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Research Article
Breast

The Spectrum of Malignant Breast lesions by Fine Needle Aspiration Cytology in a Teaching Hospital

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Background: Fine needle aspiration cytology (FNAC) is one of the preliminary tests done to detect malignant breast lesions, which help in early detection and management. Studying the cytology features of various malignant breast diseases was the aim of this study. **Methods:** This study is a cross-sectional retrospective study conducted in the Department of Pathology from 2015 to 2020. Clinical details and cytology features were collected from the Department records. **Results:** A total of 75 cases were collected during the study period. All the cases were females. The spectrum of lesions was composed of Ductal carcinoma followed by one point each of Mucinous carcinoma, Malignant Phyllodes tumour and Lobular Carcinoma. **Conclusions:** FNAC helps in rapid diagnosis and early management of malignant breast lesions.

Keywords: Breast cytology, Malignant breast lesions, FNAC

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Introduction

Breast lesions are a heterogeneous group of disorders ranging from inflammatory lesions to invasive cancers. Breast cancer is the most common malignant neoplasm among women worldwide after non-melanoma skin malignancies. Further, it is the most frequent cause of cancer-related death among women worldwide, with an estimated 2.1 million new cases annually. The survival rate varies by continent, with better rates in developed countries[1]. The implementation of breast cancer screening programs is helpful for the early detection of breast lesions that, in turn, translate to a significant decrease in mortality. Lesions suspected of malignancy should be subjected to complementary tests as soon as possible for diagnostic confirmation[2].

The most common modality for the initial evaluation of breast lesions is fine-needle aspiration cytology (FNAC). In addition, some studies recommend that small breast lesions or those suspicious for malignancy should be evaluated through histopathological examination ("core needle biopsy" or excision). However, FNAC is a more simple, low-cost technique with a low risk of complications than that observed with biopsy or excision procedures [4]. FNAC, when performed inadequate conditions, has good accuracy. The aspirated specimen can also be processed as a cell block that can be used for immunohistochemical analysis of related biomarkers (e.g., estrogen receptor, progesterone receptor, and Her2)[5]. The cellblock specimen can also be used for molecular analysis, providing additional information that can be helpful in the diagnosis and treatment by identifying predictive and prognostic markers. Early diagnosis and small lesion size significantly improve the treatment outcomes and prognosis of patients with breast lesions, especially those with malignant lesions

Breast masses are the most common complaint with which females patients present to the hospital. The majority of these lesions are either benign or non-neoplastic [6]. Fine needle aspiration cytology (FNAC) is one of the most common tests for palpable lesions. FNAC is also a part of the triple assessment test for breast masses [7]. It is minimally invasive, cost-effective and diagnostic accuracy is good [8]. Rapid turnaround times help in the same-day diagnosis of breast lesions and early management. Malignant diseases are more common after menopause [4].

Breast cancer is the most common female cancer worldwide. It accounts for nearly a quarter (25%) of all cancers, with an estimated 1.5 lakh new cancer cases diagnosed in 2016. This study was conducted to determine various forms of malignant breast lesions presented to our hospital.

Methods

Setting: Department of Pathology, Gadag Institute of Medical Sciences, Gadag

Duration of Study: 5 years six months from June 2015 to December 2020

Type of Study: Cross-sectional retrospective observational study

Sampling methods: Universal sampling

Sample Size calculation: All the cases as per inclusion criteria were included in the study

Inclusion Criteria: were cases with the diagnosis of neoplastic breast disease in females

Exclusion Criteria: All benign breast diseases in males and females were excluded from the study

Data Collection Procedure: Clinical details and demographic data were obtained from departmental records. FNAC was done by using five cc syringes with 22-23G needle under all aseptic precautions. Air-dried smears were stained with MGG stain, Leishman stain and wet smears were stained with PAP stain and H and E stain.

Ethical Clearance: Obtained from Institutional Ethical Committee

Statistical Analysis: The data obtained were entered into Microsoft Excel Spreadsheet. Categorical data were expressed in terms of rates, ratios and percentages.

