

## SEVERE FLARE-UP IN A PROSTATE CANCER PATIENT TREATED WITH LUTEINIZING HORMONE-RELEASING HORMONE ANALOGUE DEPOT

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A 65-year-old man with advanced prostate cancer was treated with a luteinizing hormone-releasing hormone (LH-RH) analogue. Four days after the initial injection of 3.6 mg of goserelin acetate, severe dyspnea developed due to worsening pleuritis carcinomatosa, which was considered as a flare-up. Chest drainage was required to save his life. Therefore, we emphasize the importance of treatment to prevent tumor flare during LH-RH analogue therapy.

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**Key words:** Prostate cancer, LHRH analogue, Flare-up

### INTRODUCTION

Luteinizing hormone-releasing hormone (LH-RH) analogue is generally accepted as a useful treatment modality in prostate cancer<sup>1)</sup>, but the flare-up phenomenon is observed in a certain percentage of patients<sup>2)</sup>. We present a case with severe respiratory symptoms which were considered the result of a flare-up.

### CASE REPORT

A 65-year-old man was referred to our hospital with dysuria and gross hematuria associated with edema of the genitalia and lower extremities. Digital rectal examination revealed an enlarged stony-hard prostate. Abnormal lymph nodes were palpable at the left supraclavicular region and right groin. He presented with symptoms of urinary retention. Laboratory values included elevated blood urea nitrogen (BUN) 40.1 mg/dl (normal 8.0 to 20.0), serum creatinine (Cr) 3.3 mg/dl (normal 0.8 to 1.2), prostate specific antigen (PSA) 292 ng/ml (normal less than 3.6) and prostatic acid phosphatase (PAP) 160 ng/ml (normal less than 3.0). Needle biopsy of the prostate showed poorly differentiated prostatic adenocarcinoma and extensive examina-

tion revealed prostatic carcinoma invading beyond the capsule into the bladder neck and seminal vesicle with multiple lymph nodes, pulmonary and osseous metastases. Pulmonary metastases was associated with pleural effusion (Fig. 1) and blood gas analysis (BGA) showed hypoxemia; pH=7.44, carbon dioxide tension=36.3 mmHg, oxygen tension=56.1 mmHg, HCO<sub>3</sub>=24.2 mmol/L, base excess=0.4 mmol/L. Serum testosterone level (T) was 261 ng/dl (normal 250 to 1,100).

LH-RH analogue depot (3.6 mg of goserelin acetate) was injected subcutaneously. Four days later, he presented with severe dyspnea with remarkable pleural effusion (Fig. 2). BGA revealed hypercapnea and marked hypoxemia; pH=7.40, carbon dioxide tension=57.1 mmHg, oxygen tension=50.3 mmHg, HCO<sub>3</sub>=34.8 mmol/L, base excess=8.3 mmol/L under supplemental oxygen administration. Chest drainage resulted in six liters of hemorrhagic pleural fluid, cytological examination was positive for adenocarcinoma. In six days, he recovered with BGA; pH=7.47, carbon dioxide tension=44.5 mmHg, oxygen tension=60.1 mmHg, HCO<sub>3</sub>=32.3 mmol/L, base excess=7.9 mmol/L, and the drainage tube was removed.

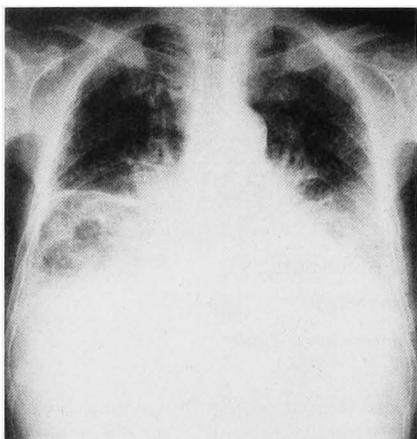


Fig. 1. Chest X-ray before treatment revealed multiple lung metastases with pleural effusion

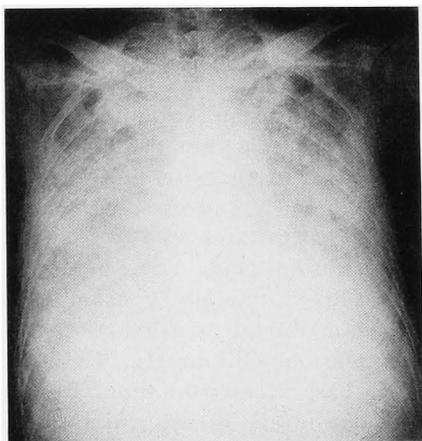


Fig. 2. Four days after the injection of 3.6 mg of goserelin acetate. Marked exacerbation of pleuritis carcinomatosa was observed

The administration of the depot was continued every 28 days. The signs and symptoms of prostate cancer improved transiently; he became able to urinate with slight hesitancy, the edema was limited at right thigh and leg, BUN 9.9 mg/dl, Cr 0.4 mg/dl, T 27.2 ng/dl, PSA 68 ng/ml, PAP 44 ng/ml. However, in three months, the disease progressed; abnormal lymph nodes increased in size and number, the prostate enlarged with marked dysuria, pleural effusion and pulmonary metastases exacerbated. PSA was 207 ng/ml, and PAP 140 ng/ml. He died of cancer four months

after the initiation of treatment.

### DISCUSSION

The LH-RH analogue is known to cause transient stimulation of luteinizing hormone (LH) and T before reaching a medically castrated status<sup>3)</sup> and this stimulation results in an exacerbation of clinical signs and symptoms in some patients. The most common one is an increase in metastatic, especially osseous, pain with a reported frequency of 2~4%<sup>2,4)</sup>. Although not common, some patients exhibit uremia from ureteral obstruction and spinal cord compression which can often be lethal<sup>2,5)</sup>. Our case presented with pulmonary insufficiency which was considered to be the result of worsening pleuritis carcinomatosa. This type of tumor flare is rare and we were unable to find any similar cases in the literature. Such a tumor flare is possible, but the relative scarcity of pulmonary metastasis in prostate cancer patients makes the incidence low.

We emphasize the importance of life-threatening flare-ups such as uremia, spinal cord compression and pulmonary insufficiency as in our patient. Moral and associates<sup>6)</sup> suggested the need of blocking the rise in T in patients with a large tumor burden. Several attempts to prevent tumor flare in LH-RH analogue treatment have included combined treatment with pure antiandrogen<sup>7)</sup> or pretreatment with DES<sup>5,6,8)</sup>, although the efficacy of some treatments is ambiguous. Therefore, we emphasize the need to prevent this flare-up phenomenon during LH-RH analogue therapy.

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## 和文抄録

### LH-RH アナログ療法により激しい Flare-up をきたした前立腺癌の 1 例

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進行性前立腺癌 (T4N2M1, 病期 D2) の 65 歳男性に初回治療として酢酸ゴセレリンを投与したところ, 4 日後に癌性胸膜炎の急激な悪化により呼吸不全に陥った. 保存的治療は無効であり, 胸腔ドレナージにて

救命しえた. LH-RH アナログ療法による flare-up は軽微なことが多いとされるが, なかには致命的なものもありその予防が必要と思われた.

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