Male Breast Cancer—Review of Literature on a Rare Microscopic Variant (Oncocytic Carcinoma)

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Abstract Breast cancer is uncommon in males. Approximately 85 % of male mammary carcinomas are of the infiltrating duct type. One of the uncommon subtypes is oncocytic carcinoma (OC). Oncocytic tumors may occur in several different anatomical sites such as meninges, choroid plexus, soft tissue, and gastrointestinal tract; they tend to affect more frequently the endocrine and glandular epithelia such as salivary gland and renal tubules that have high metabolic activity. At present, OC is a morphological entity, and there is no practical reason for including OC into everyday reports, since any significant clinical features are found. However, more cases of OC of the breast have to be studied in view of the fact that oncocytic tumors of colon, thyroid, and meninges seem to be resistant to radiation therapy, a finding that might be taken into consideration when planning the treatment in breast carcinomas.

Keywords Histopathology · Oncocytic carcinoma · Male breast cancer · Antimitochondrial antibody

Introduction

Breast cancer is uncommon in males and accounts for about 1 % of all cancers in men. Oncocytic differentiation, which has rarely been described, may present as intraductal as well as invasive lesion. Oncocytic breast carcinomas are tumors composed of no fewer than 70 % of oncocytic cells. At immunohistochemistry they are positive for antimitochondrial antibody. To date only four cases of oncocytic carcinomas of

the breast have been reported in the literature worldwide and this prompted us to document this case [1, 2].

Case Report

A 55-year-old man presented to the surgical outpatient department at Father Muller Medical College with a history of a progressively increasing lump in the right breast and history of weight loss for 1 year. Patient did not experience previous chest wall irradiation. There was no history regarding breast carcinoma or benign breast neoplasm in his female and male first degree relatives. Patient was a nonsmoker and nonalcoholic. He did not have phenotypic features of Klinefelter's syndrome and there was no history of hormonal therapy. On clinical examination, the right breast showed a lump in the central quadrant just below the nipple and areola complex. The lump measured 4 cm in diameter and was firm in consistency with a palpable 1 cm right axillary lymph node. No discharge, retraction of nipple or ulceration was noted. The lump was not fixed to the chest wall. Clinically the patient was diagnosed to have carcinoma breast stage III. Further a fine-needle aspiration cytology (FNAC) was performed, which showed tumor cells in discohesive sheets and dispersed singly. Individual cells showed sharply defined cell border, abundant densely eosinophilic and granular cytoplasm, hyperchromatic nucleus and having small nucleoli—features were suggestive of oncocytes. FNAC of the axillary lymph node showed features of reactive hyperplasia. A final cytological impression of infiltrating duct carcinoma was rendered. Histopathological correlation was suggested. Subsequently the patient underwent modified radical mastectomy. Resected specimen revealed a tumor below the nipple and areola, measuring 4 cm in diameter. Cut surface showed well-defined, solid, firm tan brown tumor as seen in the oncocytic tumor elsewhere (Fig. 1). Microscopy of the tumor

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Fig. 1 Cut surface of Mastectomy specimen showing tan coloured tumor

showed cells in solid nests separated by fibroelastic stroma. Occasional foci of papillary and cribriform pattern and focal area of atypical ductal hyperplasia were also noted. Individual tumor cells showed well-defined border, abundant granular densely eosinophilic cytoplasm, and hyperchromatic nucleus as noticed in FNAC smear (Fig. 2). Thirteen lymph nodes identified showed reactive features. Final histopathological diagnosis of infiltrating duct carcinoma, oncocytic variant was established. Further strong positivity for estrogen receptor (ER) (Fig. 3) and weak positivity for progesterone receptor (PR) (Fig. 4) were noted. For confirmation, immunohistochemistry for antimitochondrial antibody was suggested which was not performed due to nonavailability of antibody in this part of the country. The patient rejected radiotherapy and adjuvant hormonal therapy. He is asymptomatic after 2 years of follow-up.

Discussion

Male breast cancer is infrequent and represents less than 1 % of all cancers in men, and experience of it in any single institution is limited. Current understanding regarding its

Fig. 2 Microscopy showing oncocytic cells in solid nests, separated by fibrous stroma, H&E, 10x

Fig. 3 Immunohistochemistry showing strong positivity for ER receptor

biology, natural history, and treatment strategies has been extrapolated from its female counterpart. Male breast carcinoma usually presents as a painless, firm subareolar mass or a mass in the outer quadrant of the breast. Some of the risk factors implicated include alcohol intake, obesity, tobacco abuse, and conditions associated with increased estrogen or decreased androgen, medications, or radiation exposure. The clinical presentation of breast cancer in males is similar to that in females, except for higher median age at presentation in males. Male breast carcinoma tends to present at advanced clinical stages and with more lymph node metastasis due to paucity of breast tissue in males [3, 4].

