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Rare types of breast carcinoma

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Background. Breast cancer is a heterogeneous disease that encompasses several distinct entities with remarkably different characteristics. One of very important cancer characteristics is its histological type.

Materials and methods. We used Pubmed and Medscape databases and analyzed original articles and literature reviews about rare histological types of breast cancer.

Results and discussion. World Health Organization (WHO) presents a detailed classification of breast cancers. According to this classification, cancers are divided into epithelial, mesenchymal, fibroepithelial tumors. Malignant lymphoma, metastatic tumors can also be found in the breast. WHO also marks tumors of the nipple, male breast cancer and myoepithelial lesions. In this paper, only the invasive epithelial tumors are discussed. Most tumors are derived from mammary ductal epithelium, and up to 75% of the breast cancers are ductal carcinomas. The second most common epithelial tumor type is invasive lobular carcinoma which comprises 5–15% of the group. There are more than a dozen variants which are less common. They comprise less than 10% of breast tumors. Their clinical behavior can differ greatly. So, it is important to know their main characteristics in order to make the best treatment choice and to foresee prognosis. We shortly describe the epidemiology, diagnostics, clinical and immunophenotypic features, prognosis and predictive factors of rare epithelial breast tumors.

Key words: breast cancer, histological type, epithelial breast tumors, rare histological types

INTRODUCTION

Breast cancer (BC) is a heterogeneous disease that encompasses several distinct entities with remarkably different characteristics. For many decades, invasive breast carcinomas were classified according to the histological type, grade and expression of hormone receptors. More recently, improvements in our understanding of the biology of breast cancer have led to a more specific classification of tumors according to their genetic expression and imunohistochemical staining characteristics. Different forms of the disease vary with regard to clinical behaviour, management options and prognosis (1–3).

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One of very important cancer characteristics is its histological type. Histological type is associated with different epidemiology, diagnostic issues, clinical course and prognosis. World Health Organization (WHO) presents a detailed classification of breast cancers (4). According to this classification, cancers are divided into **epithelial** (such as invasive ductal carcinoma, invasive lobular carcinoma, tubular carcinoma, medullary carcinoma, mucinous carcinoma, and others), **mesenchymal tumors** (such as haemangioma, myofibroblastoma, lipoma, neurofibroma, leiomyoma, and others), **fibroepithelial tumors** (fibroadenoma, phylloides tumor, mammary hamartoma). **Malignant lymphoma** (diffuse large B-cell lymphoma, burkitt lymphoma, follicular lymphoma), **metastatic tumors** can also be found in the breast. WHO also marks **tumors of the nipple, male breast cancer and myoepithelial lesions.**

In this paper, only the invasive epithelial tumors are discussed. These cancers are divided into 19 different types:

1. Invasive ductal carcinoma, not otherwise specified;
2. Invasive lobular carcinoma;
3. Tubular carcinoma;
4. Invasive cribriform carcinoma;
5. Medullary carcinoma;
6. Mucinous carcinoma and other tumors with abundant mucin;
7. Neuroendocrine tumors;
8. Invasive papillary carcinoma;
9. Invasive micropapillary carcinoma;
10. Apocrine carcinoma;
11. Metaplastic carcinoma;
12. Lipid-rich carcinoma;
13. Secretory carcinoma;
14. Oncocytic carcinoma;
15. Adenoid cystic carcinoma;
16. Acinic cell carcinoma;
17. Glycogen-rich clear cell carcinoma;
18. Sebaceous carcinoma;
19. Inflammatory carcinoma.

Most tumors are derived from mammary ductal epithelium, actually the terminal duct-lobular unit, and up to 75% of the diagnosed infiltrating ductal carcinoma are defined as invasive ductal carcinoma, not otherwise specified (IDC-NOS). The second most common epithelial tumor type is invasive lobular carcinoma which comprises 5–15% of the group. There are more than a dozen variants which are less common, but still very well defined by the WHO classification. We will call them "rare types of breast cancer".

When we speak about breast cancer, usually we have in mind the ductal carcinoma. But the other types, which comprise less than 10% of breast tumors, are also very important. Their clinical behavior can differ greatly. So, it is important to know their main characteristics in order to make the best treatment choice and to foresee prognosis.

