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A Case of Multiple Myeloma Associated with Immune Thrombocytopenia

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Abstract Multiple myeloma with immune thrombocytopenia in an 81-year-old male is reported. He was admitted to our hospital because of paresis of lower extremities. Prednisolone therapy for autoimmune thrombocytopenia was followed by combination therapy (melphalan 8 mg/day + prednisolone 30 mg/day) against multiple myeloma. The platelet count increased to within normal range and correlated well with a decrease in PAIgG. There was no significant change in total IgG. Intermittent chemotherapy suppressed the proliferation of myeloma cells and maintained the platelet count in the normal range.

Key Words : Idiopathic Thrombocytopenic Purpura, Multiple Myeloma, PAIgG

Introduction

Thrombocytopenia is not a rare complication in patients with multiple myeloma. It is usually caused by chemotherapy or bone marrow replacement with myeloma cells[1]. Severe thrombocytopenia induced by an autoimmune mechanism, however, is not a common feature of multiple myeloma. To our knowledge, only 3 cases of multiple myeloma associated with immune thrombocytopenia have been reported[2,3]. We report a case of multiple myeloma with autoimmune thrombocytopenia and discuss the association of the two diseases. The significance of platelet-associated IgG (PAIgG) is also discussed.

Case Report

An 81-year-old male was admitted to our hospital in January, 1991, because of paresis of the lower extremities. No purpura was observed on his body. CT and MRI examinations of the central nervous system revealed no positive findings. Lumbar puncture gave a xanthochromic cerebrospinal fluid. Therefore, his paresis was thought to be caused by hemorrhage in the central nervous system. Blood examination on admission are shown in table 1. Hematologic examination revealed thrombocytopenia with a slight decrease in hemoglobin and a normal white blood cell count and differential. Blood chemical analysis revealed an increase in gamma-globulin and very mild liver dysfunction. There was a remarkable elevation of IgG with normal IgA and IgM. Platelet associated IgG (PAIgG) was markedly increased. Tests for blood coagulation disclosed no abnormal findings. Antinuclear antibody was negative and CH50 was within normal limit. There were no findings suspecting of disease or disseminated intravascular coagulation

Table 1. Laboratory findings on admission.

		(Normal Range)	
RBC	390	(450−550)	X $10^4/\mu l$
Hb	12.9	(14−18)	g/dl
Ht	36.6	(40−50)	%
Platelet	0.2	(15−40)	X$10^4/\mu l$
WBC	50	(40−100)	X$10^2/\mu l$
Neutro	66.2	(41−64)	%
Lymph	21.2	(30−46)	%
Mono	7.2	(4−10)	%
Eosino	5.0	(1−5)	%
Baso	0.4	(0−2)	%
Bleedng time	2.0	(1−3)	min
PPT	12.4	(10.5−13.0)	sec
aPTT	27.6	(23−35)	sec
Thrombo test	123	(70−130)	%
ATlll	68	(80−120)	%
FDP (serum)	5	(<10)	μg/ml
ANA	(−)		
CH50	33.2	(30.0−40.0)	U/ml
C3	60	(60−116)	mg/dl
C4	21	(15−44)	mg/dl
PAIgG	809.7	(9.0−25.0)	ng/10^7 CELLS
CRP	4.1	(<0.3)	mg/dl
TP	9.4	(6.7−8.3)	g/dl
AIb	3.4	(3.8−5.6)	g/dl
γ-GIb	43.2		%
IgG	4440	(1000−2060)	mg/dl
IgA	202	(115−440)	mg/dl
IgM	119	(74−330)	mg/dl
GOT	32	(10−27)	IU/l
GPT	35	(5−33)	IU/l
ALP	465	(96−284)	IU/l
LDH	576	(180−460)	IU/l
γ-GTP	30	(4−63)	IU/l
TB	0.6	(0.2−1.1)	mg/dl
CH-E	0.64	(0.7−1.2)	ΔPH
CHO	176	(130−250)	mg/dl
HB-Ag	(−)		
HB-Ab	(−)		
HCV-Ab	(−)		

that may cause thrombocytopenia. A bone marrow aspirate disclosed an increase in megakaryocytes with a few nuclei and no attached -platelets, and a moderate proliferation (16% of total nucleated marrow cells) of atypical plasma cells (Figures 1, 2 and Table 2). Immunoelectrophoresis of patient's serum protein confirmed the presence of a monoclonal immunoglobulin of IgG kappa type (Figure 3). Bence-Jones protein was not detected in the urine. Skeletal X-rays revealed only osteoporosis and no punched out lesion was detected. Physical examination and abdominal ultrasonography revealed no hepato -splenomegaly. These results allowed us to make a diagnosis of multiple myeloma associated with immune thrombocytopenia. The patient was started on prednisolone (30 mg/day), because it was assumed that the thrombocytes were destroyed by some immune mechanism before the diagnosis of multiple myeloma was established. Platelet count increased from 2,000/ 1 to 220,000/ 1 in a week, on the other hand, the PAIgG level decreased from 809.7 ng/10^7 cells to 53.7 ng/10^7 cells in the same period. There was an inverse

