Chronic Kidney Disease and Multiple Myeloma Case in Clinical Nephrology

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Abstract
Multiple myeloma (MM) is a neoplastic plasma cell dyscrasia identify by anemia, recurrent infections, increased serum and / or monoclonal protein in urine, osteolytic bone lesions, hypercalcemia and renal failure. MM accounts for approximately 1% of all cancer cases and 10% of hematological malignancies MM related renal failure is an important prognostic factor leading to early mortality and ranges from 20-50% depending on the frequency of kidney disease in MM. In the present paper, we report that advanced age, concomitant chronic renal failure with unknown cause and anemia should always bring MM to mind; In these cases, serum and urine immunization electrophoresis should be requested even if serum protein electrophoresis is normal.

Key words: Light chain; The immunofixation; multiple myeloma

Introduction
Multiple myeloma (MM) accounts for approximately 1% of all cancer cases and 10% of hematological malignancies (Rajkumar et al., 2014). Each year over 32,000 new cases are diagnosed in the United States, and almost 13,000 patients die of the disease (Siegel et al., 2020). The annual age-adjusted incidence in the United States has remained stable for decades at approximately 4 per 100,000 (Kyle et al., 2004). MM is more common in males (approximately 1.4 / 1), with an average age of 69 for males and 72 for females at the time of diagnosis (Barlogie et al., 2006). Multiple myeloma can be presented with three different clinical pictures: typical pattern, light chain myeloma and non-secretory myeloma. The classic findings leading to diagnosis are bone pain, hypercalcemia, sedimentation height, anemia, and lytic bone lesions (Kyle et al., 2003). Bone pain is generally felt in the
back and chest wall, less often in the extremities. In 80% of patients, lytic bone lesions, osteopenia, osteoporosis, or pathological fractures can be detected in skeletal surveys (Kyle et al., 2003). Unlike other malignancies that metastasize to bone, the osteolytic bone lesions in multiple myeloma exhibit no new bone formation (Roodman, 2009). Bone disease is the main cause of morbidity and can be best detected using low-dose whole body computed tomography (WB-CT), fluoro-deoxyglucose (FDG) positron emission tomography/computed tomographic scans (PET/CT), or magnetic resonance imaging (MRI) (Hillengass et al., 2019). Sedimentation has increased significantly and may be over 100 mm/h. (Alexandrakis et al., 2003) Anemia is generally normochromic normocytic and is seen at the time of diagnosis in 73% of patients and throughout the disease in 97% (Kyle et al., 2003). Renal involvement rate is 48% and it is more common in light chain myeloma (Winearls, 1995).

Renal involvement in MM was first described in 1845 by Henry Bence Jones detecting oxidized albumin in the urine of a myeloma patient, which would later be called Bence Jones protein (Jones, 1848). MM-related kidney failure (ESRD) is an important prognostic factor causing early mortality. The frequency of renal failure in MM varies between 20-50% depending on the definition (Alexanian et al., 1990; Eleutherakis-Papaiakovou et al., 2007). Renal failure despite being generally moderate (between stage 2 and stage 4), 10% of patients still require renal replacement therapy (Torra et al., 1995). MM damage is mainly caused by the effect of monoclonal light chains. Hypercalcemia although less frequently is another cause of kidney failure (Blade and Rosinol, 2005). Dehydration, hyperuricemia, nephrotoxic drugs, and use of contrast agents are other factors that are effective in the development of kidney failure and they cause kidney damage by increasing the effects of light chains rather than being the main cause of kidney failure (Alexanian et al., 1990; Kyle et al., 2003). It is known that with the improvement of kidney failure, negative effects on survival disappear. Therefore, it is important to identify the factors that affect the healing of kidney failure. Alongside supportive therapy such as appropriate fluid replacement, correction of hypercalcemia and avoiding nephrotoxic agents, chemotherapy for MM should be initiated quickly. With the treatment, the rate of recovery of kidney failure reaches 25-58% (Blade and Rosinol, 2005; Eleutherakis-Papaiakovou et al., 2007). In the present paper, we report that advanced age, concomitant chronic renal failure with unknown cause and anemia should always bring MM to mind; In these cases, serum and urine immunization electrophoresis should be requested even if serum protein electrophoresis is normal.

Case

An 82-year-old male patient has been followed up in the nephrology outpatient clinic for nine months due to chronic kidney damage (CKD). Five months prior, in addition to anemia, the patient with a marked sedimentation height was referred to the hematology outpatient clinic. CKD and hypertension have been present for 9 months in patient history. The medications patient was administrated were polystyrene sulfonate calcium salt, sodium bicarbonate, iron II, darbopoetin alpha. The patient did not consume alcohol or smoke.