MATERIALS AND METHODS

Searching for literature, we used Pubmed and Medscape databases. We analyzed original articles and literature reviews about rare histological types of breast cancer. This article shortly describes the epidemiology, diagnostics, clinical and immunophenotypic features, prognosis and predictive factors of rare epithelial breast tumors.

RESULTS

Tubular carcinoma

It is a type of breast carcinoma with a particularly favorable prognosis, composed of distinct well differentiated tubular structures with open lumina lined by a single layer of epithelial cells.

Epidemiology. Pure tubular carcinoma (TC) accounts for under 2% of invasive breast cancer. Higher frequencies of up to 7% are found in series of small breast cancers. This type of BC is more likely to occur in older patients compared to ductal carcinoma (5).

Diagnosis. This kind of carcinoma is usually well seen on mammograms because of its spiculated nature and is often seen at higher frequencies of 9–19% in mammographic screening series. On sonography TC is seen as an irregular mass with posterior acoustic shadowing (6).

Immunohistology. In most of the cases, estrogen receptors ER (>90%) and the progesterone receptor (PgR) are positive. The proliferation index is usually low. HER-2 and the epidermal growth factor receptor (EGFR) are negative (7).

Clinical features. When compared with invasive ductal carcinoma, TC is more likely to be smaller

in size and have substantially less nodal involvement (8). These tumors are recognized to occur in association with some epithelial proliferative lesions including well-differentiated / low-grade types of ductal carcinoma in situ (DCIS), lobular neoplasia and flat epithelial atypia (9). In addition, an association with a radial scar has been proposed (10).

Prognosis and predictive factors. Pure tubular carcinoma has an excellent long-term prognosis. Survival is not significantly different from that of the general population, even with positive axillary lymph nodes. Five-year disease-free survival (DFS) for node-positive patients was 94% (n = 64). Recurrence following mastectomy or breast conservation treatment is rare and localized tubular carcinomas are considered to be ideal candidates for breast conservation techniques (5, 11).

Cribriform carcinoma

It is a type of breast tumor when the cancer cells invade the stroma in nest-like formations between the ducts and lobules. Within the tumor, there are distinctive holes in between the cancer cells.

Epidemiology. This tumor accounts up to 3.5% of the breast cancers (12).

Diagnosis. The tumors may present as a mass but frequently they are clinically occult. At mammography, tumors typically form a spiculated mass containing microcalcifications. The ultrasound is not entirely typical for the breast carcinoma. This form should be differentiated from carcinoid tumor, adenoid cystic carcinoma and extensive cribriform DCIS.

Immunohistology. ER is positive in 100% and PgR in 69% of the cases; HER-2 is negative (13).

Clinical features. The mean age is 53–58 years. Invasive cribriform carcinoma is usually of the low grade. Multifocality is observed in 20% of the cases (12). Some authors reported 14.3% of the cases to involve axillary lymph nodes (14).

Prognosis and predictive factors. The outcome is remarkably favorable. The ten-year overall survival is 90–100%. The outcome of the mixed invasive cribriform carcinoma has been reported to be less favorable than that of the classic form, but better than the common ductal carcinoma. The biological behavior is very similar to that of the tubular carcinoma (12).

Apocrine carcinoma

It is a carcinoma showing cytological and immunohistochemical features of apocrine cells in >90% of the tumor cells.

Epidemiology. The reported incidence of apocrine carcinoma depends on the method of detection. Based on light microscopy alone, it is only 0.3–4% (15).

Diagnosis. Not specific.

Immunohistology. These tumors are reported as ER positive in 3.8%–60% of cases, PgR positive in 4.8–40%, HER-2 positive in 50%, with the proliferation index of 6.9–23.7% and p53 alteration in 46–50%. Androgen receptors are positive in 56–100% of AC (16).

Clinical features. There is no difference between the clinical or mammographic features, size and site of carcinomas among apocrine and non-apocrine lesions.

Prognosis and predictive factors. Survival analysis of 72 cases of invasive apocrine duct carcinoma compared with non apocrine duct carcinoma revealed no statistical difference (17).

Medullary carcinoma

It is a well-circumscribed carcinoma, composed of poorly differentiated cells arranged in large sheets, with no glandular structures, scant stroma and a prominent lymphoplasmacytic infiltrate.

