

Tumor lysis syndrome presenting in a patient with multiple myeloma treated with vincristine, adriamycin, and dexamethasone: a case report

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Published: 19th October, 2012

Accepted: 19th October, 2012

Received: 11th August, 2012

Revised: 13th September, 2012

Open Journal of Hematology, 2012, 3-3

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Keywords: tumor lysis syndrome, multiple myeloma, VAD, renal dysfunction

ABSTRACT

Multiple myeloma has seldom been reported to complicate tumor lysis syndrome since it is an indolent disease. We report a case with multiple myeloma who rapidly developed tumor lysis syndrome after conventional induction therapy.

A 63-year-old Japanese woman presented with dyspnea on effort was diagnosed as IgA-lambda type myeloma. According to the International Staging System, her stage was defined as III because of elevated serum beta-2 microglobulin at 72mg/L. Remission induction consisted of continuous intravenous administration of vincristine of 0.4mg/day and adriamycin of 15mg/day through days 1 to 4 and infusion of dexamethasone of 40mg/day on days 1-4 was given. On day 7, she felt general fatigue and loss of appetite and her serum uric acid, creatinine, and potassium elevated to 898.1μmol/L, 9.8mg/dL, and 6.7mmol/L, respectively. Inversely, serum calcium decreased to 2.0mmol/L. Under the diagnosis of tumor lysis syndrome, she was treated with hydration and diuretics, resulted in immediate regression of her symptoms and recovery of laboratory data.

Besides conventional chemotherapy, newly introduced agents have also been reported to cause tumor lysis in myeloma. While previous description has identified renal dysfunction to play a crucial role in the development of tumor lysis syndrome, myeloma often complicates impaired renal function. Since International Staging System is widely applied for myeloma patients, beta-2 microglobulin that represents renal function is thought to be examined in most of them. Taken together, elevated beta-2 microglobulin appears to easily predict a risk for tumor lysis syndrome. Thus, we postulate that prevention for excessive tumor lysis should be considered for myeloma patients with elevated beta-2 microglobulin.

INTRODUCTION

Tumor lysis syndrome (TLS) is recognized as a complication of malignancies that shows hyperuricemia, hyperkalemia, and hypocalcemia resulted in by massive destruction of tumor cells [1]. Among those, hyperuricemia often causes severe renal dysfunction. Since TLS is associated with large tumor burden, rapid tumor growth, or high sensitivity to cytoreductive chemotherapy, hematologists often encounter TLS when they treat hematological tumors, especially leukemia or aggressive lymphoma. However, multiple myeloma (MM) has seldom been reported to complicate TLS even after intensive chemotherapy since it is an indolent disease [2].

We report a case with MM who developed TLS shortly after conventional induction therapy consisting of vincristine, adriamycin, and dexamethasone (VAD). In addition, we discuss about an appropriate indication of TLS prevention for MM regardless of patients' characteristics or

Table: Laboratory data on admission

WBC	6.03x10 ⁹ /L	T-prot	107g/L	BUN	4.99mmol/L
RBC	2.0x10 ¹² /L	Alb	34g/L	Cr	0.73mg/dL
Hb	61g/L	AST	19μkat/L	UA	321.2μmol/L
Ht	18.5%	ALT	15μkat /L	Ca	2.4mmol/L
PLT	162x10 ⁹ /L	LDH	90μkat /L	β-2mg	72mg/L
		ALP	190μkat /L		
U-prot	1+	γ-GTP	21μkat /L	IgA	32.4g/L
				IgG	32.7g/L
				IgM	4.2g/L
				IEP	IgA-kappa
Bone marrow					
Nucleated cells	140x10 ⁹ /L				
Plasma cells	69.4%				

Remission induction of VAD that consisted of continuous intravenous administration of vincristine of 0.4mg/day and adriamycin of 15mg/day through days 1 to 4 and infusion of dexamethasone of 40mg/day on days 1-4 was given. On day 7, she complained general fatigue and loss of appetite. Her serum uric acid, creatinine, and potassium elevated to 898.1μmol/L, 9.8mg/dL, and 6.7mmol/L, respectively. Inversely, serum calcium decreased to 2.0mmol/L. Her urine volume was more than 1000ml/day. Under the diagnosis of TLS, she was treated with hydration and diuretics, resulting in immediate regression of her symptoms and recovery of laboratory data (Figure).

therapeutic agents.

