Case Report

Anaplastic Multiple Myeloma: A Report of a Rare Case with CD38 and CD117 Positivity

Anaplastik Multipl Miyelom: CD38 ve CD117 Pozitifliği Olan Nadir Bir Olgu Sunumu

Rafiye Çiftciler[1], Mustafa Erol[2], Şükrü Nail Güner[3], İsmail Reisli[3]

[1]Selcuk University Faculty of Medicine, Department of Hematology, Konya, Turkey
[2]Department of Nuclear Medicine, Konya City Hospital, Konya, Turkey
[3]Department of Pediatric Immunology, Necmettin Erbakan University, Faculty of Medicine, Konya, Turkey

ABSTRACT

Anaplastic multiple myeloma (AMM), which comprises anaplastic multiple myeloma and anaplastic plasmacytoma, is a rare illness that aggressively advances as a morphological subtype of multiple myeloma (MM). It has a poor prognosis and is believed to be particularly resistant to treatment. In this case report, we presented a 66-year-old woman diagnosed with AMM. The anaplastic morphology of MM may pose a diagnostic challenge. The need for a multidisciplinary approach to detect hematological neoplasms is highlighted in this example. For AMM instances, prompt radiographic, flowcytometry, and histological examination may assist guide effective treatment strategies.

Keywords: Anaplastic myeloma, multiple myeloma, monoclonal antibody

ÖZET

Anaplastik multipl miyelom ve anaplastik plazmasitoma içeren anaplastik multipl miyelom (AMM), multipl miyelomun (MM) morfolojik bir alt tip olarak agresif bir şekilde ilerleyen nadir bir hastalıktır. Kötü bir prognoza sahiptir ve tedaviye özellikle dirençli olduğuna inanılmaktadır. Bu olgu sunumunda AMM tanısı alan 66 yaşında bir kadın hastayı sunduk. MM'nin anaplastik morfolojisi tanısal bir zorluk teşkil edebilir. Bu örnekte hematolojik neoplazmları tespit etmek için multidisipliner bir yaklaşıma olan ihtiyaç vurgulanmıştır. AMM vakaları için hızlı radyografik, akım sitometri ve histolojik inceleme, etkili tedavi stratejilerini yönlendirmeye yardımcı olabilir.

Anahtar kelimeler: Anaplastik myelom, multiple myelom, monoklonal antikor

Introduction

Anaplastic multiple myeloma (AMM), which comprises anaplastic multiple myeloma and anaplastic plasmacytoma, is a rare illness that aggressively advances as a morphological subtype of multiple myeloma (MM). In newly-diagnosed instances of MM aberrant morphology and asynchronous immuno-phenotypic expression of plasma cells might be detected, leading to error in the initial diagnosis. It has a poor prognosis and is believed to be particularly resistant to treatment [1]. All ethnic groups and both sexes are impacted by AMM. AMM is far more common in younger patients than traditional multiple myeloma (median age of 69 years old), with a median age of 57.02 years [2, 3]. Because of its rarity, the clinical and pathological aspects of AMM have not been thoroughly understood yet. AMM

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patients are often young, with anemia or pancytopenia, dramatically reduced Ig, IgA isotype blood levels, and quickly developing extramedullary diseases [4]. Even in the presence of clinical, radiographic, and biochemical indications of the disease, a bone marrow test is necessary for the diagnosis of AMM. Using immunophenotyping, the bone marrow is evaluated both qualitatively and quantitatively. Myeloma cells are divided into 4 kinds based on their cytomorphology: mature, immature, pleomorphic, and plasmablastic [5]. AMM cells are atypical plasmacytoid differentiated cells that are widely dispersed. They have the following morphological characteristics: More than one big and irregular nucleolus; nucleoli with numerous distributed vacuoles; pleomorphic cells with significantly enriched cytoplasm [6]. Conventional chemotherapy and radiation are ineffective in the majority of AMM patients [1]. Immunotherapy, such as chimeric antigen receptor T cell immunotherapy, monoclonal antibodies, and potentially hematopoietic stem cell transplantation, might give these patients hope [1]. Chemotherapy has not been very effective in the past against this illness. It has been proposed that this aggressive phase may be the consequence of clonal evolution of the initial malignant cell rather than the emergence of a brand-new neoplasia on its own [7]. In this case report, we presented a 66-year-old woman diagnosed with AMM.

