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Original research article

Immunohistochemical profile of unusual breast lesions

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Abstract

Background: It can be difficult to diagnose breast lesions that are unusual. Nonneoplastic lesions, benign tumours, and primary and metastatic cancers are some of these lesions. This article describes a wide variety of unusual breast tumours that can manifest as breast lumps. This study's objective is to present an overview of the variety of uncommon breast abnormalities, particularly malignant tumours.

Material and Methods: The Siddhartha Medical College's Department of Pathology in Vijayawada evaluated 198 cases of breast lesions over a three-year period (August 2016-July 2019), comparing histopathological findings with imaging and IHC findings. The lesions identified were both neoplastic and non-neoplastic. 18 (35.6%) out of 198 cases of breast lesions were presented with rare findings.

Results: Out of 198 cases, 189 (95.45%) were neoplastic and 9 (4.54%) were non-neoplastic. Among neoplastic lesions, 88 (44.44%) were malignant, 1 (0.5%) was in situ and 100 (50.5%) were benign. Nineteen (9.09%) out of 198 cases presented with rare histopathological findings. The various lesions diagnosed were nodular pubertal hyperplasia, granulomatous mastitis, and rare benign tumours like intraductal papillomas, adenomyoepitheliomas, benign phyllodes, lactating adenomas, and tubular adenomas. Aside from these, only one case of Paget's disease of the nipple (0.5% of the total) was diagnosed as in situ carcinoma.

Conclusions: Understanding these unusual lesions may aid in accurate diagnosis and early patient care. This study emphasises how crucial histopathology and Immunohistochemistrylogy is in determining the diagnosis and prognosis of breast lesions.

Keywords: Neoplastic lesions, immunohistochemistry, unusual variations, breast lesions

Introduction

Several breast tumours were previously identified as duct cell carcinomas when they were all discovered at the same time. Specific tumours have, nevertheless, recently been acknowledged as different pathologic entities[2]. These lesions' distinct clinical history and imaging characteristics can be used to diagnose them. Preoperative imaging cannot always diagnose breast neoplasms, despite the use of the most advanced imaging tools. Because of this, understanding these lesions and their diagnostic characteristics aids in specific management[2,3] and prognosis. There are numerous varieties that are less prevalent (ten percent) but nonetheless well-defined by WHO classification[2]. Our analysis includes uncommon variations in all age groups, which were explored by connecting immunohistochemical results to histopathological findings[5,6].

Because of the prognostic significance of the human epidermal growth factor receptor 2 (HER2, also known as Erbb2) and the predictive heterogeneity of the oestrogen receptor (ER), breast cancer is routinely categorised in the clinical setting by the positive or negative status of the ER, PR, and HER2. The prognosis is better for ER positive cancers than ER negative tumours when using targeted Tamoxifen therapy. More aggressive than HER2 negative cancers, HER2 positive tumours respond well to trastuzumab therapy. It is crucial to do a receptor assay since ER-PR-HER2- (Triple Negative) Tumors do not react to these medicines and are therefore associated with a worse prognosis than tumours that are receptor positive [2,8].

Breast cancer is routinely classified in the clinical setting by the positive or negative status of the oestrogen receptor (ER), progesterone receptor (PR) and human epidermal growth factor receptor 2 (HER2, also known as Erbb2) because of their predictive heterogeneity and prognostic importance. ER-positive tumours show a good response to targeted Tamoxifen therapy and has more favourable prognosis than ER-negative tumours. HER2 positive tumours are more aggressive than HER2 negative tumours and are responsive to trastuzumab therapy. ER-PR-HER2- (triple-negative) tumours do not respond to these therapies and have the worst prognosis of any tumour type, emphasising the importance of performing a receptor assay[2, 8].

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Aims and Objectives

- To study the various types of breast lesions with special emphasis on rare lesions
- To study the expression of ER, PR, and HER2/neu receptors in breast cancer patients.

Methodology

The study was conducted in the Department of Pathology, Siddharha Medical College, Vijayawada, India, over a three-year period, from August 2016 to July 2019. The information includes things like age, sex, menstrual history, tumour site, and radiological findings. This study consists of 198 cases of breast lesions from all age groups admitted to the general surgery department at Siddhartha Medical College and GGH, Vijayawada throughout the aforementioned time period.