CASE PRESENTATION

A 63-year-old Japanese woman visited our department complaining of dyspnea on effort that had developed a few months before. Her skin and visible mucosa were anemic. Laboratory data showed normocytic anemia with hemoglobin level at 61g/L and hyperproteinemia containing of increased IgA at 32.4g/L (Table). Immunoelectrophoresis of her serum revealed IgA-lambda M-protein. Her serum creatinine (Cr) and glomerular filtration rate (GFR) were normal. Plasma cells occupied 69.4% of nucleated cells on bone marrow examination. The karyotype of tumor cells was 46,XX. X-ray examination found no bone lesions. International staging system (ISS) established by Greipp et al. [3] defined as stage III because of elevated serum beta-2 microglobulin (B2MG) at 72mg/L. No plasma cell was seen in her peripheral blood.

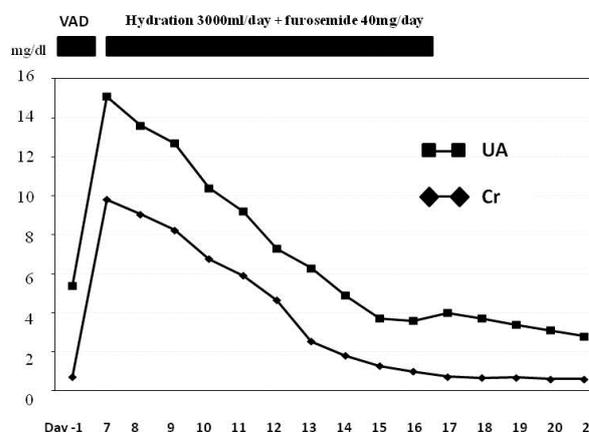


Figure: Change in various parameters of the patient. After hydration and diuresis, all markers immediately improved.

DISCUSSION

To date, only a few literatures have referred to TLS complicated with MM. Fassas et al. estimated the frequency of TLS at approximately 1% (9 of 820 MM patients) even after intermediate or high-dose chemotherapy [2]. Sezer et al. also reported that newly applied agent, bortezomib, caused TLS at only 1.4% (7 of 496 patients) [4].

Extensive bone marrow plasma cells (more than 70%), hyperproliferation, immature morphology, and unfavorable cytogenetic abnormalities are regarded as risk factors of TLS in MM [2, 5]. In addition, previous description has also identified renal dysfunction to play a crucial role in the development of TLS [6]. On the other hand, MM often complicates impaired renal function caused by deposition of MM-derived light chain, so called myeloma kidney. Although our patient showed normal serum Cr and GFR, an elevation of B2MG at presentation was seen, suggesting latent renal dysfunction. ISS has been established to evaluate prognosis of untreated MM patients using only two values of serum albumin and B2MG. If B2MG level is greater than 55mg/L, the stage is estimated as most advanced. The stage is often corresponding to tumor burden. Since ISS is widely applied for MM at the initial presentation, B2MG is now thought to be routinely examined. We additionally analyzed the relationship between elevated B2MG at the initial presentation and renal dysfunction caused by induction chemotherapy in forty seven patients with MM we have treated in the last decade. The therapeutic regimens were melphalan and prednisolone for thirteen patients, VAD for twenty four, bortezomib and dexamethasone for eight, and high-dose dexamethasone for two. Renal dysfunction was caused in four of eighteen patients with elevated B2MG greater than 55mg/L

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(22.2%) and none in the remaining twenty nine (0%). This difference was significant ($p=0.017$ by Fisher's exact test). Taken together, elevation of B2MG appears to easily predict a risk of TLS.

As Chen et al. found 4 out of 34 MM patients (11.7%) complicated TLS treated with bortezomib and thalidomide [7], we should note that the frequency of TLS might be increasing with various combinations of newly introduced agents [8, 9]. Moreover, even steroid monotherapy has been reported to induce TLS [10]. Thus, we recommend that prevention of TLS should be given to MM patients with elevated B2MG, especially in induction therapy.

Rasburicase, a recombinant urate oxidase, has recently been shown to be more effective for TLS prevention than allopurinol by a phase III study [11]. Although it is available in practical medicine and its effectiveness in MM has been described [11], it is not yet routinely used. More use of rasburicase with chemotherapy for MM might be recommended to reduce the frequency of fatal TLS.

ACKNOWLEDGEMENTS

Hiroto Kaneko and Yumina Sugahara diagnosed and managed the tumor lysis of the presented case. The two authors wrote the Case Presentation and Discussion sections of the manuscript. Toshiki Iwai, Muneo Ohshiro, and Yasuhiko Tsutsumi have treated the patients and contributed to writing Introduction. Shohei Yokota and Shigeo Horiike prepared Introduction and Discussion. Masafumi Taniwaki reviewed the draft manuscript.

CONFLICT OF INTEREST

No authors have any conflict of interest about this study.

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