JPPIPA 10(11) (2024)

Jurnal Penelitian Pendidikan IPA

Journal of Research in Science Education

http://jppipa.unram.ac.id/index.php/jppipa/index

Histopathological Features and Diagnosis of Breast Cancer

Ghina Shadrina Rienti Sepestian[1], Fathul Djannah[1*]

[1] Medical Education Study Program, Faculty of Medicine and Health Sciences, Universitas Mataram, Lombok, Indonesia

Received: July 10, 2024
Revised: September 19, 2024
Accepted: November 25, 2024
Published: November 30, 2024

Corresponding Author:
Fathul Djannah
fdjannah354@gmail.com

DOI: 10.29303/jppipa.v10i11.8469

Abstract: In Indonesia, the high number of breast cancer cases is not always followed by complete clinical and histopathological determination, even though clinical and histopathological staging is needed to determine the diagnosis and further management. Breast cancer is a malignant mass originates from the uncontrolled division of cells in breast tissue Breast cancer or mammary carcinoma is a lump that grows and develops abnormally in the cells and tissues located in the breast, such as the fat tissue and connective tissue in the breast, ducts and lobules. The histopathological examination procedure is that the patient must undergo a biopsy. Biopsy results can be used to diagnose breast cancer and also monitor the success of therapy. Mammary carcinoma can spread to surrounding tissue or to other organs through blood vessels. Breast cancer is the most common cancer in Indonesia. The prognosis of breast cancer is determined by the 5 years survival rate. The survival rate for cancer sufferers in Indonesia is low compared to other developing countries, namely 51.07%. This research is in the form of a literature review with 14 papers as references. The results obtained were that invasive ductal carcinoma was the most common mammary carcinoma and grade II-III was found to be the dominant grade.

Keywords: Breast cancer; Diagnosis; Histopathological features; Mammary carcinoma

Introduction

Breast cancer is a malignancy that originates from glandular cells and breast supporting tissue, excluding breast skin (Rädler et al., 2021; Smolarz et al., 2022). Breast cancer is also said to be a malignant proliferation of epithelial cells that line the ducts or lobes of the breast (Tabár et al., 2023). Breast cancer is a malignant mass that originates from the uncontrolled division of cells in breast tissue. Breast cancer can originate from the breast tissue itself or from other tissue which is the result of metastases from other cancers (Bonni et al., 2024; Fares et al., 2020; Huysentruyt & Seyfried, 2010; Ruscitto et al., 2022). There is no single specific cause of breast cancer, instead a series of genetic, hormonal and possibly environmental factors can contribute to the occurrence of this cancer (Giannandrea & Fargnoli, 2017; Rudolph et al., 2016; Riggio et al., 2021).

Evidence continues to emerge showing that genetic changes are associated with breast cancer, but what causes the genetic changes is still unknown (Barili et al., 2024). These genetic changes include changes or mutations in normal genes, and protein associations that either suppress or promote breast development. There are several methods used to diagnose breast cancer. Until now, the gold standard for diagnosing breast cancer is histopathological examination. Histopathological examination can determine the type of breast cancer. The histopathological examination procedure is that the patient must undergo a biopsy. Biopsy results can be used to diagnose breast cancer and also monitor the success of therapy.

The histopathological picture in question is microscopic morphology of cancer tissue from anatomical pathology which is an important parameter and the gold standard. Breast cancer or mammary carcinoma is a lump that grows and develops

How to Cite:
Sepestian, G. S. R., & Djannah, F. (2024). Histopathological Features and Diagnosis of Breast Cancer. *Jurnal Penelitian Pendidikan IPA*, *10*(11), 793–798. https://doi.org/10.29303/jppipa.v10i11.8469

abnormally in the cells and tissues located in the breast, such as the fat tissue and connective tissue in the breast, ducts and lobules. Mammary carcinoma can spread to surrounding tissue or to other organs through blood vessels (Barroso-Sousa & Metzger-Filho, 2016; Hrizat & Brachtel, 2022). Breast cancer is the most common cancer in Indonesia according to (Ng et al., 2023; Sinaga et al., 2018), the prognosis of breast cancer is determined by the 5 years survival rate. The survival rate for cancer sufferers in Indonesia is low compared to other developing countries, namely 51.07%.

