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Original Article

2 cases of multiple myeloma onset from coagulation disorder and literature review

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Abstract: This article retrospectively analyzed 2 cases of multiple myeloma (MM) with onset from coagulation disorder, and reviewed the similar cases in literatures. 2 patients all exhibited skin and mucosal bleeding as the first symptom, among who one case exhibited extended prothrombin time (PT) and thrombin time, increased D-dimer quantitation, reduced clotting factor XII, while the other case exhibited extended PT and activated partial thromboplastin time. Both cases had no associated symptom such as pain, fever, etc., and were diagnosed as MM IgG type. Combining the retrieved similar cases, it is found that MM patients with onset from coagulation disorder all belong to IgG type, and the types of the coagulation abnormality are diverse, with no special rule. The relationship between MM and coagulation disorder are complex, and the current therapeutic strategy still mainly depends on treating the basic diseases.

Keywords: Coagulation disorder, IgG type, multiple myeloma, treatment

Introduction

Multiple myeloma (MM) is characterized by malignant proliferation of monoclonal plasma cells and secretion of large amounts of monoclonal immunoglobulin. It causes extensive bone destruction, recurrent infections, anemia, hypercalcemia, hyerviscosamia and renal insufficiency, finally leading to undesirable consequences [1]. MM patients are often detected with various types of coagulation dysfunction, although the clinical severe bleeding is uncommon [2, 3]. MM patients have much more obvious bleeding trendy in the renal biopsy than non-MM patients [4]. There are less MM patients with onset from coagulation disorder but not other clinical symptoms such as bone pain or fever. Therefore, these patients are easily misdiagnosed and missed clinically. This paper reported two MM cases with onset from coagulation disorder, aiming to provide a reference for correct identifying this kind of MM and timely treatment. This study was conducted with approval from the Ethics Committee of First Affiliated Hospital of Kunming Medical University. Written informed consent was obtained from all participants.

Case 1

Male (43 years old), hospitalized on September 23, 2013 for "repeated oral mucosal bleeding for 10 days, and increased globulin for five days". On September 12, 2013, the patient came to hospital for non-incentive oral mucosal bleeding, while the bleeding volume was small and could self-cease. There was no fever, bone pain, dizziness or fatigue. Blood routine: white blood cell (WBC), 6.4×10^9/L; absolute neutrophil counting (NC), 3.2×10^9/L; red blood cell (RBC), 5.0×10^{12}/L; hemoglobin (Hb), 152 g/L; platelet (PLT), 202×10^9/L (all above were normal); prothrombin time (PT), 14.1 sec (extended); thrombin time (TT), 43.9 sec (extended). D-dimer quantitation: 1.5 ug/mL (increased). Coagulation factor XII, 76% (slightly lower); coagulation factor XII, 40.3% (lower); activated partial thromboplastin time (APTT), antithrombin III, fibrinogen quantitation, and clotting factor II, V, VII, VIII, IX and XI were normal. Von

