

Myelomatous Ascites and Pleural Effusion in Relapsed Multiple Myeloma

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Abstract

Extramedullary multiple myeloma is seen in advanced and aggressive disease and occurs due to plasma cell infiltration of sites other than the bone marrow. Myelomatous ascites or pleural effusion is seen in less than 1 % of cases and can be differentiated from infectious etiologies based on fluid cytology.

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Key Clinical Message:

Due to poor outcomes in relapsed and refractory multiple myeloma cases, it is important to identify any prominent signs or symptoms in such patients using appropriate diagnostic measures to differentiate serious entities from some common etiologies

Abstract:

Extramedullary multiple myeloma is seen in advanced and aggressive disease and occurs due to plasma cell infiltration of sites other than the bone marrow. Myelomatous ascites or pleural effusion is seen in less than 1 % of cases and can be differentiated from infectious etiologies based on fluid cytology.

Key words: Multiple myeloma, plasmacytic ascites, myelomatous pleural effusion, fluid cytology, spontaneous bacterial peritonitis

Introduction:

Multiple myeloma (MM) is a B cell neoplasm characterized by the clonal proliferation of neoplastic plasma cells in the bone marrow. [1] [2] It accounts for roughly 2 percent of all cancers and about 17 % of all hematological malignancies with an incidence rate of 7.1 % cases per 100,000 per year. Extramedullary involvement outside the bone marrow is frequently seen in advanced or refractory stages of multiple myeloma due to plasma cell infiltration of visceral organs. [3] [4] Malignant myelomatous pleural effusion or ascites is suggestive of a more advanced and aggressive disease and is seen in less than 1 % of myeloma cases. [5] [6] Ascites in MM can develop due to peritoneal infiltration or secondary causes such as hepatic amyloidosis, cardiac or renal diseases, or portal hypertension. [7] Infectious peritonitis due to tuberculosis and spontaneous bacterial peritonitis (SBP) can also be an intrinsic secondary cause of ascites but is usually differentiated from malignant plasmacytic ascites based on an ascitic fluid cytology analysis. [8] [9] Since the atypical plasma cells detected on cytology of the fluid might appear similar to reactive mesothelial cells, further testing methods such as flow cytometry, immunofluorescence, or electron microscopy should be employed. [8] Herein, we describe a case of malignant plasmacytic ascites and pleural effusion that was initially treated as SBP.

Case Presentation:

A 70-year-old male with an initial presentation of back pain and difficulty walking was diagnosed with IgD lambda subtype of International Staging System (ISS) stage II MM eight years prior to current presentation with only bony lesions and without renal disease. He was found to have a T3 tumor with lytic bone lesion which was managed by a laminectomy and radiation therapy. He was able to achieve a very good partial response with 6 cycles of lenalidomide, bortezomib, and dexamethasone (RVD). The patient underwent high dose chemotherapy followed by autologous stem cell transplant and was subsequently started on maintenance therapy with 10 mg lenalidomide. He had multiple relapses and underwent multiple lines of therapy. Most recently, the patient was on once weekly salvage therapy with carfilzomib, pomalidomide, and dexamethasone (KPD), however, he developed anemia grade 3 and neutropenia grade 4. He was hospitalized due to acute kidney injury with oliguria likely due to cast nephropathy in the setting of progressive MM. His renal function improved significantly following treatment with cyclophosphamide 1 gm/m² for 2 days, pulse dexamethasone 40 mg for 5 days, and rasburicase 3 mg due to hyperuricemia and tumor lysis syndrome. During hospital stay, the patient had significant abdominal pain and distension. Paracentesis revealed ascitic fluid with elevated white blood cell count indicating possible SBP. An abdominal ultrasound with liver doppler ruled out any liver pathology and ascitic fluid cultures were negative. The peritoneal fluid cytology demonstrated the presence of numerous atypical CD138+ plasma cells with lambda light chain restriction on kappa/lambda immunoglobulin light chain immunostaining and this confirmed our suspicion of malignant plasmacytic ascites (Figure 1A-D). The patient's condition progressed rapidly over a period of one month. Thereafter, he was further evaluated for possible non-B cell maturation antigen (BCMA) directed therapies under clinical trials. He was hospitalized multiple times for pleural effusions requiring thoracentesis and pleural catheter placement to alleviate his worsening dyspnea. The possibility of malignant effusion was considered since his respiratory symptoms were new and of sudden onset. Accordingly, a confirmatory pleural fluid cytology and immunohistochemistry was performed which revealed atypical plasma cells positive for CD138 with lambda immunoglobulin light chains restriction (Figure 2A-D). Concurrently, his serum creatinine levels rose dramatically from 0.86 mg/dL to 2.63 mg/dL and evolved to acute renal insufficiency necessitating a cystoscopy to place ureteral stent. Although the patient's kidney function improved after one cycle of cyclophosphamide, bortezomib, and dexamethasone (CyBorD), he developed an uncontrolled atrial fibrillation. The patient was transitioned to hospice care and ultimately died.