Method

Collecting some relevant literature from various references is the literature study method used in this writing. The theme raised was cholangiocarcinoma and guideline revision. Google Scholar and the National Center of Biotechnology Information (NCBI) search engine were used to conduct literature research with keywords such as "carcinoma mammae", "breast cancer", "histological features", "breast cancer diagnosis", and "histopathological examination". A total of 14 articles were used as references from various databases, including ScienceDirect, Researchgate, Proquest, and PubMed.

Results and Discussion

Epidemiology

Breast cancer is the most common cancer in Indonesia covering 16.20% of all cancer cases in Indonesia, namely 66.271. This cancer occurs more often in women than men. Most new cases of cancer were caused by breast cancer (30.10%). Mortality was highest in women and third highest in both men and women. According to (Goliwas et al., 2017), abnormal tissue and cell growth in the breast is divided into benign and malignant. Benign tumors consist of adenosis, fibroadenoma, phyllodes tumor and tubular adenoma. Based on histopathology, breast cancer is divided into ductal carcinoma in situ and invasive, mucinous carcinoma, lobular carcinoma, and papillary carcinoma.

Clinical Manifestations

The clinical manifestations of breast cancer vary between sufferers. Signs that often appear are a painless lump in the breast, retraction of the breast or nipple. Peau d'orange or thickened breast skin resembles orange peel. There is inflammation, discharge from the nipples, and asymmetrical breasts. Enlarged lymph nodes are also found in cases of breast cancer (So et al., 2021).

Histopathological Features

Histopathological examination is carried out by biopsy. Accuracy of the interpretation of histological images is a priority in the choice of biopsy technique today. Core biopsy is a diagnostic choice because of its ability to classify tumors and the number of samples obtained. The highest accuracy can be achieved by carrying out FNAB, but the classification obtained is only limited to whether it is benign or malignant (Yersal, 2014). The subtypes of breast cancer that are often found are invasive ductal carcinoma and grade II-III cancer.

Invasive ductal cancer was the highest number of cases with a percentage of 61.70% or 29 people in research at the anatomical pathology laboratory at M. Djamil Hospital Padang 2018. Cases of invasive lobular carcinoma were 13 people or 27.70% and breast cancer with other histopathology was 4 people or 8.50%. The highest histopathological grade was grade II breast cancer (74.40%). Mammary carcinoma, especially invasive ductal carcinoma and invasive lobular carcinoma, occurs mostly at the age of 26-65 years. The risk of occurrence is slight at age under 30 years and decreases after menopause (Huang et al., 2023; Kundu & Acharya, 2024). The most common subtype of breast cancer in research at Sanglah General Hospital Denpasar 2015-2016 was invasive ductal carcinoma, 84% or 483 cases. The highest degree obtained was grade III with 273 cases (47.47%) (Royce Sadler, 2014; Schindler et al., 2017).

Likewise, research at RSUD Prof. Dr. Margono Soekarjo Semarang 2022, invasive ductal carcinoma was found the most, namely 74.40% or 93 cases and cases with grade II were 65 people or 52% (Elsaeid et al., 2019). In contrast, cases of invasive ductal carcinoma in RSUD Pasar Minggu Jakarta 2020-2023 were only 7.10%, tubular carcinoma (0.80%), mucinous carcinoma (1.70%), invasive micropapillary carcinoma (2.5%) and invasive papillary (1.30%), lobular carcinoma in situ (0.40%), ductal carcinoma in situ (3.80%), and 77% of cases of carcinoma no special type. Of the 122 patients diagnosed, 83% had grade III, 1 patient had grade I (0.70%), 24 patients had grade 2 (16.30%) (Peters et al., 2023; Martinez-Calle et al., 2021; Reardon & Arvold, 2014; Sukmana et al., 2021). Histopathological evaluation of mammary carcinoma is carried out by analyzing the components obtained, such as cell type of origin, anaplasia, mitotic rate, necrosis, angiogenesis and invasion of surrounding tissue (Naponelli et al., 2024; Zarychta & Ruszkowska-Ciastek, 2022). The following are the subtypes of mammary carcinoma with their histopathological profiles:

Ductal carcinoma in situ

Cancer cells were confined to the ducts, showed varying degrees of atypia (grades I–III), and had a comedo, solid, or papillary growth pattern. Abnormal cells are found in the ductal lumen and resemble comedone paste and are solid in shape. Finger-like projections into the duct are also found in ductal carcinoma in situ (Chiang et al., 2016; Tay & Tan, 2021).

