REVIEW

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RARE BREAST TUMORS

ILIJA GUTEŠA, ANDREJ ROTH, IVAN MILAS, DANKO VELIMIR VRDOLJAK, ZVONIMIR ZORE, MIRKO GULAN and MLADEN STANEC

Department of Surgical Oncology, University Hospital for Tumors, University Hospital Center Sestre milosrdnice, Zagreb, Croatia.

Summary

Invasive breast cancer is a heterogeneous disease which occurs with different clinical presentations, pathohistological characteristics and clinical course. Most common types are invasive ductal carcinoma not otherwise specified (IDC-NOS, 70-80%) and invasive lobular carcinoma (5 – 15%). Systemic therapy of breast carcinomas is mostly determined by their molecular classification, which is based on genetic research of NOS ductal breast cancer, without the inclusion of rare histological types. Since some rare breast tumors have excellent prognosis despite unfavorable molecular characteristics, when deciding on the optimal treatment, both molecular and prognostic characteristics should be considered. Tumors of non-epithelial origin, such as sarcomas, lymphomas and phyllodes tumors also appear in breasts.

KEY WORDS: *rare breast carcinoma, molecular classification, prognosis, non-epithelial tumors*

RIJETKI TUMORI DOJKE

Sažetak

Karcinom dojke je heterogena bolest s raznolikom kliničkom slikom, patohistološkim karakteristikama i kliničkim tijekom. Najčešći tipovi karcinoma dojke su invazivni duktalni karcinom (IDC-NOS, 70-80 %) i invazivni lobularni karcinom (5-15%). Sustavno liječenje karcinoma dojke temelji se na molekularnoj klasifikaciji, koja je osnovana na genetskim istraživanjima NOS karcinoma, bez uključivanja rijetkih karcinoma dojke. Kako su neki rijetki tumori unatoč nepovoljnim molekularnim karakteristikama vrlo dobre prognoze, pri odlučivanju o načinu liječenja rijetkih tumora dojki, osim molekularnih, potrebno je uzeti u obzir i prognostičke karakteristike tih tumora. U dojkama se pojavljuju i tumori neepitelnog porijekla, poput sarkoma, limfoma i phyllodes tumora.

KLJUČNE RIJEČI: *rijetki tumori dojki, molekularna klasifikacija, prognoza, neepitelni tumori*

1. INTRODUCTION

Apart from malignant tumors of the skin, breast cancer is the most common malignant tumor in women. Invasive breast cancer is a heterogeneous disease which occurs with different clinical presentations, pathohistological characteristics and clinical course. Most cancers originate from the epithelium of the terminal ductal lobular unit. Predominant histological type is defined as an invasive ductal carcinoma not otherwise specified, IDC-NOS, which accounts for 70-80 % of all breast cancers. The second most common type of epithelial cancer is invasive lobular carcinoma, which makes 5 – 15 % of all breast cancers (1) However, there is still a significant number of breast cancer types which are less common but are clearly defined in the World Health Organization classification.

Intrisnic classification of breast cancer into five subtypes, which determines the choice of ad-

Table 1.

RARE EPITHELIAL BREAST CANCERS ACCORDING TO PROGNOSTIC CHARACTERISTICS

Good prognosis		Intermediate prognosis	Poor prognosis	Insufficient prognostic data
HR positive	HR negative			
Tubular carcinoma Cribiform carcinoma "Pure" mucinous carcinoma Invasive solid papillary carcinoma Solid neuroendocrine carcinoma	Medullary carcinoma Secretory carcinoma Adenoid cystic carcinoma Acinic cell carcinoma	Apocrine carcinoma	Pleomorphic variant of lobular carcinoma Invasive micropapillary carcinoma Metaplastic carcinoma Neuroendocrine small cell carcinoma Lipid rich carcinoma	Glycogen-rich clear-cell carcinoma of the breast Oncocytic carcinoma (malignant oncocytoma) Sebaceal carcinoma

juvant treatment (2), is defined based on genetic research of NOS ductal breast cancer, without the inclusion of rare histological types. However, without knowledge of rare histological types, some prognostically favorable rare breast cancers may be erroneously classified among the group of prognostically unfavorable tumors due to their immunohistochemical characteristics, which may result in unnecessary aggressive adjuvant treatment. Therefore, when deciding on the optimal treatment of rare breast cancer, both molecular and prognostic characteristics of rare breast cancers should be considered. However, due to a very low incidence, there are still no specific treatment recommendations for some breast tumors. It is also extremely important to stress known differences in the clinical course of rare tumors and connect all published data on rare tumors with the present molecular classification of breast cancers.

