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Assessment of histopathological evaluation of breast lesions: neoplastic and non-neoplastic lesions in females from Bihar

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Abstract
Breast neoplasms are heterogeneous. Benign breast lesions being more common than malignant tumors. The incidence of benign breast lesions begins to rise during the second decade of life, peaks in the fourth and fifth decades. Increased risk of breast cancer is associated with proliferative and atypical lesions. Diagnostic modalities such as mammography, ultrasonography, and fine-needle aspiration cytology are being increasingly used. According to Indian Council of Medical Research statistics, 10,000 breast cancers are being diagnosed every year in India and more than 70% of them are diagnosed in advanced stage. By 2020, the incidence of breast cancer in India is expected to double. Hence based on the above literature findings the present study was planned to evaluate the histopathological spectrum of neoplastic and non-neoplastic lesions of breast.

The present study was planned in the Department of Pathology, Patna Medical College and Hospital, Patna from Dec 2018 to April 2019. Total 25 cases of the breast lumps refereed to our hospital were included in our study. A working diagnosis was arrived at by analysis of history and clinical examination following which the lump was received for histopathological examination as biopsy, lumpectomy or MRM specimen in 10% formalin. The standard tissue processing protocols were followed and 5µ thick sections were cut and stained with hematoxylin and eosin for morphological analysis.

The data generated from the present study concludes that it is also important to assess a patient's risk of developing breast cancer so that the most appropriate treatment modality for each case can be established. Thus breast self-examination and education to females is very important in cases of benign breast tumors. Histopathological evaluation becomes necessary for such cases and plays a pivot role in their final diagnosis. It also becomes helpful to surgeons for making decision of further operative management of the patient.

Keywords: neoplastic, non-neoplastic, lesions of breast, histopathology, Bihar region, etc

Introduction

Due to public awareness of breast cancer, breast diseases are showing a rising trend worldwide. Benign or malignant lesions in the breast are the two most important terms to know for understanding breast injuries. The word 'lesion' comes from a Latin word 'Laesio' which means 'attack or injury'. Lesions occur due to any disease or injury. They are an abnormal change in a tissue or organ. Benign breast lesions grow in non-cancerous areas where breast cells grow abnormally and rapidly. These cells form lumps but do not lead to cancer. They occur in a vast majority in the breast but are often neglected because they are not as dangerous as malignant lesions. These types of lesions do not spread but should be removed according to their size and location. They are also removed due to their abnormal appearance. Malignant lesions are cancerous in nature and are threatening for the health after a biopsy. They are characterized by progressive and uncontrolled growth. These types of lesions must be removed immediately by a surgery.

Breast cancer is cancer that develops from breast tissue. Signs of breast cancer may include a lump in the breast, a change in breast shape, dimpling of the skin, fluid coming from the nipple, a newly-inverted nipple, or a red or scaly patch of skin. In those with distant spread of the disease, there may be bone pain, swollen lymph nodes, shortness of breath, or yellow skin [1].

The first noticeable symptom of breast cancer is typically a lump that feels different from the rest of the breast tissue. More than 80% of breast cancer cases are discovered when the woman feels a lump. The earliest breast cancers are detected by a mammogram. Lumps found in lymph nodes located in the armpits can also indicate breast cancer. Indications of breast cancer other than a lump may include thickening different from the other breast tissue, one breast becoming larger or lower, a nipple changing position or shape or becoming inverted, skin puckering or dimpling, a rash on or around a nipple, discharge from nipple/s, constant pain in part of the breast or armpit and swelling beneath the armpit or around the collarbone. Pain ("mastodynia") is an unreliable tool in determining the presence or absence of breast cancer, but may be indicative of other breast health issues [2].

Another symptom complex of breast cancer is Paget's disease of the breast. This syndrome presents as skin changes resembling eczema; such as redness, discoloration or mild flaking of the nipple skin. As Paget's disease of the breast advances, symptoms may include tingling, itching, increased sensitivity, burning, and pain. There may also be discharge from the nipple. Approximately half the women diagnosed with Paget's disease of the breast also have a lump in the breast [3].

Inflammatory Breast Cancer presents with similar effects. Inflammatory Breast Cancer is a rare (only seen in less than

5% of breast cancer diagnosis) yet aggressive form of breast cancer characterized by the swollen, red areas formed on the top of the Breast. The visual effects of Inflammatory Breast Cancer is a result of a blockage of lymph vessels by cancer cells. This type of breast cancer is seen in more commonly diagnosed in younger ages, obese women and African American women. As inflammatory breast cancer does not present as a lump there can sometimes be a delay in diagnosis [4].