Invasive ductal carcinoma

Cancer cells originate in the duct and spread to the surrounding tissue. Also shows a degree of atypia (grade I–III), and has an infiltrating, desmoplastic, or neuroendocrine growth pattern in the form of hormones. Desmoplastic occurs when the tissue around the abnormal growth turns solid as a reaction to inflammation. The most common and aggressive type of breast carcinoma is invasive ductal carcinoma (Amin et al., 2017).

Mucinous carcinoma

Mucin or slime is produced by cancer cells with a pool or signet ring growth pattern. Pool looks like a pool because of the buildup of mucin inside the cancer cells. By mucin, cancer cells are pushed to the edge and resemble a signet ring, which is called a signet ring. Mucinous carcinoma is a rarer subtype of mammary carcinoma with a good prognosis (Budzik et al., 2021; Marrazzo et al., 2020).

Lobular carcinoma

Lobular carcinoma cells originate from the lobules and are invasive with thin atypia and an infiltration pattern, called "single file" or "Indian file" (Alkhafaji et al., 2024; Davis et al., 2022; Koufopoulos et al., 2022; Makhlouf et al., 2024).

Papillary carcinoma

Papillary carcinoma shows papillary growth (solitary, multiple, or branching), cytology (cell atypia, nuclear pleomorphism, hyperchromasia, and mitosis), fibrovascular stroma (lymphocytic inflammatory infiltrate), necrosis, and vascular infiltration (Missaoui et al., 2023; Rossi et al., 2021).

Conclusion

Breast cancer (mammary carcinoma) is the most common cancer in Indonesia and is the leading cause of death in women. The clinical manifestations vary, but a painless lump in the breast is the most common sign. The diagnosis of breast cancer is made by histopathological examination of the biopsy results. Based on the histopathological appearance, mammary carcinoma is classified into several subtypes, with invasive ductal carcinoma and grade II-III cancer being the most frequently found subtypes. Histopathological evaluation is carried out by analyzing the components obtained, such as cell type of origin, anaplasia, mitotic rate, necrosis, angiogenesis, and invasion of surrounding tissue. Knowledge of the histopathological features of mammary carcinoma is very important in determining the diagnosis, prognosis and appropriate therapy for patients.

Acknowledgments

Thank you to everyone who helped with this research so that the results could be published.

Author Contributions

Conceptualization, G. S. R. S.; methodology, F. D.; validation, G. S. R. S.; formal analysis, F. D.; investigation, G. S. R. S.; resources, F. D.; data curation, G. S. R. S.: writing—original draft preparation, F. D.; writing—review and editing, G. S. R. S.: visualization, F. D. All authors have read and agreed to the published version of the manuscript.

Funding

No external funding.

Conflict of Interest

There is no conflict of interest.

Reference

Alkhafaji, S., Wolf, D. M., Magbanua, M. J. M., J. Van 'T Veer, L., Park, J. W., Esserman, L., & Mukhtar, R. A. (2024). Circulating tumor cells in early lobular versus ductal breast cancer and their associations with prognosis. *Npj Breast Cancer*, *10*(1), 17. https://doi.org/10.1038/s41523-024-00623-9

Amin, M. B., Greene, F. L., Edge, S. B., Compton, C. C., Gershenwald, J. E., Brookland, R. K., Meyer, L., Gress, D. M., Byrd, D. R., & Winchester, D. P. (2017). The Eighth Edition AJCC Cancer Staging Manual: Continuing to build a bridge from a population-based to a more "personalized" approach to cancer staging. *CA: A Cancer Journal for Clinicians*, *67*(2), 93–99. https://doi.org/10.3322/caac.21388

Barili, V., Ambrosini, E., Bortesi, B., Minari, R., De Sensi, E., Cannizzaro, I. R., Taiani, A., Michiara, M., Sikokis, A., Boggiani, D., Tommasi, C., Serra, O., Bonatti, F., Adorni, A., Luberto, A., Caggiati, P., Martorana, D., Uliana, V., Percesepe, A., … Pellegrino, B. (2024). Genetic Basis of Breast and Ovarian Cancer: Approaches and Lessons Learnt from Three Decades of Inherited Predisposition Testing. *Genes*, *15*(2), 219. https://doi.org/10.3390/genes15020219