All patients who presented with a breast lump were included, regardless of age.

Results

A total of 198 cases were examined. Table 1 displays the distribution of breast lesions by age group. Nine (4.54%) of these were non-neoplastic lesions and 189 (95.4%) of these were neoplastic lesions [Table 2]. In Table 3, several histological types were listed. With 75 cases (39.5% of all malignant tumours), infiltrating ductal cell carcinoma (NOS type) was the most prevalent form. 18 (9.09%) unusual breast lesions were identified in this investigation. Two cases of male breast cancer (1.04%) and one case of cribriform carcinoma (0.5up is reported in Table 1) were among the unusual forms studied. Nine (4.54%) of these were non-neoplastic lesions, and 189 (95.4%) of these were neoplastic lesions [Table 2]. In Table 3, several histological types were listed.

According to Table 1, the unusual types that were considered were: 2 cases of male breast cancer (1.04%) and 1 case of cribriform carcinoma (0.5up). Nine (4.54%) of these were non-neoplastic lesions, and 189 (95.4%) of these were neoplastic lesions [Table 2]. In Table 3, several histological types were listed. With 75 cases (39.5% of all malignant tumours), infiltrating ductal cell carcinoma (NOS type) was the most prevalent form. 18 (9.09%) unusual breast lesions were identified in this investigation. Two cases of invasive lobular carcinoma (1.04%), one case of cribriform carcinoma (0.5%), three cases of metaplastic carcinoma (1.5%), one case each of inflammatory carcinoma, apocrine carcinoma, mucinous carcinoma, and two cases each of invasive male breast carcinoma made up the list of unusual forms.

Two cases of male breast cancer (1.04%), one case of cribriform cancer (0.5%), three cases of metaplastic cancer (1.5%), one case each of inflammatory carcinoma (0.5%), apocrine carcinoma (0.5%), mucinous carcinoma (0.5%), two cases each of invasive lobular cancer (1.04%), one case of microinvasive cancer (0.5%), and one case of solid papillary carcinoma (0.5%) were among the rare types that were present. One case of Paget's disease of the nipple (0.5%) was identified among in situ lesions. There were 87 cases of fibroadenoma (45.3% of benign tumours), 6 cases of phyllodes (3.12%), 3 cases of intraductal papillomas (1.51%), 2 cases of lactating adenoma (1.04%), 1 case of tubular adenoma (0.5%), and 1 case of adenomyoepithelioma (0.5%). Nodular pubertal hyperplasia was present in one (0.5%) instance.

Table 1: Distribution of age group among breast lesions

Age Group	Number of Cases	Percentage
< 20	3	1.56%
20-30	6	3.1%
31-40	24	12.1%
41-50	43	21.7%
51-60	58	29.3%
61-70	49	24.5%
71-80	15	7.81%
Total	198	100%

Table 2: Distribution of nature of breast lesions

Type of Lesion	No. of Cases	Percentage
Neoplastic	189	95. 45%
Non-neoplastic	9	4. 55%
Total	198	100%

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Table 3: Morphological distribution of various breast lesions

Histological Type	No. of Cases	Percentage
Malignant		
Invasive duct cell carcinoma (NOS type)	75	39.1%
Invasive duct cell carcinoma (male breast)	2	1.04%
Invasive Lobular carcinoma	2	1.04%
Metaplastic carcinoma	3	1.5%
Apocrine carcinoma	1	0.5%
Inflammatory carcinoma	1	0.5%
Mucinous carcinoma	1	0.5%
Microinvasive carcinoma	1	0.5%
Solid papillary carcinoma	1	0.5%
cribrifrorm carcinoma	1	0.5%
Insitu carcinomas		
Paget's disease of the nipple	1	0.5%
Benign		
Fibroadenoma	87	45.3%
Benign Phyllodes	6	3.12%
Intraductal papilloma	3	1.5%
Lactating adenoma	2	1.04%
Tubular adenoma	1	0.5%
Adenomyoepithelioma	1	0.5%
Non neoplastic		
Nonspecific mastitis	6	3.12%
Granulomatous mastitis	2	1.04%
Nodular pubertal hyperplasia	1	0.5%
Total	198	100%

