International Journal of Urology (2003) **10,** 625–626

Case Report

Interstitial pneumonitis induced by bicalutamide and leuprorelin acetate for prostate cancer

KOICHI SHIOI, MINORU YOSHIDA AND NAOKI SAKAI
Department of Urology, Yokosuka Hokubu Kyosai Hospital, Kanagawa, Japan

Abstract Maximal androgen blockade therapy is the standard endocrine treatment for advanced prostate cancer. We report here an unusual case of interstitial pneumonitis induced by bicalutamide and/or leuprorelin acetate treatment for metastatic prostate cancer.

Key words interstitial pneumonitis, maximal androgen blockade therapy, prostate cancer.

Introduction

Androgen deprivation is essential for the treatment of prostate cancer. Antiandrogen with orchiectomy or luteinizing hormone-releasing hormone (LH-RH) agonists (maximal androgen blockade, MAB) is the standard endocrine treatment for advanced prostate cancer. Non-steroidal antiandrogens and LH-RH agonists rarely cause significant side-effects. Interstitial pneumonitis induced by MAB is an extremely uncommon adverse reaction. Only a few cases have been reported in the literature.[1–5] We report here an unusual case of interstitial pneumonitis after bicalutamide and leuprorelin acetate for prostate cancer.

Case report

A 79-year-old man was evaluated due to serum prostate specific antigen (PSA) level of 18 ng/mL. Prostate biopsy and bone scan revealed adenocarcinoma with multiple bone metastases. The patient had rheumatoid arthritis, which had been treated with bucillamine for 50 years. He was not a cigarette smoker and had no respiratory disease.

Hormonal therapy comprising oral 300 mg fosfestrol daily was initiated in April 1999. Despite undetectable PSA, 80 mg bicalutamide and 3.75 mg leuprorelin acetate MAB was initiated in December 2001, because MAB is now the standard endocrine treatment and the production of fosfestrol is to be ceased. In January 2002, after 4 weeks of bicalutamide (2 weeks of leuprorelin) treatment, the patient presented with severe dyspnea, cough and fever. Lung auscultation revealed bilateral fine crackles. Arterial blood gas showed oxygen partial pressure 52 mmHg. Chest X-ray showed a diffuse bilateral reticulonodular shadow (Fig. 1). Laboratory studies showed elevated white blood count without eosinophilia and C reactive protein level. A lymphocyte stimulation test was not performed. After obtaining sputum and blood cultures, imipenem/cilastatin was administered; however, the patient's condition did not improve. Because both cultures were negative for bacteria and fungus, and computed tomography was consistent with interstitial pneumonitis (Fig. 2), the patient received steroid pulse therapy (methylprednisolone sodium succinate 1000 mg for 3 days) and the antibiotics were discontinued. Following steroid therapy the patient's symptoms resolved and chest X-ray improved. He has now been free of respiratory disease for more than 10 months following steroid therapy.

After marked improvement of interstitial pneumonitis, we discontinued MAB therapy and did not administer any therapy for prostate cancer. However, the patient's PSA level has not been detected for more than a year.

Discussion

Maximal androgen blockade (antiandrogen and LH-RH agonists) is the standard endocrine treatment for

Correspondence: Naoki Sakai MD, Department of Urology, Yokosuka Hokubu Kyosai Hospital, Funakoshi, Yokosuka, Kanagawa 237-0076, Japan.
Email: fwnd2088@mb.infoweb.ne.jp
Received 21 November 2002; accepted 19 May 2003.

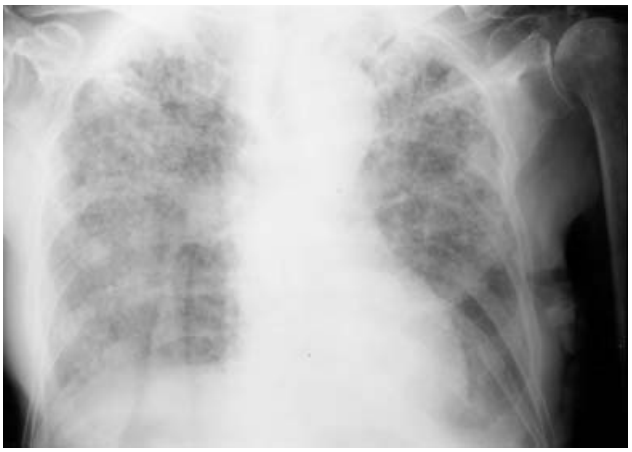

Fig. 1 Chest X-ray shows diffuse bilateral reticulonodular infiltration.

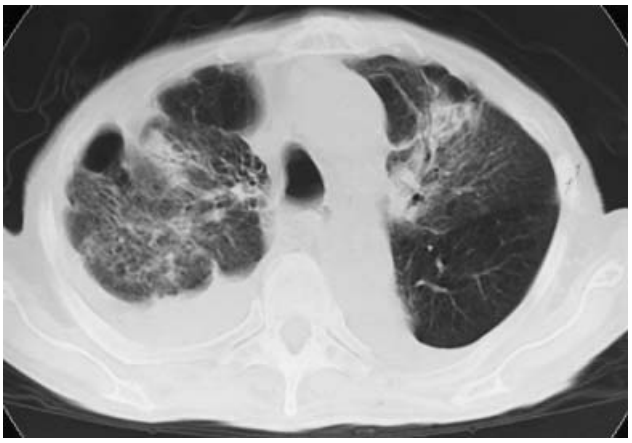

Fig. 2 Computed tomography of chest shows reticulonodular pattern.

prostate cancer. Significant adverse reactions to MAB therapy are uncommon and serious hepatic failure is rare. Interstitial pneumonitis due to MAB therapy is an extremely rare and severe adverse condition. Nilutamide,[1,2] bicalutamide[3] and flutamide[4] have been reported to induce interstitial pneumonitis. LH-RH agonists could also induce interstitial pneumonitis.[2,4,5] The onset of interstitial pneumonitis has been reported 2–8 months after non-steroidal antiandrogen treatment.[1–5]

In the case presented here, negative blood and sputum cultures, poor response to antibiotics and excellent response to steroid treatment suggest that it was unlikely that an organism induced the pneumonia. Bucillamin could also induce interstitial pneumonitis; however, the patient had been receiving bucillamine for 50 years and had not developed respiratory disease. The patient developed dyspnea 4 weeks after bicalutamide treatment. Although there was no pathological evidence, this response indicates that bicalutamide and/or leuprolide acetate induced interstitial pneumonitis in the patient. However, we cannot determine which drug was responsible for the respiratory disease.

Although the condition is extremely rare, physicians should be aware of MAB induced interstitial pneumonitis.

References

1 Pfitzenmeyer P, Foucher P, Piard F *et al.* Nilutamide pneumonitis: a report on eight patients. *Thorax* 1992; **47**: 622–7.
2 Wieder JA, Soroway MS. Interstitial pneumonitis associated with neoadjuvant leuprolide and nilutamide for prostate cancer. *J. Urol.* 1998; **159**: 2099.
3 McCaffrey JA, Scher HI. Interstitial pneumonitis following bicalutamide treatment for prostate cancer. *J. Urol.* 1998; **160**: 131.
4 Azuma T, Kurimoto S, Mikami K, Oshi M. Interstitial pneumonitis related to leuprorelin acetate and flutamide. *J. Urol.* 1999; **161**: 221.
5 Crayton H, Bohlmann T, Sufit R, Graziano FM. Drug induced polymyositis secondary to leuprolide acetate (Lupron) therapy for prostate carcinoma. *Clin. Exp. Rheumatol.* 1991; **9**: 525–8.