Case report

A 66-year-old female was admitted to the hematology clinic with increased fatiguability and night sweats. Physical examination revealed splenomegaly but was otherwise unremarkable. Hemogram revealed anemia (Hemoglobin = 9.1 g/dL), and thrombocytopenia (Platelet count = 74 × 10^6/L). Biochemical tests resulted in total protein: 105 g/L, albumin level of 35 g/L, creatinine 0.9 mg/dL, LDH 250 U/L. Roll formation was observed in erythrocytes in peripheral blood smear as depicted in Figure 1 (A). High lambda (207 mg/L) compared to kappa (10.8 mg/L) with a ratio of 19.1 verified the lambda light chain limitation in neoplastic cells by free light chain test. IgG isotype blood level was 64.12 g/L (7-16 g/L). Hypercellular particles with decreased trilineage hematopoiesis were seen on bone marrow aspiration. The aspirate smear of bone marrow was densely infiltrated with cohesive clusters/sheets of extremely pleomorphic neoplastic cells, many of which had anaplastic shape. There are numerous big atypical pleomorphic cells with a high nucleo-cytoplasmic ratio, basophilic cytoplasm, and a central eccentric nucleus with an uneven nuclear border as depicted in Figure 1 (B). Flowcytometric evaluation of bone marrow showed a CD45 negative cell population expressing CD38, CD117, and lambda on their surface without CD138 and CD56 expressions. (Figure 2). These cells were plasma cells and negative for surface expressions of CD19, CD20, CD22, and CD23, and also negative for intracytoplasmic CD79a. Positron emission tomography was reported as pleural nodular thickening, spleen 25 cm, diffusely increased involvement, multiple soft tissue lesions in the pelvic region, and multiple foci of involvement in bone structures and bone marrow as depicted in Figure 3 (maximum SUVmax value: 13.6). Based on the morphological and immuno-phenotypic findings, the patient was diagnosed with AMM. The patient is now being treated with bortezomib, lenalidomide, and dexamethasone, and is being followed up. After chemotherapy, autologous stem cell transplantation treatment is planned.

Discussion

AMM is a kind of plasma cell myeloma that has a very aggressive clinical course and a poor prognosis. One of the most frequent signs of AMM was anemia, and 9.6% of patients had thrombocytopenia when they were diagnosed, which is probably due to the

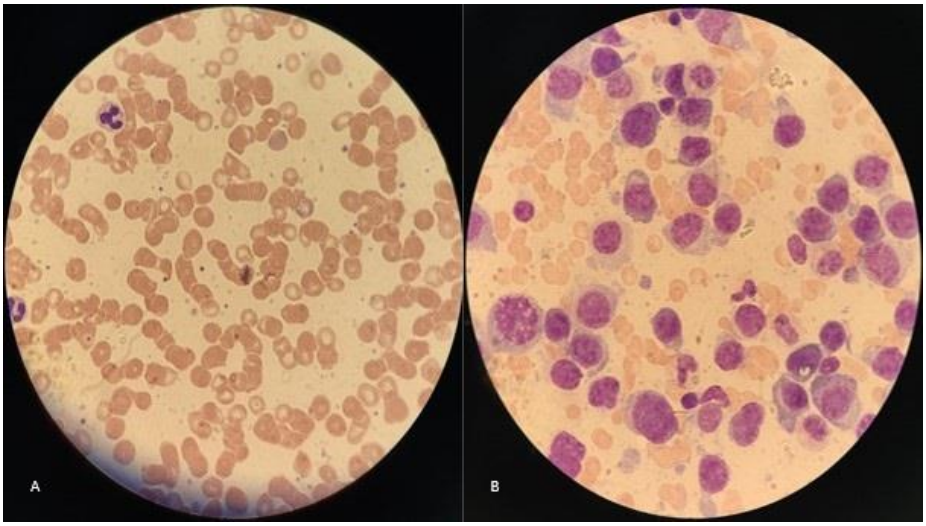

Figure 1. (A) Roll formation was observed in erythrocytes in peripheral blood smear, (B) Numerous big atypical pleomorphic cells with a high nucleocytoplasmic ratio, basophilic cytoplasm, and a central eccentric nucleus with an uneven nuclear border were seen in bone marrow aspiration.

