

Case Report

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A Man with Breast Cancer Following Hormonal Treatment for Prostate Cancer

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Abstract

Male breast cancer is rare with an annual incidence of less than 1% in Hong Kong. Some postulate the effect of estrogen as an important risk factor for development of male breast cancer. With the increasing use of hormonal therapy for patients with prostatic cancer, it may result in hormonal imbalance with a relative hyper-estrogenic state, which may increase the risk of male breast cancer. However so far there is no clinical evidence of its causal effects. Here we report a case of development of breast cancer in male patient after hormonal treatment (luteinizing hormone releasing hormone analog and anti-androgen) for prostatic cancer, and followed by a review of the literature for the association between them.

Keywords: Male breast cancer, Prostate cancer, Hormonal therapy

Introduction

Male breast cancer is rare in Hong Kong. Unlike female breast cancer, its risk factors are less studied. Some postulate the effect of estrogen level as an important risk factor for development of male breast cancer. Hormonal therapies for prostatic cancer are frequently used nowadays and it will result in a relative hyper-estrogenic state, thereby increasing the risk of male breast cancer. However there is no clinical evidence of its causal effects so far. The objective of this article is to report an uncommon association of development of male breast cancer after hormonal therapy (luteinizing hormone releasing hormone analog and anti-androgen) for prostatic cancer.

Case

A 73 years old gentleman presented to private surgeon in January 2005 for acute urinary retention. Prostate specific antigen (PSA) level was elevated up to 50.18 ng/mL. Trans-rectal ultrasound guided biopsy showed no evidence of malignancy. Trans-ureteral resection of the prostate (TURP) was performed and pathology confirmed prostatic adenocarcinoma with combined Gleason grade 7 (3+4). Further workup with magnetic resonance imaging (MRI) showed features suggestive of carcinoma in the remaining prostate with involvement of the seminal vesicles. No local infiltration to the urinary bladder, pelvic muscle or enlarged pelvic or para-aortic lymph node was noted.

Adjuvant hormonal therapy with luteinizing hormone releasing hormone analog (LHRH) for 2 years with radiotherapy was planned after discussion with the patient. He was given 6 months of LHRH analog (leuprorelin acetate 11.25 mg) with androgen cover (flutamide 250 mg) for 2 weeks. However further hormonal therapy was refused by patient after 6 months due to financial reason and he was given radiotherapy treatment afterwards. The PSA level remained low upon subsequent follow up assessment (below 0.5 mg/mL).

However he complained of a growing mass over right chest four years later and was referred to our surgical clinic for assessment. Physical examination showed a 6 cm mass over the right chest just beneath the nipple. Ultrasound findings were suggestive of malignant lesion and subsequent fine needle aspiration confirmed ductal carcinoma. Operation with right modified radical mastectomy was performed and was uneventful. Final pathology showed invasive ductal carcinoma of male breast with cystic component with a close deep margin of 1mm. There was no axillary lymph nodes involvement. Both Estrogen and progesterone receptor were positive whereas C-erb-B2 was negative. Post mastectomy radiotherapy was given in view of close margin followed by adjuvant hormonal therapy with tamoxifen. Upon latest follow up in our clinic, there is no evidence of locoregional recurrence and he remains asymptomatic.

Discussion

Breast cancer is the most common cancer in women in Hong Kong, with the annual incidence of 2962 cases in 2009. It is considered rare in men. However, men's breast tissue can also undergo malignant changes. There were a total of 17 cases of breast cancer identified in men in 2009, accounting for 0.57% among all cases [1]. Male breast cancer was generally believed to have a poor prognosis. Patients usually presented late. It was believed to be due to the low level of awareness of patient and the low level of suspicion by physician, resulting in poorer survival statistics. However, recent studies have shown that the prognosis is similar to that of women at any given stages [2]. Treatment modalities are similar to female breast cancer which is primarily surgical based. Majority (more than 70%) of male breast cancer is hormonal sensitive, and hormonal therapy is commonly utilized as an adjuvant therapy. But due to the rarity of male breast cancer, there is lack of evidence about its uses. Unlike female breast cancer, the risk factors for male breast cancer are less well studied. Studies have shown that a familial history of breast cancer is the major risk factor for male breast cancer (from 15-20% vs. 7% in general population). BRCA2 gene mutation is also a significant risk factor. Some postulate the effect of estrogen level as an important risk factor for male breast cancer. Conditions that results in imbalance between estrogen and androgen are associated with an increased risk of male breast cancer e.g. Klinefelter syndrome, use of exogenous estrogen in transsexuals, cirrhosis, obesity, testicular defect or injury etc. [3].

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Androgen ablation therapy is frequently used for the treatment of metastatic prostate cancer and may also result in hormonal imbalance. Several large prospective randomized controlled trials have established the benefits of androgen ablation therapy in the treatment for localized prostate cancer, resulting in an increasing trend of their uses at earlier stages of the disease. Studies by Tellenberg et al. [4] have shown that there was a significantly increased risk of male breast cancer in patients with history of prostate cancer before the 1990's (1958 and 1996), when the use of estrogen was common for therapy of prostate cancer. There were several reports of breast cancer developed in men receiving estrogen therapy for prostate cancer, although evidence was limited regarding the association of its use. Nowadays estrogenbased hormonal therapy are rarely used for prostate cancer, but rather androgen ablation therapy in form of monotherapy with anti-androgen alone or LHRH analog alone or combined androgen blockade [5]. The mechanism of anti-androgen monotherapy is that it blocks androgen receptors from binding testosterone, effectively inhibiting testosterone activity. However it will stimulate the negative feedback mechanism and increase in serum testosterone level, in which it will also increase the estrogen level via peripheral conversion. This results in a relative hyper-estrogenic state that causes gynaecomastia and possibly increasing the risk of male breast cancer. In contrast, LHRH analog mimics gonadotropin-releasing hormone and constantly stimulates its production, and thus down regulating the production of testosterone to castrate levels. Traditionally people believed that LHRH analog based androgen ablation therapy does not result in hyper-estrogenic state as it blocks the testicular androgen production. However, there were case reports studying on the development of male breast cancer during the treatment with leuprolide for prostate cancer. The postulated mechanism is that the use of LHRH analog does not eliminate the production of adrenal androgen, which provides another source of estrogen through peripheral conversion, despite its suppression of

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In our case report, our patient was given a course of anti-androgen and LHRH analog for six months' time, resulting in a relative hyperestrogenic state as the mechanism mentioned above. There are case reports on the use of different modalities of hormonal therapy for prostatic cancer with subsequent development of male breast cancer. But there is no definite statistical proof of their causal relationship with male breast cancer in the literature currently. Regular screening and higher index of suspicion is needed for possibilities of male breast cancer in this group of patients. Further studies about the relationship of hormonal therapy and the risk of developing male breast cancer are needed.

Declaration

testicular androgen.

We certify that we have no conflict of interest in this manuscript.

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