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LETTER TO THE EDITOR

IgD myeloma indicated by plasma cells in the peripheral blood and massive pleural effusion

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Dear Editor,

Multiple myeloma, a B-cell malignancy characterized by clonal proliferation of plasma cells in the bone marrow, has been associated with unique clinicopathologic features, genetic abnormalities, and response to therapy [1–3]. Immunoglobulin D (IgD) myeloma is a rare disease, accounting for about 2% of all myelomas. Pleural effusions occur in 6% of myeloma patients. The etiology is multifactorial and effusions due to pleural myelomatous involvement are rare, occurring in <1% of the cases [4].

We experienced a patient with IgD λ multiple myeloma, which was first indicated by plasma cells in the peripheral blood. Furthermore, cytogenetic study of the pleural effusion revealed several abnormalities. We reviewed the clinical and cytogenetic features of this case and report the findings in detail.

An 82-year-old man was admitted to our hospital in February 2002 with the chief complaint of dyspnea on effort and arrhythmia. His medical history included myocardial infarction in 1991. Chest X-ray results showed cardiomegaly and bilateral pleural effusion. He was diagnosed with acute heart failure as a result of previous myocardial infarction. The administration of diuretics and an antiarrhythmic resulted in a rapid improvement. However, the recovery did not last; the pleural effusion slowly increased and diuretics were ineffective. Moderate anemia worsened and transfusion was necessary. Hematological examination revealed plasma cells in the peripheral blood and a hematologist was consulted. On physical examination, there was anemia in the connective pulp, and heart sounds showed a systolic murmur. There was a decrease in breath sounds at the base of both lungs. Bilateral presidia-pitting edema was evident. Hematological examination revealed anemia (hemoglobin 7.7 g/dl) with plasma cells in the peripheral blood (18%). Total serum protein was 6.0 g/dl with 64.9% albumin and 14.5% γ-globulin. Creatinine 1.35 mg/dl, blood urea nitrogen 27 mg/dl, uric acid 13.3 mg/dl, and lactate dehydrogenase 679 IU/L (reference range 230–460). Immunoelectrophoresis showed monoclonal IgD (λ) in the serum and Bence Jones protein (λ) in the urine. Quantitative immunoglobulin determination showed a marked increase in IgD, 934 mg/dl, while IgG, IgA and IgM levels were decreased (Table 1). Bone marrow aspiration resulted in dry tap and biopsy results showed multiple myeloma. Chest X-ray results showed bilateral pleural effusion, whereas X-ray examination of the rest of the body was normal. Echocardiography results did not indicate amyloid deposition in the myocardium, but the ejection fraction was decreased because of a previous myocardial infarction.

The patient also underwent thoracentesis. Cytological examination of the pleural effusion showed numerous plasma cells. There were two sizes of atypical plasma cells: small, round-shaped, mature plasma cells, and large, round-shaped, immature plasma cells. Clusters of differentiation 38 (CD38) and CD138 surface markers were investigated in the pleural effusion and found to be positive in 99.4% and 91.5% of the cells, respectively. Metaphase cytogenetic study on the pleural effusion revealed abnormal karyotypes by G-banding. In the abnormalities, 11q13, 14q32 was evident and +9, −13, −22 were also detected. After the first cycle of combination chemotherapy with cyclophosphamide, vincristine, melphalan, predonisone

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Table 1 Laboratory findings

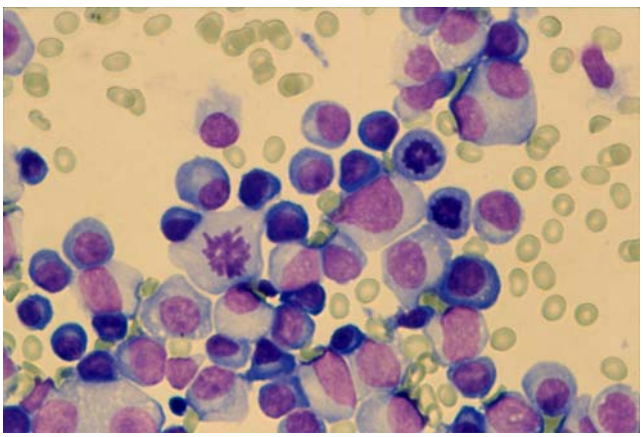
Blood picture		Blood chemistry				Immunoglobulin		Coagulation work		Pleural fluid	
RBC	224×10^4 per microliter	CRP	0.2 μg/dl	BUN	27.0 mg/dl	IgG	373 mg/dl	PT	13.3 s	Surface marker	
Hb	7.7 g/dl	Na	143 mM	Cr	1.35 mg/dl	IgA	33 mg/dl	APTT	35.4 s	CD19	0.7%
Hct	23.4%	Cl	11 mM	UA	13.3 mg/dl	IgM	10 mg/dl	Fbg	375 mg/dl	CD20	0.6%
MCV	105.0 μm^3	K	4.2 mM	GOT	32 IU/l	IgD	934 mg/dl	FDP	2.0 μg/dl	CD27	3.0%
MCH	34.5 pg	Ca	9.1 mg/dl	GPT	29 IU/l					CD83	99.4%
MCHC	33.0%	P	4.7 mg/dl	γ-GTP	62 IU/l					CD138	91.5%
PLT	5.7×10^4 per microliter	TP	6.0 g/dl	ChE	217 IU/l					Chromosome analysis	
WBC	4,000 per microliter	Alb	64.90%	LDH	679 IU/l					47,XY,del(1)del(1)(p11p13)ins(1;?)(q21:?),add(3)(p13)(,−8,+9),	
Eos	5.0%	α 1-gl	3.70%	ALP	241 IU/l					t(11;14)(q13;q32),add(12)(p11),−15add(17)(p11),−22,+mar (ten cells)	
Seg	28.0	α2-g l	9.10%							47,idem,add(3)(p11) (nine cells)	
Lym	39.0	β-g l	7.80%							46,idem,−9,−13,−21,−22,+3mar (one cell)	
Aty. Lym	17.0	γ-g l	14.50%							IL-6	3,970 pg/ml
Mono	10.0										