Gross Images

Fig 1: Phyllodes tumor, cut section shows grey white leaf like pattern of lesion of size 6*6 cm. and573/19, Gross picture of Invasive Duct cell carcinoma-NOS,showing irregular grey white lesion ofsize 4*2 cm

Fig 2: 670/20,Gross picture of Metaplastic carcinoma,Showing grey white lesion of size 4.5*4 cm. and 44/19,Gross picture of Solid papillary carcinoma,well circumscribed grey white lesion of size 4*3 cm and 655/19,Gross picture Invasive lobular carcinoma, Showing well circumscribed lesion of size 2*2 cm.

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Histopathological images

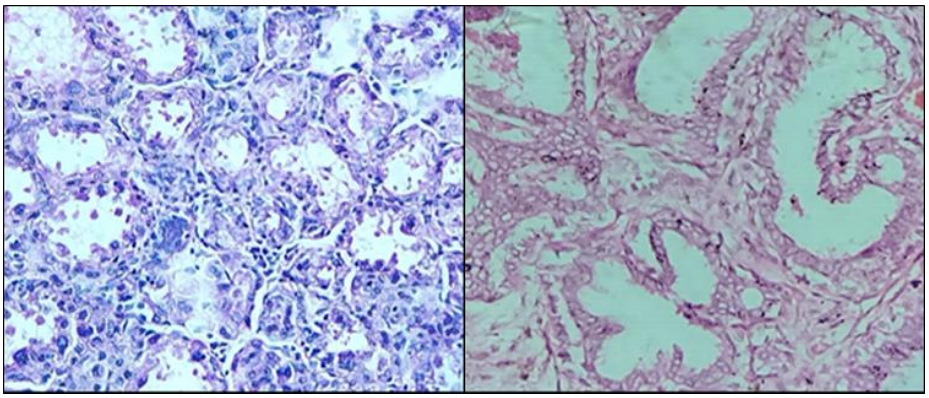

Fig 3: Lactating adenoma, glands lined by actively secreting cuboidal or hobnail shaped cells and Adenomyoepithelioma,Biphasic proliferation of epithelial and myoepithelial cells

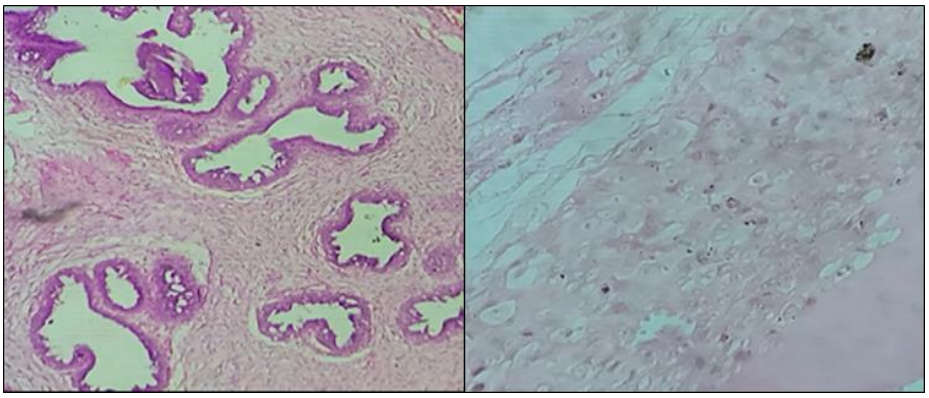

Fig 4: Nodular pubertal hyperplasia, showing epithelial hyperplasia in papillary pattern along with myoepithelial hyperplasia and Pagets disease of Nipple,clusters of pagetoid cells throughout the epidermis

