BANTAO Journal 2020; 18(2): 75-78

BJ
BANTAO Journal

Case report

Plasma Cell Dyscrasia Presenting with Severe Hypertension and Acute Kidney Injury

Atakan Ozdogan[1], Rafet Bilgic[1], Alican Yuruk[1], Demircan Guler[1], Aybuke Olgun[2], Gulen Gul[3] and Harun Akar[1]

[1]University of Health Sciences, Department of Internal Medicine, [2]Hematology and [3]Pathology. Tepecik Education and Research Hospital, Izmir, Turkey

Abstract

Plasma cell dyscrasia may occur with different clinical pictures, in addition to being caused by neoplastic overgrowth of a single plasma cell clone. Although the kidneys are one of the target organs for plasma cell dyscrasias, acute kidney injury is rarely the first presentation sign of multiple myeloma. We wanted to share a patient who presented with severe hypertension and elevated serum creatinine and was eventually diagnosed with plasma cell neoplasia. In our case, severe hypertension, hematuria, proteinuria predominantly suggested nephritic syndrome, while the high erythrocyte sedimentation rate and the increase in kappa/lambda ratio led us to plasma cell dyscrasias. In the case of severe hypertension and increased serum creatinine, accompanying erythrocyte sedimentation rate above 100 mm/hour, it is of paramount importance to include plasma cell dyscrasias among the possible diagnoses.

Keywords: Plasma cell dyscrasia, severe hypertension, nephritic syndrome

Introduction

Plasma cell dyscrasia is caused by neoplastic overgrowth of a single plasma cell clone. In general, the diagnosis of plasma cell dyscrasia is based on demonstrating monoclonality by immunohistochemical examination of bone marrow biopsy and serum immunofixation electrophoresis (SIFE) and urine immunofixation electrophoresis [1]. Plasma cell dyscrasias can present with different faces and in different clinical ways. Multiple myeloma (MM) is a neoplastic plasma cell disease. MM is manifested by clonal proliferation of malignant plasma cells in the bone marrow, monoclonal proteins in blood or urine, and associated organ dysfunction [2,3]. In clinical practice, the diagnosis of multiple myeloma is based on bone marrow aspiration, biopsy and a series of clinical laboratory tests [4]. Kidneys are one of the target organs of plasma cell dyscrasias, and relatively rarely cases presenting with acute kidney injury may be the first sign of multiple myeloma [4]. We wanted to share a patient who presented with acute nephritic syndrome, severe hypertension, elevated erythrocyte sedimentation rate, increase in serum kappa light chain level and kappa/lambda ratio and was diagnosed with plasma cell neoplasia.

Case

A 48-year-old male patient with hypertension was admitted to the emergency room with weakness and vomiting. With the pre-diagnosis of acute kidney injury (AKI), he was hospitalized in the internal medicine service to investigate the etiology. The patient's blood pressure at the time of admission was 195/105 mm Hg, and Nitroglycerin IV+ amlodipine p.o was administered for blood pressure control. The laboratory values of the patient were as follows; urea: 109 mg/dl, creatinine: 4.1 mg/dl, potassium: 4.5 mmol/L, sodium: 140 mmol/L, calcium: 10.5 mg/dl, sedimentation: 104 mm/hour, hemoglobin:

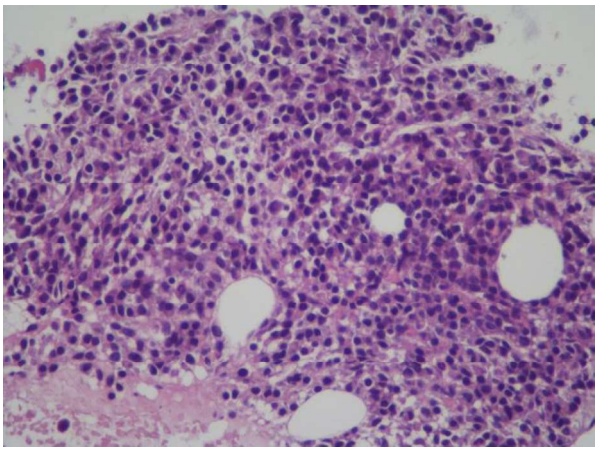

Fig. 1. Neoplastic plasma cells forming large groups, hematoxylin and eosin stain (400x)

Correspondence to: Harun Akar, Saglık Bilimleri Universitesi, Izmir Tepecik SUAM, Ic Hastaliklari Klinigi, Izmir; E-mail address: harunakar.md@gmail.com