Barroso-Sousa, R., & Metzger-Filho, O. (2016). Differences between invasive lobular and invasive ductal carcinoma of the breast: Results and therapeutic implications. *Therapeutic Advances in Medical Oncology*, *8*(4), 261–266. https://doi.org/10.1177/1758834016644156

Bonni, S., Brindley, D. N., Chamberlain, M. D., Daneshvar-Baghbadorani, N., Freywald, A., Hemmings, D. G., Hombach-Klonisch, S., Klonisch, T., Raouf, A., Shemanko, C. S., Topolnitska, D., Visser, K., Vizeacoumar, F. J., Wang, E., & Gibson, S. B. (2024). Breast Tumor Metastasis and Its Microenvironment: It Takes Both Seed and Soil to Grow a Tumor and Target It for Treatment. *Cancers*, *16*(5), 911. https://doi.org/10.3390/cancers16050911

Budzik, M. P., Fudalej, M. M., & Badowska-Kozakiewicz, A. M. (2021). Histopathological analysis of mucinous breast cancer subtypes and comparison with invasive carcinoma of no special type. *Scientific Reports*, *11*(1), 5770. https://doi.org/10.1038/s41598-021-85309-z

Chiang, C.-L., Liang, H.-L., Chou, C.-P., Huang, J.-S., Yang, T.-L., Chou, Y.-H., & Pan, H.-B. (2016). Easily recognizable sonographic patterns of ductal carcinoma in situ of the breast. *Journal of the Chinese Medical Association*, *79*(9), 493–499. https://doi.org/10.1016/j.jcma.2016.03.009

Davis, A. A., Gerratana, L., Clifton, K., Medford, A. J., Velimirovic, M., Hensing, W. L., Bucheit, L., Shah, A. N., D'Amico, P., Reduzzi, C., Zhang, Q., Dai, C. S., Denault, E. N., Bagegni, N. A., Opyrchal, M., Ademuyiwa, F. O., Bose, R., Gradishar, W. J., Behdad, A., … Cristofanilli, M. (2022). Circulating tumour DNA characterisation of invasive lobular carcinoma in patients with metastatic breast cancer. *eBioMedicine*, *86*, 104316. https://doi.org/10.1016/j.ebiom.2022.104316

Elsaeid, Y. M., Elmetwally, D., & Eteba, S. M. (2019). Association between ultrasound findings, tumor type, grade, and biological markers in patients with breast cancer. *Egyptian Journal of Radiology and Nuclear Medicine*, *50*(1), 53. https://doi.org/10.1186/s43055-019-0048-1

Fares, J., Fares, M. Y., Khachfe, H. H., Salhab, H. A., & Fares, Y. (2020). Molecular principles of metastasis: A hallmark of cancer revisited. *Signal Transduction and Targeted Therapy*, *5*(1), 28. https://doi.org/10.1038/s41392-020-0134-x

Giannandrea, F., & Fargnoli, S. (2017). Environmental Factors Affecting Growth and Occurrence of Testicular Cancer in Childhood: An Overview of the Current Epidemiological Evidence. *Children*, *4*(1), 1. https://doi.org/10.3390/children4010001

Goliwas, K. F., Richter, J. R., Pruitt, H. C., Araysi, L. M., Anderson, N. R., Samant, R. S., Lobo-Ruppert, S. M., Berry, J. L., & Frost, A. R. (2017). Methods to Evaluate Cell Growth, Viability, and Response to Treatment in a Tissue Engineered Breast Cancer Model. *Scientific Reports*, *7*(1), 14167. https://doi.org/10.1038/s41598-017-14326-8

Hrizat, A., & Brachtel, E. (2022). Metastatic Breast Cancer: Cytology Diagnosis with Implications for Treatment. *Journal of Molecular Pathology*, *4*(1), 1–14. https://doi.org/10.3390/jmp4010001

Huang, S., Gongye, R., Zou, S., Hee, J. Y., & Tang, K. (2023). Menopausal status, age at menopause and risk of all-cause mortality among Chinese women: Findings from a 10-year prospective study. *BMJ Public Health*, *1*(1), e000332. https://doi.org/10.1136/bmjph-2023-000332