Apart from carcinomas, tumors of non-epithelial origin, which will be described later in this article, also appear in breasts.

2. RARE EPITHELIAL MALIGNANT BREAST TUMORS

2.1. Pure tubular carcinoma

Pure tubular carcinoma is very rare (less than 2% of invasive breast carcinoma) and appears more often in elderly patients. They are most commonly small and regional lymph nodes are rarely affected (3).These tumors are almost always ER and PR positive, well differentiated and HER-2 negative. The prognosis for pure tubular carcinoma is excellent, and local recurrence is rare. They are most commonly treated with breast-conserving surgery followed by irradiaton (4). Due to the excellent prognosis, the need for determining the axillary stage of the disease is questionable (3). However, the incidence of axillary metastases can be found on 4 – 17 % of cases (,6). SLNB can be considered in patients where positive test results of lymph nodes could influence the choice of adjuvant treatment. Finally, survival of patients with tubular carcinoma is similar to the survival of the general population and there is no evidence that the addition of adjuvant treatment for positive SLN affects survival.[3]

2.2. Invasive cribiform carcinoma

Invasive cribiform carcinoma (ICC) is rare (up to 3.5% of all breast cancers). The tumor is often low graded and slowly growing. It is often difficult to diagnose it radiologically so it is frequently discovered as a palpable mass. It is most often ER and PR positive and HER-2 negative. The prognosis is excellent, similar to life expectancy of general population (7). Distant metastases are rarely found. There is no clear specific treatment for this cancer type.

2.3. Mucinous carcinoma

Mucinous carcinoma has low frequency (1-4% of all breast cancers), with a better prognosis than invasive ductal carcinoma (8). It is characterized by abundant production of intra- and extracellular mucin. Mucinous carcinoma is divided into pure and mixed type. The pure type contains above 90% mucin-producing cells, while the mixed type (50% - 90% purity) also contains invasive ductal carcinoma cells which do not produce mucin (9). The pure type is more often well differentiated and has a higher incidence of positive ER and PR. Mucinous carcinoma shows a lower

incidence of lymphadenopathy in relation to invasive ductal carcinoma (10). It is usually diagnosed in older age group (median 71 years) (10). Mucinous carcinoma clinically manifests as a palpable mass with the lobular lesion clearly visible on the mammogramy. Isoechogenicity on ultrasound also makes it difficult to detect the tumor (11). MRI may be decisive in diagnostics as it shows some typical characteristics of this cancer type (12,13). Due to its benign appearance, mucinous carcinoma is often diagnosed late, but late diagnosis does not worsen the clinical outcome (14). Five, ten,fifteen and twenty-year survival is respectively 94 %, 89 %, 85%, and 81 % (15). Axillary metastatic lesions are a negative prognostic factor and appear more commonly in the mixed type. In tumors smaller than 1 cm axillary lymph nodes are affected in less than 5% of cases (6). However, in those cases a SLNB is recommended,since affection of lymph nodes is the most important risk factor of poor prognosis. Patients with pure mucinous carcinoma without invasion of the skin are candidates for breast conserving surgery. Adjuvant systemic therapy is based on treatment recommendations for common breast cancers (10).

2.4. Solid papillary carcinoma

Solid papillary carcinoma makes up 1.7% of all breast cancers. It is characterized by a round node with clear margines and low grade ductal cells divided by fibrovascular septums. Solid papillary carcinomas often exhibit neuroendocrine and mucinous differentiation (16). The tumors are mostly ER and PR positive and HER2 negative. A clinical examination reveals a centrally located mass or a bloody discharge from the nipple in elderly women. On mammography, the tumor most commonly appears as a soft tissue mass with calcifications present in less than 50 % of the cases (17). In tumors without invasive components the prognosis is excellent (16). There are still no specific treatment guidelines for solid papillary carcinoma.