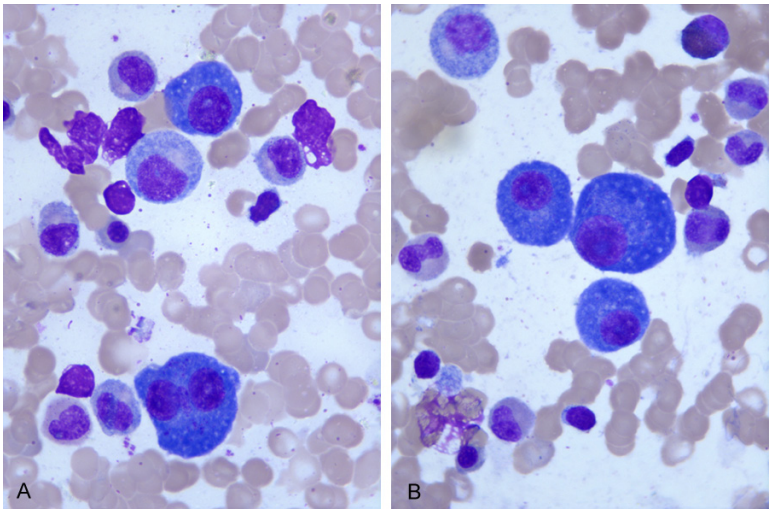

Figure 1. Bone marrow aspiration smear. A. In case 1, plasma cells accounted for 32% of nucleated cells. Naive plasma cells were obvious, accounting for 21% in classification. B. In case 2, plasma cells accounted for 43% of classification. Naive plasma cells were obvious, accounting for 31% in classification.

Willebrand factor antigen VWF/Ag, protein C and protein S were normal. Blood chemical indicators: total protein, 107.3 g/L; albumin, 35.7 g/L; globulin, 71 g/L. Hepatonephric function and normal serum calcium were normal. Immunoglobulin indicators: immunoglobulin G, 64.30 g/L; immunoglobulin M, 0.17 g/L; immunoglobulin A, 0.23 g/L; light chain of immunoglobulin λ, 15.80 g/L; light chain of immunoglobulin κ, 0.54 g/L; free light chain ratio, 0.034; light chain of urinary immunoglobulin λ, 138.00 mg/L; light chain of urinary immunoglobulin κ, 11.50 mg/L; urinary β2 microglobulin, 0.21 mg/L. Bone marrow aspiration smear indicated active hyperplasia of nucleated cells in bone marrow and significant proliferation of plasma cell system (**Figure 1A**), accounting for 32% of classification. Naive plasma cells were obvious, accounting for 21% of classification. Urine: urinary occult blood, 1+. The rest indexes were normal. Skull, vertebrae and pelvic X-ray examinations showed no obvious bone destruction. Diagnosis: phase I of MM IgG type λ light chain group A. Treatment: chemoradiation (vincristine, 2 mg, 1 day; pirarubicin, 20 mg, 1-3 days; prednisolone, 90 mg, 1-5 days). After the first course of treatment, the bleeding did not appear. The patient was discharged after improvement. The parameters related to MM and coagulation factors before and after treatment were summarized in **Table 1**.

Case 2

Male (40 years old), admitted for "repeated epistaxis for six months, dizziness and fatigue for one week". From January 2012, He presented recurrent epistaxis (small volume), and could self-cease, thus paid no serious attention. Since July 2012, he felt dizziness and fatigue, thus came to our hospital for treatment. There was no fever, bone pain or other special discomfort. Blood routine: WBC, 5.37×10^9/L; absolute NC, 2.26×10^9/L; RBC, 2.8×10^{12}/L; Hb, 70 g/L; mean corpuscular volume, 67 fL; mean corpuscular hemoglobin, 18 pg; mean corpuscular hemoglobin concentration, 280 g/L; PLT, 179×10^9/L (small cell hypochromic anemia). Coagulation indicators: PT, 18.2 sec (extended); APTT, 67.2 sec (extended), the rest had no exception. Blood chemical indicators: total protein, 124.1 g/L; albumin, 36.1 g/L; globulin, 88 g/L; hepatonephric function and serum calcium, normal. Immunoglobulin indicators: immunoglobulin G, 69.80 g/L; immunoglobulin M, 0.21 g/L; immunoglobulin A, 0.17 g/L; light chain of immunoglobulin λ, 0.41 g/L; light chain of immunoglobulin κ, 16.84 g/L; free light chain ratio, 0.024; light chain of urinary immunoglobulin λ, 12.0 mg/L; light chain of urinary immunoglobulin κ, 142.50 mg/L; urinary β2 microglobulin, 0.76 mg/L. Bone marrow aspiration smear indicated active hyperplasia of nucleated cells in bone marrow and significant proliferation of plasma cell system (**Figure 1B**), accounting for 43% of classification. Naive plasma cells were obvious, accounting for 31% of classification. Iron staining indicated extra-iron negative. Bone marrow picture was consistent with that of MM. Skull, vertebrae and pelvic X-ray examinations showed no obvious bone destruction. Diagnosis: phase I of MM IgG type κ light chain group A; iron deficiency anemia. The patient gave up treatment for family reason.

