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Endocrine Combination Therapy for Prostate and Metastatic Breast Cancer in a Male Patient

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Key Words

Breast cancer, male · Prostate cancer · Prostate-specific antigen · PSA · Endocrine therapy

Summary

Background: Breast cancer in men is rare and requires therapy concepts including health considerations different from those in female patients. **Case Report:** We report on a 64-year-old male patient with metastatic breast cancer in the lung and cervical lymph nodes. Upon metastasis, initial adjuvant endocrine therapy with tamoxifen was changed to anastrozole. After 1 year of treatment, the patient was found to have rising prostate-specific antigen (PSA) levels, and diagnostic workup confirmed the diagnosis of early prostate cancer. Because of simultaneous progressive disease of metastatic breast cancer, chemotherapy with 6 cycles of docetaxel was administered resulting in a partial remission of both tumor types. The patient is currently treated with an endocrine combination therapy of fulvestrant, goserelin, and bicalutamide. He is in good clinical condition, and tumor markers for both tumor types are stable. **Conclusion:** Elevated PSA levels under therapy with aromatase inhibitors have been described in individual cases but always warrant a careful diagnostic workup to exclude prostate cancer as an important differential diagnosis. Genetic counseling has to be taken into consideration in the case of male breast cancer as well as in the case of coincidence of different tumor types, such as breast and prostate cancer, due to the possibility of e.g. BRCA mutations in these patients.

Schlüsselwörter

Brustkrebs beim Mann · Prostatakarzinom · Prostataspezifisches Antigen · PSA · Endokrine Therapie

Zusammenfassung

Hintergrund: Brustkrebs beim Mann ist eine seltene Erkrankung, die vom behandelnden Arzt eine andere Herangehensweise erfordert als bei der weiblichen Patientin und andere Differentialdiagnosen einschließen muss. **Fallbericht:** Wir berichten über einen 64-jährigen Patienten mit Mammakarzinom, der unter Tamoxifen eine lymphatische und pulmonale Metastasierung entwickelte. Ein Jahr nach Umstellung der endokrinen Therapie auf Anastrozol fielen steigende PSA-Werte auf. Die Diagnostik ergab ein frühes Prostatakarzinom. Aufgrund der progredienten Mammakarzinomerkrankung wurde eine Chemotherapie mit Docetaxel durchgeführt, welche zur partiellen Remission beider Tumorentitäten führte. Aktuell ist der Patient unter einer endokrinen Dreierkombination aus Fulvestrant, Goserelin und Bicalutamid praktisch beschwerdefrei. Die Tumormarker beider Karzinome weisen im Verlauf stabile Werte auf. **Zusammenfassung:** Steigende PSA-Werte unter Therapie mit Aromatasehemmern sind zwar im Einzelfall beschrieben, müssen jedoch immer eine sorgfältige diagnostische Abklärung nach sich ziehen, um ein simultanes Prostatakarzinom auszuschließen. Außerdem sollte beim Auftreten eines Mammakarzinoms beim Mann wie auch beim Vorliegen mehrerer Tumorentitäten wie Mamma- und Prostatakarzinom den Patienten eine genetische Beratung empfohlen werden, da die Möglichkeit einer Genmutation, z.B. in einem der BRCA-Gene, besteht.

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Introduction

Male breast cancer is a rare disease with an annual prevalence of 1 in 100,000 [1]. Contributing etiologic factors are exposure to radiation, hyperestrogenism (from external sources or due to endogenous diseases like liver cirrhosis or Klinefelter's syndrome) or hereditary factors [2, 3]. Due to the rare occurrence of breast cancer in men, there is a substantial lack of clinical trials to evaluate optimal treatment options and derive evidence-based guidelines. Thus, our understanding of the disease in male patients and our clinical approach are in fact derived from trials and experience in female breast cancer patients.

Case Report

We report on a 62-year-old male patient who was diagnosed with invasive ductal breast cancer in 2002. The tumor stage was pT2 pN1biii (12/13) M0 G3, estrogen receptor (ER)- and progesterone receptor (PgR)-positive, Her2/neu-negative. The patient underwent mastectomy and axillary lymph node dissection, received 6 courses of adjuvant FEC (fluorouracil, epirubicin, cyclophosphamide) chemotherapy (500/100/500 mg/m^2 q21d) and subsequent loco-regional radiation therapy, and was then put on adjuvant tamoxifen 20 mg daily. In 2003, he presented to our hospital for cosmetic correction of his mastectomy scar. Preoperative routine chest X-ray showed a pulmonary mass suspicious of metastasis; all other staging examinations were normal and the patient was in excellent clinical condition. Endocrine therapy was therefore changed to anastrozole 1 mg daily. At the same time, rising prostate-specific antigen (PSA) levels were detected during the patient's annual screening tests. Literature research and a query at the medical scientific department of AstraZeneca, Wedel, Germany, yielded evidence of 2 patients worldwide with elevated PSA levels under anastrozole therapy [4–6]. In 2005, a prostate biopsy was taken. It showed moderately differentiated adenocarcinoma of the prostate gland, Gleason score 5.