2.5. Neuroendocrine carcinoma

Neuroendocrine carcinoma of the breast is very rare (less than 0.1% of all breast cancers, less than 1% of all neuroendocrine tumors) (18). It is characterized by neuroendocrine markers (mainly chromogranin or synaptophysin) in more than 50% of cells (19, 20). Histologically, neuroendocrinecarcinomas are divided into four subtypes: small cell carcinoma (SCC), large cell carcinoma, solid neuroendocrine carcinoma and atypical carcinoid tumors. Neuroendocrine carcinoma is clinically diagnosed as a palpable mass with clear margins on images (21). The tumors are most commonly hormone dependent and HER-2 negative. Immunoprofile of solid neourendocrine carcinoma usually corresponds to luminal A subtype, which is why it is assumed this tumor has good prognosis, which cannot be said with certainty due to very small number of cases. On the other hand, SCC is an ER positive tumor with worse prognosis. There are still no specific treatment strategies for the treatment of neuroendocrine tumors of the breast.

2.6. Medullary carcinoma

Medullary carcinoma accounts for 5% of all breast cancers (3). It can be divided into classical (lymphocytic infiltrate involves the entire lesion) (22), and atypical (proportion of lymphocytic infiltrate is reduced) (23,24). Medullary carcinoma is mostly diagnosed at a younger age compared to ductal invasive carcinoma. The average age of detection is between 45 and 52 years (10). Clinical examination reveals a soft consistency tumor with sharp edges. ER and HER2 are mostly negative and p53 mutation is positive(10). Although it is highly proliferative, the prognosis for medullary carcinoma is more favorable compared to invasive ductal carcinoma (25). Regional lymph node involvement is low (from 16% to 21%) in relation to other types of breast cancer (10). BRCA1 positive tumors with high grade, negative hormone receptors and p53 somatic mutation have a poor prognosis (24). Such patients usually have pathological N stage. Recommended treatment includes breast conserving surgery, axillary staging and adjuvant treatment.

2.7. Secretory breast carcinoma

Secretory breast carcinoma accounts for less than 0.15% of all types of breast cancer. It is characterized by younger age of onset and indolent course. Histological secretory breast cancer pertains to the phenotypic spectrum of basal-like breast carcinoma, which are characterized by presence of intracellular and extracellular secre-

tory material. It is most commonly detected as a painless and hard mass. The carcinoma is mostly ER, PR and HER2 negative. Basal-like breast cancer marker (epidermal growth factor receptor) is present in 90% of the cases. Reported frequency of axillary metastases is 20-30%. Nodal involvement is rare in children and adolescents. Treatment is primarily surgical, including SLNB. The efficiency of adjuvant chemotherapy and radiation is not clear yet. This tumor is associated with high rate of long-term survival (26).

2.8. Adenoid cystic carcinoma

Adenoid cystic carcinoma (ACC) of the breast is a very rare tumor responsible for less than 0.1% of all breast cancers (27). ACC of the breast can be classified as cribriform, tubular and solid. The cribriform type is most common. The mean age of patients is 50-65 years (28). This tumor presents as a 2-3 cm sized nodule. ER, PR and HER 2 are mostly negative (27). The prognosis is good. Lymphadenopathy and distant dissemination are rare (27,29,30). Patients with negative hormone receptors have a better prognosis. ACC is best treated with surgery and adjuvant irradiation. Systemic therapy is not recommended (27,28).

2.9 Acinic cell carcinoma

Acinic cell carcinoma was described in 1996 as the equivalent of an identical parotid gland tumor (31). It is very rare, as only 19 cases have been documented so far (32,33). The average age of patients is 56 years (34,35). Histologically, it is characterized by infiltrative growth of small glandular structures made of cells similar to acinic cells of salivary glands. ER, PR and HER2 are negative. The prognosis is usually good. Due to the low incidence, there is no consensus on the optimal treatment choices.

2.10. Apocrine carcinoma

Apocrine breast carcinoma is microscopically defined as a type of invasive ductal breast carcinoma accounting for 0.3-4% of all breast cancers (36,37). Apocrine breast carcinoma is clinically manifested as a palpable, often multifocal/multicentric mass. The tumor usually expresses the androgen receptor (AR), and is ER and PR negative (37). On the other hand, HER2 is often overexpressed (36). This tumor has a good prognosis (38). Apocrine HER2 negative carcinoma has a better prognosis than non-apocrine triple negative carcinoma of the breast due to lower proliferation rate. There are no specific treatment recommendations for apocrine breast cancer. Hormonal therapy targeted against AR may be applied. Adjuvant chemotherapy is recommended for triple negative apocrine carcinoma (36).