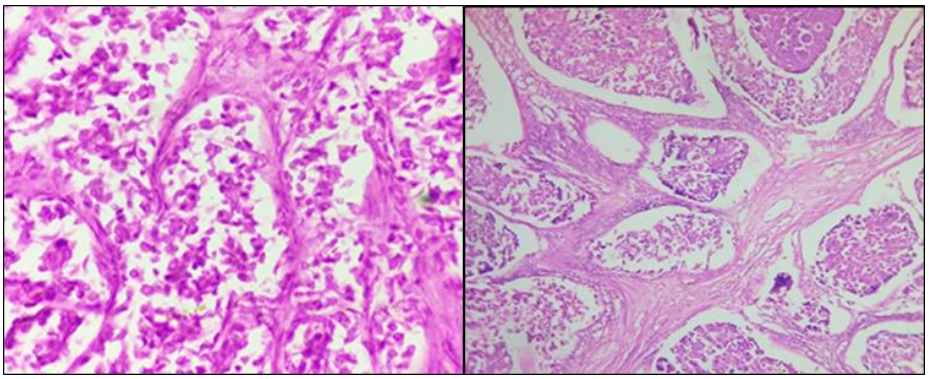

Fig 5:573/19 Neoplastic cells permeating surrounding stroma and distrupting normal ductal epithelium,Invasive Duct cellcarcinomaNOS,H&E, 400X. and 2752/19, showing sieve like pattern incribriformcarcinoma, H&E, 40X.

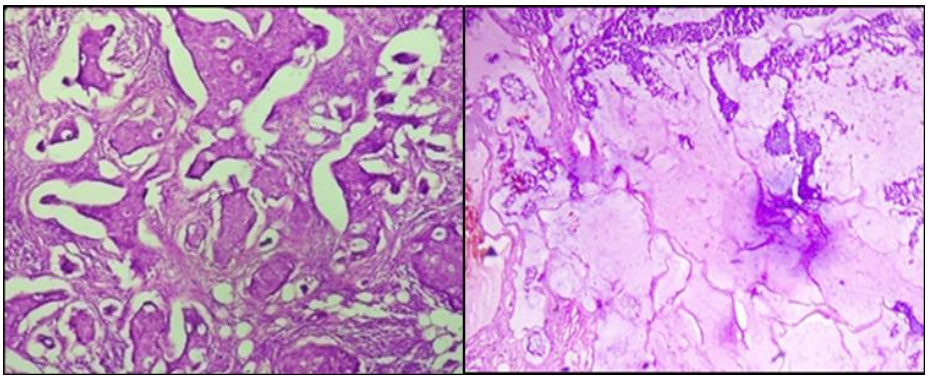

Fig 6: 2469/19,Squamous metaplasia in Metaplastic carcinoma,H&E,100X and 1383/19,Mucin pools suggesting Mucinous carcinoma,H&E,100X.

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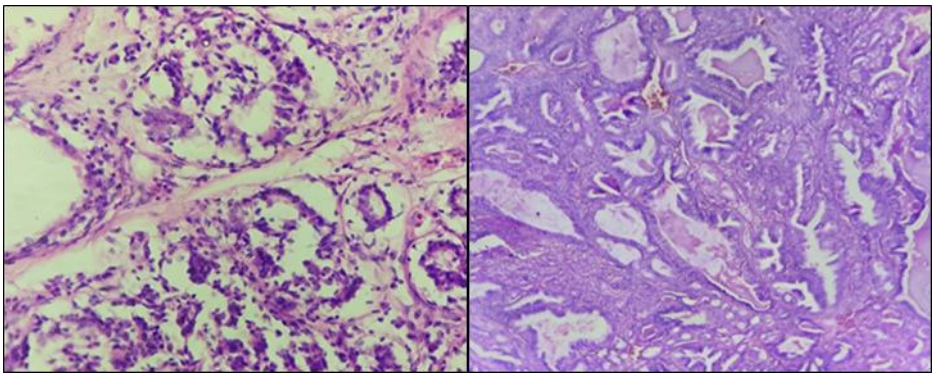

Fig 7: 39/19,Showing microinvasion suggesting Microinvasive carcinoma,H&E,100x and44/19,Showing Solid papillary carcinoma devoid of myoepithelial cell layer with ragged contours create a geographical jigsaw pattern in desmoplasticstroma,in H&E, 100X