Epidemiology. Medullary carcinoma (MC) represents 1–7% of all breast carcinomas, depending on the stringency of diagnostic criteria used (18).

Diagnosis. Mammographically, MC is typically well-circumscribed and may be confused with a benign lesion (19).

Immunohistology. MC shares common characteristics with the basal type breast cancer. Most of the tumors are hormone receptor and HER-2 negative and CKT 5/6 positive (94%) (20).

Clinical features. The mean age of women with MC ranges from 45 to 52 years (21). In a large series of almost 1,500 patients with MC, only 27% had involved nodes.

Prognosis and predictive factors. MC has been reported to have a better prognosis than the common invasive ductal carcinoma, but this has been questioned by the others. The overall 10-year survival, reported for MC, varies from about 50% and could reach more than 90%. Such big disparity can occur due to differences in diagnostic criteria (18, 22).

Mucin producing carcinoma

In this type of cancer, the tumor is formed from abnormal cells that "float" in pools of the mucin. A variety of carcinomas in the breast are characterized by the production of abundant extracellular and / or intracellular mucin: colloid carcinoma, mucinous cystadenocarcinoma, columnar cell mucinous carcinoma and signet ring cell carcinoma.

Epidemiology. Pure mucinous carcinomas represent 1–4% of all the breast cancers.

Diagnosis. The tumors usually present as a palpable lump. Mamographically, mucinous carcinoma appears as a well-defined, lobulated lesion. On the magnification or the compression views, a less defined margin may become more evident. The mamographic resemblance to a benign process increases with the increasing mucin content. Pure mucinous carcinomas present an imaging challenge due to their isoechogenic appearance on ultrasound.

Immunohistology. These are mostly well-differentiated lesions frequently associated with the positive ERs (>90%) and PgRs (81.5%) and HER-2-negative disease (23).

Clinical features. This form presents at the one of the oldest median ages (71 years). The tumors range in size from less than 1 cm to over 20 cm, with an average of 2.8 cm (23). Despite often having a large tumor size, the axillary lymph nodes are rarely involved. Frequency of lymph nodes metastases depends on the form: only 3–15% of the pure variety show axillary node metastases compared to 33–46% of the mixed type. Lymph node metastases were found only in 13% of the cases. Node positivity was associated with the larger tumor size (24).

Prognosis and predictive factors. In general, pure mucinous carcinomas have a favorable prognosis. Prognosis worsens in case of cellular tumors. The ten-year survival ranges from 80 to 100%. Pure mucinous carcinomas have a far better prognosis than the mixed variety with at least 18% difference in the survival rates. About 10% of women with the pure form die from their cancer compared to 29% of those with the mixed type (24).

Neuroendocrine tumors

Primary neuroendocrine (NE) carcinomas of the breast are the group, which exhibits morphological features similar to those of NE tumors of both gastro intestinal tract and lung. They express neuroendocrine markers in more than 50% of the cell population.

Epidemiology. NE breast carcinomas represent about 2–5% of breast carcinomas (4).

Diagnosis. It usually appears as a circumscribed mass on mammographic and ultrasound examination.

Four different subtypes are distinguished: small-cell carcinoma (SCC), large-cell carcinoma, solid NE carcinoma and atypical carcinoid tumor.

Solid NE

Immunohistology. Typically, these tumors are ER and PgR positive and HER-2-negative (25).

Clinical features. Most patients are in the 6th or 7th decades of life (26). There are no notable or specific differences compared to other tumor types. Endocrine hormone related syndromes are exceptionally rare.

Prognosis and predictive factors. The outcome of these cancers does not differ from that of other carcinomas and depends very much on the histological grade (27, 28).

SCC

Immunohistology. The tumor often expresses ERs and PgRs and this correlates with the degree of differentiation; well-differentiated tumors are more likely to express hormone receptors. Her-2 status is typically negative (29, 30).

Clinical features. Patients with small cell carcinoma often present at an advanced stage.

Prognosis and predictive factors. SCC tumor is considered as an aggressive tumor with a poor prognosis (31). However, there are some reports about long-term survival when the diagnosis is made early (32).

Invasive papillary carcinoma

This cancer characteristically has papillae with focal solid areas.