2.11 Metaplastic carcinoma

Metaplastic carcinoma accounts for 1% of all breast cancers and is characterized by presence of two cell lines, most commonly malignant epithelial and mesenchymalcomponents (39,40). Average size at the time of diagnosis is 3.5- 5 cm (41-44); it rarely affects axillary lymph nodes (42,45). The mean age of detection is over 50 years of age(41,43,46). Hormonal receptors and HER2 are rarely positive (39). This tumor has a high local reccurence and metastatic potential, and therefore, a poor prognosis. Mastectomy with axillary dissection is a preffered surgical choice in the literature (1,39,43). Adjuvant treatment is based on clinical guidelines for invasive adenocarcinoma of the breast(39).

2.12 Pleomorphic variant of lobular carcinoma (PLC)

Pleomorphic variant of lobular carcinoma is a rare variant of invasive lobular carcinoma which constitutes less than 1% of all breast cancers (47). The mean age of detection is 58.9 years with frequent multifocal and bilateral localization (47,48). The tumor is characterized by higher levels of Ki67, low ER and PR expression and high HER2 amplification. This tumor is aggressive and has a poor prognosis. The treatment is similar to other invasive lobular carcinomas.

2.13 Papillary breast carcinoma

Papillary breast carcinoma accounts for 0.5% of all invasive breast cancers. The tumor is composed of epihelialcells arranged around fibrovascular cores, forming a circumscribed mass (49). Papillary breast carcinoma can be a divided into several histologically subtypes: in situ ductal carcinoma which grows inside intraductal papiloma, in situ papillary ductal carcinoma, incapsulated

papillary carcinoma, solid and invasive papillary carcinoma. Unlike benign intraductal papilloma, papillary carcinoma does not have a layer of myoepithelial cells within the papilla. These tumors clinically manifest with a bloody discharge, palpable lump or suspicious mammographic findings (50). Hormonal receptors are mostly positive and HER2 is negative. The tumor has a good prognosis. There is no specific treatment for papillary carcinoma for now.

3. RARE NON-EPITHELIAN BREAST MALIGNANCIES

3.1 Sarcomas

Sarcomas account for less than 1% of all breast tumors. Various histological types have been described. They most commonly appear in the 5th and 6th decade as palpable, painless lumps (51). Tumor size varies greatly. The prognosis depends on tumor size and histological type. The tumor can spread directly or through the blood (52,53). Lymphatic dissemination is very rare (54,55). Treatment is multidisciplinary and includes surgery, chemotherapy and radiation.

3.1.1 Primary breast lymphoma (PBL)

Primary breast lymphoma (PBL) denotes malignant lymphomas which primarily appeared in the breast in the absence of earlier discovered lymphoma in other location. PBL represents less than 0.5% of all malignant lymphomas (56). B-cell type is more common than T-cell type. A painless, fast-growing mass is dominant in the clinical setting (56). Differentiation of primary and secondary lymphoma is difficult, and the following criteria are used:

1. availability of adequate tumor sample
2. presence of both breast tissue and lymphomatous infiltrate in the sample
3. no distanced disease and previous extramammary lymphoma
4. ipsilateral axillary lymph node involvement is acceptable (57)

Treatment includes surgery, chemotherapy and radiation. Chemotherapeutic treatment of stage 2 is defined and can be found in the literature. Irradiation is used for local control (56). Five-year survival is 53%. Local relapse occurs in 12% of patients, and systemic relapse occurs in 55% of patients. Favorable prognostic factors are:early stage, applicable breast conserving surgery, applied radiation and applied combined treatment (58).

3.1.2 Phyllodes tumor

Phyllodes tumor accounts for less than 1% of all breast tumors. The tumor is biphasic, consisting of a stromal and epithelial components. Phyllodes tumor occurs in benign, borderline and malignant subtypes. It most commonly appears as a fast-growing lump in women in their 40s and 50s. Phyllodes tumors are similar to fibroadenomas on ultrasound, mammography and even on core biopsy specimens. Recurrences usually occur locally. Recurrence risk factors are tumor positive edges, proliferation of connective tissue into the surrounding breast tissue and tumor necrosis. Hematogenous metastases are very rare and occur most commonly in the lungs. Mortality due to phyllodes tumor is very low (2%). The treatment of choice is surgery with a margin greater than 1 cm. Mastectomy is needed only if it is not possible to achieve negative margins with breast conserving surgery. Since phyllodes tumor rarely metastasizes to the axillary lymph nodes, removal of axillary lymph node is not necessary unless they are clinically positive. The role of adjuvant irrradiation is not completely clear and further research is needed. Although epithelial components are often positive for hormone receptors, efficacy of endocrine treatment has not been proven so far. There is also no evidence of the effectiveness of chemotherapy. Local recurrences are treated by a wide excision with negative surgical margins, and some members of the NCCN committee recommend local radiation after the resection of recurrence (59,60).