In rare cases, what initially appears as a fibroadenoma (hard, movable non-cancerous lump) could in fact be a phyllodes tumor. Phyllodes tumors are formed within the stroma (connective tissue) of the breast and contain glandular as well as stromal tissue. Phyllodes tumors are not staged in the usual sense; they are classified on the basis of their appearance under the microscope as benign, borderline or malignant.

Malignant tumors can result in metastatic tumors—secondary tumors (originating from the primary tumor) that spread beyond the site of origination. The symptoms caused by metastatic breast cancer will depend on the location of metastasis. Common sites of metastasis include bone, liver, lung, and brain. When cancer has reached such an invasive state, it is categorized as a stage 4 cancer, cancers of this state are oftentimes fatal. Common symptoms of stage 4 cancer include unexplained weight loss, bone and joint pain, jaundice and neurological symptoms. These symptoms are called non-specific symptoms because they could be manifestations of many other illnesses [5].

Most symptoms of breast disorders, including most lumps, do not turn out to represent underlying breast cancer. Less than 20% of lumps, for example, are cancerous, and benign breast diseases such as mastitis and fibroadenoma of the breast are more common causes of breast disorder symptoms [6].

Breast cancer, like other cancers, occurs because of an interaction between an environmental (external) factor and a genetically susceptible host. Normal cells divide as many times as needed and stop. They attach to other cells and stay in place in tissues. Cells become cancerous when they lose their ability to stop dividing, to attach to other cells, to stay where they belong, and to die at the proper time.

Normal cells will commit cell suicide (programmed cell death) when they are no longer needed. Until then, they are protected from cell suicide by several protein clusters and pathways. One of the protective pathways is the PI3K/AKT pathway; another is the RAS/MEK/ERK pathway. Sometimes the genes along these protective pathways are mutated in a way that turns them permanently "on", rendering the cell incapable of committing suicide when it is no longer needed. This is one of the steps that causes cancer in combination with other mutations. Normally, the PTEN protein turns off the PI3K/AKT pathway when the cell is ready for programmed cell death. In some breast cancers, the gene for the PTEN protein is mutated, so the PI3K/AKT pathway is stuck in the "on" position, and the cancer cell does not commit suicide [7].

Mutations that can lead to breast cancer have been experimentally linked to estrogen exposure. Additionally, G-protein coupled estrogen receptors have been associated with various cancers of the female reproductive system including breast cancer. Abnormal growth factor signaling in the interaction between stromal cells and epithelial cells can facilitate malignant cell growth. In breast adipose tissue, overexpression of leptin leads to increased cell proliferation and cancer [8].

Most types of breast cancer are easy to diagnose by microscopic analysis of a sample—or biopsy—of the affected area of the breast. Also, there are types of breast cancer that require specialized lab exams. The two most commonly used screening methods, physical examination of the breasts by a healthcare provider and mammography, can offer an approximate likelihood that a lump is cancer, and may also detect some other lesions, such as a simple cyst [9].

When these examinations are inconclusive, a healthcare provider can remove a sample of the fluid in the lump for microscopic analysis (a procedure known as fine needle aspiration, or fine needle aspiration and cytology—FNAC) to help establish the diagnosis. A needle aspiration can be performed in a healthcare provider's office or clinic. A local anaesthetic may be used to numb the breast tissue to prevent pain during the procedure, but may not be necessary if the lump isn't beneath the skin. A finding of clear fluid makes the lump highly unlikely to be cancerous, but bloody fluid may be sent off for inspection under a microscope for cancerous cells. Together, physical examination of the breasts, mammography, and FNAC can be used to diagnose breast cancer with a good degree of accuracy.

Other options for biopsy include a core biopsy or vacuum-assisted breast biopsy [10]. which are procedures in which a section of the breast lump is removed; or an excisional biopsy, in which the entire lump is removed. Very often the results of physical examination by a healthcare provider, mammography, and additional tests that may be performed in special circumstances (such as imaging by ultrasound or MRI) are sufficient to warrant excisional biopsy as the definitive diagnostic and primary treatment method.

Breast cancer is usually classified primarily by its histological appearance. Most breast cancers are derived from the epithelium lining the ducts or lobules, and these cancers are classified as ductal or lobular carcinoma. Carcinoma in situ is growth of low-grade cancerous or precancerous cells within a particular tissue compartment such as the mammary duct without invasion of the surrounding tissue. In contrast, invasive carcinoma does not confine itself to the initial tissue compartment [11].