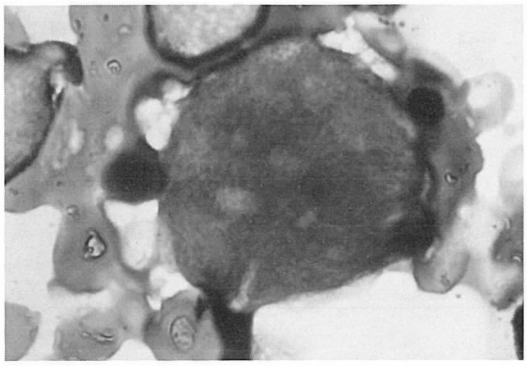

Fig. 1. Bone marrow aspirate on admission, showing megakaryocytes with no platelets attached. Wright stain, ×1000.

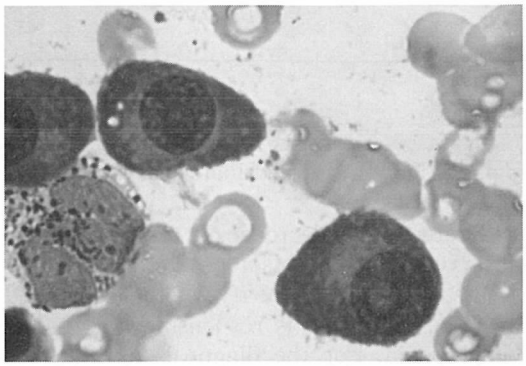

Fig. 2. Bone marrow aspirate on admission, showing atypical plasma cells with a large nucleus. Wright stain, ×1000.

relationship between the platelet count and PAIgG as shown in Figure 4. By the intermittent chemotherapy (melphalan 8 mg/day + prednisolone 30 mg/day for 4 days), the patient's serum IgG level and the number of myeloma cells in the bone marrow decreased gradually to 2630 mg/dl and 2.4%, respectively, in a month. Daily prednisolone was tapered, and chemotherapy with melphalan and prednisolone was carried out

Table 2. Findings of bone marrow aspirate.

NCC		$20\times10^4/\mu l$
Megakaryocyte count		$0.1\times10^4/\mu l$
Promegakaryocyte		2.0%
Megakaryocyte		79.0%
Metamegakaryocyte		18.0%
Naked megakaryocyte		1.0%
Differential		
Erythroid series		27.4%
Proerythroblast		0.0%
Basophilic erythroblast		5.6%
Polchromatic erythroblast		21.8%
Orthochromatic erythroblast		0.0%
Myeloid series		47.2%
Neurophil	Promyelocyte	6.4%
	Myelocyte	11.2%
	Metamyelocyte	8.2%
	Band	11.6%
	Segment	4.0%
Eosinophil		5.6%
Basophil		0.2%
Lymphocyte		8.0%
Monocyte		0.4%
Plasma cell		16.2%

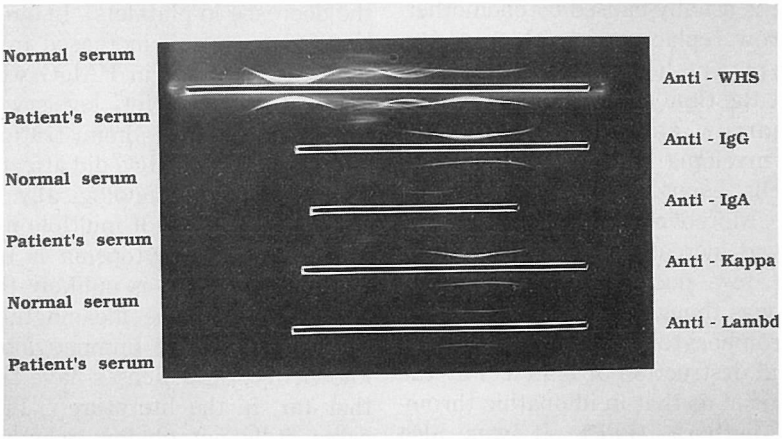

Fig. 3. Immunoelectrophoresis of serum protein, demonstrating a monoclonal kappa type IgG in the patient's serum.