2 months later, the patient was admitted to the Ear, Nose and Throat (ENT) department for progressive enlargement of cervical lymph nodes. A diagnostic extirpation was performed, and histology revealed metastasis of invasive ductal breast cancer, hormone receptor-positive, Her2/neu-negative. Computed tomography (CT) scan of the chest showed progressive pulmonary metastatic disease. The patient's treatment options were discussed at our multidisciplinary tumor conference, and we finally opted for chemotherapy with docetaxel 100 mg/m^2 q21d, a therapy regimen that is effective in both tumor types. After 3 chemotherapy cycles, partial remission was achieved, and a total of 6 courses yielded further consolidation of disease. The challenge now was to tailor an effective endocrine therapy encompassing both breast and prostate cancer with as little side effects and drug interactions as possible. The patient was put on a triple combination therapy of fulvestrant (Faslodex™, AstraZeneca, 250 mg q28d i.m.), goserelin (Zoladex™, AstraZeneca, 3.6 mg q28d s.c.), and bicalutamide (Casodex™, AstraZeneca, 50 mg daily p.o.). The patient consented after careful and thorough information regarding the limited evidence basis for this treatment. Since the beginning of therapy 6 months ago, the patient is in excellent clinical condition, only suffering from mild dyspnea on exertion and hot flushes. The tumor marker PSA is within normal limits (< 0.10 ng/ml), and CA 15–3 is slightly elevated on a stable level (27 U/ml).

Discussion

90% of male breast cancers are hormone receptor-positive [1, 7]. Therefore, endocrine therapy has been a hallmark of breast cancer therapy in men both in the adjuvant and in the advanced setting. Adjuvant tamoxifen has been shown to improve disease-free and overall survival [8, 1]. However, there is no clear data for optimal duration of treatment. Aromatase inhibitors have not been systematically studied as adjuvant therapy for male patients, and their role in the advanced setting remains controversial [9–12]. Furthermore, there is no large-scale experience with the anti-estrogen fulvestrant in male patients [13]. Carcinoma of the prostate gland is another hormone-related cancer, with the androgen receptor being expressed in nearly all prostate cancers [14].

In the case outlined above, we tailored the endocrine combination therapy as follows: The patient had progressed under both tamoxifen and anastrozole, so the next endocrine treatment option – analogous to the situation in a female patient – would be fulvestrant, an ER antagonist without agonistic effects which downregulates the ER [15]. To treat the prostate cancer, the nonsteroidal antiandrogen bicalutamide was chosen and combined with the gonadotropin-releasing hormone (GnRH) agonist goserelin to achieve optimal androgen blockade by suppressing elevated follicle-stimulating hormone (FSH) and luteinizing hormone (LH) levels [16, 17]. So far, there has been no documented experience in the literature regarding the efficacy or drug interactions of this triple therapy regimen apart from 1 case report describing the combination of an LHRH agonist and flutamide in a male patient with metastatic breast cancer [18].

Genetic susceptibility to breast cancer has been studied extensively in women, identifying multiple genes involved in breast cancer development. Probably best known and most relevant for familial breast cancer are BRCA1 and BRCA2 [19]. Autosomal dominant inheritance attributable to gene mutations in BRCA1 or BRCA2 is suspected in 4–40% of male breast cancer cases, and 20% of men with breast cancer are found to have first degree relatives with the same disease [1]. Prostate cancer is found with a higher prevalence among carriers of BRCA2 mutations [20, 21, 3]. Although there was no history of breast or prostate cancer in this patient's family, we recommended counseling in our specialist clinic for hereditary tumor syndromes and cancer genetics to evaluate a potential genetic background for the coincidence of the patient's 2 cancer types.

Conclusion

Given the rare occurrence of male breast cancer, optimal long-term treatment remains a challenge. Approach to the disease and patient care require taking health issues into account that are specific for the male patient. Due to the lack of large-scale prospective clinical trials, therapeutic decisions will be made in accordance to treatment of female patients and will have to be tailored individually – like in this case where 2 tumor types had to be treated simultaneously. Moreover, in the case of male breast cancer or coincidence of several different cancer types or familial breast cancer, genetic counseling should be recommended to the patient.

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