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Review

Rare breast tumors: Review of the literature

Catalina Acevedo[a,*], Claudia Amaya[a], Jose-Luis López-Guerra[b]

[a] Department of Radiation Oncology, Fundación Valle del Lili, Cali, Colombia
[b] Department of Radiation Oncology, Virgen del Rocío University Hospital, Seville, Spain

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ABSTRACT

Breast cancer tumors have different morphological phenotypes and specific histopathological types with particular prognostic and clinical characteristics. The treatment of rare malignant lesions is frequently controversial due to the absence of trials to determine the optimal managements. This review describes the spectrum of rare breast tumors indicating the clinical, epidemiological and treatment characteristics.

1. Background

Breast cancer is the most common cause of death from cancer in women worldwide. In 2012, an estimated of 100,000 cases of invasive breast cancer were diagnosed in the United States. The histology type is predominantly ductal in 70–80% of all cases followed by invasive lobular carcinoma in 5–15% of patients.[1] These tumors had been studied in randomized trials to determine the optimal treatment approach including surgery, endocrine, and chemo or radiation therapy. In these types of tumors, the therapeutic approach is generally well defined. However, breast tumors exhibit a wide range of morphological phenotypes and rare specific histopathological types (less of 2% of all breast cancer) have particular prognostic or clinical characteristics.[2–4] Because of the rarity of these tumors, there is no consensus regarding optimal treatment and it is difficult to allow large studies to define the optimal adjuvant treatment. Most cases have been treated with standard therapy as there are no data to indicate special protocols. The management of uncommon tumors is often controversial due to the lack of large single-institution studies or randomized trials to define optimal treatment. In this article, we describe the spectrum of rare breast tumors indicating the clinical, epidemiological and treatment characteristics.[2]

Including all the histological types, Ellis et al.[5] compared 10-year survival in 1621 cases of primary breast cancer. Ductal carcinoma *in situ*, cribriform and tubular carcinoma presented excellent prognoses, with 10-year survival rates of 92%, 91% and 90%, respectively, compared to 80% for mucinous carcinoma, 51% for medullary carcinoma, 54% for lobular carcinoma and 47% for invasive ductal carcinoma. Table 1 summarizes the main rare breast cancer classified in epithelial and non-epithelial breast tumors. Additionally, Table 2 shows the main characteristics of rare breast cancers.

2. Rare epithelial breast cancers

2.1. *Pure tubular carcinoma*

Pure tubular carcinoma is a very rare breast cancer that accounts for less than 2% of invasive breast cancers in most

* *Corresponding author at*: Department of Radiation Oncology, Fundación Valle del Lili, Av. Simón Bolívar Cra 98 18-49, Cali, Colombia. Tel.: +57 2 3319090; fax: +57 2 680 5757.
E-mail address: catalina.acevedo@hotmail.com (C. Acevedo).

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Table 1 – Rare breast cancer classified in epithelial and non-epithelial breast tumors.

Rare epithelial breast cancer
Tubular carcinoma
Invasive cribriform carcinoma
Mucinous carcinoma
Invasive solid papillary carcinoma
Apocrine carcinoma
Neuroendocrine tumors
Medullary carcinoma
Secretory breast carcinoma
Adenoid cystic carcinoma
Acinic cell carcinoma
Metaplastic carcinoma
Glycogen-rich clear-cell carcinoma
Oncocytic carcinoma (malignant oncocytoma)
Sebaceous carcinoma
Primary squamous cell carcinoma
Pleomorphic variant of lobular carcinoma
Papillary Carcinoma of the Breast
Rare non-epithelial breast cancer
Sarcomas
Phylloides tumor
Lymphomas