Epidemiology. Invasive papillary carcinoma represents less than 1–2% of all the breast cancers.

Diagnosis. Mammographically, invasive papillary carcinoma is usually characterized by the nodular densities which may be multiple and frequently lobulated. The sonographic features are indistinguishable from the papillomas. The only differential finding between noninvasive and invasive

papillary cancers was the circumscribed margins. Macroscopically, invasive papillary carcinoma is grossly circumscribed (33).

Clinical features. Typically, papillary carcinoma presents in postmenopausal women with only 15% of the reported cases occurring under the age of 50. These patients often exhibit axillary lympadenopathy suggestive of metastatic disease, but which on pathological examination is due to the benign reactive changes. Tumors are often of Grade 2, or of the moderate grade, on a scale of 1 to 3. In most of the cases of invasive papillary carcinoma, ductal carcinoma in situ (DCIS) is also present.

Immunohistology. In total, 100% of the tumors are ER positive and HER-2 negative, and 80–100% are PgR positive (34).

Prognosis and predictive factors. There are only limited data on the prognostic significance of the invasive papillary carcinoma. Of the 1,603 breast cancers reviewed in the National Surgical Adjuvant Breast and Bowel Project (NSABP)-04 study, 35 had papillary features and only three experienced treatment failure after 5 years. Node-negative patients, who had been enrolled in the NSABP B-06 study, revealed an improved survival after 10 years of the follow-up compared with IDC-NOS (35).

Invasive micropapillary carcinoma

It is a carcinoma composed of the small clusters of the tumor cells lying within the clear stromal spaces. The pure variant is extremely rare.

Diagnosis. Invasive micropapillary carcinoma usually presents as a solid mass. Pure micropapillary carcinoma has a lobulated outline due to the expansive mode of the growth. Mammography tumor appears like the high density mass in >80% of the cases. The margins are spiculated, sometimes indistinct or microlobulated. Microcalcifications are present in 43.8% of patients. Masses are typically hypoechoic, with only 60% of the masses showing posterior acoustic shadowing (36).

Clinical features. The mean age is 52.5 years (range 33–78). This growth pattern is correlated with the presence of the vascular invasion and the axillary lymph node metastases; 70% of the patients present with the involved axillary lymph nodes. In 72.3% to 91% of the cases lymphatic invasion is found. However, a micropapillary growth pattern has no independent significance for the survival.

*Immunohistology. A*bout two-thirds of the cases are ER positive and up to 68% are PgR positive, one-third to one-half of the patients present with HER-2-positive status and 66% with Bcl-2 positive. p53 overexpression was identified in 48% of the cases. No basal-like immunostaining pattern was detected (37).

Prognosis and predictive factors. Carcinoma with micropapillary features harbors a poor survival; it is related to the number of involved axillary lymph nodes. In the 5-year follow-up (range 4–199 months) of 98 patients, 10-year OS was 48% and breast-specific survival was 63.3%. The outcome of the patients did not differ significantly from that of the infiltrating ductal carcinomas of similar node status (38).

Metaplastic carcinoma

It is a general term referring to a heterogeneous group of the neoplasms, characterized by an intimate admixture of adenocarcinoma with dominant areas of spindle cell, squamous, and / or mesenchymal differentiation.

Epidemiology. The incidence of metaplastic carcinoma is <1% of all the invasive breast carcinomas.

Diagnosis. Mammographically, either a circumscribed or an indistinct lesion is typical. On the ultrasound, the metaplastic carcinoma reveals more benign features, characterized by an oval, round or lobular solid hypoechoic mass with circumscribed margins.

Clinical features. This form is commonly diagnosed in women >50 years of age. Metaplastic carcinoma is usually diagnosed with T2 disease, with a mean size 3.4–4.4 cm (39).

Immunohistology. Most of these high-grade neoplasms show a basal-like phenotype, few being positive for the hormone receptors or HER-2 overexpression (0–8%).

Prognosis and predictive factors. These tumors have a high metastatic potential. More than 50% of these tumors are associated with the local or distal recurrence. The spread is hematogenous rather than lymphatic. According to the literature, the mean OS is 37 months. The median survival from detection of metastatic disease is only 8–12 months (40).

