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The Patient Presenting with Renal Failure Due to Multiple Myeloma Associated with Celiac Disease: Case Report

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ABSTRACT

Celiac disease (CD) is an autoimmune disorder induced by gluten intake in susceptible individuals, and characterized by intestinal and extraintestinal findings due to malabsorption caused by intestinal mucosa inflammation and villus atrophy. CD is an important risk factor for the development of malignancy including lymphoma and gastrointestinal tumors and renal failure. In this paper we present a 65 years old male patient with multiple myeloma, who was monitored for chronic renal failure (CRF) and diagnosed with CD. He is the first case with multiple myeloma associated with CD in the literature.

Keywords: Celiac disease, Multiple myeloma, Chronic renal failure

ÖZET

Multipl Myeloma Bağlı Böbrek Yetmezliği ile Başvuran Hastada Eşlik Eden Çölyak Hastalığı: Olgu Sunumu

Çölyak hastalığı (ÇH), oto-immün kökenli, glutene karşı hassasiyet sonucu ince bağırsak mukozasında inflamasyon ve villüs atrofisi sonucu gelişen malabsorbsiyona bağlı olarak intestinal ve ekstraintestinal bulgularla karakterize bir hastalıktır. ÇH malignite ve böbrek yetmezliği gelişimi için önemli bir risk faktörüdür. ÇH olanlarda başta lenfoma ve gastrointestinal sistem tümörleri olmak üzere malignite sıklığı artmıştır. Makalemizde, kronik böbrek yetmezliği (KBY) tanısı ile izlenen, multipl miyeloma tanısı konulan ve ÇH saptanan 65 yaşında erkek hasta sunulmuştur. Olgumuz literatürde bildirilen ÇH'na eşlik eden ilk multipl miyelom olgusudur.

Anahtar Kelimeler: Çölyak hastalığı, Multipl miyelom, Kronik böbrek yetmezliği

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INTRODUCTION

Celiac disease (CD) is an immune-mediated disorder in which the ingestion of dietary gluten causes chronic inflammatory changes, including intestinal mucosa inflammation, crypt hyperplasia, lymphocyte infiltration, and villous atrophy. A gluten-free diet rapidly improves symptoms and mucosal changes.[1] Patients with CD show 1.9 to 3.8 times increase in mortality. The main mortality factors are malignant diseases.[2] Prior studies have suggested that the incidence of some neoplastic disorders, particularly malignant lymphoma, small intestinal adenocarcinoma and esophageal carcinoma, are increased in CD compared to patients without CD.[3,4] Gluten-free diet for one to five years can prevent the risk of development of malignant disease.[2]

Multiple myeloma (MM) is a malignancy characterized by a clonal accumulation of malignant plasma cells, infiltration of plasma cells in the bone marrow, osteolytic bone lesions, renal failure, and immune deficiency. MM is the second most common hematological malignancy after non-hodgkin's lymphoma, accounting for 1% of all malignancies and 13% of the diagnoses of hematological malignancies.[5]

Although it is known that the malignancy incidence has increased[3,4], only one case with plasma cell dyscrasia was reported in literature. This case had plasma cell dyscrasia but didn't meet all MM criteria.[6] Our patient is the first case of multipl myeloma associated with celiac disease in the literature.

CASE

A 65-year-old male farmer presented with 1.5-years history of itching and 2-months history of fatigue, flank pain and frequent urination. Even though he was prescribed some medications in different health centers, his complaint of itching remained unchanged. In addition he had nausea and vomiting. He was referred to our unit with diagnosis of renal failure by the last visited health center. He had thyroid surgery 1.5 years ago and has 2-months history of hypertension. He was taking levothyroxin and cilazapril. The physical examination findings were as follows: blood pressure, 190/80 mmHg; pulse rate, 76/min; general condition was moderate; he was conscious, cooperation, orientation and

