IMAJ • VOL 12 • FEBRUARY 2009

Dyspnea and Pleural Effusion as Presenting Clinical Manifestations of Multiple Myeloma

Gal Neuman MD and Yaron Denekamp MD MSc

Department of Medicine, Carmel Medical Center, and Faculty of Medicine, Technion-Israel Institute of Technology, Haifa, Israel

KEY WORDS: multiple myeloma, dyspnea, pleural effusion

IMAJ 2009;11:118–119

The most common presenting clinical findings of multiple myeloma are fatigue, bone pain and recurrent infections [1]. We report an extremely rare case of a patient presenting with effort dyspnea due to a pleural effusion in whom a diagnosis of multiple myeloma was established after a thorough investigation.

PATIENT DESCRIPTION

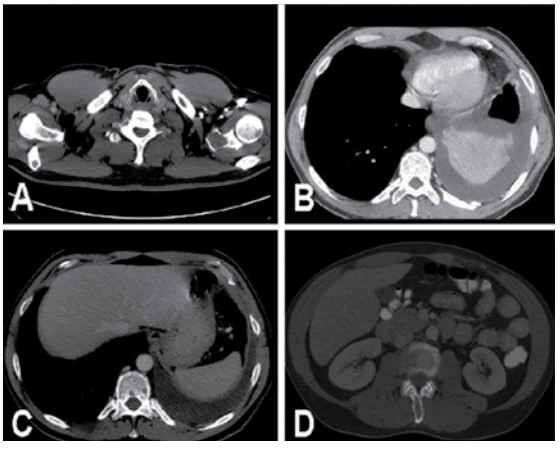
A 47 year old man presented to the emergency department with effort dyspnea, pleuritic chest pain and dry cough of 4 months duration. Three months previously he completed one trial of an antibiotic course, macrolide, which did not alleviate his complaints. Two days before the admission he had presented to the emergency department with exacerbation of the aforementioned complaints, including pleuritic chest pain, but without fever or sputum production. Laboratory analysis revealed normal complete blood count and blood chemistry values. Chest radiograph showed pleural thickening in the diaphragmatic, costal and apical margins of the left lung. Treatment with bronchodilator inhalations significantly improved the patient's condition. He was discharged with bronchodilator treatment and was referred to a pulmonologist for further evaluation but returned 2 days later with the initial complaints.

The patient was a heavy smoker and until 4 years before the admission had been an intravenous cocaine abuser. He denied weight loss, night sweats, bone pain, lethargy and hemoptysis, His vital signs included oxygen saturation 96% in room air and respiratory rate 26 breaths per minute; he was hemodynamically stable and his temperature was normal. His physical examination was normal apart from decreased breath sounds and dullness on percussion over the left lung. The only abnormality in CBC analysis was mild leukocytosis. Blood chemistry including calcium level was within the normal reference range. D-dimer level was very high (4022 µg/L). Chest radiograph demonstrated a moderate amount of left pleural effusion. Computed tomography-angiography of the chest showed no evidence of pulmonary embolism. The patient was hospitalized in the internal medicine department for further evaluation. Repeated CBC and basic blood chemistry did not disclose any abnormalities. Erythrocyte sedimentation rate was mildly elevated (48 mm/hour), as were serum lactate dehydrogenase levels (368 IU/L). Broad serology for bacterial, viral and collagen vascular diseases was normal.

Tumor markers such as carcinoembryonic antigen, CA19-9 and prostate-specific antigen were normal. β-microglobulin level was within normal range at 2410 µg/L. Bacterial, fungal and mycobaterial cultures that were taken from the patient's blood and sputum were all negative. Sputum cytology did not show tumor cells. Serum protein electrophoresis (including albumin, alpha-, beta-, and gammaglobulin) was normal. Immune electrophoresis that was then performed revealed normal immunoglobulin levels.

Urine dipstick showed elevated protein, and analysis of a 24 hour urine collection revealed 250 mg protein. A spiral CT of the patient's neck, chest and abdomen was performed, demonstrating multiple lytic lesions in the left aspect of the patient's maxilla, left scapula, and several spinal vertebrae (L1, L2, L5), left pleural effusion in a moderate quantity, with a consolidation in the left lung representing passive atelectasis, hepatomegaly and bilateral inguinal lymphadenopathy [Figure].