Huysentruyt, L. C., & Seyfried, T. N. (2010). Perspectives on the mesenchymal origin of metastatic cancer. *Cancer and Metastasis Reviews*, *29*(4), 695–707. https://doi.org/10.1007/s10555-010-9254-z

Koufopoulos, N., Pateras, I. S., Gouloumis, A. R., Ieronimaki, A. I., Zacharatou, A., Spathis, A., Leventakou, D., Economopoulou, P., Psyrri, A., Arkadopoulos, N., & Panayiotides, I. G. (2022). Diagnostically Challenging Subtypes of Invasive Lobular Carcinomas: How to Avoid Potential Diagnostic Pitfalls. *Diagnostics*, *12*(11), 2658. https://doi.org/10.3390/diagnostics12112658

Kundu, S., & Acharya, S. S. (2024). Exploring the triggers of premature and early menopause in India: A comprehensive analysis based on National Family Health Survey, 2019–2021. *Scientific Reports*, *14*(1), 3040. https://doi.org/10.1038/s41598-024-53536-9

Makhlouf, S., Atallah, N. M., Polotto, S., Lee, A. H. S., Green, A. R., & Rakha, E. A. (2024). Deciphering the Clinical Behaviour of Invasive Lobular Carcinoma of the Breast Defines an Aggressive Subtype. *Cancers*, *16*(10), 1893. https://doi.org/10.3390/cancers16101893

Marrazzo, E., Frusone, F., Milana, F., Sagona, A., Gatzemeier, W., Barbieri, E., Bottini, A., Canavese, G., Rubino, A. O., Eboli, M. G., Rossetti, C. M., Testori, A., Errico, V., De Luca, A., & Tinterri, C. (2020). Mucinous breast cancer: A narrative review of the literature and a retrospective tertiary single-centre analysis. *The Breast*, *49*, 87–92. https://doi.org/10.1016/j.breast.2019.11.002

Martinez-Calle, N., Isbell, L. K., Cwynarski, K., & Schorb, E. (2021). Treatment of elderly patients with primary CNS lymphoma. *Annals of Lymphoma*, *5*, 2–2. https://doi.org/10.21037/aol-20-30

Missaoui, A. M., Hamza, F., Belabed, W., Mellouli, M., Maaloul, M., Charfi, S., Jardak, I., Sellami-

Boudawara, T., Rekik, N., & Abid, M. (2023). Warthin-like papillary thyroid carcinoma: A case report and comprehensive review of the literature. *Frontiers in Endocrinology*, *14*, 1210943. https://doi.org/10.3389/fendo.2023.1210943

Naponelli, V., Rocchetti, M. T., & Mangieri, D. (2024). Apigenin: Molecular Mechanisms and Therapeutic Potential against Cancer Spreading. *International Journal of Molecular Sciences*, *25*(10), 5569. https://doi.org/10.3390/ijms25105569

Ng, B., Puspitaningtyas, H., Wiranata, J. A., Hutajulu, S. H., Widodo, I., Anggorowati, N., Sanjaya, G. Y., Lazuardi, L., & Sripan, P. (2023). Breast cancer incidence in Yogyakarta, Indonesia from 2008–2019: A cross-sectional study using trend analysis and geographical information system. *PLOS ONE*, *18*(7), e0288073. https://doi.org/10.1371/journal.pone.0288073

Peters, A., Keating, M.-M., Nikonova, A., Doucette, S., & Prica, A. (2023). Management of Marginal Zone Lymphoma: A Canadian Perspective. *Current Oncology*, *30*(2), 1745–1759. https://doi.org/10.3390/curroncol30020135

Rädler, P. D., Wehde, B. L., Triplett, A. A., Shrestha, H., Shepherd, J. H., Pfefferle, A. D., Rui, H., Cardiff, R. D., Perou, C. M., & Wagner, K.-U. (2021). Highly metastatic claudin-low mammary cancers can originate from luminal epithelial cells. *Nature Communications*, *12*(1), 3742. https://doi.org/10.1038/s41467-021-23957-5

Reardon, D., & Arvold, N. (2014). Treatment options and outcomes for glioblastoma in the elderly patient. *Clinical Interventions in Aging*, 357. https://doi.org/10.2147/CIA.S44259