Discussion

We have retrieved the cases related to MM with onset from coagulation disorder in recent years

Table 1. Changes of MM related parameters and coagulation factors before and after treatment in case 1

		Before treatment	After two courses of chemotherapy	After four courses of chemotherapy
Blood biochemical index	GLP (g/L)	71	54.3	46.8
	ALB (g/L)	36.3	34.7	34.1
	TP (g/L)	107.3	89	80.9
Blood	IgG (g/L)	64.3	42.4	30.7
	λ light chain (g/L)	15.8	10.8	9.8
	κ light chain (g/L)	0.54	0.68	0.53
	κ/λ	0.034	0.063	0.055
	β_2-MG (mg/L)	1.36	2.11	2.13
Urine	λ light chain (g/L)	138	30.1	7.25
	κ light chain (g/L)	11.5	6.81	11.5
Blood routine	WBC ($\times 10^9$)	6.4	5.72	3.67
	N (%)	50	40.8	42.3
	Hb (g/L)	152	121	122
	PLT ($\times 10^9$)	202	164	156
Bone marrow aspiration smear		Stage-III proliferation; plasma cells, 32%; naive plasma cells, 21%	Stage-II proliferation; plasma cells, 22%	Stage-II proliferation; plasma cells, 20%; naive plasma cells, 10%
Coagulation function	PT (s)	14.1	13.2	12.6
	TT (s)	43.9	27.4	27.8
	APTT (s)	36.2	36	33.8
	Fib (g/L)	3.31	4.09	3.11
Coagulation factors	D-Dimer (ug/mL)	1.5	Normal	Normal
	Coagulation factor X (%)	76	96	92
	Coagulation factor XII (%)	40.3	78	75
	Antithrombin III, coagulation factor II, V, VII, VIII, IX, XI, vWF antigen, protein C, protein S	Normal	Normal	Normal
Others	Liver and kidney function, blood Ca, skull, thoracic vertebrae and lumbar vertebrae, pelvis X-ray	Normal	Normal	Normal

Table 2. 6 MM cases with onset from coagulation disorder

Gender	Age	Type*	Situation of coagulation abnormality	Reference
Male	72	A	Paraprotein, 85.75 g/L; TT, 76.8 sec; APTT, 39.5 sec; PT, 23.5 sec; reptilase time, 72 sec; increased fibrinogen	[5]
Male	59	B	TT, 50.7 sec; APTT, 52.8 sec; PT, 15 sec; bleeding time, 17 sec	[6]
Female	43	B	APTT, 84.4 sec (extended); VIII factor, 6% (reduced); rest was normal; titer of VIII factor inhibitor, 10 BU/mL.	[7]
Female	57	C	PT, 19.1 sec (increased); APTT, 128.6 sec (increased); slightly increased fibrinogen; XII factor: 45% (reduced); rest was normal.	[8]
Male	49	C	TT, > 10 sec (extended); APTT, 56.2 sec (extended); vWF antigen, 6% (reduced); vWF: RC, < 6% (reduced); bleeding time, > 10 sec; activity of VIII factor, 11% (reduced)	[9]
Unknown	56	B	Paraprotein, TT and reptilase time were increased	[10]

*A, Phase III of MM IgG κ light chain type group A; B, MM IgG κ light chain type; C, MM IgG λ light chain type.

[4-10] (**Table 2**). It is found that, this kind of MM is very rare. Two cases in this study and the reported cases are all diagnosed as IgG type. However, due to small sample size, this may not represent all cases. The types of the coagulation abnormality in these cases are diverse, with no special rule. In treatment, there is no systematic scheme to be referred.

Disclosure of conflict of interest

None.

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