(VCMP)–vincristine, saimerine, Adriamycin, predonisone (MCNU-VMP; Table 1), the plasma cells in the peripheral blood disappeared; chest radiograph showed a reduction of pleural effusion and the anemia improved. IgD levels decreased rapidly to 44.7 mg/dl after completion of four cycles of chemotherapy. The patient was discharged from our hospital in early June. In outpatient clinic, the patient was treated two more times with the same chemotherapy, but high fever persisted and bilateral pleural effusions increased. He was readmitted in late August and treated with antibiotics and an antifungal agent, but the clinical course was aggressive, and he died of septic complications and progression of the disease.

IgD myeloma was first reported in 1965 by Row and Fahey [5], and the pathological and clinical features were described by Jancelewicz et al. [6] and Hobbs and Corbett [7]. IgD myeloma is characterized by a small monoclonal IgD peak, occurrence in younger subjects, primarily in men, a high incidence of both Bence Jones proteinuria and renal insufficiency, an exceptionally high prevalence of λ light chains over κ light chains, and frequent occurrence of extraosseous spread. The difficulty in the diagnosis of IgD myeloma is based on the lack of an M component. IgD exhibits a very short biological half-life in peripheral blood. The rate of catabolism of IgD is 26% per day, compared with 3~6% per day for IgG, and 10~15% per day for IgA.

Myelomatous pleural effusion has been considered as a late manifestation in the natural history of multiple myeloma or as an expression of the aggressive behavior of the disease. Pleural effusions occur in approximately 6% of patients with myeloma. The etiology is multifactorial, and effusions due to pleural myelomatous involvement are rare, occurring in <1% of the cases [4]. In previous reports of myelomatous pleural effusions, 80% were due to IgA, whereas the others were mostly due to IgG.

Pleural effusions in myeloma may be due to nephrotic syndrome, pulmonary embolism, congestive heart failure secondary to amyloidosis, secondary neoplasms and infiltration of myeloma cells from adjacent skeletal or parenchymal locations, direct implantation of plasma cells on the pleura, and mediastinal lymph node infiltration with lymphatic obstruction [8–10]. Extramedullary plasmacytoma is a rare type of tumor, comprising approximately 4% to 6% of the plasma cell malignancies [8, 11].



In our case, a variety of chromosomal abnormalities were detected from the pleural effusion. Translocations involving the immunoglobulin heavy chain (IgH) region at chromosome region 14q32 are regularly involved in human B-cell malignancies and may upregulate existing oncogenes or create new hybrid genes with transforming properties. For example, Burkitt lymphoma shows a specific t(8;14)(q24;q32). This case demonstrated t(11;14)(q13;q32), which commonly results in the fusion of the *BCL-1* locus, although the break points in myeloma may be different from those observed in mantle cell lymphoma. The protooncogene c-myc is translocated to the IgH locus at 14q32, resulting in increased expression of the oncogene because of strong immunoglobulin enhancers [12]. 14q32 has been detected in 74% of patients with multiple myeloma, by fluorescence *in situ* hybridization, and in 85% of plasma cell leukemia cases [2]. 14q32 is one of the factors related to a poor prognosis. These translocations are found in the earliest stage of the disease, suggesting that such translocations are an early and possibly initiating event in the disease development [13]. The detection of genetic changes is important, not only because of their association with clinical prognosis, but also because they can be used as measurable targets for response to treatment.

Malignant effusions can occur in the terminal stage of the disease and are difficult to treat. This particular case of multiple myeloma had a poor prognosis and required appropriate therapy. In general, with the appearance of malignant effusions, systemic chemotherapy and drainage are necessary. In IgD myeloma, most patients tend to be younger than other myeloma patients, and there are likely a large number of eligible cases. As a therapeutic approach for IgD myeloma, especially the λ type, we consider that peripheral blood stem cell transplantation will result in a good prognosis after conventional chemotherapy.

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