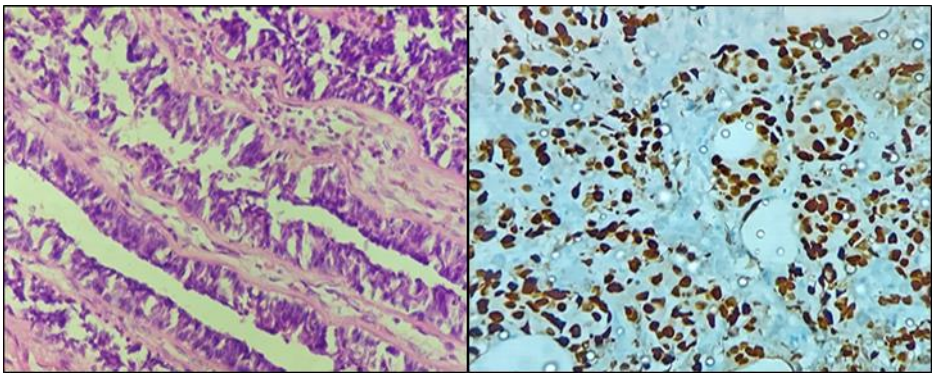

Fig 8: 655/19, showing Indian file pattern suggesting Invasive Lobular carcinoma, 100XH&E,400X and 655/19-ERpositive on IHC

Immunohistochemistry images

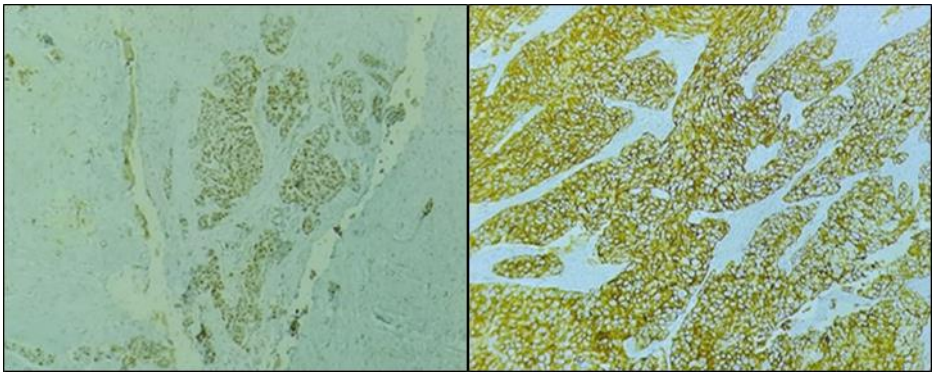

Fig 9: 573/19,Invasive duct cell carcinoma-NOS, PR positive,IHC,100X and 573/19, Invasive duct cell carcinoma-NOS, HER2-Positive,IHC,400x

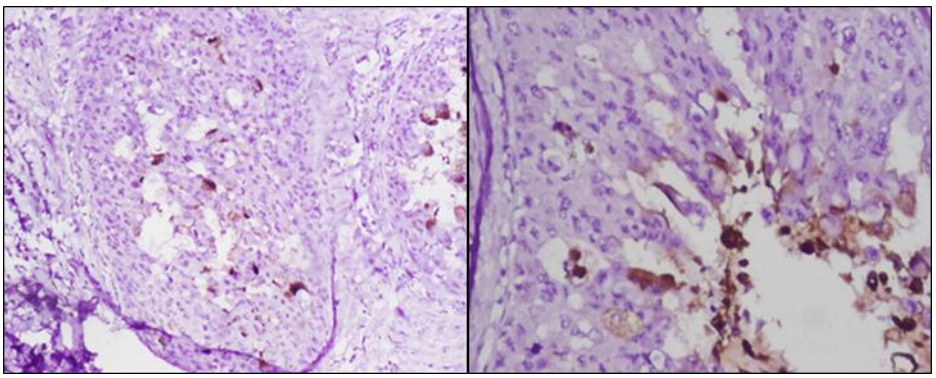

Fig 10: 3170/19, Invasive duct cell carcinoma-NOS, showing ER-Negativity 1+ in tumor nuclei on IHC 100X and 3170/19, Invasive duct cell carcinoma-NOS,PR positivity 2+ in focal tumor cell nuclei, IHC: PR,400

