer's exact test.

Results

During the period of study, a total of sixty consecutive patients were selected who had absolute polycythemia. They were further subdivided into polycythemia vera and idiopathic erythrocytosis according to the diagnostic criteria.

Twenty six patients fulfilled the diagnostic criteria of polycythemia vera. Mean age at the presentation was 51.3 years. Median age was 57.5 years.

Seven (37%) patients were less than 40 years of age.

Table 1. Clinical features of patients.

Clinical features at presentation	Polycythemia vera (n=26)	Idiopathic Erythrocytosis (n=34)
Mean age (years)	51.3	40.8
Median age (years)	57.5	42
Male to female ratio	21:5	34:0
Incidental Diagnosis	6 (23%)	15 (44.1%)
Headache	10 (38%)	8 (23.5%)
Generalized Weakness	12 (46.1%)	5 (14.7%)
Hypertension	4 (15.3%)	6 (17.6%)
Cigarette Smoking	1 (3.8%)	1 (2.9%)
Cerebrovascular accident	4 (15.3%)	1 (2.9%)
Splenomegaly	8 (30.7%)	0 (0%)

Ten (38%) patients belonged to the age group of 40-59 years, while nine (35%) patients were of more than 60 years of age. Male to female ratio was 21:5.

Thirty-four patients had idiopathic erythrocytosis. The mean age was 40.8 years. Median age was 42 years. Fourteen (41%) patients were less than forty years of age, 17 (50%) belonged to the age group of 40-59 years and 3 (8%) were more than 60 years of age. All patients were males. The remaining clinical features and laboratory investigations of both groups are given in Tables 1 and 2 respectively.

Table 2. Laboratory findings.

	Polycythemia vera (n=26)	Idiopathic erythrocytosis (n=34)
Mean hemoglobin gm/dl	18.2 ±1.8	17.7±0.8
Hb more than 18gm/dl	13 (50%)	9 (26.4%)
Mean hematocrit (%)	56.2%±5.7	52.8±0.8
Hematocrit >55%	12 (46.2%)	5 (14.7%)
Mean RBC count / cumm	7.3±1.2	5.9±0.3
RBC > 6.5 million / cumm	26 (100%)	2 (5.8%)
Mean white cell count	18.2 ±10	8.8±2.2
White cell > 12x10^9/L	20 (76.9%)	2 (5.8%)
Mean platelet countx10^9/L	544±276	227±50.6
Platelet > 400x10^9/L	21 (80.7%)	0 (0%)
Mean erythropoietin (u/ml)	2.2 ±1.2	6.8±2.4
Erythropoietin <3.3 u/ml	15/16 (93.7%)	1/10 (10%)

Table 3. Comparison of the statistically significant variables.

Variable	Polycythemia vera (n=26)	Idiopathic Erythrocytosis (n=34)	P value
Mean age (years)	51.3	40.8	<0.01
Weakness	12 (46.2%)	5 (14.7%)	<0.007
Hematocrit >55%	12 (46.2%)	5 (14.7%)	<0.007
RBC >6.5million/cumm	26 (100%)	2 (5.9%)	<0.000
White cell >12,000/cumm	20 (76.9%)	2 (5.9%)	<0.000
Platelet >400,000/cumm	21 (80.8%)	0 (0%)	<0.000
Erythropoietin <3.3 iu/L	15/16 (93%)	1/10 (10%)	<0.000

Statistically significant variables were mean age, generalized weakness at presentation, splenomegaly, hematocrit more than 55%, red blood cell count more than 6.5 million/ cumm, white cell count more than 12.0x10^{9}E/L, platelet count more than 400x10^{9}E/L and low serum erythropoietin level (less than 3.3 i.u/ml). This is summarized in Table 3.

Discussion

This study primarily focused on the two groups, that is the polycythemia vera and idiopathic erythrocytosis. The patients with idiopathic erythrocytosis were relatively younger (40.8 years versus 51.3 years, P valve <0.01) and

all were males. The male preponderance was also seen in another study.[7] However, since there is under representation of females to seek medical attention in our part of the world, male preponderance in this study could be an incidental finding. Although generalized weakness is a non-specific symptom, however, it was more common in polycythemia vera (p valve <0.007). Similarly splenomegaly in the presence of absolute polycythemia is almost diagnostic of polycythemia vera.[8]

Among the other statistically significant variables, white cell count more than $12.0x10^9$E/L (P value <0.000), platelet count more than $400x10^9$E/L (P value <0.000) and low serum erythropoietin level (P value <0.000) are already established either as a major or minor criteria to make a diagnosis of polycythemia vera.[9-12] This study further supports the above-mentioned variables to differentiate polycythemia vera from idiopathic erythrocytosis. Low serum erythropoietin level is now considered as a minor criterion for the diagnosis of polycythemia vera.[1] It was found normal in nine out of ten patients of idiopathic erythrocytosis in this study whereas its level was high in twelve out of 25 patients in another study.[13] Thus low serum erythropoietin level supports the diagnosis of polycythemia vera but normal or high level is non contributory.

Red blood cell count was more than 6.5 million/cumm in all patients of polycythemia vera. It was only seen in 2 (5.9%) patients (P value <0.000) in idiopathic erythrocytosis. Similarly hematocrit is more than 55% was noted in 12 (46%) patients of polycythemia vera as compared to 5(14.7%) cases of idiopathic erythrocytosis which is statistically significant.

It is concluded that the idiopathic erythrocytosis and polycythemia vera are the two major groups of disorders in patients who present with absolute polycythemia. Both of these disorders have been seen in relatively younger people and predominantly in males. It is also noted that with simple clinical and laboratory parameters, it is possible to differentiate between polycythemia vera and idiopathic erythrocytosis in most cases. Sophisticated investigations such as in vitro culture of erythroid colonies, karyotyping etc. may only be needed in occasional patients.

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