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Case Report

Case report of immunoglobulin M multiple myeloma: A rare hematologic malignancy

Damla Çağla Patır[1], Sibel Demiral Sezer[1], Aybüke Olgun[2], Harun Akar[1]

[1]*Department of Internal Medicine, University of Health Sciences, Izmir Tepecik Training and Research Hospital, Izmir, Turkey*
[2]*Department of Hematology, University of Health Sciences, İzmir Tepecik Training and Research Hospital, Izmir, Turkey*

ABSTRACT

Immunoglobulin M (IgM) multiple myeloma is a very rare hematologic malignancy which comprises less than only 0.5% of multiple myeloma (MM) cases. Immunoglobulin M multiple myeloma and Waldenstrom's macroglobulinemia (WM) are two distinct hematologic entities with the common finding of IgM monoclonal gammopathy. This article presents a case of IgM multiple myeloma with increased monoclonal IgM overlapping with multiple myeloma.

Keywords: Immunoglobulin M, multiple myeloma, Waldenstrom's macroglobulinemia.

Multiple myeloma (MM) is a hematologic malignancy characterized by uncontrolled and monoclonal increase in plasma cells, the mature form of B lymphocytes. In most patients, monoclonal characterization of immunoglobulin G (IgG) (52%) or IgA (21%) is detected in serum and urine.[1] Immunoglobulin M multiple myeloma is a very rare hematological malignancy accounting for only less than 0.5% of MM cases.[2] It is critical to differentiate this disease from more common but still rare hematological diseases such as Waldenstrom's macroglobulinemia (WM). Immunoglobulin M monoclonal gammopathy is a common finding of both diseases.[3] The presence of lytic bone lesions, hypercalcemia, plasma cell infiltration, and monoclonal Ig elevation in bone marrow leads to MM diagnosis, whereas lymphadenopathy, hepatosplenomegaly, and monoclonal IgM elevation supports the diagnosis of WM.[4] Hyperviscosity is not specific to WM, but can be observed in IgM multiple myeloma due to the large structure of IgM immunoglobulin.[3] Immunoglobulin M MM is a different disease than WM and should be considered when the clinical findings of WM are not accompanied by this clinical presentation. Diagnosis should be confirmed with cytogenetic analysis of malignant cells in clinically overlapping cases.[5,6] In this article, we present a case of IgM multiple myeloma with a serum IgM level of 7,700 mg/dL and plasma cell infiltration of over 20% in bone marrow biopsy.

CASE REPORT

A 67-year-old male patient was admitted to our internal medicine outpatient clinic with complaints of weight loss and fatigue. Anemia and elevated sedimentation were determined and the patient was hospitalized for general examination and treatment. Initial examination of patient revealed body temperature of 37.6° C, BP: 128/62 mmHg, heart rate: 72 bpm, and RR: 18 bpm. Physical examination revealed no organomegaly. Peripheral lymphadenopathy was

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Correspondence: Damla Çağla Patır, MD. Sağlık Bilimleri Üniversitesi, İzmir Tepecik SUAM, İç Hastalıkları Kliniği, 35180 Yenişehir, Konak, İzmir, Türkiye.
Tel: +90 539 - 273 05 92 e-mail: damlapatir@yahoo.com

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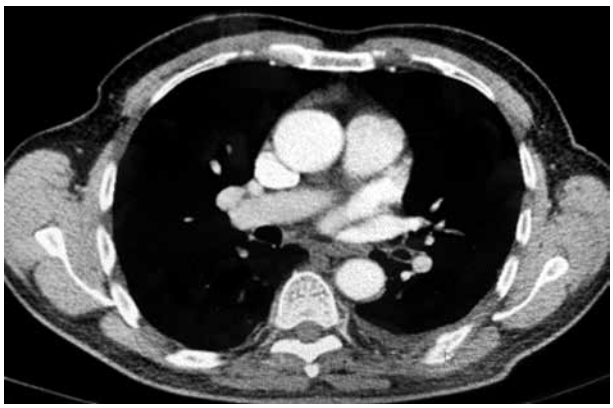

Figure 1. Computed tomography of the patient revealed bilateral fractures in ribs 7 and 10 in the first costa.

