International Journal Of Health Medicine and Current Research
E - ISSN : 2528 - 3189
P - ISSN : 2528 - 4398

International Journal of Health Medicine and Current Research
Vol. 2, Issue 01, pp.226-230, March, 2017

DOI:
10.22301/IJHMCR.2528-3189.226

Article can be accessed online on:
http://www.ijhmcr.com

CASE REPORT

INTERNATIONAL JOURNAL OF HEALTH MEDICINE AND CURRENT RESEARCH

A MALE WITH NON-SECRETORY MULTIPLE MYELOMA : A CASE REPORT

LWA Rotty[1], H Haroen[2], P Lasut[3], C Hendrata[4], A Pradipta[5]

[1] Professor, Head of Department of Hemato-Oncology, Sam Ratulangi Medical Institute, Prof Dr R D Kandou General Hospital, Manado.

[2] Consultant, Department of Hemato-Oncology, Sam Ratulangi Medical Institute, Prof Dr R D Kandou General Hospital, Manado.

[3] Consultant fellowship, Department of Hemato-Oncology, Sam Ratulangi Medical Institute, Prof Dr R D Kandou General Hospital, Manado.

[4] Consultant fellowship, Department of Hemato-Oncology, Sam Ratulangi Medical Institute, Prof Dr R D Kandou General Hospital, Manado.

[5] Resident, Department of Hemato-Oncology, Sam Ratulangi Medical Institute, Prof Dr R D Kandou General Hospital, Manado.

ARTICLE INFO

Article History:
Received 05th January, 2017
Received in revised form
04th February, 2017
Accepted 16th March, 2017
Published online 30th March, 2017

Key words:
Multiple Myeloma.

Correspondence to Author:
LWA Rotty
Professor, Head of Department of Hemato-Oncology, Sam Ratulangi Medical Institute, Prof Dr R D Kandou General Hospital, Manado

E-mail:
linda_rotty@yahoo.com

ABSTRACT

Non-secretory multiple myeloma is a rare case of hematological malignancies, also a rare variant of multiple myeloma. Several studies have been published, yet the exact mechanism about the absence of M protein still debatable. We described a 61-years-old man with lower back pain due to pathological fracture on fourth lumbar vertebrae, anemia, hypercalcemia, renal impairment, and bone lytic lesion on cranial bone. The absence of M protein in serum protein electrophoresis was a diagnostic dilemma while the patient had all the CRAB manifestations. Serum immunotyping still could not exclude monoclonal gammopathy. We further obtain immunofixation on patient's serum and the result shows biclonal gammopathy identified from IgG kappa and IgG lambda paraproteins. This patients diagnosed with non-secretory multiple myeloma and managed with zoledronic acid injection routinely and melphalan prednison (MP) regimen as a definitive treatment modality available here. This case report suggested that non-secretory type of multiple myeloma is a diagnostic challenge for physician with several difficulties include treatment response monitoring due to absence of M protein.

Citation: LWA Rotty[1], H Haroen[2], P Lasut[3], C Hendrata[4], A Pradipta[5], 2017 "**A Male With Non-Secretory Multiple Myeloma : A Case Report**", *International Journal of Health Medicine and Current Research*, 2, (01), 226-230.

INTRODUCTION

Multiple myeloma (MM) is a hematological malignancy in the bone marrow characterized by proliferation of neoplastic plasma cells that produce monoclonal paraprotein (M protein), immunoglobulin or one of its chain. These malignancies include 1% of all cases and 10% of all hematologic malignancies. The median age of patients 65 years of age and is more common in men.[1] In the United States, MM reach 1.8% of all new cases of malignancy, with 5-year survival rate was 48.5% .[2] The incidence of MM in Indonesia has not been much reported.

