Polycythemia vera and essential thrombocythemia with monoclonal gammopathy: experience of a single institution

We studied the incidence of monoclonal gammopathy (MG) in 382 consecutive cases of polycythemia vera or essential thrombocythemia (MPD) and in 500 normal controls, stratified by age. A non-significant higher incidence of MG was seen in the oldest group of MPD. The occurrence of MG in such MPD is therefore likely coincidental.

Polycythemia vera (PV) and essential thrombocythemia (ET) are clonal diseases of middle/advanced age and may develop common features including a small potential for transforming into acute leukemia. Monoclonal gammopathy (MG) affects old people too and its etiology remains unknown. Concomitant cases of MG with PV or ET have been described in the literature (Table 1).

We retrospectively evaluated the data of 382 patients (170 males, 212 females, 164 PV and 218 ET, mean age 54.75±1.61, median follow-up 6.83 years), with a thrombocytosis over 500×10^9/L. The diagnoses were made in agreement with the Polycythemia Vera Study Group criteria[1] and all patients with myeloproliferative disease (MPD) underwent a bone biopsy. It is noteworthy that the diagnostic criteria for ET[2] comprehend the exclusion of secondary causes of thrombocytosis such as hematologic malignancies and in the presence of MG, which is a clonal anomaly, the diagnosis of ET may be difficult. Five hundred subjects without hematologic pathologies matched for sex and age (200 males, 300 females, mean age 53.28±2, median follow-up 7.2 years) were used as controls.

The patients and the controls were divided into: group A (younger than 55 years), group B (55–70 years) and group C (over 70 years). In the presence of a MG, monoclonal protein (M-protein) immunofixation electrophoresis was performed, immunoglobulins and β2-microglobulins assayed, Bence Jones proteinuria searched for, and bone marrow cytological and cytochemical studies carried out.

An M-protein was observed in 3.1% of MPDs, occurring in 3.2% of patients with ET, in 3 % of those with PV, and in 2% of controls. The M protein was detected in 2 patients of group A (1%), in 6 of group B (4.8%) and in 4 (5.8%) of group C and in 4 controls (1.6%) of group A, 4 (2.7%) of group B and 2 (2%) of group C. These prevalences were not statistically different. One ET patient with MG had a mild increase of reticulin fibers (less than 1/3 of the biopsied area)[3] while other patients with MPD had no marrow fibrosis. No lymphoid aggregates were found in our patients. The main characteristics of MPDs with M-protein are summarized in Table 2.

The general frequency of MG should be considered to be about 1% in the adult population[4] which increases with the increase of age, since it occurs in about 4–5 % of octogenerians.[5]

The occurrence of MG in our PV and ET patients is similar to that observed in the general population. In contrast, Economopoulos[6] reported 8.2% cases of MG in his group of patients with MPD with no MG among the 7 patients with ET and 3 in patients with PV.[7]

The effect of radiophosphorus and alkylating agents on the development of acute leukemia in patients with MPD has been recognized[8] but a relation between such therapy and the occurrence of MG may only be a matter of speculation.

A higher incidence of MG in MPD patients than in the controls was observed but without this being statistically significant, when both patients and controls were divided by age.

The development of MG in an individual diagnosed and treated for ET or PV is probably coincidental, but perhaps MG could arise from a separate clone or from the same stem cell as the megakaryocytes and red cells precursors.[9,10]

Table 1. Summary of the cases of monoclonal gammopathy (MG) associated with polycythemia vera (PV) or essential thrombocythemia (ET) published in the last 50 years.

MPD (30 cases)	Plasmacell dyscrasia	Chemotherapy for MPD before the diagnosis of MG
7 ET	5 MM	1 ^{32}P
	1 MGUS	4 alkylating agents
	1 light chains	1 none
21 PV	14 MM	3 ^{32}P
	6 MGUS	0 alkylating agents
	1 unknown	13 none

MM = multiple myeloma, MGUS = monoclonal gammopathy of unknown significance, MPD = myeloproliferative disorder, ^{32}P = radiophosphorus.

Table 2. Main characteristics of our patients with MPD and M-protein.

	Sex	Age	MPD	M-protein (gr/L)	Years between MPD and M-protein observation	Therapy for MPD
1	F	70	PV	IgM (1.53)	1	ASA
2	M	47	PV	IgG (11.9)	16	^{32}P, ASA, BU
3	F	63	ET	IgM (18.3)	0	none
4	F	45	ET	IgG (5.3)	5	ASA
5	M	68	ET	IgG (7.4)	0	none
6	F	78	PV	IgG (2.5)	4	ASA, HU
7	M	27	PV	IgG (1.7) IgM (3)	3	none
8	M	61	PV	IgG (2.5)	10	ASA, phlebotomy
9	M	60	ET	IgM (7.97)	0	none
10	F	66	ET	IgG (9.1)	3	none
11	F	74	ET	IgG (2)	0	none
12	M	49	ET	IgM (3.2)	10	^{32}P, ASA, BU

PV= polycythemia vera, ET= essential thrombocythemia, ASA= aspirin, ^{32}P= radiophosphorus, BU= busulfan, HU= hydroxyurea, MPD= myeloproliferative disorders.

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