Lipid-rich carcinoma

It is a breast carcinoma in which approximately 90% of the neoplastic cells contain abundant cy-

toplasmic neutral lipids. Many pathologists do not consider this type as a separate entity.

Epidemiology. The tumor accounts for 1–2% of all breast cancers (41).

Diagnosis. Most patients have palpable nodules. These tumors present with a higher density than the adjacent tissue at mammography (42).

Immunohistology. In the largest series (n = 49), 100% of the patients presented with the ER-negative status. The vast majority (90%) were PgR negative as well. Her-2 overexpression was found in 71.4% of this kind of neoplasm (43).

Clinical features. 84% of the reported patients were at the age <50. In one series, 80% were diagnosed with involved axillary lymph nodes and most of them had more than three positive lymph nodes. In total, 71% (35 of 49) were diagnosed with stage III disease.

Prognosis and predictive factors. Prognosis is unfavorable. The 2-year and 5-year OS rates were 64.6% and 33.2%, respectively, with a median OS of 35 months.

Secretory breast carcinoma (SC)

It is a rare, low-grade carcinoma with a solid, microcystic and tubular architecture, composed of cells that produce abundant intracellular and extracellular secretory (milk-like) material. Its synonym is juvenile carcinoma.

Epidemiology. This is a rare tumor, with a frequency below 0.15% of all breast cancers (44).

Diagnosis. The tumor usually manifests as indolent, mobile lumps located near the areola. On sonography SC frequently appears as a small benign / intraductal lesion (45).

Immunohistology. This subtype has the triple-negative phenotype (ER, PgR, and HER-2 negative).

Clinical features. A recent report disclosed 67 patients. Twenty-five (37%) were aged less than 20 years, 21 (31%) older than 30 years and the remaining 21 in between (46). Nodal involvement is seen in 15% of the patients at the time of diagnosis (47).

Prognosis and predictive factors. SC has an extremely favorable prognosis for children and adolescents, but seems to be slightly more aggressive for older patients.

Oncocytic carcinoma

It is a breast carcinoma composed of more than 70% oncocytic cells. Only the occasional cases have been described. However, the incidence in the breast is probably underestimated as oncocytes are easily overlooked or misdiagnosed as apocrine elements. All described patients have been over 60 years old. The follow up and number of reported cases are too small to allow meaningful discussion of prognosis (4).

Acinic cell carcinoma

Acinic cell carcinoma (ACCA) is the breast counterpart of similar tumors that occur in the parotid gland and show acinic cell (serous) differentiation.

Epidemiology. ACCA is a rare tumor. Eighteen cases have been reported in the literature (48).

Diagnosis. A well defined mass is usually seen on mammograms (49).

Immunohistology. This neoplasm is characterized by the lack of ER, PgR and HER-2 expression (50).

Clinical features. It affects women between 35 and 80 years (mean 56 years).

Prognosis and predictive factors. The literature categorizes this tumor as a favorable one; however, even within a short follow-up period, systemic and local recurrences were recorded. Larger series are required for definite conclusions.

Adenoid cystic carcinoma

These tumors are characterized by a mixture of proliferating glands, myoepithelial cells and stromal / basement elements.

Epidemiology. The tumor represents 0.1% of the breast carcinoma. Data in the literature is based on 200 cases.

Diagnosis. About 50% of these tumors are found in the sub-periareolar region. They may be painful or tender and unexpected cystic. Pain is a prominent symptom due to the neural involvement. A discrete nodule is the most common presentation. Adenoid cyst carcinoma must be distinguished from the benign collagenous spherulosis and from cribriform carcinoma (51).

Immunohistology. Histologically it is similar to the salivary gland counterpart, has a low aggressive potential. Generally, the tumor displays triple-negative phenotype (52). MIB-1 antibody (monoclonal antibody that is immunoreactive with Ki-67) stains demonstrate a low proliferative fraction (53).

Clinical features. Tumors are diagnosed predominantly in postmenopausal women. The size varies from 0.7 cm to 12 cm, with an average amongst most reported cases of 3 cm. Most of the reports document a low rate of axillary involvement of 0–4.6%; however, there are some small series that report on up to 27% lymph node metastases (53).