Riggio, A. I., Varley, K. E., & Welm, A. L. (2021). The lingering mysteries of metastatic recurrence in breast cancer. *British Journal of Cancer*, *124*(1), 13–26. https://doi.org/10.1038/s41416-020-01161-4

Rossi, E. D., Pantanowitz, L., & Hornick, J. L. (2021). Cytologic and histological features of rare nonepithelial and nonlymphoid tumors of the thyroid. *Cancer Cytopathology*, *129*(8), 583–602. https://doi.org/10.1002/cncy.22404

Royce Sadler, D. (2014). The futility of attempting to codify academic achievement standards. *Higher Education*, *67*(3), 273–288. https://doi.org/10.1007/s10734-013-9649-1

Rudolph, A., Chang-Claude, J., & Schmidt, M. K. (2016). Gene–environment interaction and risk of breast cancer. *British Journal of Cancer*, *114*(2), 125–133. https://doi.org/10.1038/bjc.2015.439

Ruscitto, F., Roda, N., Priami, C., Migliaccio, E., & Pelicci, P. G. (2022). Beyond Genetics: Metastasis as an Adaptive Response in Breast Cancer. *International Journal of Molecular Sciences*, *23*(11), 6271. https://doi.org/10.3390/ijms23116271

Schindler, L. A., Burkholder, G. J., Morad, O. A., & Marsh, C. (2017). Computer-based technology and student engagement: A critical review of the literature. *International Journal of Educational Technology in Higher Education*, *14*(1), 25. https://doi.org/10.1186/s41239-017-0063-0

Sinaga, E. S., Ahmad, R. A., Shivalli, S., & Hutajulu, S. H. (2018). Age at diagnosis predicted survival outcome of female patients with breast cancer at a tertiary hospital in Yogyakarta, Indonesia. *Pan African Medical Journal*, *31*. https://doi.org/10.11604/pamj.2018.31.163.17284

Smolarz, B., Nowak, A. Z., & Romanowicz, H. (2022). Breast Cancer—Epidemiology, Classification, Pathogenesis and Treatment (Review of Literature). *Cancers*, *14*(10), 2569. https://doi.org/10.3390/cancers14102569

So, W. K. W., Law, B. M. H., Ng, M. S. N., He, X., Chan, D. N. S., Chan, C. W. H., & McCarthy, A. L. (2021). Symptom clusters experienced by breast cancer patients at various treatment stages: A systematic review. *Cancer Medicine*, *10*(8), 2531–2565. https://doi.org/10.1002/cam4.3794

Sukmana, D. J., Mentari, I. N., & Anjelin, D. P. (2021). Study of Creatinin Levels of Patients Receiving Antipsycotic Treatment at Mutiara Sukma Psychiatric Hospital, Nusa Tenggara Barat. *Medicra (Journal of Medical Laboratory Science/Technology)*, *4*(2), 83–87. https://doi.org/10.21070/medicra.v4i2.1616

Tabár, L., Bozó, R., Dean, P. B., Ormándi, K., Puchkova, O., Oláh-Németh, O., Németh, I. B., Veréb, Z., Yen, M.-F., Chen, L.-S., Chen, H.-H., & Vörös, A. (2023). Does Diffusely Infiltrating Lobular Carcinoma of the Breast Arise from Epithelial–Mesenchymal Hybrid Cells? *International Journal of Molecular Sciences*, *24*(13), 10752. https://doi.org/10.3390/ijms241310752

Tay, T. K. Y., & Tan, P. H. (2021). Papillary neoplasms of the breast—Reviewing the spectrum. *Modern Pathology*, *34*(6), 1044–1061. https://doi.org/10.1038/s41379-020-00732-3

Yersal, O. (2014). Biological subtypes of breast cancer: Prognostic and therapeutic implications. *World Journal of Clinical Oncology*, *5*(3), 412. https://doi.org/10.5306/wjco.v5.i3.412

Zarychta, E., & Ruszkowska-Ciastek, B. (2022). Cooperation between Angiogenesis, Vasculogenesis, Chemotaxis, and Coagulation in Breast Cancer Metastases Development: Pathophysiological Point of View. *Biomedicines*,

10(2), 300. https://doi.org/10.3390/biomedicines10020300