Morphological growth patterns seen in infiltrating duct carcinoma in the male breast duplicate those encountered in the female breast. Oncocytic differentiation has rarely been described and has to be differentiated from apocrine carcinomas. Oncocytic breast carcinomas are tumors composed of no fewer than 70 % of oncocytic cells. A thorough sampling is essential for an accurate histopathological diagnosis of such cases. Oncocytes and apocrine cells share

Fig. 4 Immunohistochemistry showing weak positivity for PR receptor

similar morphological features at the hematoxylin–eosin level. At immunohistochemistry, ER and PR are usually negative in apocrine carcinoma. Positivity for ER and PR receptor noted in the index case rules out apocrine carcinoma. However, there are some ultra structural differences that allow a confident distinction between these two cell types. Mitochondria in apocrine cells usually are in perinuclear location and are not so numerous and diffusely dispersed as in oncocytes. At immunohistochemistry apocrine cells are strongly positive for GCDFP (gross cystic disease fluid protein) -15 and negative for antimitochondrial antibody [3–6].

Oncocyte means “swollen cell” from ancient Greek. The term was coined in salivary glands by Hamper in 1931 to describe a special type of epithelial cell showing, at light microscopy, large size and deeply acidophilic granular cytoplasm. In thyroid, the same cell was first described by Askanazy whereas the designation “Hurthle cell” is a misinterpretation because what Hurthle described were the ultimobranhial body-derived parafollicular calcitonin-producing cells. Electron microscopy subsequently evidenced that oncocytic cells were enlarged as a consequence of an increase in the number and size of mitochondria, which also imparted the cytoplasmic granularity. The proposal by Ghadially that 60 % of the total cytoplasm volume loaded by mitochondria has become the generally accepted cut-off value for the designation of oncocyte. In definition of oncocytoma, the proportion of neoplastic cells exhibiting oncocytic features varies in different organs—being 70 % in breast, 75 % in thyroid neoplasm, and 100 % in renal tumors. In breast, the primary oncocytic carcinoma (OC) was defined as tumors composed of no fewer than 70 % of oncocytic cells. In spite of rare reports, the incidence of OCs of the breast was felt to be underestimated probably because of histological similarities between oncocytes and apocrine cells [1, 5].

To date only four cases of oncocytic breast carcinomas have been reported in the literature. They include two invasive carcinomas and one carcinoma in situ; all patients were older than 70 years, and all cases showed remarkably good prognosis. Our patient was 55-year-old and has been doing well after 2 years of follow-up. Histologically, the four cases were well-differentiated tumors composed of large cells having well-defined borders and abundant eosinophilic granular cytoplasm. The case of carcinoma in situ reported by Damiani et al. [5] had a papillary appearance as noted in case under discussion. The focus of atypical ductal hyperplasia was also noted in the index case. In all cases, the oncocytic nature of the neoplastic cells was proved by ultrastructure and also by immunohistochemistry in the three cases reported by Damiani et al. All three cases expressed estrogen receptor (ER) with positivity found in

10–90 % of the neoplastic cells. Progesterone receptor (PR) was negative in one case and positive in the remaining three cases, with percentages of positive cells ranging from 5–20 %. Strong positivity for ER and weak positivity for PR were noted in the present case under discussion. Damiani concluded that reported cases were too limited for any conclusion, and a study of more cases was advocated [1, 4, 5].

Modified radical mastectomy followed by external radiation therapy is the standard treatment for male breast cancer. Hormonal therapy, as an adjuvant treatment, is the first-line approach in a majority of patients, and chemotherapy is reserved for patients with poor prognostic factors. In male breast carcinoma, several series reported a higher percentage of hormonal receptor positivity than in female breast cancers. In case under discussion, strong positivity for ER and weak positivity for PR were noted. Costa and Silverberg [6] have studied that pathological features and the presence of estrogen receptor are biochemically distinct from apocrine carcinoma. A study done by Rodriguez et al. [3] showed that ER-positive patients appeared to have a better survival than ER-negative patients. PR expression did not correlate with treatment or survival [4, 5].

In the present case, the patient is a manual laborer and he has been doing his routine work as usual. He has rejected radiotherapy and has been physically fit for 2 years. At present, OC is a morphological entity, and there is no practical reason for including OC into everyday reports, since any significant clinical features are found. However, more cases of OC of the breast have to be studied in view of the fact that oncocytic tumors of colon, thyroid, and meninges seem to be resistant to radiation therapy, a finding that might be taken into consideration when planning the treatment in breast carcinomas [1].

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