

BREAST CANCER IN AN OLD MALE WITH KLINEFELTER SYNDROME: AWARENESS AND KNOWLEDGE

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Abstract

We describe a case of an old man affected by Klinefelter Syndrome (47, XXY) in which has been diagnosed a breast cancer with metastatic axillary and supraclavicular lymph nodes. The case analyzed the role of bilateral gynecomastia and of pharmacological replace therapy in the evaluation of breast cancer risk in these patients . The usefulness of breast cancer screening could be evaluated in a retrospective cohort study.

Key words: Klinefelter Syndrome, gynecomastia, male breast cancer

Introduction

A 70-year-old man, D.C., with a diagnosis of Klinefelter syndrome 25 years before by genetic testing (47XXY), came to our Hospital for breast palpable mass on left side. The patient underwent clinical breast exam and breast ultrasonography; US was performed using a Logiq S6 scanner (GE Healthcare, Waukesha, WI, USA) with a multifrequency matrix-array linear transducer (7-14 MHz); Colour Doppler US was also performed to study intralesional vascularity. The patient received a medical report at the end of the examination. The exam showed bilateral gynecomastia and, in the site of the palpable mass, a hypoechoic lesion with smooth margins and inhomogeneous internal echopattern (14 mm diameter) associated to round, hypoechoic lymph node in left axilla and supraclavicular region (mm 11 max diameter) (Figure 1). The patient underwent us-guided fine needle aspiration cytology that confirm the malignancy of the lesion (C5) [1].

The patient underwent also Chest CT that revealed cylindrical bronchiectasis on lower segments; lymph nodes enlargement in supraclavicular region, abdominal ultrasonography that showed hepatic steatosis; prostatic hyperplasia; abdominal aorta calcifications. The result of thyroid ultrasonography was a diffuse inhomogeneity without focal lesions; reactive lymphadenomegaly, of testes ultrasound was low testicular volume and absence of focal lesions. Echocardiography and ecocolor Doppler was within normal limits.

Discussion

Klinefelter syndrome is one of the most common congenital chromosome disorders associated to hypogonadism and infertility; the incidence is 1 to 2 per 1000 neonates (47, XXY karyotype) and the life expectancy is 11.5 years less than general population. The most frequent disorders are small testes, cognitive impairment and hypergonadotrophic hypogonadism with risk of metabolic syndrome, type 2 diabetes and cardiovascular disease (varicose veins, thrombosis, embolism), gynecomastia (38% of patients), osteoporosis and epilepsy; may occur also with other syndrome, such as the rare Job's Syndrome. However, the diagnosis of Klinefelter Syndrome is carried out only in 25% of patients and at an adult age (mid-30s yo). A Klinefelter Syndrome associated to male breast cancer was first suggested by Bauer and Erickson in 1955 [2,3]; even if breast cancer and extragonadal germ cell tumors are more frequent in patients with Klinefelter

Syndrome, such as in other hereditary syndromes [4,5], cancer risk is generally stackable to general population. The base condition is gynecomastia, a benign situation characterized by enlargement of the male breast due to proliferation of glandular tissue; it is common in normal males during the neonatal period, at early puberty, and with increasing age, but can be pathological in some hereditary/iatrogenic conditions. The rarity of old patients suffering from Klinefelter Syndrome justify this case of a breast cancer in an old man (47 XXY). During puberty, Klinefelter Syndrome patients is exposed to elevated levels of gonadotrophins and decreased levels of testosterone, that determine the characteristic body proportions and gynecomastia; during adulthood, low testosterone in relation to estradiol levels result in increased estrogen-to-androgen ratios [6] that can explain the relationship between bone fractures and an increased risk of male breast cancer.