Breast neoplasms are heterogeneous. Benign breast lesions being more common than malignant tumors. The incidence of benign breast lesions begins to rise during the second decade of life, peaks in the fourth and fifth decades. Increased risk of breast cancer is associated with proliferative and atypical lesions. Diagnostic modalities such as mammography, ultrasonography, and fine-needle aspiration cytology are being increasingly used. According to Indian Council of Medical Research statistics, 10,000 breast cancers are being diagnosed every year in India and more than 70% of them are diagnosed in advanced stage. By 2020, the incidence of breast cancer in India is expected to double. Hence based on the above literature findings the present study was planned to evaluate the histopathological spectrum of neoplastic and non-neoplastic lesions of breast.

Methodology

The present study was planned in the Department of Pathology, Patna Medical College and Hospital, Patna from Dec 2018 to April 2019. Total 25 cases of the breast lumps refereed to our hospital were included in our study. A working diagnosis was arrived at by analysis of history and

clinical examination following which the lump was received for histopathological examination as biopsy, lumpectomy or MRM specimen in 10% formalin. The standard tissue processing protocols were followed and 5µ thick sections were cut and stained with hematoxylin and eosin for morphological analysis.

All the patients were informed consents. The aim and the objective of the present study were conveyed to them. Approval of the institutional ethical committee was taken prior to conduct of this study.

Results and Discussion

Lump or Mass in the breast is an issue of worry or anxiety particularly for female patients of all age groups and sometimes produces diagnostic difficulty for both Clinicians as well as Pathologists. Benign breast Diseases is defined as any non-malignant breast condition and encompasses a wide range of clinical and pathologic disorders [12]. It is one of the most common diseases in the females of any society [13]. Though majority complains are neglected [14]. In order to provide relief to the patients from anxiety, timely, precise and accurate diagnosis is must. Accuracy and Precision save a patient's life in breast cancers and in cases of non-malignant lesions, they avoid unnecessary mutilating radical surgery and preserve patient's breast. In other words one can say that to prevent unnecessary loss of breast, perfect diagnosis of non-malignant lesions is of utmost importance.

Non-malignant lesions include both non-neoplastic and neoplastic lesions. Histopathological examination is now considered a gold standard approach to the diagnosis of breast lump [15]. They also include tumor like conditions e.g. Hamartomas. The incidence of benign breast lesions begins toriseduring the second decades of life and peaks in the fourth and fifth decades [16, 17]. So in our present study, we have used the more accurate term "Non-malignant" instead of the term "Benign".

Breast tissue is well developed only in female; in men it remains rudimentary throughout the life [18]. Breast is a superficially located organ subject to many changes during a woman's life and sensitive to hormones particularly estrogen and progesterone. Benign neoplasms of the breast are more common than the malignant neoplasms and are completely curable. However, these are overshadowed by the magnitude of the problems of malignant tumors of the breast. More than half of all women will develop some form of benign breast disease (BBD) after age 20. Although a history of BBD indicates some increase in risk for breast cancer (BC), only a small fraction of those diagnosed ever develop malignant disease [19].

Table 1: Age & Sex Distribution

Age Group	Number of Cases
21 – 30 years	1
31 – 40 years	2
40 – 50 years	3
51 – 60 years	15
Above 60 years	4
Total	25

Table 2: Showing the Incidence of Presenting Complaints

SR. No.	Presenting Complaint	No. of Cases
1	Breast Lump	19
2	Breast Lump with Pain	3
3	Diffuse Pain	1
4	Bloody Nipple Discharge	1
5	Skin Ulceration	1
	Total	25

Table 3: Incidence of Benign and Malignant Lesions of Breast

Sl. No.	Lesions	Frequency
1	Non Neoplastic	3
2	Neoplastic: Benign Malignant	 9 13
	Total	25

Table 4: Distribution Pattern of Malignant Lesions of the Breast

Sl. No.	Malignant Lesions	No. of Cases
1	Invasive Ductal Carcinoma (IDC)-NST	7
2	Invasive Lobular Carcinoma (ILC)	2
3	IDC+ ILC	0
4	Invasive Papillary Carcinoma	1
5	Medullary Carcinoma	1
6	Carcinoma with Neuroendocrine Differentiation	1
7	Metaplastic Carcinoma	1
	Total	13