Chest spiral CT of the chest. **[A]** Lytic lesion of the left scapula. **[B]** Left-sided pleural effusion with passive atelectasis. **[C]** Lytic lesions in the body of the spinal vertebra. **[D]** Lytic lesions of the spinous processes of the spinal vertebra.



CBC = complete blood count

Pleural fluid aspiration revealed indices of an exudate. Some atypical cells were demonstrated, probably mesothelial, with no evidence of tumor cells. Adenosine deaminase in the pleural fluid was normal. Pan bacterial and pan fungal cultures were all negative. Cytopathological testing of the pleural fluid, including markers for CD138, was negative. Immune electrophoresis of the urine showed high levels of Bence-Johns protein, kappa light chain type. Fine needle aspiration of the lytic lesion in the left scapula demonstrated a large number of plasma cells, positive for immunohistochemical markers CD138 and kappa light chain. These findings prompted a bone marrow biopsy that demonstrated a markedly hypercellular bone marrow (cellularity 95–100%), which consisted almost entirely of diffuse infiltrate of plasma cells (95% of marrow cells). Immunohistochemically, the plasma cells were positive for CD138 and kappa light chain. The patient's symptoms subsided following the pleural fluid aspiration. A diagnosis of light chain multiple myeloma was confirmed by a second histopathological revision of the bone marrow aspirate. The patient is a candidate for autologus stem cell transplantation.

COMMENT

Multiple myeloma is a plasma cell malignancy that accounts for approximately 10% of hematological malignancies. The most common presenting manifestations are fatigue, bone pains and recurrent infections. Other, less common, presenting symptoms and signs [2] include cardiac/respiratory, gastroenteric, renal, neurological and musculoskeletal symptoms and signs. One of the first descriptions of multiple myeloma presenting as recurrent pleural effusion was published in 1978 [3].

Pleural effusion occurs in approximately 6% of patients with multiple myeloma during the course of the disease [3] and not as a presenting sign. Pleural myelomatous effusion is even rarer, occurring in less than 1% of patients [3], during the course of the disease. The etiology of pleural effusions in multiple myeloma is multifactorial. The following mechanisms are possible [4]:

- infiltration of the pleural fluid by malignant plasma cells (i.e., myelomatous pleural effusion)
- direct infiltration of the pleural fluid from adjacent tissues
- nephrotic syndrome (secondary to renal tubular infiltration with paraprotein and the development of glomerular damage)
- pulmonary embolism
- congestive heart failure secondary to amyloidosis
- secondary neoplasms
- lymphatic drainage obstruction by tumor infiltration.

In our patient the etiology may have been lymphatic drainage obstruction by tumor mass. Direct myelomatous effusion is less probable because there were no myeloma cells detected on cytology, nor was it positive for CD138 and/or kappa light chain.

In summary, we report a rare case of a patient presenting with dyspnea resulting from pleural effusion, with biochemical parameters of an exudate not containing any plasma cells. Skeletal radiographs showed the lytic bone lesions, leading to a subsequent diagnosis of multiple myeloma.

Correspondence
Dr. G. Neuman
13 Shimkin Street, Haifa 34750, Israel
Tel/Fax: (972-4) 822-1045
email: g_neuman@rambam.health.gov.il

References

1. Rajkumar SV, Kyle RA. Multiple myeloma: diagnosis and treatment. *Mayo Clin Proc* 2005; 80(10): 1371–82.
2. Ong F, Hermans J, Noordijk EM, Wijermans PW, Kluin-Nelemans JC. Presenting signs and symptoms in multiple myeloma: high prectentages of stage III among patients without apparent myeloma-associated symptoms. *Ann Hematol* 1994; 70(3): 149–52.
3. Shoenfeld Y, Pick AI, Weinberger A, Ben-Bassat M, Pinkhas J. Pleural effusion – presenting sign in multiple myeloma. *Respiration* 1978; 36(3): 160–4.
4. Alexandrakis MG, Passam FH, Kyriakou DS, Bouros D. Pleural effusions in hematologic *malignancies, Chest* 2004; 125; 1546–55.

"I am a part of all that I have met"

Lord Alfred Tennyson (1809-1892), British Poet Laureate who remains one of the most popular English poets

"Democracy, to me, is liberty plus economic security"

Maury Maverick (1895-1954), U.S. attorney and Democratic congressman. He was best known for coining the term "gobbledygook" for obscure and euphemistic bureaucratic language