Typical clinical manifestations are generally characterized by hypercalcemia, renal disorders, anemia, and lytic bone lesions are commonly referred CRAB. Diagnosis according to The International Myeloma Working Group in 2014 established if obtained plasma cells > 10% on bone marrow biopsy and accompanied CRAB clinical manifestations or myeloma defining events (MDEs).[3,4]

Non-secretory multiple myeloma (NSMM) is a rare variant of MM, characterized by the absence of the M protein detected either in blood or urine. The incidence of only 1-5% of all cases MM.[4] absence of M protein may be a diagnostic dilemma in patients with clinically overt disease. Since it was first reported in 1958, estimated that only approximately 80 cases published since 1972 to 2009. The absence of M protein in NSMM allegedly caused by a decrease in protein synthesis due to increased immunoglobulin M cytoplasmic, increased degradation and impaired intracellular transport of immunoglobulins.[5] Management of NSMM was no difference with secretory MM in general, and show the same prognosis of secretory type.[6]

CASE ILLUSTRATION

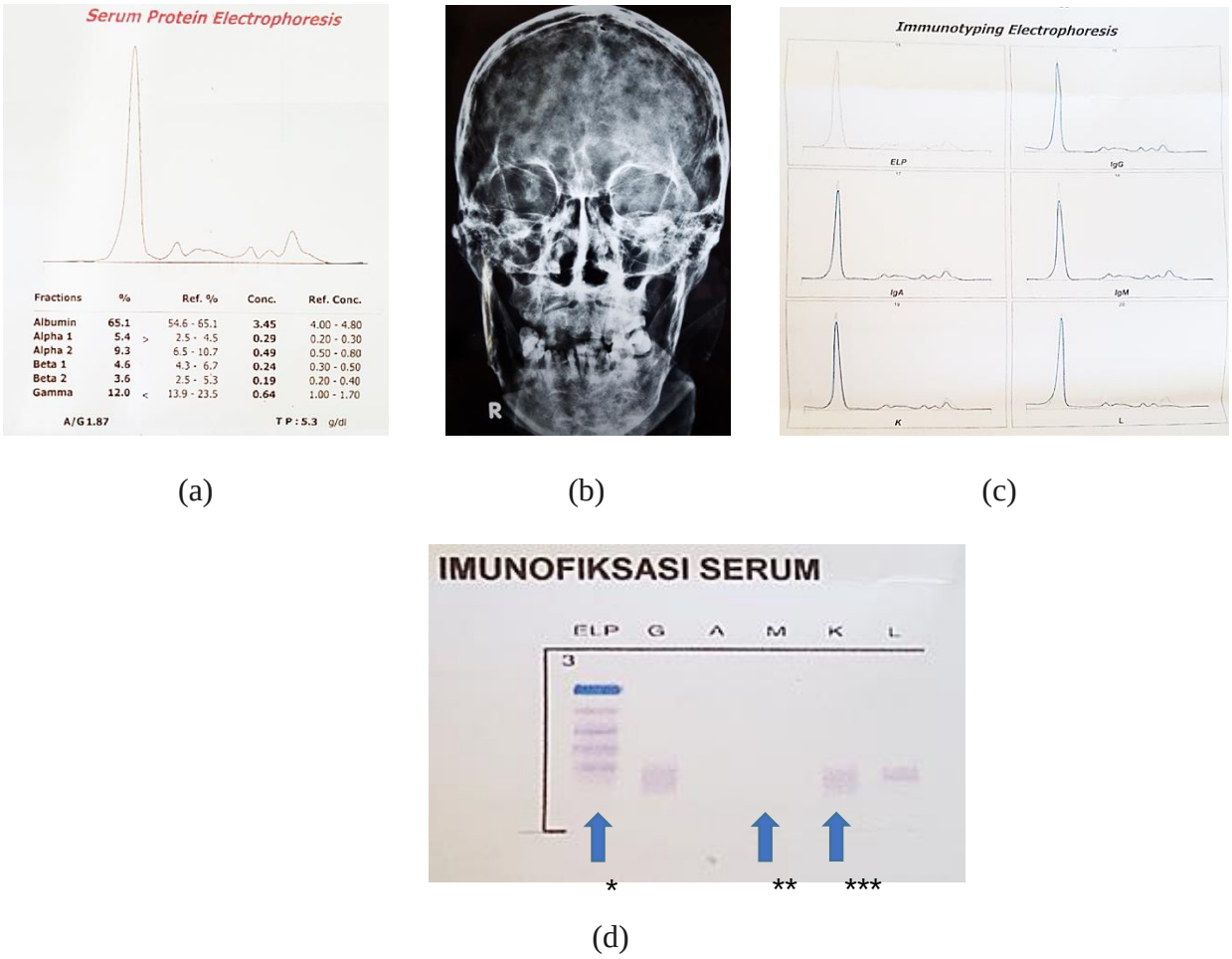
A 61-years-old Minahasans male, a veteran soldiers have gone to the emergency department with a chief complaint of lower back pain. Lower back pain is localized and worsened from one week prior to service. Continuous pain, especially when moving, making it difficult for the patient to sit and stand. Pain has been started since four months ago when the patient had fallen from seat. Patients was treated at a local hospital and found a compression fracture in the spine with a low hemoglobin level and renal impairment. A history of hypertension and increased uric acid known since 5 years ago but did not seek treatment regularly. History of diabetes mellitus, history of heart disease, lung, liver denied. No familial history who suffer with the same complaint. Smoking and alcohol denied.