4. CONCLUSION

Despite breast conserving treatment, survival in histologically favorable subtypes is very high, even comparable to survival of women without breast cancer. Patients with tubular, mucinous and medullary carcinoma, and malignant phyllodes tumor have such low death rates that an even more conservative approach is recommended in some cases. Since some of these tumors are

very rare, specific treatment recommendations still cannot be defined. For that reason treatment of rare carcinoma is still based on treatment guidelines for common breast cancers. However, when deciding on the choice of treatment, known clinical characteristics of rare tumors need to be taken into consideration, and individualized multidisciplinary approach should be adopted.

REFERENCES

1. Yerushalmi R, Hayes MM, Gelmon KA. Breast carcinoma – rare types: review of the literature. Ann Oncol. 2009;20:1763–1770.
2. Goldhirsch A et al. Personalizing the treatment of women with early breast cancer: highlights of the St Gallen International Expert Consensus on the Primary Therapy of Early Breast Cancer 2013. Ann Oncol. 2013; 24: 9:2206-2223.
3. Diab SG, Clark GM, Osborne CK, Libby A, Allred DC, Elledge RM. Tumor characteristics and clinical outcome of tubular and mucinous breast carcinomas. J Clin Oncol. 1999;17:1442–1448.
4. Vo T, Xing Y, Meric-Bernstam F, et al. Long-term outcomes in patients with mucinous, medullary, tubular, and invasive ductal carcinomas after lumpectomy. Am J Surg. 2007;194:527–531.
5. Soares A, Gonçalves J, Azevedo I, et al. Lobular ectopic breast carcinoma: a case-report. Rep Pract Oncol Radiother. 2013;18:189–191.
6. Maibenco DC, Weiss LK, Rawlish KS, Severson RK. Axillary lymph node metastases associated with small invasive breast carcinomas. Cancer. 1999;85: 1530–1536.
7. Colleoni M, Russo L, Dellapasgua S. Adjuvant therapies for special types of breast cancer. Breast. 2011; Suppl 3:S153–S157.
8. André S, Cunha F, Bernardo M, Meneses e Sousa J, Cortez F, Soares J. Mucinous carcinoma of the breast: a pathologic study of 82 cases. J Surg Oncol. 1995; 58:162–167.
9. Tan PH, Tse GMK, Bay BH. Mucinous breast lesions: diagnostic challenges. J Clin Pathol.2008;61:11–19.
10. Reimer T. Management of rare histological types of breast tumours. Breast Care (Basel). 2008;3:190–196.
11. Memis A, Ozdemir N, Parildar M, et al. Mucinous (colloid) breast cancer: mammographic and US features with histologic correlation. Eur J Radiol. 2000; 35(1):39-43.
12. Kawashima M, Tamaki Y, Nonaka T, et al. MR imaging of mucinous carcinoma of the breast. Am J Roentgenol. 2002;179(1):179-183.
13. Okafuji T, Yabuuchi H, Sakai S, et al. MR imaging features of pure mucinous carcinoma of the breast. Eur J Radiol. 2006;60(3):405-413.