12 g/dl, MCV: 91.7fL, leukocyte: 8100x10∧3/uL, platelet: 159000x10∧3/uL, albumin: 3.6 g/dl, globulin: 3.6 g/dl, kappa light chain: 2930mg/l, lambda light chain: 10.3 mg/l, kappa lambda ratio: 284.4, immunoglubulin A: 16.2 g/L, immunoglubulin M: 0.19 g/L, immunoglubulin G: 3.18 g/In L, complete urinalysis, +3 erythrocyuria, 2+ proteinuria, 2.2 g/day proteinuria were detected. Echocardiographic findings were as follows: ejection fraction: 60%, left atrium dilated, left ventricular concentric hypertrophy and left ventricular diastolic dysfunction were noted. In the fundus examination, stage 2 hypertensive retinopathy was detected. Upon the suppression of two series in immunoglobulin tests and abnormality in kappa-lambda ratio was detected, bone marrow aspiration and biopsy were performed with the possible diagnosis of cast nephropathy.
Microscopic examination of the bone marrow aspiration showed an increase in plasma cells at a rate of 45%, some of them with atypical binuclear appearance. Over 10% increase in CD38 positive neoplastic plasma cells was observed in bone marrow biopsy (Figure 1), and almost all of these plasma cells were evaluated as kappa positive (Figure 2a and Figure 2b). Bone marrow Congo red stain was negative. The patient with monoclonal plasma cell increase in the bone marrow, acute kidney damage, anemia, and diffuse lytic bone lesions on PET-CT was evaluated as multiple myeloma. The patient was transferred to the hematology clinic and VCD (Cyclophosphamide, bortezomib, dexamethasone) chemotherapy protocol and zoledronic acid treatment for lytic bone lesions was initiated. At the end of the first course of chemotherapy treatment, improvement was noted in serum urea (51mg/dl) and creatinine (1.16 mg/dl) values, and the patient was discharged with a control recommendation to receive the second course of treatment.

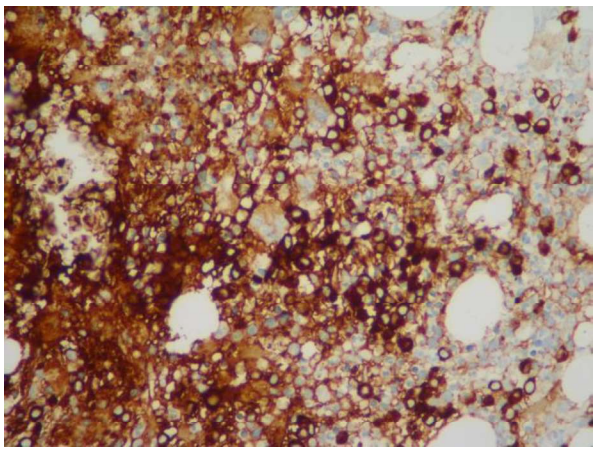

Fig. 2a. kappa positivity in plasma cells immunohistochemically (400x)

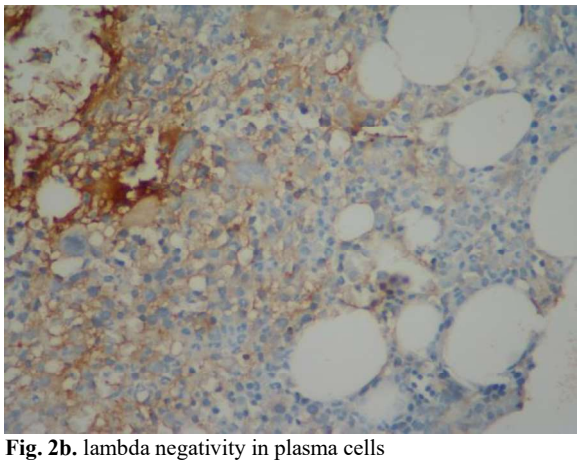

Fig. 2b. lambda negativity in plasma cells immunohistochemically (400x)