clinical series. This specific histological type is more likely to occur in older patients, and it is characterized by small size (the majority are less than 1 cm), and less nodal involvement.[6] This tumor is nearly always estrogen (ER) and progesterone receptor (PR)-positive, well-differentiated, and mostly human epidermal growth factor receptor type 2 (HER2)-negative. Patients with pure tubular carcinoma have an excellent prognosis compared with invasive ductal carcinoma with low ipsilateral recurrence rates. Therapy is based on radiation treatment after breast conserving surgery.[7] The effect of adjuvant radiotherapy reducing local failure following breast conservative surgery has been described in the literature.[6] Due to the excellent survival rate of patients with breast tubular cancer, the need of axillary staging in these patients is questionable.[6] However, the incidence of axillary metastases may range from 4% to 17%.[4,8] Thus, the use of sentinel lymph node biopsy (SLNB) should be considered for patients with tubular carcinoma if the positive biopsy finding will modify adjuvant treatment.[2] However, the survival of patients with tubular carcinoma is similar to that of the general population, and there is no evidence that adjuvant therapy due to positive SLNB influences survival.[6]

2.2. *Invasive cribriform carcinoma*

Breast invasive cribriform carcinoma (ICC) is a rare tumor reported to range from 0.3% to 3.5% of all breast cancers. The new definition of the World Health Organization (WHO) describes pure ICC as a carcinoma with infiltrating components presenting more than 90% of cells of invasive cribriform pattern.[9] The tumor may present as a frequently occult mass, difficult for radiological detecting. For this reason, the lesions are usually large at presentation although they grow slowly. ER and PR expression is common in these tumors. Prognosis of ICC is excellent, approaching that of the general population mainly in pure ICC tumors.[10] At present, distant metastasis of pure ICC has rarely been reported. Treatment guidelines are extrapolated from other breast cancers without clear validation.

2.3. *Mucinous carcinoma*

This rare tumor accounts for 1–4% of breast tumors and is characterized by a better prognosis than infiltrative ductal cancer.[11] This breast type is characterized by production of abundant extracellular and/or intracellular mucin. Pure and mixed variants of mucinous carcinoma have been described. The pure type consists of tumor tissue with extracellular mucin production (90% purity), while the 'mixed' form of mucinous carcinoma (50–90% purity) also contains infiltrating ductal epithelial component without mucin.[12] The pure type shows a better differentiation with low grade and expression of ER (to 94%) and PR (80%) and the majority of cases. Compared to infiltrating ductal carcinoma, mucin tumors are smaller and present less nodal involvement.[2]

The diagnosis age ranges from 25 to 85 years, with a median age at diagnosis of 71 years in a large retrospective review of 11,400 breast cancer cases.[2] Clinically, mucinous carcinoma manifests as a palpable lump, with a mammographic appearance of well-defined and lobulated lesion. Due to the benign course, a late diagnosis does not worsen the clinical outcome.[13] This benign pattern is confirmed in a large retrospective series that shows that 10-year survival is more than 90%.[2] Only 3–15% of the pure variety of mucinous carcinomas show axillary node metastases compared to 33–46% of the mixed type.[8] This involvement is a marker of poor prognosis. However the incidence of nodal involvement is less that 5% in mucinous tumor of $\leq$1 cm of diameter. Thus, some authors recommend that axillary node staging is not beneficial in tumors measuring less of 1 cm.[8] Nevertheless, SLNB should be considered also in these cases because positive nodal status seems to be the most important factor associated with worse prognosis. Patients with pure mucinous carcinomas without skin invasion are candidates for a breast-conserving therapy. Concerning the systemic adjuvant therapy, there are no consensus, thus the treatment is based on classical breast cancer strategies.[2]

2.4. *Solid papillary carcinoma*

Solid papillary carcinomas of the breast are rare tumors (to 1.7% of all breast cancers), characterized by round, well-defined nodules composed of low-grade ductal cells separated by fibrovascular cores. Pathologically, solid papillary carcinomas exhibit low-grade features, and the tumors often display neuroendocrine and mucinous differentiation.[14] ER and PR are generally positives and her2 negative. Clinically, these tumors present as a palpable, centrally located mass or as bloody nipple discharge and affects older women (mean age 66 years). The most common mammographic appearance of a papillary tumor is as a soft-tissue mass, with calcification present in less than half of cases.[15] The treatment for solid papillary carcinomas is based on surgical excision. When invasive carcinoma is not present, the prognosis is excellent.[14] There are limited studies focused solely on treatment strategies for papillary carcinoma. The absence of definitive guidelines for