Physical examination shows a good general state, compost mentis, blood pressure of 140/80 mmHg; pulse 89 x / min regular and sufficient; respiratory 20 x / min, body temperature 36,8^{o}C. Visual analogue scale (VAS) 7. Body weight (BW) is estimated 60kg and 165cm in height with a body mass index of 22.03 kg / m2, body surface area (BSA) of 1.66 m2. Examination of the head obtained anemic conjunctiva, no jaundice. There were no enlarged lymph nodes. Examination of the heart and lungs within normal limits. Abdominal examination found no hepatosplenomegaly and no abdominal tenderness. There is tenderness in the lower back region with restricted of active and passive movement of vertebrae due to pain. Examination of the extremities shows no tophy, pedal edema nor cyanosis.

Laboratory tests of hemoglobin (Hb) of 7.3 g / dL; hematocrit (Ht) 20.0%; leukocytes 5,600 / mm3; platelets 168,000 / mm 3; MCV 83.3 fl; MCH 30.4 fl; MCHC 36.5 fl; random blood glucose (RBG) 88 mg / dL; ureum 54 mg / dL; creatinine 1.9 mg / dL; total protein 6,2 g/dL; albumin 4,16 g/dL; globulin 2,04 g/dL; total cholesterol 118 mg/dL; HDL 25 mg/dL; LDL 61 mg/dL; triglyceride 159 mg/dL; Na 128 mEq / L; K 3.50 mEq / L; Cl 101 mEq / L; Calcium 11.56 mg / dL; magnesium 2.09 mg / dL. Estimated glomerular filtration rate (eGFR) 37.2 mL / min / 1,73m2 (CKD-EPI). Urinalysis obtained a pH of 6.0, a specific gravity of 1.020, positive leukocyte (+2), nitrite negative, positive protein (+1), glucose negative. Peripheral blood smear shows erythrocytes normocytic and normochrom, no polikromatophily, no normoblast, no rouleaux formation. leukocyte impression normal amount and morphology (0% / 0% / 28% / 44% / 20% / 8%), platelets impression normal amount and morphology. Protein serum electrophoresis is obtained and M protein is not found, still the impression of the pattern can not get rid of monoclonal gammopathy (figure 1(a)). Electrocardiography (ECG) results of sinus rhythm 74x / minute and left anterior hemiblock. Chest X-ray examination is within normal limits. Lumbosacral X-ray showed a compression fractures in vertebrae L4. Plain skull X-ray obtained and shows multiple osteolytic lesions impression of multiple myeloma (figure 1(b)).

Patient treated with saline infusion, analgesics for pain management and packed-red-cells transfusion to reach desireable hemoglobin level. Zoledronic acid 4mg is given intravenous once, and repeat regularly per month. Patient then referred to the medic rehabilitation department for physioteraphy and further pain

management. Bone marrow aspiration still can not be performed because the patient can not face down as a result of pain and restricted range of vertebral motion. Patient scheduled for examination of serum immunotyping and immunofixation for further diagnostic test. The serum immunotyping results obtained can not exclude the presence of a monoclonal protein (figure 1(c)) and confirmation by serum immunofixation showed biclonal gammopathy identified from IgG kappa and IgG lambda paraproteins result (figure 1(d)). Patients diagnosed with a non-secretory multiple myeloma (Durie-Salmon stadium IIIA) based from light chains gammopathy and CRAB manifestation. Definitive treatment modality available here was melphalan prednison (MP) regimen. Given orally melphalan 14mg (8mg/m^2) and prednison 100mg (60mg/m^2) in divided dose for four days and cycle repeated every four weeks. Patients allowed to discharge from hospital and routinely control to hematology clinic for further clinical monitoring and adverse effect evaluation.