Disscussion

Multiple myeloma constitutes 1% of all malignancies and 10% of hematological malignancies [5,6]. MM often presents with severe weakness, bone pain, and recurrent infections [7,8]. Clinical findings in MM cases are classified under 4 main headings: anemia, hypercalcemia, bone lesions and acute kidney injury. Laboratory findings include anemia, high erythrocyte sedimentation rate, impaired renal function, inversion in the albumin/globulin ratio, and hypercalcemia [9]. In our case, severe hypertension, hematuria, proteinuria (2.2 g/day) predominantly suggest nephritic syndrome, while the high erythrocyte sedimentation rate (104 mm/hour) and the apparent increase in kappa/lambda ratio lead us to plasma cell dyscrasias in differential diagnosis. Severe hypertension, hematuria, nephritic proteinuria accompanying high erythrocyte sedimentation rate and marked increase in kappa/lambda ratio should prompt us to consider plasma cell dyscrasias in the differential diagnosis. MM may cause acute kidney damage with glomerular, tubular and interstitial involvement. One of the mechanisms underlying acute kidney injury (AKI) occurs when the toxic effects of light chains cause tubulointerstitial damage. Subtypes of tubulointerstitial kidney injury caused by plasma cell dyscrasias include isolated proximal tubular epithelial cell cytotoxicity, tubulointerstitial nephritis, and cast nephropathy, also known as myeloma kidney. Hypercalcemia, hyperuricemia, dehydration, intravenous radiocontrast agents themselves cause AKI primarily and/or by contributing to the toxic effects of light chains. Production of monoclonal free light chains (FLC) increases in plasma cell dyscrasias and increases hundreds of times above normal [10]. This increase exceeds the absorption capacity of the proximal tubules and abundant FLCs pass first into the tubular fluid and then into the urine, FLCs seen in urine are traditionally called Bence Jones proteins. FLCs may cause proximal tubule damage or the formation of intratubular cast by binding to Tamm Horsfall (THP) mucoprotein and then precipitation in the distal

nephron lumen [10]. Intraluminal casts also trigger inflammation and fibrosis by activating a series of chemokines. Here, the first line of treatment is to treat the underlying disease process, monoclonal plasma cell neoplastic overgrowth. Early initiation of chemotherapy with adequate hydration may prevent kidney damage that does not develop cast nephropathy. In our case, early diagnosis and treatment prevented the development of permanent kidney damage. Interestingly, the patient described in this case presented with severe hypertension, azotemia, hematuria, and nephritic level proteinuria. The most important thing in this context is the necessity to consider plasma cell dyscrasia as an etiology. In appropriate clinical situations, it is important to screen for the presence of potentially nephrotoxic monoclonal Free Light Chains (FLC) during etiology investigation in AKI. Quantitative measurement of serum FLCs by protein electrophoresis (with or without immunofixation) or nephelometric immunoassays can be used in the evaluation. With this last method, quantitative measurement of κ and λ FLCs is obtained; Overproduction of one of the monoclonal FLCs in the case of renal function impairment will cause the κ/λ FLC ratio to deviate outside the normal range (0.26-1.65), providing diagnostic benefit [10]. Multiple myeloma should be considered among our differential diagnoses in patients with kidney failure of unknown cause.

The three most common subtypes of monoclonal Ig-mediated kidney disease are cast nephropathy, monoclonal Ig deposition disease (MIDD), and AL amyloidosis [11]. Blood pressure can be a useful distinguishing feature because patients with amyloid often have hypotension with or without orthostasis as a result of coexisting myocardial amyloid, whereas patients with MIDD and kidney disease typically have hypertension [11]. Light chain deposition disease (LCDD) is the most common type of Monoclonal immunoglobulin deposition disease and renal involvement due to LCDD manifests itself with renal lesions, hypertension, microscopic hematuria, and proteinuria [12].

It is thought that the renin angiotensin system plays a role in hematopoietic stem cell plasticity [13]. It has been suggested that circulating ACE may be associated with clonal proliferation of malignant plasma cells in the bone marrow microenvironment [14]. It was hypothesized that the JAK-STAT pathway might serve as a crosstalk point between RAS components locally present in the bone marrow and hematopoiesis [15]. It has been noted that RAS components such as the ACE2 enzyme and ANG- (1-7) peptide may provide new targets for cancer therapy [16]. It is thought that RAS determines the processes of angiogenesis, cellular proliferation, inflammation and fibrosis and the cross-interaction between them, which will determine the tumor potential [16]. We need to know more about the complex role of RAS in dysproteinemias.

Chari *et al*. in their study investigating the incidence rates of hypertension and malignant hypertension in newly treated MM patients, they reported a 30% increase in hypertension risk for MM versus non-MM patients [17]. In this study, comorbid conditions that significantly increase the risk of malignant hypertension in MM patients with a history of hypertension; cardiomyopathy, kidney failure, and diabetes mellitus has been reported [17].

As a limitation of our study, we could not perform renal biopsy in our case, partially due to the effect of the Covid-19 pandemic process. After the diagnosis of plasma cell dyscrasia, the patient was transferred to the hematology clinic immediately and chemotherapy treatment was started energetically, and rapid improvement in renal functions was documented. In this Covid-19 Era, we thought the most prudent management of this case was to transfer the patient to the hematology clinic in order to be administer to apply specific treatment for plasma cell dyscrasia.

Conflict of interest statement. None declared.

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