Characteristic Patients with Multiple Myeloma at Dr. Kariadi Hospital Semarang

Santosa Iva, Catharina Suharti, Mika Lumban Tobing, Suyono, Eko Adhi Pangarsa

Division of Hematology-Medical Oncology, Department of Internal Medicine,
Diponegoro University-Dr. Kariadi Hospital Semarang

ABSTRAK.

Latar belakang. Multiple myeloma (MM) adalah keganasan yang membedakan karakter B-limfosit ditandai dengan akumulasi sel plasma klon dalam sumsum tulang (BM), adanya imunoglobulin monoklonal (Ig) dalam serum atau urine, dan lesi tulang osteolitik.[1] Komplikasi penyakit ini terdiri dari infeksi bakteri berulang, anemia, lesi osteolitik dan penurunan fungsi ginjal.[2-5] MM adalah penyebab 1% kematian dari kematian akibat kanker di negara-negara Barat. Insiden MM adalah 1% dari semua keganasan dan 10% dari keganasan hematologi di ras Kaukasia dan 20% di ras Afro Amerika.[2]
Tujuan. Tujuan dari penelitian ini adalah untuk mengetahui data deskriptif karakteristik pasien dengan Multiple Meyloma di Rumah sakit dr. Kariadi Semarang.
Metode. Meskipun pembangunan di manajemen pasien, MM masih penyakit yang tak tersembuhkan, dengan tingkat ketahanan hidup 5 tahun lebih rendah dari 40%. Ada banyak perbedaan di myeloma dan manifestasi klinis. Beberapa pasien dapat bertahan di bulan sampai lebih dari 10 tahun.[5,6,7] Kelangsungan hidup rata-rata adalah 33 bulan, jumlah ini sama dalam studi Asia.[8,9]
Hasil.Ada beberapa faktor prognostik dalam manajemen myeloma, seperti β2-mikroglobulin (β2m), albumin serum, serum kreatinin, persentase sel plasma di sumsum, tulang litik lesi, β2m anemia.[10-13] merupakan faktor prognostik yang digunakan oleh Sistem Staging Internasional (ISS)[11] untuk menentukan stadium dan prognosis di MM. β2m berkorelasi dengan faktor-faktor lain, seperti kreatinin serum, anemia, mekanisme kerusakan tulang pada pasien MM.[11,13]
Kesimpulan. MM di Indonesia belum diteliti secara komprehensif sedangkan pengukuran β2m mahal dan tidak tersedia secara luas.

Kata kunci: *Multiple Myeloma, Sumsum tulang, Prognosis Factors*

ABSTRACT

Background. Multiple myeloma (MM) is a malignancy of differentiated B-lymphocytes characterized by accumulation of clonal plasma cells in the bone marrow (BM), the presence of a monoclonal immunoglobulin (Ig) in the serum and/or urine, and osteolytic bone lesions.[1] Complications of this disease consist of recurrent bacterial infection, anemia, osteolytic lesion and decreased renal function.[2-5] MM is the cause of death in 1% of cancer death in Western countries. MM incidence is 1% of all malignancies and 10% of hematologic malignancies in Caucasian race and 20% in the Afro American race.[2]
Aim. The aim of the study is to know the descriptive data of characteristic of patients with MM at dr. Kariadi Hospital Semarang.
Metode. Despite of development in patient management, MM is still an incurable disease, with 5-year survival rates lower than 40%. There are many differences in myeloma and its clinical manifestations. Some patients can survive in the months until over than 10 years.[5, 6, 7] The median survival was 33 months, this number is similar in Asian studies.[8, 9]

Results. There are several prognostic factors in myeloma management, such as β_2-Microglobulin (β_2m), serum albumin, serum creatinine, plasma cell percentage in marrow, bone lytic lesion, anemia.[10-13] β_2m is a prognostic factor used by the International Staging System (ISS)[11] to determine stadium and prognosis in MM. β_2m correlates with other prognostic factors, such as serum creatinine, anemia, mechanism of bone destruction in MM patients.[11, 13]

Conclusion. MM in Indonesia has not been studied comprehensively and the β_2m measurement is expensive and not widely available.