In the physical examination of a middle aged male patient with no acute ailments, decreased skin turgor, dry tongue, pale skin was found and a fever of 37°C, blood pressure of 140/80 mmHg, 96/min pulse and respiratory rate of 18 per minute is recorded. Respiratory sounds were normal in auscultation. Cardiac sounds were normal during the cardiac examination. Abdominal examination revealed no distention, tenderness, and organomegaly. Intestinal sounds were normal. There was no costovertebral angle sensitivity. No edema was detected in both lower extremities. No lymphadenopathy was detected in the cervical, axillary and inguinal regions. No feature present in neurological examination. Other system examinations were normal.

In Hemogram WBC 11430 ul, Hb 10.5 gr / dl, Hct 33.2 %, MCV 91.7 fl, RBC 3.62 x 10^6 / ul, Neu 6410 ul, Monocyte 620 ul, Lymphocyte 3560 ul, PLT 193.000 ul.

Routine biochemistry Glucose 86 mg /dL urea 49.2 mg /dl, creatinine 1.58 mg / dl, sodium 140 mEq /L, potassium 6.13 mEq / L, calcium 9.6 mg / dl, chloride 104 mEq / L, phosphorus 3.4 mg / dl, uric acid 5.5 mg / dl, AST 21 U/L, ALT 13 U/L, Total protein 8.4 g / dl, albumin 4.1 g / dl, CK 107 U / L, sedimentation 105 mm / h, CRP was 1.3 mg / L, LDH 189 UL. Iron 100.8 ug / dl, TDBK 230.8 ug / dl, ferritin 860.7 ng / mL, folate 2.85 ng / mL, vitamin B12 357.7 pg / mL, reticulocyte count 1.17 ng / mL, Parathormone 70.91 ng / mL, 25-OH D 16.81 ng was / mL. PT was 16.9 sec, aPTT 40.7 ng / mL, INR 1.22 ng / mL.
CASE REPORT

Complete urine examination and sediment
Density 1013, pH 5, leukocyte negative, erythrocyte negative, protein +1, glucose negative, nitrite negative, urobinoligen negative, ketone negative.

Venous blood gas pH 7.28, HCO3 18.6, PCO2 39.8, PO2 32.3
In advanced examination and examination of hematemia outpatient clinic Serum beta-2 microglobulin is found as 6.51 mg / L.

Immunization electrophoresis-serum quantitative monoclonal protein was IgA 908 mg / dL, IgG 1724 mg / dL, IgM 56.5 mg / dL, Kappa light chain was 4.16 g / L, Lambda light chain was 3.31 g / L. Hemoglobin electrophoresis was; HbA 97.4%, HbA2 2.57% HbF 0%. ARB (-) in sputum, Sputum culture: no reproduction.

Discussion
Multiple myeloma is malignant proliferation of advanced plasma cells; seen in elderly, often presenting with renal failure and hypercalcemia. As with many types of malignancies, the benefit of early diagnosis is indisputable, and further evaluations are often required aside a presence of high clinical suspicion. Clinical and laboratory findings in light chain myeloma often resemble typical MM.

The revised International Myeloma Working Group criteria for the diagnosis of multiple myeloma requires the presence of one or more myeloma defining events (MDE) in addition to evidence of either 10% or more clonal plasma cells on bone marrow examination or a biopsy-proven plasmaclymota. MDE consists of established CRAB (hypercalcemia, renal failure, anemia, or lytic bone lesions) features as well as 3 specific biomarkers: clonal bone marrow plasma cells ≥60%, serum free light chain (FLC) ratio ≥100 (provided involved FLC level is ≥100 mg/L), and more than one focal lesion on MRI. (Rajkumar, 2020)

Serum protein electrophoresis alone is insufficient in MM. In the presence of a typical pattern MM, M protein can be detected by serum protein electrophoresis at a rate of 82%, which increases to 97% if serum and urine immunofaction electrophoresis is added (Kyle et al., 2003).

In 20% of all MM cases, only light chain is present in serum and urine, and in this table, also called light chain myeloma, one third of patients are presented with renal failure. In light chain myeloma, serum or urine kappa and lambda type light chains can be detected by serum and urine immunofaction electrophoresis.

Conclusion
Advanced age concomitant chronic renal failure with unknown cause and anemia should always bring MM to mind; In these cases, serum and urine immunization electrophoresis should be requested even if serum protein electrophoresis is normal.

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