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Caso clinico

Case report

Male breast cancer in an HIV-infected patient: a case report

Un caso di tumore della mammella in un uomo con infezione da HIV

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INTRODUCTION

Breast cancer is the most common cancer and the leading cause of female cancer death among women in Italy and worldwide [1, 2]. Conversely, male breast cancer (MBC) is extremely rare: it accounts for almost 1% of all breast malignancies, and its incidence in Northwest Europe and North America is approximately one per 100,000 [3, 4].
Breast cancer is classified among the non-AIDS-defining malignancies and it does not seem to increase in incidence within the HIV-infected population [5]. To date, very few cases of breast cancer in HIV-infected patients are reported in the literature [6].

CASE REPORT

The patient, a 65-year-old heterosexual man, had been diagnosed with HIV infection in June 2000. He observed a regular follow-up in the Institute of Infectious Diseases of Brescia (Northern Italy), with haematological and chemical analysis and a physical examination every three months. He smoked 20 cigarettes/day during 24 years and was a former drinker. He did not report family history of any type of cancer. His medical history included a secondary syphilis and a liver cirrhosis, due to chronic hepatitis C. He has had no opportunistic infections or other diseases associated with AIDS. Nadir CD4+ T-cell count, defined as the lowest value since HIV diagnosis up until breast cancer diagnosis, was 238 cells/mm^3. He started antiretroviral therapy immediately after HIV diagnosis with a great adherence.
In May 2008 he developed a painless nodule near the nipple of his left breast, which, at physical examination, had 1 cm at its larger diameter, was hard and not mobile. He underwent fine-needle aspiration biopsy that was positive for malignant epithelial cells. He was submitted to mastectomy and axillary dissection. Histology confirmed a ductal carcinoma 1.2 cm wide, grade 2, with vascular invasion.
Only one out of 20 axillary nodes was found to be involved by metastatic breast carcinoma. The stage of the disease was performed by using chest X-ray, abdomen ultrasonography and bone scintigraphy: no other pathologic sites were identified. Staging resulted in pT1c/pN1a/M0 (tumor, node and metastatic involvement). It was positive for the presence of oestrogen/progesterone receptors, negative for the human epidermal growth factor receptor-2 (HER-2). The patient was treated with local radiotherapy, followed by a treatment with tamoxifen using a dosage of 20 mg daily. At breast cancer diagnosis, he was receiving HAART with abacavir, lamivudine and unboosted atazanavir with undetectable HIV viral load, and his CD4+ T-cell count was 445 cells/mm^3.
In April 2011, he had a diagnosis of a basal cell carcinoma of the scalp, treated with surgical extirpation. In the meantime, he had also a diagnosis of an anal high-grade squamous intraepithelial lesion. Because of the latter, he stopped tamoxifen and he has been receiving

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chemotherapy with capecitabine and 25 sessions of radiotherapy. The patient is now being monitored, to date without signs of breast cancer disease or metastasis.

DISCUSSION

In our cohort of 5,096 HIV-infected patients followed in the Clinic of Infectious Diseases and Tropical Medicine in Brescia (Northern Italy), ten breast cancer cases have occurred between 1999 and 2009: among these, the one here described was in a man. Thus, the male: female ratio among our cohort HIV-infected individuals was about 1:10, so much higher than described in the general population, were is about 1:100 [7, 8]. We calculated a standardized incidence ratio (SIR) of 8.63 (IC95% 1.22-61.3) in our area. Breast cancer occurred in our HIV-infected man showed many characteristics similar to MBC in the general population. It did not occur in a patient younger than expected, as the mean age at breast cancer diagnosis is 63.4 years, while women with breast cancers are on average approximately 10 years younger. It was an infiltrating ductal carcinoma, as 85-90% of MBC and it was stage II, as more than 50% of MBC, compared to ~35% of female breast cancer (FBC) [9, 10]. It was positive for both oestrogen- and progesterone- receptors: this positivity is proportionally higher in MBC than FBC, so thus hormone therapies should be at least as effective in males and patients can receive endocrine therapy. The tumour was also HER-2 negative, as MBC are ~3 time less likely to be HER-2 positive than FBC [11, 12]. It metastasized to the axillary lymph nodes, accordingly about half of MBC diagnosed: the axilla nodal status at the time of the diagnosis is the most important prognostic factor [10].

Family history of our patient was negative for any kind of cancer, while 20% of men with breast cancer have a relative with breast or ovarian cancer [13]. A strong susceptibility to breast cancer is seen in Klinefelter's syndrome, which is characterized by an extra X chromosome, feminization, hypogonadism, gynecomastia and obesity, but clinical features of this syndrome were absent in our HIV-infected man [14]. A chromosomal analysis was not performed, so we do not know about the presence of an inherited mutation in the BRCA2 gene, which is currently considered as the strongest known risk factor for MBC, or other genetic predispositions that increase risk for MBC, as Cowden syndrome, the CHEK2 1100delC mutation, mutations in the gene encoding the androgen receptor or in the CYP17 gene [15-19].