Results

A total of 514 cases were there in which FNAC was done, of which malignancy was detected in 75(14.6%) cases. All the cases were females. The most common presenting complaint was a lump in the breast 72(97%) cases. The mean age of presentation of all malignant breast diseases was 49 years. The mean age of the most common malignant neoplasm (Ductal carcinoma breast) was 49 years. The following were the cytological diagnosis: Ductal carcinoma-72 cases(97%) followed one case each of Mucinous carcinoma

(1%), Malignant Phyllodes tumour (1%) and Lobular Carcinoma(1%) as shown in Table 1.

Table 1: Spectrum of Malignant Breast Lesions on FNAC

Malignant breast neoplasms	Number of Cases	Percentage (%)
Ductal carcinoma breast	72	97%
Mucinous carcinoma breast	1	1%
Malignant Phyllodes tumour	1	1%
Lobular carcinoma	1	1%

Table 2: Comparison of Malignant Breast lesions among various studies.

Study	Malignant breast lesions
Modi et al [25]	16.7%
Georgieva et al[26]	22.5%
Bajwa et al[27]	10.3%
Sunita et al[28]	37.1%
Panwar et al [29]	8.4%
Present Study	14.6%

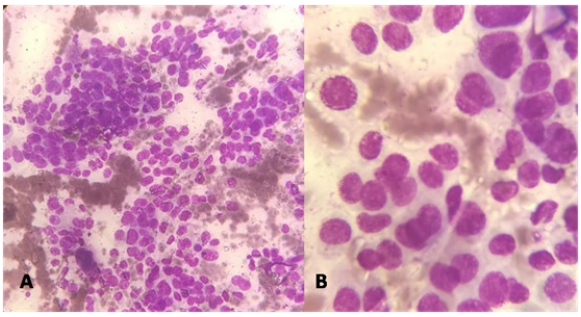

Figure 1: Smears studied shows malignant ductal epithelial cells seen in dyscohesive clusters. These tumour cells have a high N/C ratio with a moderate to scanty amount of cytoplasm. These features are suggestive of Ductal Carcinoma Breast(1A: Leishman stain, 10 X and 1B: Leishman stain, 40 X)

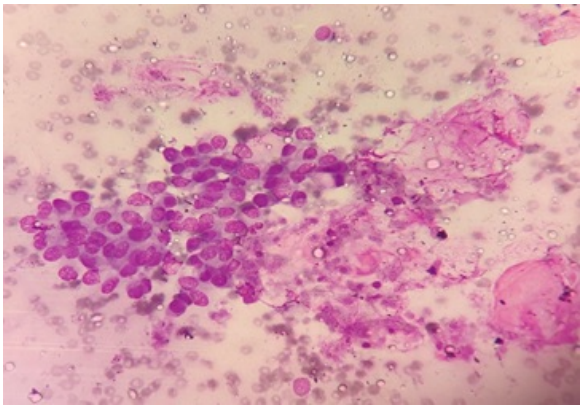

Figure 2: Smear studied shows clusters of tumour cells with mild to moderate nuclear Pleomorphism, floating in extracellular pools of mucin, suggestive of Mucinous carcinoma breast (Leishman stain 40X)

Discussion

Breast lumps are very common, most of the lumps are benign, and the prevalence of malignant lumps increases with age[9]. Breast cancer is one of the commonest cancers amongst women in India, with approximately 75,000 new cases estimated every year[10].

The following are the risk factors for breast cancer: Family history, Genetic predisposition, Estrogen exposure, Radiation exposure, Breast density and Obesity. The following are the Precancerous conditions: Complex fibroadenoma, moderate or florid hyperplasia without atypia, sclerosing adenosis and solitary papilloma without atypical ductal hyperplasia are associated with slightly increased risk (1.5-2times) whereas, atypical ductal hyperplasia and atypical lobular hyperplasia are associated with moderately increased risk (4 -5 times) of breast cancer[11].