Keywords: *Multiple Meyloma, bone marrow, prognostic factors*

MATERIAL AND METHOD

This is a cross sectional study. The design and conduct of the study complied with the principles of good clinical practice, in accordance with the Declaration of Helsinki. The study was approved by local ethics committees and written informed consent was obtained from all patients before enrollment. The patients are older than 14 years old, who are new and old patients diagnosed with MM that referred to dr. Kariadi Hospital Semarang.

Patients were evaluated for physical examination, laboratory measurement, and bone survey. Complete blood count was analyzed using ABX Micros 60®. Creatinine serum was measured from blood clot using Gas-chromatography-isotope dilution mass spectral method. Albumin serum was measured using Bromocresol green method. Beta-microglobulin was analyzed using Enzyme-linked immunosorbent assays (ELISA) method. Immunofixation was analyzed using the Hellabio Immunofixation Electrophoresis (IFE).

Data Analysis

Data were analyzed using SPSS 12 evaluation version. The data showed as descriptive method.

RESULTS

Demographic Characteristic

Between January and December 2010, 25 patients with clinical diagnosis of MM were included in this study. The demographic characteristics were shown in Table 1. Median age was 56 (SE ±1.8). The study population was mostly men (79%). Private employee, government employee, farmer, entrepreneur, and others were 13 patients (52%), 7 patients (28%), 2 patients (8%), 2 patients (8%), and 1 patient (4%), respectively. The main complaint was bone pain, this occurred in 15 patients (60%), followed by shortness of breath in 4 patients (16%), swelling of shoulder in 1 patient (4%), forehead tumor in 1 patient (4%), petechiae in 1 patient (4%), fatigue in 1 patient (4%), weakness in 1 patient (4%), bone pain in 1 patient (4%), and bone fracture in 1 patient (4%).

Laboratory characterizations were shown in Table 2. The majority of patients have anemia with mean Hb level of 9.4 g/dL (SD±2.7). Leukocyte and Platelet counts were normal, 7.4 g/dL (SD ±2.9) and 200.3 x 10^3 /mm^3(SD±124) respectively. The mean creatinine level was 1.7 mmol/L (SD±1.1). There was hypoalbuminemia with mean albumin level of 2.6 g/dL (SD±0.6), hyperglobulinemia with mean globulin level of 6.9 g/dL (SD ± 1.8) and normal calcium level with a mean of 2.3 mmol/L (SD± 0.4). The mean β_2m level was 9.6 g/dL (SD±8.9).

Table 1. The demographic data of 25 patients with MM

Characteristic	All patient (N= 25)
Age at diagnosis, year *	56 (1.8)
Sex, Man/Woman (%)	76/24
Occupation (%)	
Farmer	2 (8)
Government employee	7 (28)
Private employee	13(52)
Entrepreneur	2 (8)
Others	1(4)
Main complaint (%)	
Shoulder swelling	1 (4)
Tumor in forehead	1 (4)
Ecchymosis	1 (4)
Fatigue	1 (4)
Weakness	1 (4)
Bone pain	15 (60)
Bone fracture	1 (4)
Shortness of breath	4 (16)
Complication (%)	
Fracture	4 (16)
Recurrent infection	5 (20)
Renal failure	1(4)
Bleeding	1 (4)
Thrombosis	1 (4)
Neuropathy	2 (12)
Compression fracture of column vertebra	10 (40)
History of the past treatment (%)	
No treatment	13 (52)
With treatment	12 (48)
Durie-Salmon staging (%)	
I	0
II	1 (4)
IIIA/IIIB	24(96)
International System Staging (ISS)	
I	4 (16)
II	5 (20)
III	16 (64)
*Median , (SE Median)	

The most complication in patients with MM is fracture; compression of lumbar vertebra 10 cases (40%) and fracture another site 4 cases (16%). According to Durrie Salmon staging system, 96% patients have stage III A/IIIB. However, according to the International staging system, 64% patients have stage III.

According to immunoisotype, total case of IgG κ , IgA κ, IgA λ, biclonal λ light cain and IgG λ were 11 patients (44%), 2 patients (8%), 1 patient (4%), and 1 patient (4%), respectively. Thirty six (36%) patients have not been classified. The Bone survey examination showed that most of the patients have bone lytic lesion, 21 patients (88%).