Predisposing for the occurrence of breast cancer in men are also all factors that lead to an hormone imbalance, with an altered ratio of oestrogen to testosterone. This could be related to many conditions associated with decreased testosterone levels, as undescended testes, mumps orchitis, congenital inguinal hernia, orchitis, orchiectomy or testicular trauma. Similarly, it could be caused by an increase in oestrogens, as a result of obesity or of drug related exceeding supply with oestrogens as seen in the treatment of prostate cancer. Moreover, increased oestrogens levels are frequently seen in males with cirrhosis, which can increase the MBC risk 9- to 13-fold: this liver affection is a frequent disease in HIV-infected patients, due to the co-infection with hepatitis viruses, as the patient described in our case report [20]. We have also to remember that we follow many patients who are trans-sexuals, taking oestrogen therapies for prolonged periods: an increased incidence of breast cancer has been reported in these subjects [21]. In our HIV-infected patients, habits such as alcohol intake, smoking and physical inactivity are more frequent than in the general population: these lifestyle factors have been investigated as risk factors for MBC, but none has consistently been associated with higher risk. Our patient developed also a basal cell carcinoma of the scalp: the occurrence of a dual neoplastic disease is not uncommon in HIV-infected patients, [22].

Understanding of male breast cancer comes from studies of female breast cancer, which undoubtedly provides an inaccurate picture. The rarity of MBC has precluded the large clinical trials that are necessary for formal recommendations and guidelines on screening, diagnosis and treatment. Thus recommendations for MBC have a poor strength and a low quality of evidence as they are extrapolated from FBC studies, along with retrospective analyses of smaller MBC studies.

The low incidence of MBC in the general population renders mammographic screening of all men impractical [23]. Mammography is more often utilized as a diagnostic tool to evaluate breast symptoms, that are usually caused by benign abnormalities such as gynecomastia [24]. In post-adolescent adults, medications are responsible for up to 20% of cases of gynecomas-

tia. These drugs include many of those used to treat HIV: protease inhibitors have been frequently involved, but reports linking gynecomastia to either nucleoside analogs or non-nucleosides have equally appeared in the literature [25-27]. This enlargement of the male mammary gland should be unilateral or bilateral: physicians usually think of it as part of the lipodystrophy syndrome and do not further investigate breast cancer risk of the male patient they are evaluating. Men in the increased risk category for developing breast cancer (strong family history of breast cancer, genetic predisposition, prior personal history of male breast cancer) should be advised to carry out a monthly breast self examination, a semi-annual clinical breast examination, and baseline mammography followed by annual mammography if gynecomastia and/or breast density are seen on baseline as suggested in the current guidelines [28]. Genetic testing should be also considered, when appropriate, as informing family members of risk and genetic testing options [28].

CONCLUSIONS

Patients with infection of HIV have a bigger cancer risk due to immunosuppression: it concerns not only AIDS-defining malignancies, but also other types of cancer. Within the HIV-infected population, the total risk of breast cancer has been noted to be relatively lower as compared with the general population [29]. Male breast cancer is rare, but an increased risk of 4-fold has been calculated among HIV-positive men: a heightened awareness of this cancer by both physicians and patients is needed, as it may result in earlier detection and in better management [30].

Keywords: HIV, breast cancer, cancer prevention.

SUMMARY

Male breast cancer is rare and few cases of breast cancer in human immunodeficiency virus (HIV)-infected patients are reported. We describe the case of breast cancer in a 65-year-old HIV-positive man who presented a nodule near the nipple of his left breast. He did not report risk factors for breast cancer, but he had liver cirrhosis. Biopsy of the lesion revealed a ductal carcinoma and he was submitted to mastectomy and axillary dissection. Staging resulted in pT1c/pN1a/M0; it was positive for the presence of oestrogen/progesterone receptors, negative for the human epidermal growth factor receptor-2. He was also treated with local radiotherapy and tamoxifen. At cancer diagnosis, he received highly active antiretroviral therapy (HAART) with undetectable HIV viral load, and his CD4+ T-cell count was 445 cells/mm^3.
Patients with HIV infection have a higher cancer risk due to immunosuppression: it concerns not only malignancies related to human acquired immunodeficiency syndrome (AIDS), but also other cancers. A heightened awareness of male breast cancer by HIV specialists is needed, especially for particular risk categories, such as trans-sexuals who take oestrogen therapies, and for the presence of breast conditions, such as gynecomastia, usually considered as part of the lipodystrophy syndrome.

RIASSUNTO

Il tumore della mammella nell'uomo è estremamente raro e, ad oggi, pochi casi sono descritti in pazienti con infezione da HIV. Un paziente sieropositivo di 65 anni presentava all'esame obiettivo un nodulo indolente al margine dell'areola della mammella sinistra. La biopsia della lesione ha evidenziato un carcinoma duttale, per cui il paziente è stato sottoposto a mastectomia sinistra e allo svuotamento del cavo ascellare omolaterale. Lo stadio è risultato pT1c/pN1a/M0 e il tumore esprimeva i recettori per estrogeni e progesterone, ma non per il recettore umano del fattore di crescita 2. Il paziente è stato sottoposto anche a radioterapia locale e ha assunto tamoxifene. Al momento della diagnosi, era in terapia antiretrovirale con viremia di HIV soppressa ed una conta di linfociti T CD4+ pari a 445 cellule/mm^3. I pazienti con infezione da HIV hanno un maggior rischio di sviluppare tumori, sia AIDS-definenti che di altro tipo. Gli specialisti nel trattamento dell'infezione da HIV devono essere più consapevoli del tumore della mammella, anche maschile, soprattutto per la presenza di categorie a rischio, come i transessuali che assumono terapie ormonali sostitutive, e per la presenza di condizioni, come la ginecomastia, che vengono spesso trascurate poiché considerate parte della sindrome lipodistrofica.

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