14. Dhillon R, Depree P, Metcalf C, Wylie E. Screen detected mucinous breast carcinoma: potential for delayed diagnosis. Clin Radiol. 2006;61:423–430.
15. Di Saverio S, Gutierrez J, Avisar E. A retrospective review with long term follow up of 11,400 cases of pure mucinous breast carcinoma. Breast Cancer Res Treat. 2008;111(3):541-547.
16. Saremian J, Rosa M. Solid papillary carcinoma of the breast: a pathologically and clinically distinct breast tumor. Arch Pathol Lab Med. 2012;136:1308–1311.
17. Brookes MJ, Bourke AG. Radiological appearances of papillary breast lesions. Clin Radiol. 2008;63: 1265–1273.
18. Singh S, Aggarwal G, Kataria SP, Kalra R, Duhan A, Sen R. Primary neuroendocrine carcinoma of breast. J Cytol. 2011;28:91–92.
19. Sapino A, Righi L, Cassoni P, Papotti M, Pietribiasi F, Bussolati G. Expression of the neuroendocrine phenotype in carcinomas of the breast. Semin Diagn Pathol. 2000;17:127–137.
20. Moriya T, Kanomata N, Kozuka Y, et al. Usefulness of immunohistochemistry for differential diagnosis between benign and malignant breast lesions. Breast Cancer. 2009;16:173–178.
21. Stita W, Trabelsi A, Gharbi O, Mokni M, Korbi S. Primary solid neuroendocrine carcinoma of the breast. Can J Surg. 2009;52:E289–E290.
22. Ridolfi RL, Rosen PP, Port A, Kinne D, Mike V. Medullary carcinoma of the breast: a clinicopathologic study with 10 year follow up. Cancer. 1977;40:1365–1385.
23. Lakhani SR. The pathology of familial breast cancer: morphological aspects. Breast Cancer Res. 1999;1: 31–35.
24. Marcus JN, Watson P, Page DL, et al. Hereditary breast cancer: pathobiology, prognosis, and BRCA1 and BRCA2 gene linkage. Cancer. 1996;77:697–709.
25. Pedersen L, Holck S, Schiodt T. Medullary carcinoma of the breast. Cancer Treat Rev. 1988;15:53–63.
26. Li D, Xiao X, Yang W, et al. Secretory breast carcinoma: a clinicopathological and immunophenotypic study of 15 cases with a review of the literature. Mod Pathol. 2012;25:567–575.
27. Khanfir K, Kallel A, Villette S, et al. Management of adenoid cystic carcinoma of the breast: a Rare Cancer Network study. Int J Radiat Oncol Biol Phys. 2012; 82:2118–2124.
28. Wang S, Ji X, Wei Y, Yu Z, Li N. Adenoid cystic carcinoma of the breast: review of the literature and report of two cases. Oncol Lett. 2012;4:701–704.
29. Millar BA, Kerba M, Youngson B, Lockwood GA, Liu FF. The potential role of breast conservation surgery and adjuvant breast radiation for adenoid cystic carcinoma of the breast. Breast Cancer Res Treat. 2004; 87:225–232.
30. Ro JY, Silva EG, Gallager HS. Adenoid cystic carcinoma of the breast. Hum Pathol. 1987;18:1276–1281.