not detected. Lung sounds were normal. Heart sounds were rhythmic and without extra sounds or murmur. She had pain and tenderness on the chest. The patient's blood biochemistry and complete blood count results were as follows: blood glucose: 97 mg/dL, creatinine: 0.8 mg/dL, AST: 10 U/L, ALT: 10 U/L, Na: 139 mmol/L, K: 4.18 mmol/L, Cl: 105 mmol/L, Ca: 8.9 mg/dL, albumin: 3.2 g/dL, globulin: 5.9 g/dL, spot urine protein/creatinine: 1.7 g, IgA: 7.82 mg/dL, IgG: 443 mg/dL, IgM: 7,770 mg/dL, WBC: $3,300\times10^9$/L, Hgb: 8.3 g/dL, PLT: 250×10^9/L, sedimentation: 140 mm/h. Thoracic computed tomography (CT) of the patient revealed bilateral fractures in ribs 7 and 10 in the first costa (Figure 1). Evaluation of the patient's peripheral smear showed leukocyte counts were compatible with hemogram and normal lymphocyte morphology. Erythrocytes were normocytic and hypochromic and there was a Rouleaux formation. Bone marrow aspiration and biopsy were performed. Bone marrow biopsy revealed 20% plasma cell infiltration. Biopsy results were compatible with myeloma. Serum immunofixation analysis showed monoclonal elevation of IgM and was consistent with IgM myeloma. Serum immunofixation electrophoresis showed that free kappa/lambda ratio: 416 mg/dL (170-370) and 15.41 (1-35-2.65). The patient was ultimately diagnosed with IgM-kappa-type MM. The patient was transferred to the hematology department with a diagnosis of multiple myeloma. Prednisolone and lenalidomide were initiated as treatment.

DISCUSSION

Diagnosis of IgM MM is a difficult subject considering the rarity of the disease and the few reported cases in the literature. The differentiation between IgM MM and WM are important due to differences between the two diseases in terms treatment and prognosis. Overlapping clinical presentation and diagnostic difficulties in biopsy make differentiation challenging. In most cases, the clinical factors used in distinguishing between the two diseases may overlap. For example, some patients with IgM MM had organomegaly, one of the most common findings of WM.[3] The presence of lytic bone lesions or translocation t (11; 14) may show differences between IgM MM and WM, but these findings are not present in 20% of patients.[7] Currently, the diagnostic criteria of IgM MM are as follows: IgM monoclonal gammopathy with presence of plasma cells above 10% in bone marrow biopsy; lytic bone lesions or translocation t (11; 14); bone marrow infiltration requires widespread, interstitial or nodular involvement of surface Ig; and CD5-, CD10-, CD19 +, CD20 +, CD23- in bone marrow biopsy.[9] There is a strong association between IgM MM and t (11;14) and the presence of this translocation is specific for IgM MM.[10] Avet-Loiseau et al.[11] described the presence of t (11; 14) (q13q32) as the most common cytogenetic anomaly present in 83% of IgM MM cases, while CD20 (+) is most common in Waldenstrom's macroglobulinemia.[10] Once IgM MM diagnosis is established, treatment of patients suitable for transplantation includes induction therapy with a drug regimen, usually containing lenalidomide, bortezomib (or other proteasome inhibitor) followed by autologous stem cell transplantation. Non-transplant candidates with good performance status include drug regimens including melphalan, prednisone, thalidomide; melphalan, prednisone and bortezomib; modified revlimid, velcade, dexamethasone (mRVD); cyclophosphamide, bortezomib, dexamethasone (CyborD).[12] In our case, it was observed that bone marrow was infiltrated by plasma cells. Immunohistochemical staining did not reveal CD20 staining in these cells, but staining with lambda light chain was identified. Serum IgM was elevated and IgG and IgA protein levels were normal. Radiographic examination revealed fractures due to lytic lesions. The patient was diagnosed with IgM

myeloma and accordingly treated. In patients with IgM monoclonal gammopathy, multiple myeloma diagnosis should not be ignored; it should be kept in mind in the differential diagnosis. In patients who cannot be diagnosed due to overlapping clinical features, cytogenetic analysis should be used to increase diagnostic accuracy.

Declaration of conflicting interests

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