Prognosis and predictive factors. The 5-year, 10-year and 15-year OS rates were 85–88%, 75% and 60%, respectively, for adenoid cystic carcinoma (54). Adenoid cyst carcinoma is a low-grade malignant tumor generally cured by the simple mastectomy. It rarely spreads via lymphatic stream. Only two cases of axillary node metastases have been reported. Metastases are rare and have been reported to spread many years from diagnosis and without prior nodal disease. Local recurrence is related to the incomplete excision. Distant metastases occur in about 10% of the cases and the lungs are frequently involved. The most frequent site of metastases is lung; patients may live many years with metastases.

Glycogen-rich, clear cell carcinoma

This is defined as a carcinoma in which >90% of the neoplastic cells have abundant clear cytoplasm containing glycogen.

Epidemiology. The incidence is 1.4–3% of all breast cancers (55).

Diagnosis. These tumors show similar presentation features to the ductal carcinoma.

Immunohistology. In a series of 20 patients, 35% and 30% were positive to ER and PgR, respectively. In total, 20% presented with HER-2-positive status. Enzyme chemistry and immunohistochemistry are useful to differentiate this tumor from other clear cell tumors (56).

Clinical features. This form presents at the median age of 57. Tumor size ranges from 1 cm to 8 cm. The incidence of axillary lymph node invasion is significantly higher than in other forms, and the histological grade is from intermediate to high.

Prognosis and predictive factors. There is debate regarding this tumor's behavior, as some small series report high axillary lymph nodal rate involvement of more than 50%, whereas others report a much lower rate – 35% (n = 20). Fewer than 100 cases have been reported; thus, it is difficult to draw definitive conclusions. Most of the authors have found that this tumor has a poor prognosis; and they suggest that these tumors are more aggressive than typical ductal carcinoma. Also disease-free and overall survival is significantly worse in glycogen-rich carcinomas (56).

Sebaceous carcinoma

This carcinoma is characterized by a lobular or nested growth pattern of tumor cells variably admixed with those displaying sebaceous differentiation.

Epidemiology. Only seven cases have been reported in the literature.

Diagnosis. Margins are sharply delineated.

Clinical features. The age ranges from 43 to 83 years. The tumor ranges in size from 7.5 cm to 20 cm. Sebaceous tumor may precede internal malignancies and a genetic consultation to rule out Muir-Torre Syndrome should be considered.

Immunohistology. The hormone receptor status is typically positive. No HER-2 overexpression was detected. Percentage of Ki-67-positive tumor cells was relatively high and ranged from 16% to 38%.

Prognosis and predictive factors. Not much is known about the behavior of these tumors. Sebaceous carcinoma is generally felt to have a worse prognosis than other cutaneous carcinomas. Due to the only scant published data, it is difficult to compare it with other breast carcinomas (57).

Summary of the features of rare histological BC types are presented in the Table.

DISCUSSION

These epithelial tumors are far too rare to have been studied with specific randomized clinical trials to determine the optimal surgical, radiation, chemotherapeutic or endocrine treatment. Surgery is the first step in treating most of early-stage breast cancers. The standard of care is lumpectomy / mastectomy with sentinel node biopsy (SNB). Many of special types such as tubular, cribriform, medullary and mucinous carcinomas have a low risk for regional involved lymph nodes but without more data it is not clear whether SNB can be safely omitted. Adjuvant radiation therapy has shown its benefit in breast cancer as a local control procedure and it prolongs survival. The significant parameters related to local recurrence were still the traditional ones: age, margins, lymphovascular invasion and extensive DCIS (5, 58–59).