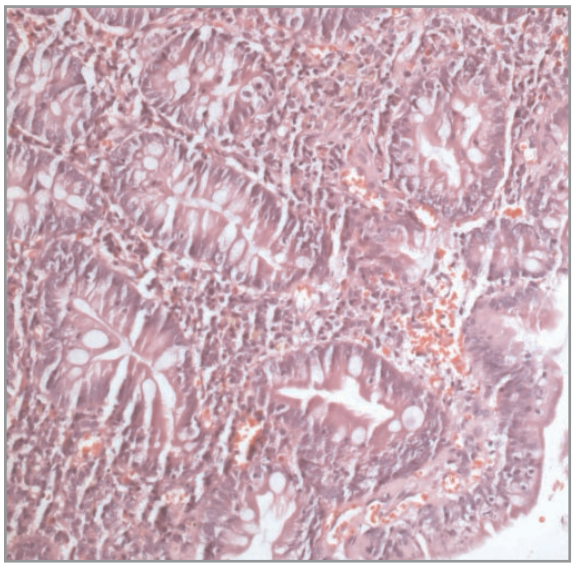

Figure 1. Atrophy and blunting due to loss of microvilli in brush border as well as increased intraepithelial lymphocyte count were seen in sections. On the other hand crypts seem elongated and hyperplastic. In addition, chronic inflammatory infiltrate in lamina propria contains lymphocytes, eosinophils and plasma cells (H&E stain, x20 objective).

turgor of mucosa were normal, and his mucosa were pale. He had hepatomegaly of 1 to 2 cm as well as bilateral anterior cervical lymphadenopathy. Laboratory findings on admission were as follows: hemoglobin, 8.4 g/dL; hematocrit, 23.6%; MCV, 88,8 fl; platelet count, 227.000/mm^3; leukocyte count, 5.200 /mm^3; erythrocyte sedimentation rate, 78 mm/h; glucose, 90 mg/dL; BUN, 72 mg/dL; creatinine, 7.2 mg/dL; uric acid, 8.5 mg/dL; Ca, 9.2 mg/dL; P, 6.7 mg/dL; total protein, 12,6 mg/dL; albumin: 3.3 mg/dL; Na, 128 meq/L; K, 6,1 meq/L. The liver function tests were within the normal range. Complete urine analysis revealed: density, 1009; protein, 100 mg/dL; glucose was negative; and there was 4 erythrocyte and 4 leukocyte per microscopic field. Urinary protein/creatinine ratio was 1893 mg/L / 54 mg/L. PTH, 191 ng/mL (Normal range: 0-72 ng/mL); ferritin, 527 pg/mL. IgA anti-endomysium antibodies were positive. IgG, IgA, IgM and IgE levels were 67.6 g/L (Normal range 7-16), 0,22 g/L (Normal range 0.7-4), 0,17 (Normal range 0.4-2.30), and 11.9 IU/mL (Normal range 0.0-100), respectively. Urinary system USG revealed that both kidney size were within normal ranges and there was grade II increased echogenicity.

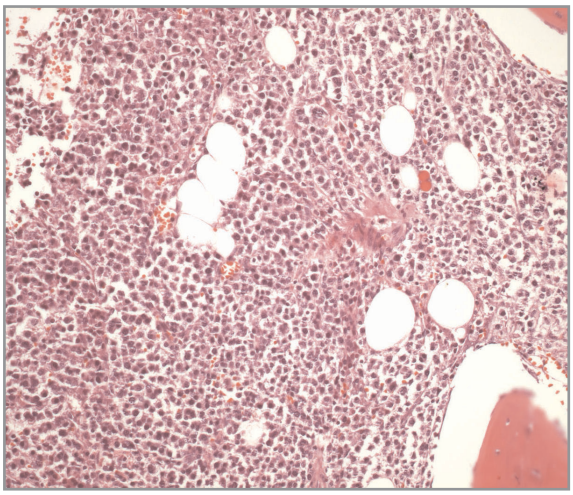

Figure 2. Histopathologic sampling revealed infiltration focuses, composed of plasma cellls, in bone marrow parenchyma.

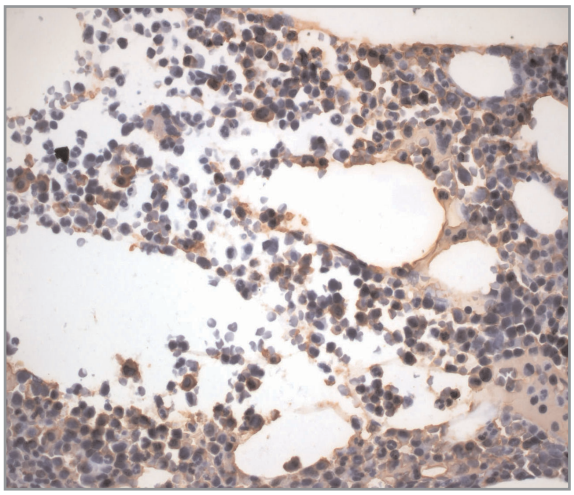

Figure 3. Immunohistochemical study showed monoclonal staining pattern, which is positive for kappa and negative for lambda in plasma cells.