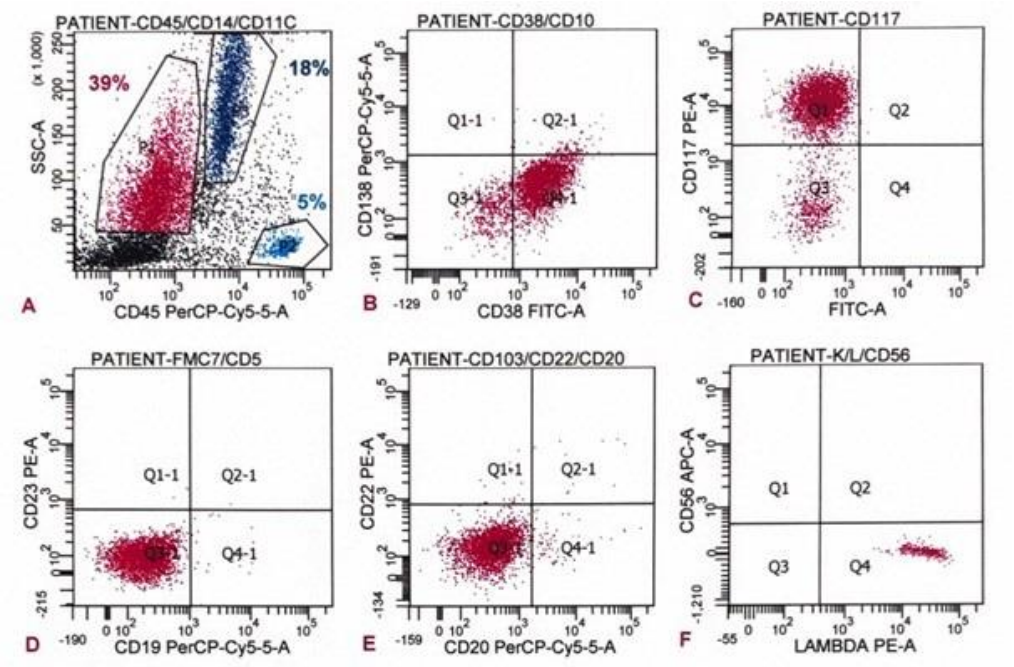

Figure 2. Flowcytometry showed (A) plasma cells account for 39%; were negative for CD45; (B) positive for CD38, negative for 138; (C) positive for CD117, (D) negative for CD19 and CD23; (E) negative for CD20 and CD22; (F) negative for CD56 and positive for lambda chain (FACS Canto, Becton Dickenson).

disease's aggressiveness and the significant anaplastic plasma cell infiltration of the bone marrow [3, 8]. Because of their unusual form, they might be difficult to diagnose. By morphology, they might seem like high-grade lymphoma or non-hematopoietic cancer. Anaplastic morphology can be detected in the early stages of myeloma or as the disease progresses. Infiltration of the extramedullary space is prevalent [9]. For the proper diagnosis, a combination of clinical symptoms, morphology, biochemical data, and immunophenotype are required. We reported a 66-year-old woman diagnosed with AMM in this case report. After further examination, multiple extramedullary infiltrates were detected in the patient. AM cells resemble "immunoblasts" at times, and