(a) (b) (c)

(d)

Figure 1. (a) Serum protein electropharesis result shows no M protein detected. (b) Plain skull x-ray shows multiple punch out lesion impression of bone lytic lesion in multiple myeloma. (c) Serum immunotyping result shows no monoclonal protein detected. (d) Serum immunofixation result a biclonal gammopathy, identified the paraprotein as an IgG antibody (arrow*) with kappa light chain (arrow**) and lambda light chain (arrow***).

DISCUSSION

Multiple myeloma (MM) is hematological malignancy in bone marrow, characterized by neoplastic plasma cells proliferation that produce monoclonal paraprotein (M protein), immunoglobulin or one of its chain. The median age of patients 65 years of age and is more common in men. Highest incidence in african-american and pasific islanders, then caucasian, and low indicence in asian and developing countries.[7]

Lower back pain is the most common symptoms accounts to 70% of all cases. Pathological fracture may occur and presenting a localized persistent pain. Lytic lesion usually present in cranial, vertebrae and proximal part of long bones , due to tumour cells proliferation and activation of osteoclast. Calcium mobilization from this lytic process induce hypercalcemia in MM patients.[7]

Nephropathy occurs in 20-25% MM patients, mostly due to hypercalcemia. Other factors are infiltration of MM cells, amyloid deposition, and tubular damage due to excessive light chains excretion.[8] Anemia accounts up to 80% cases, usually normocytic normochrom due to direct hematopoiesis inhibiton as a result from abnormal plasma cells profliferation in bone marrow. Hence, granulocytopenia and thrombocytopenia not always present.[9]

The International Myeloma Working Group in 2014 established a revision of diagnostic criteria for MM : 1) obtained plasma cells > 10% on bone marrow biopsy and 2) accompanied one or more CRAB clinical manifestations or 3) myeloma defining events (MDEs), like: a) Clonal plasma cells 60% or more in bone marrow examination, 2) Serum involved / uninvolved free light chain ratio >100, 3) more than one focal lesion >5mm detected from magnetic resonance imaging (MRI). The new diagnostic criteria revision aimed for early detection and management MM patients before progressive organ involvement occurs [10,11]

Non-secretory multiple myeloma (NSMM) is a rare variant of MM, characterized by the absence of the M protein detected either in blood or urine, while it had the same CRAB manifestation. The incidence of only 1-5% of all cases MM. Absence of M protein may be a diagnostic dilemma for physician to diagnose patients with clinically overt disease and treatment monitoring. The theory approaced to explain the absence of M protein in NSMM still controversial. There is opinion that conventional protein electropharesis technique we used may not detect the pathological immunoglobulin secretion, or due to low tumour mass.[12] In 2007, Kartika,et al from Indonesia once published a rare case of NSMM in Cipto Mangunkusumo hospital.[13]

Durie-Salmon criteria had been used as a MM staging system from decades. Study in Dharmais hospital, Jakarta, showed that majority of MM patients diagnosed first time on Durie-Salmon stage IIIA. [14] Bacterial infection is a common complication from MM patients, as a result from impaired immunoglobulin production and low antibody responses. A large scale study showed that meningitis, septicemia, pneumonia, osteomyelitis, cellulitis and pielonephritis were the common complications.[15,16]

European Myeloma Network Guidelines in 2015 reccomended zoledronic acid as a best option treatment for manage hypercalcemia and bone lytic lesions. Symptomatic and persistent anemia may managed by erythropoietic-stimulating agents (ESA) administration. Influenza and pneumococcus vaccines may benefit for MM patients. [17,18] MM is an incurable disease. Best definitive treatment for MM nowadays are autologous stem-cell transplantation (ASCT) and bortezomib based therapy.[19] In patients who unable to have a transplant procedure, melphalan based therapy is still an option. However, melphalan can destruct stem cells reserve in bone marrow and must be avoided for transplant candidates. Melphalan and prednison (MP) regimen was a standard therapy since 1960 and had successful respons up tp 60% in 18 months. Although melphalan, prednison with addition talidomid (MPT) or bortezomib (MPB) give superior results than MP alone in various study, it still a best option in facilities who did not have an access to those novel agents. Melphalan 8mg/m^2 and prednison 60mg/m^2 is given for four days consecutively and this cycle repeated every four weeks until complete response acquired.[20] From various cases reported, prognostic and survival rate of NSMM are the same with the usual secretory type.[21]

CONFLICT OF INTERESTS

The authors declare that there is no conflict of interests regarding the publication of this paper.