Clinical Course

The patient was given 3000 cc/day isotonic fluid replacement. Amlodipin 10 mg daily was started for hypertension. He underwent upper gastrointestinal system endoscopy, and gastroduodenitis was defined. Pathological examination demonstrated microvillous atrophy, crypt hyperplasia, and lymphocytic infiltration (Figure 1). After detection of hypergammaglobulinemia, protein electrophoresis was performed, and significant "M" band was shown. The urine was positive for Bence Jones protein. A bone marrow biopsy showed 90% plasma cells stained with kappa. The patient was diagnosed as IgG-kappa myeloma with criteria of >30% plasmacytosis in bone marrow, > 35 g/L IgG, and > 1 g Bence Jones protein level in the 24-hour urine (7) (Figures 2 and 3). He was started on a regimen of VAD. He developed polyuria under treatment regimen. The daily urine output increased up to 8500 cc, creatinine levels decreased, and reached a steady level of 4-4.5 mg/dL. After the first cycle, the second one was given on 28th day. He developed neutropenia 8 days after the second cycle, then fever, cough, nausea, and vomiting were observed. After 10 days of second cycle, the patient deteriorated and died of lung infection due to neutropenia.

DISCUSSION

Our patient is the first case with multiple myeloma associated with CD in the literature. CD is an autoimmune disorder induced by gluten intake in susceptible individuals, and characterized by small intestinal mucosal injury. Mucosal lesions may be related to direct toxic effect of gluten or gluten products over small intestine epithelium.[8] The prevalence of malignant tumors is 1.5 times higher in CD patients compared with that of the general population.[4] CD patients are at increased risk of some malignancies, particularly lymphoma and gastrointestinal system tumors. Indeed, they have 5-fold increased risk of melanoma, 6-9 times of non-Hodgkin lymphoma, 12 times of osephageal cancer, and 24-34 times of primary gastrointestinal lymphoma.[4,9] The mechanisms that cause increased malignancy in CD is not well-established, but increase in mucosal permeability, exposure to environmental carcinogens, chronic inflammation, chronic antigenic stimulation, pro-inflammatory cytokine release, and malnutrition may be involved in tumor development.[8,10] Although it is known that the incidence of cancer has increased, no case of CD associated with MM has been reported in the literature. Although, a case of CD associated with plasma cell dyscrasia was previously reported, that case did not meet the criteria for the diagnosis of MM.[6] In spite

of the fact that endoscopic and histopathologic findings were compatible with CD, our case was diagnosed by positive EMA. Positive EMA is considered as a predictive value in the diagnosis of CD, which has sensitivity of 96% and specificity of 100%.[2]

CD has been reported to be an important risk factor for the development of chronic renal failure (CRF), but the reason of this increase has not been well-established. CD is frequently associated with glomerulonephritis, particularly IgA nephropathy, and type-I diabetes mellitus. All of these illnesses can cause CRF.[11] The cause of the renal failure in our case was likely due to MM rather than CD. Approximately 50% of the patients with MM will develop renal involvement during the course of disease. Besides, hypercalcemia, dehydration, non-steroidal anti-inflammatory agents, and contrast substances may contribute to renal failure. Since the disease load in patients with renal failure is high, it should be kept in mind that clinical course of the disease might be aggressive.[12,13] In many cases renal failure responds to fluid replacement, treatment of the hypercalcemia, withdrawal of toxic agents, and steroid use.[12] Our case showed partial improvement with above mentioned therapy measures. But he died due to lung infection.

It has been reported in the literature that autoimmune diseases, such as systemic lupus erythematosus, rheumatoid arthritis, myasthenia gravis, pernicious anemia, are associated with increased risk of MM development.[14] Although CD is an immune-mediated disease[1], the data related to its contribution to increased risk of MM development is limited. Our case suggests that MM can develop in patients with CD.[14] Further studies with more patients are required to define the relationship between CD and MM.

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