Table 4: Comparison of Incidence of Neoplastic and Non-Neoplastic Lesions

Sr. No.	Study	Neoplastic Lesions		Non-Neoplastic Lesions	
		No. of Cases	%	No. of Cases	%
1	Samir S *et al* (1995).3	52	48.1%	56	51.9%
2	M S Siddiqui *et al* (2003).4	2357	71.8%	922	28.2%
3	Naseer Ahmed Shaik *et al* (2012).5	2186	81%	507	18.83%
4	Present study	22	88%	3	12%

The breast specific biphasic stromal tumors fibroadenoma and phyllodes tumor arise from intralobular stroma. This specialized stroma may elaborate growth factors for epithelial cells, resulting in the proliferation of the non-neoplastic epithelial component of these tumors. Fibroadenoma is the most common benign tumor of the female breast. Most occur in women in their 30s to 50s, and they are frequently multiple and bilateral. Young women usually present with a palpable mass and older women with a mammographic density or mammographic calcifications. The epithelium of the fibroadenoma is hormonally responsive, and an increase in size due to lactational changes during pregnancy, which may be complicated by infarction and inflammation, can mimic carcinoma. Phyllodes tumors can occur at any age, most present in the sixth decade, 10 to 20 years later than the peak age for fibroadenomas. The majority are detected as palpable masses, but a few are found by mammography. The tumors vary in size from a few centimeters to massive lesions

involving the entire breast. The larger lesions often have bulbous protrusions ("leaflike") due to the presence of nodules of proliferating stroma covered by epithelium.

In a study done by Kulkarni Sangeeta *et al* [20], out of 176 cases, non-malignant breast lesions constituted 80.7% while malignant lesions constituted 19.3%. Malik *et al* [21] reported non-malignant lesions in 72.97% and malignant lesions in 27.03%.Pudale S *et al* [22] reported non-malignant lesions in 71.15% and malignant lesions in 28.85%. So we can say that incidence of both non-malignant as well as malignant breast lesions are comparable in all studies.

Chronic mastitis followed by granulomatous mastitis was frequently observed in nonneoplastic lesions in our findings, whereas past studies reported highest occurrence of breast abscess followed by chronic mastitis. [23, 14] Fibroadenoma forms highly movable, asymptomatic, compact, callus, and frequently palpable mass in the breasts. Their formation can be independent or multilateral, and frequently observed in the early reproductive age of women, which was similar to our results. Of all benign neoplastic lesions, 50% were found to be fibroadenoma, this was in similar with the accessible literature on benign breast disease [25, 26]. The prevalence of invasive ductal carcinoma in malignant lesions was reported by Sheikh NA *et al.* [23] and Vissa Shanti *et al.* [27] reported that 45.8% of the malignant lesion cases had metastasis in axillary lymph node out of 100 cases, which was found to be the identical with our studies. NGS was used to histologically grade the breast cancer.

Conclusion

The data generated from the present study concludes that it is also important to assess a patient's risk of developing breast cancer so that the most appropriate treatment modality for each case can be established. Thus breast self-examination and education to females is very important in cases of benign breast tumors. Histopathological evaluation becomes necessary for such cases and plays a pivot role in their final diagnosis. It also becomes helpful to surgeons for making decision of further operative management of the patient.

