

An Unusual Presentation of Multiple Myeloma: Plasmacytic Ascites Complicated by Duodenal Involvement

Multiple Myeloma'nun Nadir bir Prezantasyonu: Duodenal Tutulum ile Komplike olan Plazmasitik Asit

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Abstract: The incidence of gastrointestinal system involvement during the course of multiple myeloma (MM) is rare. The usually affected sites of GI tract are small and large bowel, stomach, and rarely esophagus. Only a few MM cases are also known with myelomatous ascites at presentation. In this report, we present a 67-year old patient who developed myelomatous ascites. Although rare, MM can involve extramedullary areas such as duodenum and different kinds of complications may occur. In addition to standard diagnostic and treatment methods, individualized diagnostic and therapeutic options should be considered for such patients.

Key words: multiple myeloma, ascites, duodenal involvement

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Öz: Multiple myeloma (MM) seyrinde gastrointestinal sistem tutulumu nadirdir. Gastrointestinal sistemde sıklıkla ince ve kalın bağırsak, mide ve nadiren de özefagus tutulur. MM vakalarında myeloma bağlı asit ile başvuran hasta sayısı çok azdır. Bu vaka sunumunda myeloma bağlı asit gelişen 67 yaşında bir erkek hasta sunulmuştur. Nadir görülmesine rağmen MM duodenum gibi extramedüller bölgeleri tutabilir ve buna bağlı farklı komplikasyonlar gelişebilir. Bu tür hastalarda standart tanı ve tedavi yöntemlerine ek olarak, bireyselleştirilmiş tanı ve tedavi seçenekleri de düşünülmelidir.

Anahtar Kelimeler: multiple myelom, asit, duodenal tutulum

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1. Introduction

Plasma cell neoplasms are classically categorized into four groups; multiple myeloma (MM), plasma cell leukemias, solitary plasmacytomas of the bone (SPB), and extramedullary plasmacytomas (EMP) (1). Plasmacytomas are extramedullary accumulations of plasma cells and can occur nearly in 20% of MM patients (1). The incidence of gastrointestinal (GI) involvement during the course of MM is approximately 10–13% (2). The usually affected sites of GI tract are small and large bowel, stomach, and rarely esophagus (3). Only a few MM cases are also known with myelomatous ascites at presentation (4).

Here in, we present an unusual presentation of MM with plasmacytic ascites complicated by duodenal involvement.

2. Case Report

A male of sixty-seven old presented with a 2-month history of abdominal distention, fatigue, and low back and leg pain. On physical examination conjunctivas were pale, skin and sclera were icteric and moderate ascites was found. His complete blood count revealed hemoglobin 11g/dl, hematocrit 32%, white blood cell counts 5900/UL with normal differential; and platelets 156.000/UL. Erythrocyte sedimentation rate was 123 mm/hour. Blood chemistries showed an elevated LDH of 712 U/L (normal range, 240-480), an ALP of 904 U/L (98-270), GGT of 494 U/L (8-50), total bilirubin of 9.59 mg/dl (0.1-0.9), and direct bilirubin of 6.7 mg/dl. Total proteins were 9.18g/dl (6-8.5) with albumin 4.13 g/dl (3.5-5.0) and calcium of 10.4 mg/dl (8.5-10.5). Beta-2 microglobulin was 5.47 (1.42-3.21) in the serum. AST and ALT were elevated at 246 U/L (7-39) and 259 U/L (2-40), respectively. Renal function and serum electrolytes were within normal limits. Serum protein electrophoresis disclosed monoclonal gammopathy with an elevated IgA of 3390 mg/dl (82-453), and a low IgG of 409 mg/dl (751-1560), and an IgM of 7.55mg/dl (46-304) while free kappa light chain was detected. Plain film skeletal survey revealed multiple osteolytic lesions of the lumbar spine, pelvis, clavícula and skull. Paracentesis demonstrated clear ascites fluid

with a level of 2.54 g/dl protein, 0.91g/dl of albumin and 9.88 mg/dl of beta-2 microglobulin. Ascitic fluid electrophoresis also demonstrated a monoclonal gammopathy. By flow cytometric analysis, CD38/138 ratio was found as 65% on bone marrow aspiration sample and 14% in ascites fluid. Plasma cells were shown in peripheral smear of ascites fluid (Figure 1A). Since the patient developed hematemesis, an upper gastrointestinal system endoscopy was performed on which a giant ulcer was detected in the second portion of the duodenum. The biopsy of the ulcer showed marked monoclonal plasma-cell infiltration by immunohistochemistry and immunoperoxidase stain for CD138 showed diffuse and strong positivity (Figure 1B). A F-18 fluorodeoxyglucose (FDG) whole body Positron Emission Tomography (PET) in combination with computed tomography (CT) scan was performed and revealed an increased F18 FDG accumulation in anterior portion of left inferior quadrant abdomen which was matched to colon trace, in the localization of pancreas in the left inguinal area, in the anterior portion of thoracal vertebrae and in the soft tissue localization of the anterior sacrum. Additionally, thorax images revealed a focal activity which was matched with lymphadenopathy in the left lateral of the middle mediastine (Figure 2). According to these findings, the patient was diagnosed as Ig type A MM with plasmacytic ascites and duodenal involvement and VCMP (vincristine, cyclophosphamide, melphalan, prednisolone) chemotherapy protocol was begun. Upper gastrointestinal bleeding was treated conservatively with proton pump inhibitors. Although his ascites and icter disappeared after two courses of VCMP, there was no resolution of the abdominal lesion in PET/CT. Bortezomib therapy was recommended and the patient agreed to receive this agent. After one course of bortezomib, he again developed upper gastrointestinal bleeding and was managed with proton pump inhibitors. Since then, the patient and his family refused further cytotoxic treatment and instead chose to receive supportive therapy. Then, patient has not come to routine follow-up and couldn't get contact from the family.

