Malignant Pleural Effusion From Prostatic Adenocarcinoma Resolved With Hormonal Therapy*

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A 73-year-old man presented with dyspnea, right-sided pleural effusion, and bilateral pulmonary infiltrates. The pleural fluid revealed adenocarcinoma cells that stained positively for prostatic specific antigen (PSA), which confirmed this uncommon metastatic involvement from prostate cancer. The dyspnea, effusion, and infiltrates disappeared after therapy with flutamide and leuprolide was started. This report demonstrates both the usefulness of immunocytochemical staining for PSA in ascertaining the origin of malignant pleural effusion in men and the effectiveness of the aforementioned endocrine therapy in such setting.

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Prostatic adenocarcinoma has become the most common newly diagnosed cancer in male patients.1 We describe a case of metastatic pleural effusion from prostate cancer confirmed by a positive tumor cell stain for prostatic specific antigen (PSA) and successfully treated with flutamide and leuprolide.

CASE REPORT

A 73-year-old male nonsmoker was referred to the outpatient clinic because of nonproductive cough and progressive exertional dyspnea for the past 4 months. He denied any other complaints. He drank alcoholic beverages occasionally. Prostatectomy had been performed 2 years earlier in another hospital to relieve bladder outlet obstructive symptoms. The pathologic study disclosed prostatic adenocarcinoma and no further specific therapy had been prescribed. The physical examination disclosed no abnormalities except for some bilateral rales and wheezes. Routine laboratory tests included a complete blood cell count, coagulation studies, serum biochemistry profile with calcium and alkaline phosphatase, and a urinalysis. The erythrocyte sedimentation rate was 60 mm/h. Arterial blood gas levels while breathing room air showed a PaO2 of 56 mm Hg, a PaCO2 of 40 mm Hg, and an alveolar-arterial oxygen pressure difference of 46 mm Hg. A chest-x-ray film revealed bilateral diffuse pulmonary infiltrates both alveolar and interstitial, Kerley B lines, and a small right-sided pleural effusion (Fig 1).

Doppler echocardiography only demonstrated minimal left ventricular hypertrophy. Vital capacity was 2.31 L (61.8 percent of predicted) and the FEV1 was 1.37 L (50.1 percent of predicted) with a Tiffeneau index of 59.52 percent (74.07 percent). The total lung capacity was 4.51 L (68.6 percent) and the residual volume was 2.20 L (84.3 percent). The pleural effusion was a straw-colored exudate containing cells suggestive of an adenocarcinoma which stained positively with an immunocytochemical marker for PSA (immunoenzymometric assay, Dakopatts, Glostrup, Denmark). A technetium-99m-DPD bone scan revealed metastases involving the thoracic and lumbar spine, ribs on the right side, pelvic bones, sternum, and right femur. By that time, we received

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the results of a test for serum prostatic acid phosphatase; the level was 197 U/L (normal, ≤4.5 U/L). Therapy with flutamide, 250 mg, given by mouth three times a day, and leuprolide acetate, 7.5 mg, given intramuscularly monthly, was begun without other associated medications. One month after the onset of therapy, he denied exertional dyspnea, the chest x-ray film showed marked improvement, and the prostatic acid phosphatase value decreased to 18 U/L. At follow-up 22 months later, the patient remains asymptomatic and his chest x-ray film discloses no significant abnormality (Fig 2). The pulmonary function tests show clear improvement and the prostatic acid phosphatase level is 1.7 U/L.

**DISCUSSION**

Prostatic cancer has become the third leading cause of cancer deaths in males, after lung and colon cancer. In autopsy series, its reported frequency is up to 12 to 46 percent in men more than 50 years old.

At the time of presentation, 24 percent of patients already have distant metastases, lymph nodes and bones being the most frequent sites involved followed by the lungs and the liver. The incidence of clinically recognized pulmonary metastases has been reported to range from 5 percent at presentation to 25 percent in advanced prostate cancer, although chest x-ray films show evidence of disease in less than 6 percent of cases. In fact, Crawford et al. found only 14 cases of lung or pleural metastases in their series of 603 patients with disseminated previously untreated prostate cancer.

The recognized patterns of intrathoracic involvement in metastatic prostate cancer are, in order of decreasing frequency, nodular pulmonary metastases, mediastinal lymphadenopathy, lymphangitis carcinomatosa, isolated pleural effusion, and microscopic tumor emboli.

Prostatic specific antigen, a glycoprotein produced exclusively by normal and neoplastic prostate cells and not found in other normal or neoplastic tissues, is considered the most sensitive marker of prostatic cancer. Moreover, a positive immunocytochemical stain for PSA identifies the prostate as the primary site of malignancy. In the present case, such an assay was the diagnostic procedure performed.

Since its introduction in 1941 by Huggins and Hodges, androgen deprivation remains the mainstay of therapy for metastatic prostatic cancer. The goal is to suppress androgens in order to inhibit further tumor development. However, following initial hormonal deprivation, the hormone-independent cells gradually repopulate the tumor and therefore hormonal therapy is not curative. Therapy consisting of flutamide, a nonsteroidal antiandrogenic agent that inhibits the binding of androgens to the cell nucleus, in combination with leuprolide, an analog of luteinizing hormone-releasing hormone that inhibits the release of gonadotropins, has been used in the treatment of disseminated prostate cancer, with a communicated progression-free survival of 16.5 months and a median length of survival of 35.6 months.

In the present case, the usefulness of hormone therapy in the management of patients with prostate cancer and intrathoracic metastases is emphasized. The progression-free survival of our patient is 22 months until now, and the therapy has been well tolerated all the time. Lymphangitis carcinomatosa was suspected because of the chest x-ray film, the initial clinical picture, and its resolution with the aforementioned treatment, but we do not have histologic confirmation of the diagnosis.

In summary, we would recommend that immunocytochemical staining for PSA be performed in all male patients with metastatic pleural adenocarcinoma of unknown origin. If positive, combination therapy with flutamide and leuprolide seriously should be considered owing to its effectiveness and safety.

**REFERENCES**