Table. Summary of the features of rare histological BC types

Histological type	Frequency	Age	ER / PR	HER2	Lymph nodes	Prognosis
Cribriform carcinoma	5–6%	53–58 years	+	–	14% positive	excellent
Mucin producing carcinoma	2%	>60 years	ER+, <70% PR+	–	3–15% positive	favorable
Papillary carcinoma	1–2%	postmeno-pausal	+	–	negative	relatively good
Micropapillary carcinoma	2%	52.5 years	60–70% ER+, 68% PR+	50%+ positive	72–77% positive	poor
Metaplastic carcinoma	<1%	mean 55 years	–	–	negative (0–8%+)	poor
Adenoid cystic carcinoma	0.1%	postmeno-pausal	–	–	negative (0–27% positive)	moderate (similar to ductal carcinoma)
Glycogen-rich, clear cell carcinoma	1–3%	41–78 years, mean 57 years	35% ER+, 30% PR+	20%+	often positive (35–50%)	poor (few cases for conclusion)
Sebaceous carcinoma	<1%	45–62 years	+	–	negative	poor (few cases for conclusion)
Tubular carcinoma	<2%	older patients	+	–	usually absent	excellent
Lipid-rich carcinoma	1–2%	<50 years	–	usually positive	present	poor
Oncocytic carcinoma	occasional cases	Na	Na	Na	Na	Na
Apocrinic carcinoma	0.3–4%	Ns	ER positive 3.8–60%, PgR positive 4.8–40%	HER-2 positive 50%	Ns	Ns
Secretory carcinoma	<0.15%	young, children	–	–	<15%	excellent
Medullary carcinoma	1–7%	45–52 years	–	–	27%	better than ductal carcinoma
Neuroendocrine carcinomas	2–5 %	>60 years	+	–	Ns	no difference with other types for solid NE, poor for SCC

Ns – not specific; Na – not applicable.

We cannot create systemic treatment algorithms using randomized trials with Level 1 evidence because of the rarity of all these tumors; we can only analyze small case reports. Maybe systemic adjuvant therapy and node dissection may be avoided in many patients with tubular carcinoma, because axillary node involvement is not a poor prognostic feature in this type of carcinoma (5).

However, further data are required before completely changing our guidelines for these tumors. For example, adenoid cystic carcinoma does not often respond to chemotherapy, but there are new data that this type has some response to anthracyclines and 5-fluorouracil as well as to paclitaxel (60).

Large series, however, are not available.

CONCLUSIONS

Rare epithelial breast cancers are a heterogeneous group of malignancies with different behaviors and prognoses. Although histopathology has been standard, there is now the question of whether it is

time to apply new technologies such as microarrays and deep gene analysis to further understand these rare tumors. Are they all really unique subtypes or not? Can they be classified according to their molecular or genetic features? Are the older histological subtypes of value in understanding the behavior of these rare tumors and are they really classifying specific tumors or not?

It is important that investigators from around the world gather a sizable number of these rare tumor types, and try to group them with outcome and treatment data. So treatment algorithms and guidelines can be established.

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RETI KRŪTIES NAVIKŲ TIPAI

Santrauka

Įvadas. Krūties vėžys – heterogeninė liga, apimanti keletą skirtingų tipų, kurių charakteristikos reikšmingai skiriasi. Vienas svarbių krūties naviką apibūdinančių bruožų yra jo histologija.

Medžiaga ir metodai. Ieškant literatūros šaltinių naudotasi Pubmed ir Medscape duomenų bazėmis. Išanalizuoti originalūs straipsniai bei literatūros apžvalgos apie retus histologinius krūties vėžio tipus.

Rezultatai ir aptarimas. Pagal Pasaulinę Sveikatos Organizaciją (PSO), krūties navikai skirstomi į epitelinius, mezenchiminius, fibroepitelinius, taip pat krūtyje gali būti aptiktos limfomos, metastatiniai navikai. PSO dar išskiria vyrų krūties navikus, spenelio navikus bei mioepitelinius pakenkimus. Šiame straipsnyje aptariami tik epiteliniai navikai. Dauguma navikų kilę iš krūties kanaliukų epitelio. Apie 75 % krūties navikų sudaro duktalinės karcinomos. Antras dažniausias tipas – invazyvi lobulinė karcinoma (apie 5–15 % visų navikų). Daugybė retesnių variantų sudaro mažiau nei 10 % krūties navikų. Navikų klinikinės savybės gali gerokai skirtis, todėl labai svarbu žinoti pagrindinius jų bruožus, kad būtų galima parinkti tinkamiausią gydymą bei numatyti prognozę. Šiame straipsnyje trumpai aprašoma retų krūties navikų epidemiologija, diagnostika, klinikinės bei imunofenotipinės savybės, taip pat prognozė bei predikciniai veiksniai.

Raktažodžiai: krūties navikai, histologinis tipas, epiteliniai krūties navikai, reti histologiniai tipai