The vast majority of breast malignancies are adenocarcinomas arising from the ducts or lobules. Traditionally, these were categorized by morphology. The most common histologic type of breast cancer is invasive ductal carcinoma or carcinoma of no special type (40%-75%) (Figure 1). The remainder of carcinomas is classified as specialized types. These include but are not limited to lobular carcinoma (5%-15%), mucinous carcinoma (2%), tubular carcinoma (2%), medullary carcinoma(< 1%) and metaplastic carcinoma(0.2%-5%) [12].

Lobular carcinoma is the most common type of breast cancer following ductal carcinoma and is composed of dyscohesive monomorphic cells that lack tubule formation [12]. The dyscohesion is due to the inactivation of the cell adhesion molecule E-cadherin. These tumours are invariably ER-positive in 60% to 70% of tumours and generally negative for HER2. The prognosis of this tumor is favorable; however, this type is associated with a worse long-term outcome relative to ductal carcinoma in terms of higher incidences of mortality, recurrence, and distant metastasis [13]. In mucinous carcinoma, well to moderately differentiated neoplastic cells are clustered in small groups within large pools of mucin (see Figure 2). This type of carcinoma is typically ER-positive and HER2-negative.

Mucinous carcinoma has an excellent 5-year survival rate and a low rate of distant and local recurrence. [13]. Tubular carcinoma is composed of well-formed tubules, often shaped like teardrops [12]. This type of carcinoma is uncommon, at only 2% of invasive breast carcinomas, and is associated with an excellent prognosis. Tubular carcinoma is generally ER-positive/HER2-negative[13].

Metaplastic carcinoma is a heterogeneous category of neoplasms that have differentiated into squamous or mesenchymal cells. Greater than 90% of metaplastic carcinomas are ER-negative/HER2-negative. Compared with other TNBCs, metaplastic carcinoma has a worse clinical outcome and lower chemotherapy response rate [13]. Medullary carcinoma comprises solid syncytial sheets of pleomorphic cells with prominent nucleoli, a lymphoplasmacytic infiltrate numerous mitoses, and a pushing border[12]. These tumours are typically triple-negative and often associated with BRCA mutations. Traditionally, these tumors were reported to have a relatively favorable prognosis; however, due to the low level of reproducibility for the diagnosis and the poor prognosis associated with TNBCs, these tumors are now termed "carcinomas with medullary features" and treated with aggressive therapy [13].

Molecular gene expression profiling studies heralded a new era in the classification of breast carcinomas. In addition to morphology, breast carcinomas now are categorized into 1 of 3 subtypes based on the tumour's expression of HER2 and E.R.s. Although testing is almost always performed for P.R. as well as E.R., descriptions of molecular classifications generally use E.R. status as a surrogate marker for P.R. as well. The three subtypes are ER-positive/HER2-negative (50%-65% of tumours). HER2-positive (10%-20% of tumors). ER-negative/HER2-negative (10%-20% of tumors) [14].

ER-positive/HER2-negative breast cancers: These are often associated with losses of chromosome 16q and gains in chromosome 1q, as well as activating mutations in PIK3CA, a growth factor receptor signalling molecule. This type of breast carcinoma often progresses through a sequence that can include flat epithelial atypia, atypical ductal hyperplasia, ductal carcinoma in situ (DCIS), and eventually invasive ductal carcinoma. This subtype is primarily treated with hormone therapy instead of chemotherapy because few of these carcinomas respond to chemotherapeutic drugs.

HER2-Positive Invasive Carcinomas: These tumors are defined by HER-2 positivity, regardless of E.R. status. The HER2-positive carcinomas are characterized by mutations in tumor suppressor TP53, which amplify HER2 on chromosome 17q. The suggested precursor lesion for this type of carcinoma is atypical apocrine adenosis that progresses to DCIS. This subtype is more common in nonwhite and young women and patients with LiFraumeni syndrome (hereditary TP53 mutation). These cancers can metastasize early, often to the brain and viscera, even when small. The drug trastuzumab (Herceptin) is a monoclonal antibody that inhibits HER2 and vastly improves survival. Once metastasized, survival is uncommon[14].