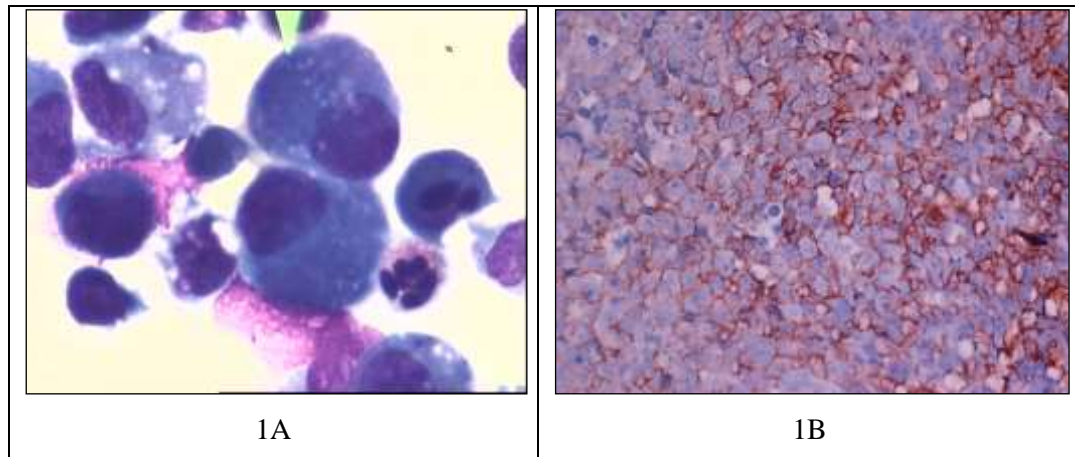


Figure 1: *1A.* Representative plasma cells present in the ascitic fluid (Wright's stain) (X100). *1B.* Immunoperoxidase stain for CD138 shows diffuse and strong positivity in neoplastic plasma cells in the biopsy of the duodenal ulcer (x200)

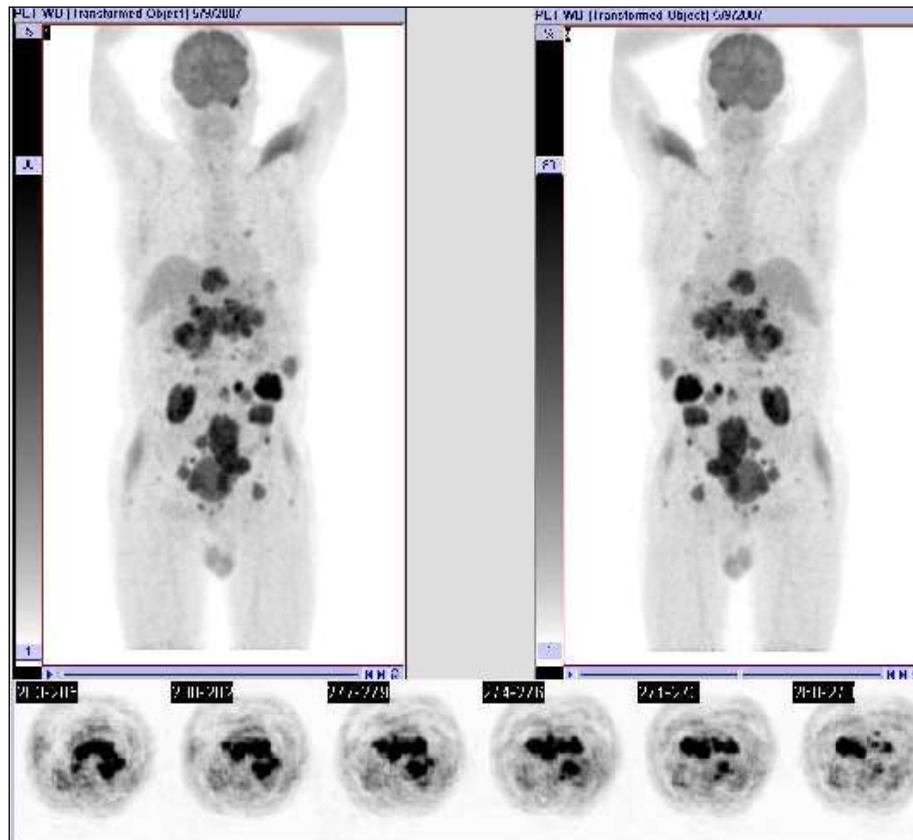


Figure 2. *Heterogen, irregular restricted, hypermetabolic images obtained at ductus choledochus, duodenum and pancreas regions with transaxial and whole body F-18 FDG PET.*