Table 2. The Laboratory data of patient with Multiple myeloma

Variable	Mean (± SD)
Hemoglobine, gr/dL	9.4 ± 2.7
Leucocyte x 103/mm^3	7.4 ± 2.9
Platelet x103/mm^3	200.3 ±124
Creatinine, mmol/L	1.7±1.1
Albumin, g/dL	2.6 ±0.6
Globulin, g/dL	6.9 ± 1.8
Calcium, mmol/L	2.3 ± 0.4
β_2m, mg/dL	9.6 ±8.9

Table 3. Patient clasification with MM based on monoclonal protein

Immunoisotipe	total (%)
IgG κ	11 (44)
IgA κ	2 (8)
IgA λs	1 (4)
Biclonal λ *light cain* and IgG κ	1(4)
Light-chain κ	1 (4)
Not classified	9 (36)

Table 4. Osteolytic Lesion of patient with MM

Number of osteolytic bone, %	Total (%)
0 (no osteolytic)	4 (12)
1	1 (4)
2	12(48)
3	4 (16)
4	2 (8)
5	1 (4)
6	0
7	1 (4)

DISCUSSION

The median age of this study population was 56 years. Median age in a study in Taiwan was 62 years.[14] Median age in Royal Free Myeloma Clinic study was 67 years for

men, and 63 years for women.[15] Median age, according to Dispezieri (2009) was 71 years. [5] Median age of Kariyawasan CC study (2007),[16] was 66 years. The median age in our study was lower than other studies. Man to woman ratio was 3.1: 1, this number is similar to the studies in other countries. The incidence of patients with MM was higher in men than in women, this result similar to another study.[5, 17]

Bone pain was the main complaint of MM patients in this study, 60%. In a study by Kariyawasan CC, et al (2007),[17] 56% patients experienced bone pain ranging from mild, moderate, to severe. Bone involvement rather than symptomatic bone pain, bone lytic lesion and/or severe osteoporosis were the main features in patients with MM. [18]

Other complaints were swelling, tumor mass, petechiae, fatigue, fracture and sort of breath. Bone swelling and bone mass were caused by bone destruction. When a solitary mass appeared, this bone mass was called plasmacytoma. [19,20]

The complication of infection is usually found in MM patients. Patients with MM have decreased of immunity that resulted in susceptibility to infection. Disturbance in humoral immunity and leucopenia make patients with MM prone to infection. Patients with multiple myeloma were more susceptible to bacterial infections, especially from encapsulated microorganisms, such as pneumococcus, as well as a viral infection.[21] The study in Japan revealed that patients with MM have risk of bacterial infection include Streptococcus pneumoniae, Haemophilus influenzae, and Escherichia coli. Sulfamethoxazole – trimethoprim oral for at least the first 2 months of chemotherapy were important prophylaxis for bacterial infection.[22]

Hypercalcemia was due to bone destruction in MM. Bone destruction mechanism and disability of osteoblast to repair bone lesions in clinical remission phase have been understood.[23] Incidence of hypercalcemia in patients with MM was 20%, however all of the patient in this study have no hypercalcemia.

Most of the patients with MM came to hospital in advanced stage. According to Durrie Salmon staging system, 96% patients have stage III A or IIIB. However, according to the international staging system, 64% patients have stage III. These were caused by delay diagnosis and referral. Many patients came to a Neurologist, Nephrologist, and Orthopedist. Diagnosing MM in early stage is difficult, as shown in the result of this study; we should have more awareness in patients with bone pain.

The study in Taiwan revealed a correlation between farming exposure and MM. However, in this study, almost all of the population were private employees that have no farming exposure. There are many risk factors for MM. Although there were correlations between toxin, dietary source, environment pollution and increasing MM incidence, these findings still need epidemiology analysis in the future. [14]

All patients in this study have anemia. Anemia in patients with MM is anemia of chronic disease that caused by blunting of response to erythropoietin (EPO) and disorder of iron metabolism.[24]

This study has some limitations, because there were no analysis of parameters such as performance status, C reactive protein, chromosome 13 abnormalities, and plasma cell labeling index (PCLI).

CONCLUSION

The characteristic data of patient with MM at dr. Kariadi Hospital similar to other

center. Almost the patient came to the hospital with advanced stage, bone complication, infection etc. There, interest data was the age patients with MM were younger than another center.

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