The ER-negative/HER2-negative cancers, also known as triple-negative as P.R., is also negative, are the least understood of the subtypes of invasive ductal carcinoma. This subtype arises through a pathway independent from changes in HER-2 and E.R.s. Most carcinomas in women with BRCA1 mutations are triple-negative. These cancers grow and metastasize quickly to the brain and viscera. Approximately 30% respond to chemotherapy, and they tend to recur within five years. Triple-negative breast carcinomas (TNBCs) tend to be poorly differentiated[14].

In patients presenting with a breast lump, the diagnosis should be made by clinical assessment. Radiological imaging and tissue sample have been taken either for cytology or histology analysis: the so-called Triple Test. There are several competing approaches to a breast biopsy, such as surgical excision biopsy, core needle biopsy and biopsy by aspiration or Fine-needle aspiration (FNA) [15]. FNAC has become an increasingly popular technique for assessing breast lumps. It is a minor invasive technique for obtaining a cytological diagnosis and is highly accurate if done by experienced personnel [16].

The worldwide-accepted protocol for diagnosing breast lumps is the "Triple Assessment", which includes clinical examination, mammography and pathological diagnosis. Fine needle aspiration cytology (FNAC) has become a diagnostic tool to assess the nature of palpable breast lesions [17,18].

It forms an important part of the pathological assessment since it is easy, relatively painless, quick and a cost-effective technique. It also helps in the planning of treatment of breast lump [19].

Moreover, FNAC has good sensitivity, specificity and accuracy in the diagnosis of both malignant and non-malignant breast lumps. Accuracy can be improved by multiple sampling from different angles and by using ultrasound guidance in very small lumps [20]. Malignant breast lesions were found in all age groups. This finding follows a study by Rahman et al.[21], who also concluded that most malignant lesions were found in the middle age group of 31 to 50 years. Similar results from other studies in India like Muddegowda et al.[22].and Khemka et al [23]were reported. However, reports from the western world depict the 5th and 6th decades as the predominant age group for breast cancer [24]. Present study findings of 14.6% cases are similar to a study done by Modi et al. [25], which found 16.7% cases. The other comparison studies are shown in Table 2. The management of breast disease needs a deliberate, synchronized diagnostic and treatment strategy. Fine-needle aspiration cytology (FNAC) is an essential diagnostic tool for the preoperative diagnosis of palpable and non-palpable breast lesions. Our study has the limitation of having a small sample size, and being a retrospective study, there will be deficiencies incomplete data collection. However, it provides baseline data of the patient population presenting to our hospital.

Conclusion

For diagnosing the nature of palpable breast lesions, FNAC is considered a highly accurate procedure with sensitivity and specificity as high as 95%. Its use has been recommended in literature as a preliminary treatment on an outpatient basis. Early diagnosis is of paramount importance to decrease the mortality and morbidity associated with these lesions. FNAC is a relatively simple procedure with good patient acceptance and low morbidity. It is an accurate, safe and repeatable procedure in the diagnosis of various breast lesions –both malignant and non-malignant. Repeated passes should be made for a greater yield of cytological material. FNAC should be used earlier and more frequently to shorten the diagnostic interval and allow more prompt therapy for malignant breast lesions.

What new this study adds to existing knowledge

FNAC helps in rapid diagnosis and early management of malignant breast lesions.

This study gives an insight into the various malignant breast lesions in this country region with a description of few rare lesions.

Authors Contribution

Dr Manika Alxeander: Data collection, Literature review, Manuscript preparation, Manuscript editing, Final approval. **Dr Mallikarjun A Pattanashetti:** Patients Selection, Collection of Samples, Data Analysis, Statistical analysis and Manuscript preparation.

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