Indeed, both hormones are involved in bone maintenance and osteoporosis among men and androgens decrease during aging with the consequent predilection for bone loss and fractures; conversely the androgen replace therapy can increase male breast cancer as a iatrogenic effect of exogenous hormones [7]. It has been demonstrated the transition from atypical proliferative ductal epithelium in gynecomastia to carcinoma in Klinefelter Syndrome patients, supporting the notion of abnormal hormonal stimulation of cell proliferation in the mammary ductal epithelium [8]; perhaps XXY males may inherit the same predisposition to breast cancer as XX females [9]. However, the risk, although elevated, is still considerably lower than that of women in the general population [10]; therefore, the level of risk does not justify prophylactic mastectomy, also for psychological effects [11], but could be useful patient education with breast self-examination ever 30 days and periodical clinical and ultrasound examination conducted by a breast radiologist [12] and/or mammography [13], also to avoid incorrect clinical-anamnestic association [14]. In future, to evaluate the risk of breast cancer in Klinefelter Syndrome patients, could be useful a retrospective cohort study, in which a cohort of patients with Klinefelter Syndrome is enrolled from historical records that can allow the subsequent assessment of cancer development. Psychiatric examination disclosed paranoid ideation, delusional convictions of influence and broadcasting, ideas of reference, associative thinking and preoccupations with religious themes. There was a marked lack of insight. Mood was slightly euphoric and effect was inappropriate.

Psychomotor behaviour was somewhat agitated and mild pressure of speech was noticed. Hallucinatory experiences of any kind were not present. Extensive neuropsychological assessment disclosed low average to average intelligence (Kaufman adolescent and adult intelligence test - KAIT - total intelligent quotient (IQ): 86; Crystallised IQ:90; Fluid IQ: 84; National Adult Reading Test - NART - IQ: 88) [15,16]. Cognition was characterised by dysfunctions in attention such as distractibility, executive dysfunctions and impulsivity. In addition, memory problems and fragmented perception were found, partially related to attentional deficits. His personality showed marked traits of extraversion combined with eccentricity. Based on the findings obtained in psychiatric and neuropsychological examination, a final diagnose of schizotypal personality disorder (diagnostic and statistical manual of mental disorders-IV: 301.22; international classification of diseases-10: F-21) was made with eccentric behaviour, anomalies of thinking and affect, paranoid ideas and circumstantial speech as most prominent symptoms. In this report, the psychiatric disorder of the patient was characterised by quasi-psychotic episodes with intense illusions, circumstantial thinking and speech, delusion-like ideas occurring without external provocation and odd eccentric behaviours. The symptom profile matched a schizotypal personality [17,18].

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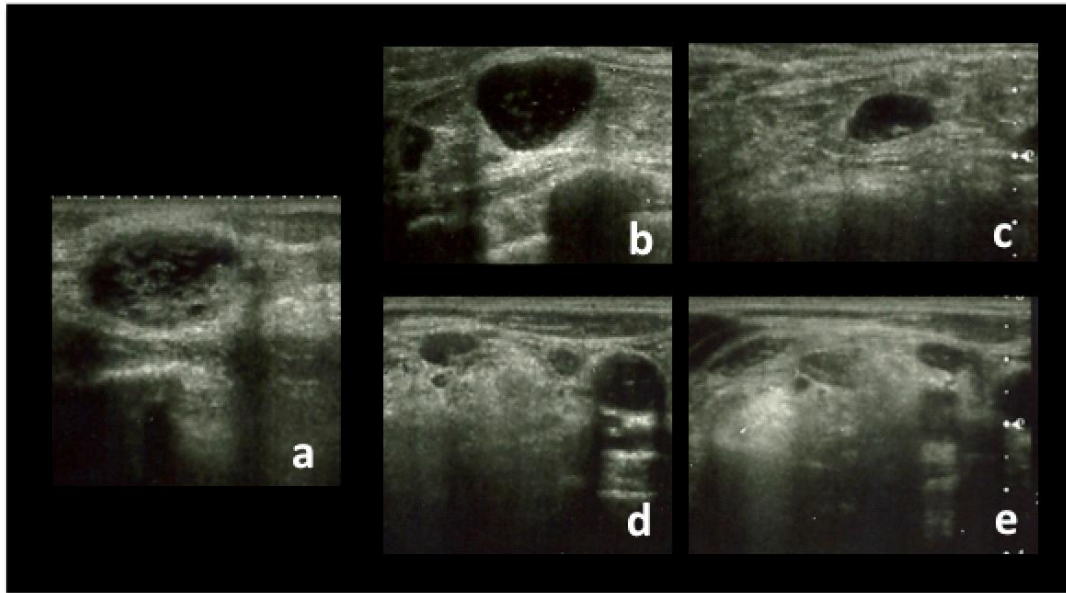


Figure 1. Male, 70 yo – ultrasonography shows a) the ovalar hypoechoic lesion in upper medial right breast, associated to suspected lymph nodes in axillary (b, c) and sovraclavicular regione (d,e).