31. Roncaroli F, Lamovec J, Zidar A, Eusebi V. Acinic cell-like carcinoma of the breast. Virchows Arch. 1996;429: 69–74.
32. Matoso A, Easley SE, Gnepp DR, Mangray S. Salivary gland acinar-like differentiation of the breast. Histopathology. 2009;54:262–263.
33. Damiani S, Pasquinelli G, Lamovec J, Peterse JL, Eusebi V. Acinic cell carcinoma of the breast: an immunohistochemical and ultrastructural study. Virchows Arch. 2000;437:74–81.
34. Tanahashi C, Yabuki S, Akamine N, Yatabe Y, Ichihara S. Pure acinic cell carcinoma of the breast in an 80-year-old Japanese woman. Pathol Int. 2007;57:43–46.
35. Hirokawa M, Sugihara K, Sai T, et al. Secretory carcinoma of the breast: a tumour analogous to salivary gland acinic cell carcinoma? Histopathology. 2002; 40:223–229.
36. Tsutsumi Y. Apocrine carcinoma as triple-negative breast cancer: novel definition of apocrine-type carcinoma as estrogen/progesterone receptor-negative and androgen receptor-positive invasive ductal carcinoma. Jpn J Clin Oncol. 2012;42:375–386.
37. Ogiya A, Horii R, Osako T, et al. Apocrine metaplasia of breast cancer: clinicopathological features and predicting response. Breast Cancer. 2010;17:290–297.
38. Vranic S, Tawfik O, Palazzo J, et al. EGFR and HER-2/neu expression in invasive apocrine carcinoma of the breast. Mod Pathol. 2010;23:644–653.
39. Shah DR, Tseng WH, Martinez SR. Treatment options for metaplastic breast cancer. ISRN Oncol. 2012; 2012:706162.
40. Esbah O, Turkoz FP, Turker I, et al. Metaplastic breast carcinoma: case series and review of the literature. Asian Pac J Cancer Prev. 2012;13:4645–4649.
41. Oberman HA. Metaplastic carcinoma of the breast: a clinicopathologic study of 29 patients. Am J Surg Pathol. 1987;11:918–929.
42. Chao TC, Wang CS, Chen SC, ChenMF. Metaplastic carcinomas of the breast. J SurgOncol. 1999;71:220–225.
43. Rayson D, Adjei AA, Suman VJ, Wold LE, Ingle JN. Metaplastic breast cancer: prognosis and response to systemic therapy. Ann Oncol. 1999;10:413–419.
44. Luini A, Aguilar M, Gatti G. et al. Metaplastic carcinoma of the breast, an unusual disease with worse prognosis: the experience of the European Institute of Oncology and review of the literature. Breast Cancer Res Treat. 2007;101:349–353.
45. Beatty JD, Atwood M, Tickman R, Reiner M. Metaplastic breast cancer: clinical significance. Am J Surg. 2006;191:657–664.
46. Kaufman MW, Marti JR, Gallager HS, Hoehn JL. Carcinoma of the breast with pseudosarcomatous metaplasia. Cancer. 1984;53:1908–1917.
47. Gupta A, Sharma N, Jha AK, Gandhi A, Singh UR. Pleomorphic variant of lobular carcinoma breast: a rare case report with review of the literature. J Cancer Res Ther. 2012;8:320–322.
48. Middleton LP, Palacios DM, Bryant BR, Krebs P, Otis CN, Merino MJ. Pleomorphic lobular carcinoma: morphology, immunohistochemistry, and molecular analysis. Am J Surg Pathol. 2000;24:1650–1656.
49. McCulloch GL, Evans AJ, Yeoman L, et al. Radiological features of papillary carcinoma of the breast. Clin Radiol. 1997;52:865–868.
50. Pal SK, Lau SK, Kruper L, et al. Papillary carcinoma of the breast: an overview. Breast Cancer Res Treat. 2010;122:637–645.
51. Barnes L, Pietruszka M. Sarcomas of the breast: a clinicopathologic analysis of ten cases. Cancer. 1977;40: 1577–1585.
52. Adem C, Reynolds C, Ingle JN, Nascimento AG. Primary breast sarcoma: clinicopathologic series from the Mayo Clinic and review of the literature. Br J Cancer. 2004;91:237–241.
53. Sandhya B, Babu V, Parthasarathy G, Kate V, Ananthakrishnan N, Krishnan R. Primary leiomyosarcoma of the breast: a case report and review of literature. Indian J Surg. 2010;72:286–288.
54. Lee JY, Kim DB, Kwak BS, Kim EJ. Primary fibrosarcoma of the breast: a case report. J Breast Cancer. 2011;14:156–159.
55. Madigan MN, Dempsey PJ, Krishnamurthy S. Ultrasound-guided fine needle aspiration cytodiagnosis of leiomyosarcoma metastatic to the breast: a case report. Acta Cytol. 2003;47:783–786.
56. Meerkotter D, Rubin G, Joske F, Angunawela P, Khalafallah A. Primary breast lymphoma: a rare entity. J Radiol Case Rep. 2011;5:1–9.
57. Wiseman C, Liao KT. Primary lymphoma of the breast. Cancer. 1972;29:1705–1712.
58. Jeanneret-Sozzi W, Taghian A, Epelbaum R, et al. Primary breast lymphoma: patient profile, outcome and prognostic factors. A multicentre Rare Cancer Network study. BMC Cancer. 2008;8:86.
59. Macdonald OK, Lee CM, Tward JD, Chappel CG, Gaffney DK. Malignant phyllodes tumor of the female breast. Cancer. 2006;107:2127–2133.
60. Chaney AW, Pollack A, Mcneese MD, et al. Primary treatment of cystosarcoma phyllodes of the breast. Cancer. 2000;89:1502–1511.

Author's address: Ilija Guteša, Department of Surgical Oncology, University Hospital for Tumors, University Hospital Center Sestre milosrdnice, Ilica 197, 10000 Zagreb, Croatia. E-mail: ilija.gutesa@gmail.com