Discussion:

This case illustrates an aggressive form of multiple myeloma that presented with both plasmacytic ascites and pleural effusion in the late stages of disease. The incidence of extra-medullary involvement in MM is about 7%, and that of malignant effusions is 1-2% which is usually associated with a poor prognosis. [9] [10] [11] Classic presenting symptoms and signs of MM include anemia, bone pain, renal failure, infections, and hypercalcemia. Effusions due to MM commonly occur due to secondary involvement of other organs like heart and kidney. Malignant ascites can occasionally be a presenting feature in MM, but myelomatous pleural effusion rarely manifests at initial diagnosis. [11] [12] [13] Four out of seven cases of MM with a malignant effusion that were reported by Gochhaitt et al presented with pleural effusion during their treatment with no other sites of involvement. All the four MM cases were first recognized based on the typical clinical presentation of hypercalcemia–renal function–anemia–bone lesion (CRAB). [10] Mitra et al reported case of an elderly male who was evaluated for ascites with abdominal pain and distension with high total protein but normal bilirubin and liver enzymes. Computed tomography (CT) scan of the abdomen revealed multiple peritoneal nodules, mesenteric and omental thickening. Both this and another MM patient reported by Abdulsamad et al presented with ascites at initial diagnosis unlike our patient who suffered from multiple relapses over 7 to 8 years and ultimately developed extra-osseous complications at an advanced stage of MM. [7, 8]

The body cavities are not unusual sites of metastasis, but the pathophysiology of their involvement is poorly understood. A pleural or peritoneal biopsy may show extensive plasma cell infiltration, but it is not necessary for diagnosis. [12] [13] The diagnosis of plasmacytic effusion can be confirmed based on detection of atypical plasma cells on fluid cytological analysis derived via paracentesis and/or thoracocentesis supplemented by immunofixation of proteins and identification of cytoplasmic immunoglobulin, kappa or lambda light chains, and high CD38 and/or CD138 expression on their immunophenotypic analysis. [12] [14] An abdominal paracentesis in the case reported by Mitra did not reveal any significant findings. Histopathological examination of centrifuged peritoneal deposits showed CD138 positive plasma cells on immunohistochemistry. Serum electrophoresis confirmed the presence of IgG heavy chains and lambda light chains that led to the diagnosis of MM, IgG lambda, ISS Stage III. Similar findings were noted on flow cytometric immunophenotyping in the four patients described by Gochhaitt et al. [10] In one patient as described by Stoos-Veic et al, a diagnosis of myelomatous ascites was confirmed by flow cytometry immunophenotyping and presence of IgG kappa light chains on ascitic fluid immuno-electrophoresis. [15] Ghorbel et al described a case of an adult female diagnosed with MM Stage IIIa based on a serum electrophoresis, imaging, and bone marrow aspiration. Her clinical presentation was typical with worsening bone pain and classic fatigue but in about five months of treatment initiation, new respiratory symptoms led to the diagnosis of myelomatous pleural effusion based on a chest X-ray, thoracentesis, and a pleural biopsy. [16]

To help rule out secondary causes of effusion in MM such as infections, secondary tumors, renal or heart failure, ascitic fluid can be examined to calculate the serum ascites albumin gradient (SAAG) ratio, pleural fluid for pleural fluid/serum lactate dehydrogenase (LDH) ratio, adenosine deaminase (ADA) and glucose levels, and both for cell counts and cultures. [13] [17] Imaging modalities like skeletal survey, PET-CT scan and MRI are also commonly used to corroborate a diagnosis of MM bone disease and extra-medullary MM. [18] Alegre et al documented a disease presentation of similar nature as our patient, i.e., development of features of extramedullary MM in the form of ascites and pleural effusion later in the disease course. After remaining asymptomatic with a stage IA IgG multiple myeloma for 8 years after induction treatment, she abruptly presented with moderate ascites, unexplained fever, and pancytopenia due to bone marrow infiltration. A paracentesis demonstrated 93% atypical plasma cells on fluid cytology and monoclonal cytoplasmic kappa light chains on immunohistochemistry. [19]

Finally, myelomatous effusions seems to predict poor outcomes with short time to demise in the relapsed and refractory setting [15] [16] [19] [20] [21] it is important to recognize this entity as it might help differentiate infectious etiologies versus disease relapses in MM patients.

Conclusion:

Based on the varying patient presentations encountered in the setting of myelomatous involvement of body cavities, it can be stressed that ascitic or pleural fluid cytology is an important diagnostic method in the presence of atypical MM symptoms. Cytological examination may be useful in early diagnosis of a plasma cell neoplasm. It is also helpful in identifying extra-medullary progression in some cases where it is indicative of an aggressive form of the disease requiring prompt evaluation and treatment.

Conflict of Interest

M.B, M.A.M, K.L, L.J, V.A, V.R, T.S, A. C-K, and R.D.P have no conflicts of interest to declare.

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Authors' Contributions

M.B. and M.A.M.: wrote the manuscript; K.L. and L.J.: obtained the pathology images for the case; M.B, K.L, L.J, V.A, V.R, T.S, A.C-K, S.A, R.D.P, and M.A.M edited and finalized the manuscript.

Ethical Statement:

We hereby confirm that the present study conforms to the ethical standards and guidelines of the journal.

Data Availability Statement:

All the data supporting the findings of this study are available within the article. No additional data is available.

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