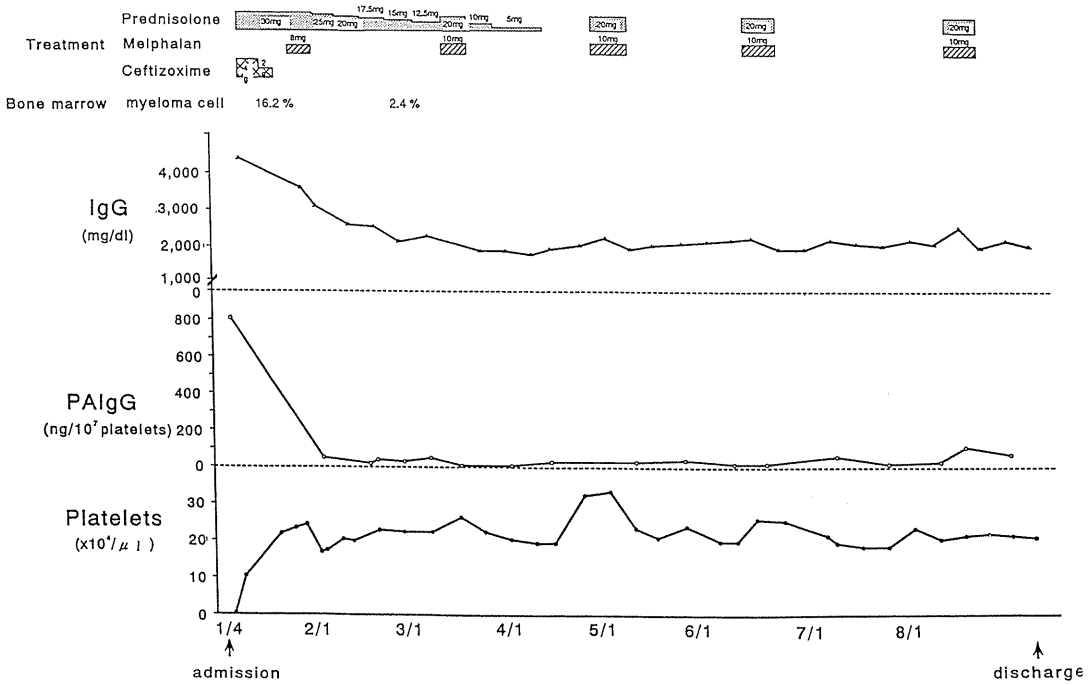

Fig. 4. Clinical course and time course of the IgG, PAIgG and Platelets.

every 6 weeks. After discharge, the patient remained on the same chemotherapy regimen, and IgG level, percent myeloma cells in the bone marrow and platelet count were under good control.

Discussion

Thrombocytopenia in patients with multiple myeloma is usually caused by chemotherapy or marrow replacement with myeloma cells[1]. In our patient, however, no medication was given at the time of first admission and his bone marrow aspirate showed only 16.2 % of myeloma cells, no increase in myeloma cells enough to replace normal marrow cells. Moreover, the number of megakaryocytes was increased and many of them had only a few nuclei and no platelets attached. It was thought, therefore, that this patient's thrombocytopenia was caused by the peripheral destruction of platelets by the same mechanism as that in idiopathic thrombocytopenic purpura (ITP). It was also proved by the fact that rapid increase in the thrombocyte count and decrease in PAIgG without enough decrease in total IgG were observed after prednisolone therapy.

It is important to clarify whether a marked increase in PAIgG is responsible for thrombocytopenia. For the diagnosis of ITP, the specificity of PAIgG is poor[4]. Moreover, McGrath et al. reported that the PAIgG level was increased in patients with hypergammaglobulinemia, including IgG myeloma without the decrease in platelets[5]. In our case, thrombocyte count was increased in combination with the decrease in PAIgG when total immunoglobulin and IgG levels were still high after prednisolone administration. Therefore we believe that PAIgG did affect the patient's thrombocytes immunologically.

The association of multiple myeloma with immune thrombocytopenia is unusual. This may be because it is unlikely that myeloma cells produce some meaningful quantity of functionally active immunoglobulin. To our knowledge, only 3 cases have been reported, thus far, in the literature[2,3]. In all of these cases, it is not obvious whether idiopathic thrombocytopenic purpura was associated with multiple myeloma or immune throm-

bocytopenia was caused by multiple myeloma, in other words, whether non-neoplastic plasmocytes or neoplastic plasmocytes, that is myeloma cells, produced immunoglobulin with anti-platelet activity. We hope to solve this problem, however so far we have no additional blood specimen available to confirm whether the abnormal IgG produced by myeloma cells results in the peripheral destruction of thrombocytes or not. It is necessary to cautiously follow the patient's platelet count to elucidate the mechanism of thrombocytopenia.

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