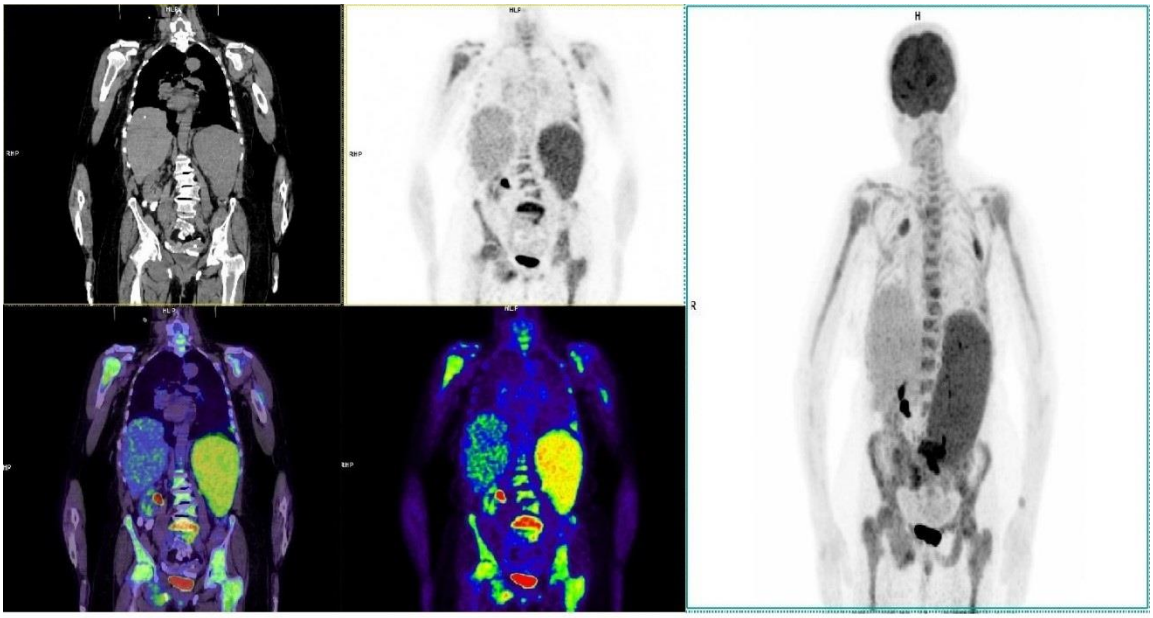

Figure 3. FDG uptake of tumor tissue in the skeletal system, spleen, bilateral pleura, and the lesion adjacent to L5 vertebra anterior in the coronal plane and MIP images observed in 18F-Fluorodeoxyglucose (FDG) positron emission tomography (PET) / computed tomography (CT)

they're frequently mistaken as other low-differentiated malignancies such as malignant melanoma, Burkitt lymphoma, and sarcoma. As a result, immunohistochemistry and flow-cytometry play a crucial role in differential diagnosis. AM cells typically express CD38, CD138, and MUM1 with little light chain expression, while lymphocyte markers CD20, CD19, and CD3 are absent [1]. This is in line with our findings. AM cells may also express CD56 and CD117 on their surface. Vinho Do et al. reported a case of AMM. In this case, flow cytometric analysis was positive in an expanded panel of CD138, CD56, and CD117 together with the kappa light chain. They reported that plasma cells account for 81.0% and those cells are negative for CD45, positive for CD138, negative for CD38, and positive for CD117 [10]. After this case report reported by Vinho Do et al. in the literature, flowcytometric analysis of the bone marrow showed CD117 positivity in our case.1q21 amplification [13], 17p (p53) deletion, t(4;14), and/or chromosomal 13 abnormalities are all prevalent [11]. Conventional chemotherapy and radiation are ineffective in the majority of AMM patients. As a result, combining stronger chemotherapies with new drugs may increase response. According to one case series, 66.7% of patients receiving VRD (Bortezomib, Lenalidomide, and Dexa-methasone) and VCD (Bortezomib, Cyclophosphamide, and Dexamethasone) conventional myeloma treatment regimens had an inadequate response. In two patients, VD-PACE (bortezomib, dexamethasone, cisplatin, doxorubicin, cyclophosphamide, and etoposide) regimen was used along with VRD prior to hematopoietic stem cell transplantation consolidation and was able to achieve remission for over 2 years [3]. Immunotherapy, such as chimeric antigen receptor T cell immunotherapy, monoclonal antibodies, and potentially hematopoietic stem cell transplantation, may offer these patients fresh therapeutic hope [1]. We applied bortezomib (1.3 mg/m^2), lenalidomide (25 mg), and dexamethasone (40 mg) chemotherapeutic in this case we presented. In conclusion, the anaplastic morphology of MM

may pose a diagnostic challenge. The need for a multidisciplinary approach to detect hematological neoplasms is highlighted in this example. For AMM instances, prompt radiographic, flow cytometry, and histological examination may assist the diagnosis

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Corresponding author e-mail: rafiyesarigul@gmail.com

Orcid ID:
Rafiye Çiftciler 0000-0001-5687-8531
Mustafa Erol 0000-0003-3121-5330
Şükrü Nail Güner 0000-0002-8860-6132
İsmail Reisli 0000-0001-8247-6405

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