REFERENCES

1. Syahrir M. Mieloma multiple dan penyakit gamopati lain. Dalam: Sudoyo A, Setiyohadi B, Alwi I, Simadibrata M, Setiati S, editor. Buku ajar ilmu penyakit dalam. Edisi keenam. Jakarta. Pusat Penerbitan Departemen Ilmu Penyakit Dalam Fakultas Kedokteran Universitas Indonesia 2014. h2700-7.
2. Myeloma SEER stat fact sheets. In: Surveillance, epidemiology, and end results program. US National Cancer Institute. 2016.
3. Munshi NC, Longo DL, Anderson KC. Plasma cell disorders. In: Fauci, Braunwald, Kasper, Hauser, Longo, Jameson, Loscalzo editors. Harrison's Principles of Internal Medicine. 18th ed. Vol I. New York. McGraw Hill 2012. p1684-95.
4. Kilic OB, Oguz AK, Ergun I, Baydar DE, Ayli M. Nonsecretory multiple myeloma and AL amyloidosis presenting with nephrotic range proteinuria. Case Report in Nephrology 2015; 635974: 1-4.
5. Middela S, Kanse P. Nonsecretory multiple myeloma. Indian J Orthop 2009; 43(4): 408–411.

6. Lonial S, Kaufman JL. Non-secretory myeloma : a clinician's guide. Oncology 2013; 27(9): 924-8.
7. Munshi NC, Longo DL, Anderson KC. Plasma cell disorders. In: Fauci, Braunwald, Kasper, Hauser, Longo, Jameson, Loscalzo editors. Harrison's Principles of Internal Medicine. 19th ed. Vol I. New York. McGraw Hill 2015; 710-24.
8. Katagiri D, Noiri E, Hinoshita F. Multiple myeloma and kidney disease. The Scientific World Journal 2013; 487285: 1-9.
9. Bouchnita A, Eymard N, Moyo TK, Koury MJ, Volpert V. Bone marrow infiltration by multiple myeloma causes anemia by reversible disruption of erythropoiesis. Am J Hematol 2016; 91(4): 371-8.
10. Rajkumar SV. Updated diagnostic criteria and staging system for multiple myeloma. Am Soc Clin Oncol Educ Book 2016; 35: 418-23.
11. International Myeloma Working Group. Criteria for the diagnosis of multiple myeloma. a Research Division of Myeloma Foundation. 2016.
12. Euch ME, Fredj FI, Rezgui A, Karmani M, Derbeli F, Amri R and Kechrid EL. Non-secretory multiple myeloma with lytic bone lesions about a new observation. J Clin Cell Immunol 2012; 3: 120.
13. Kartika WTH, Purwanto I, Kurnianda J, Mangunsudirjo S, Harijadi A, Puntodewo P. Non secretory multiple myeloma – a case report. Med J Indones 2007; 16: 257-60.
14. Tadjoedin H, et al. Multiple Myeloma in Indonesia. Indonesian Journal of Cancer 2011; 2: 76-81.
15. Blimark C, Holmberg E, Mellqvist UH, Landgren O, Björkholm M, Hultcrantz M, et al. Multiple myeloma and infections: a population-based study on 9253 multiple myeloma patients. Haematologica 2015; 100 (1): 107-113.
16. Bladé J, Rosiñol L. Complications of multiple myeloma. Hematol Oncol Clin North Am 2007; 21(6): 1231-46.
17. Terpos E, Kleber M, Engelhardt M, et al. European Myeloma Network Guidelines for the management of multiple myeloma-related complications. Haematologica. 2015; 100(10): 1254-1266.
18. Meletios AD, Sonneveld P, Leung N, Merlini G, Ludwig H, Kastritis E, et al. International Myeloma Working Group recommendations for the diagnosis and management of myeloma-related renal impairment. CJASN. 2016.
19. Rajkumar SV. Multiple myeloma: 2012 update on diagnosis, risk-stratification, and management. American Jornal of Hematology 2012;87:79-88.
20. Multiple myeloma. In : NCCN clinical practice guidelines in oncology version 2. National Comprehensive Cancer Network. 2014.
21. Chawla S, Kumar SK, Dispenzieri A, Greenberg AJ, Larson DR, Kyle RA, et al. Clnical course and prognosis of non-secretory multiple myeloma. European Journal of Haematology 2015; 95(1): 57-64.

****