References

1. Saunders, Christobel; Jassal, Sunil (2009). Breast cancer (1. ed.). Oxford: Oxford University Press. p. Chapter 13. ISBN 978-0-19-955869-8. Archived from the original on 25 October 2015.
2. Merck Manual of Diagnosis and Therapy (February 2003). "Breast Disorders: Breast Cancer". Archived from the original on 2 October 2011. Retrieved 5 February 2008.
3. Ashikari, Roy; Park, Keun; Huvos, Andrew G.; Urban, Jerome A. "Paget's disease of the breast". Cancer. 1970; 26 (3):680-685. doi:10.1002/1097-0142(197009) 26:33. 0.CO; 2-P(inactive 20 August 2019). ISSN 1097-0142.
4. Kleer, Celina G, Van Golen, Kenneth L, Merajver, Sofia D. Molecular biology of breast cancer metastasis Inflammatory breast cancer: clinical syndrome and molecular determinants. Breast Cancer Research. 2000; 2(6):423-429. doi:10.1186/bcr89. ISSN 1465-542X. PMC 138665. PMID 11250736.
5. National Cancer Institute. Metastatic Cancer: Questions and Answers. Archived from the original on. Retrieved, 2008.
6. Merck Manual of Diagnosis and Therapy, Breast Disorders: Overview of Breast Disorders". Archived from the original on 2003-2011. Retrieved 5 February 2008.
7. Adrian Lee, Carlos Arteaga 32nd Annual CTRC-AACR San Antonio Breast Cancer Symposium (PDF). Sunday Morning Year-End Review. Archived from the original (PDF) on, 2009-2013.
8. Jardé T, Perrier S, Vasson MP, Caldefie-Chézet F. Molecular mechanisms of leptin and adiponectin in breast cancer. Eur. J. Cancer. 2011; 47(1):33-43. doi:10.1016/j.ejca.2010.09.005. PMID 20889333.
9. Saslow D, Hannan J, Osuch J, Alciati MH, Baines C, Barton M. Clinical breast examination: practical recommendations for optimizing performance and reporting. CA: A Cancer Journal for Clinicians. 2004; 54(6):327-344. doi:10.3322/canjclin.54.6.327. PMID 15537576.
10. Yu YH, Liang C, Yuan XZ. Diagnostic value of vacuum-assisted breast biopsy for breast carcinoma: a meta-analysis and systematic review. Breast Cancer Research and Treatment. 2010; 120(2):469-79. doi:10.1007/s10549-010-0750-1. PMID 20130983.
11. Merck Manual, Professional Edition Archived 10 at the Wayback Machine, Ch. 253, Breast Cancer, 2011.
12. Rangabashyam N, Gnanaprakasam D, Krishnaraj B, *et al*. Spectrum of benign breast lesions in Madras. J R Coll Surg Edinb. 1983; 28(6):369-73.
13. Guray M, Sahin AA. Benign breast diseases: classification, diagnosis, and management. Oncologist. 2006; 11(5):435-49. DOI:10.1634/theoncologist.11-5-435.
14. Srivatsava A, Dhar A. Benign breast disease: a neglected entity. Recent Adv Surg. 2006; 10:175-201.
15. Hughes LE, Mansel RE, Webster DJT. The approach to diagnosis and assessment of benign breast lumps benign disorders and diseases of the breast concepts and clinical management, 2ndedition. London: WB Saunders, 2005, 35.
16. Kelsey JL, Gammon MD. Epidemiology of breast cancer. Epidemiol Rev. 1990; 12:228-40.
17. Cole P, Mark Elwood J, Kaplan SD. Incidence rates and risk factors of benign breast neoplasms. Am J Epidemiol. 1978; 108(2):112-20.
18. Omene C, Tiersten A. The differences between male and female breast cancer. In: Legato MJ, editor. Principles of gender specific medicine, vol1. 2nd ed. London: Elsevier, 2010, 459.
19. Worsham MJ, Abrams J, Raju U, Kapke A, Lu M, *et al*. Breast cancer incidence in a cohort of women with benign breast disease from a multi-ethinic, primary health care population. Breast J. 2007; 12(2):115-121.
20. Kulkarni Sangeeta, *et al*. Histopathological spectrum of breast lesions with reference touncommon cases. J Obstet Gynecol India. 2009; 59(5):444-452.
21. Malik R, Bharadwaj VK. Breast lesions in young females--a 20-year study for significance of early recognition. Indian J Pathol Microbiol. 2003; 46(4):559-62.
22. Pudale S, *et al*. A histopathological study of non-malignant breast lesions. Int J Res Med Sci. 2015; 3(10):2672-2676.
23. Sheikh NA, Farzana C, Ikram-ud-din U, Jawaid AR. Breast diseasespattern at Lumhs, 10 years experience of consecutive referral to public sector medical university

at Hyderabad. Professional Medical J, 2012, 19.
24. Bagale P, Bagale NV, Bagale S, Ahire N. Clinicopathological study of benign breast diseases. IJHSR. 2013; 3:47-54.
25. Parajuli S, Koirala U, Khatri R, Acharya L, Suwal A. Histopathological spectrum of Breast lesions. J Nepal Health Res Counc. 2011; 9:48-51.
26. Olu-Eddo AN, Ugiagbe EE. Benign breast lesions in an African population: A 25-year histopathological review of 1864 cases. Niger Med J. 2011; 52:211-6.
27. Vissa Shanthi, Kashmir Ali, Nandam Mohan Rao. Clinicopathological study of breast lesions in females with assessment of correlation between tumor grade and prognostic factors. J Biosci Tech. 2011; 2:367-78.