3. Discussion

Our patient is one of few MM cases in the literature with significant bleeding from a duodenal plasmacytoma and ascites (3). The presentation with ascites of MM is also a rare condition. In the literature research and case

report of Greer et al (5) there was not any case presenting with ascites. In 1987 Karp and Shareff have reported that especially Ig type G MM could be presented with ascites (6). Ascites formation in a myeloma patient is

usually associated with extensive liver infiltration with plasma cells causing portal hypertension, but may be secondary to infectious peritonitis, or very rarely, to myelomatous peritoneal infiltration. Systemic amyloidosis, tuberculous peritonitis, hemangioendothelial sarcoma, plasma cell sarcoma, and spontaneous splenic ruptures are the other possible etiologies of ascites in MM patients (7). The low serum ascit-albumin gradient (SAAG) without the myelomatous infiltration of the liver and the presence of the malignant plasma cells in the ascitic fluid supports myelomatous peritoneal involvement (7). Also the high serum and ascitic level of beta-2 microglobulin could be attributed to its cytokine-mediated hyperproduction by tumor cells or by activated infiltrated cells (8). Although SAAG was 3.22 in our case, increased levels of beta 2 microglobulin was detected both in the serum and the ascites.

Aggressive myelomas rarely invade organs outside the bone marrow, lymphatics or reticuloendothelial system. Also diffuse intra-abdominal seeding caused by myelomatous ascites or biliary obstruction is extremely rare (9). When myeloma cells spread to the intraabdominal cavity reticuloendothelial system and kidneys are the most common involved parts. In autopsy studies, over two-thirds of myeloma cases were associated with microscopic infiltration of these organs (10, 11). If myeloma affects the liver, diffuse infiltration leading to intrahepatic cholestasis and jaundice is typically seen. Extrahepatic biliary obstruction caused by a hilar plasmacytoma, as in this case, is uncommon, with limited reports noted in the English literature (9). In our case, there was an obstructive icter which could not be shown by imaging methods and necessitated an extrahepatic bilier drainage.

Plasma cell tumors rarely invade the gastrointestinal tract. In a review of 36 patients with gastrointestinal plasmacytomas, the stomach was most frequently involved, followed by the jejunum, ileum, colon, rectum, and rarely the duodenum (2). Gastrointestinal tract involvement incidence during the course of MM is approximately 10–13% (2), whereas solitary extramedullary plasmacytoma of the GI tract is noted in only 3–7% of patients with EMP (12).

In our case the endoscopic imaging and pathological examination of duodenal ulcer biopsy revealed duodenal involvement. A review of the English-language literature in 1999 revealed only 19 cases of significant hemorrhage complicating multiple myeloma or solitary EMP of the GI tract. Only two of these have experienced overt hemorrhage due to duodenal plasmacytoma (3). To the best of our knowledge, ours is the third reported case of significant bleeding from a duodenal plasmacytoma. The standard therapy approaches for GIS plasmacytomas are radiotherapy and chemotherapy. A surgical procedure may be necessary for acute bleedings while there are also case reports offering angiographic embolization to control massive bleeding (3). In our case bleeding was treated successfully by conservative methods.

The differential diagnosis of gastrointestinal blood loss in a patient with multiple myeloma should include poorly differentiated neoplasms, mucosa-associated lymphoid tissue (MALT) lymphoma and amyloidosis, as well as ulcer related and unrelated gastrointestinal bleeding disorders, such as peptic ulcer disease, arteriovenous malformation, polyps, or carcinoma. The endoscopic appearance of the gastrointestinal plasmacytoma resembles poorly differentiated neoplasms, MALT lymphoma and amyloidosis. As the management of these clinical settings differs, it is very important to have the right diagnosis (13-15). Flow cytometric analysis and histochemical examination may help in the differential diagnosis (16). In our case, there was a giant ulcer in duodenum in which CD38/138 positive cells were shown by immunohistochemical examination. For us, the differential diagnosis of gastrointestinal bleeding in MM is important since failure to recognize myelomatous involvement of gastrointestinal tract may result in achieving inappropriate treatment modalities of surgery, radiotherapy and/or chemotherapy.

4. Conclusion

Aggressive MM can involve extramedullary areas and different kinds of complications may occur. We suggest that individualized diagnostic and therapeutic options should be considered for such patients.

KAYNAKLAR

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