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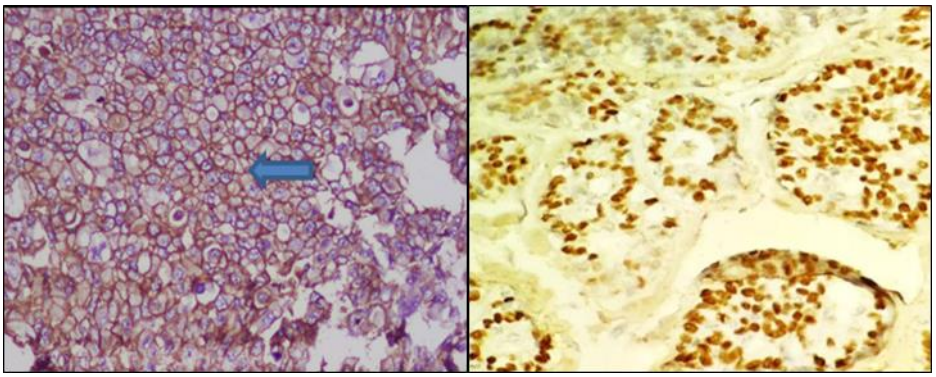

Fig 11: 3170/19,Invasive duct cell carcinoma-NOS, Membrane staining of cells showing HER2/neu receptor-Positive 3+, IHC:HER2, 100x and 2752/19, cribriform carcinoma, ER-Positive, 3+,in tumor cell nuclei, IHC:ER, 400X

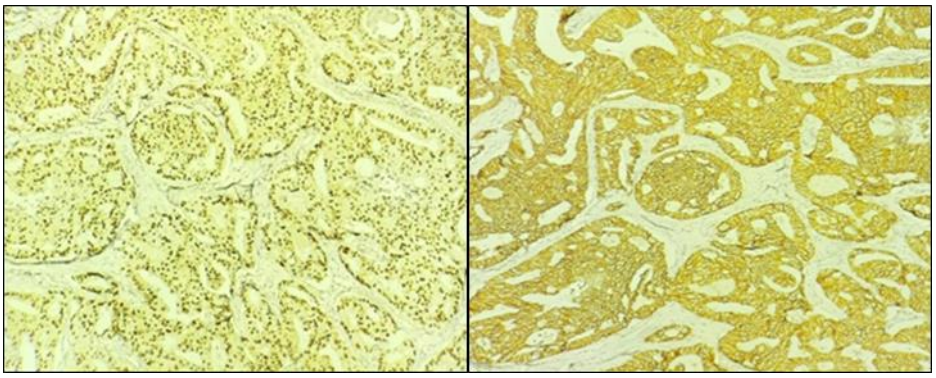

Fig 12: 2752/19,Cribriformcarcinoma,PR-Positive, IHC:PR,400X.2752/19,Cribriform carcinoma, HER2/neu-Positive, IHC:HER2/neu, 400x

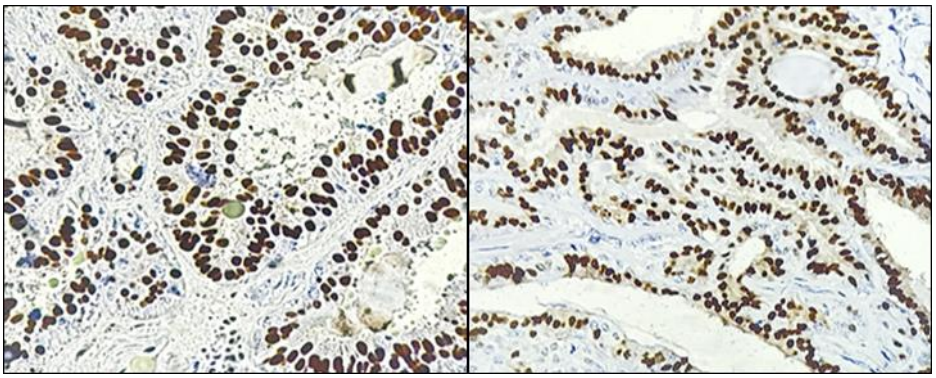

Fig 13: 44/19, Solid papillary carcinoma, showing ER-Positive 4+,IHC:ER,100X and 44/19, Solid papillary carcinoma,Showing PR-Positive 4+,IHC:PR, 40X

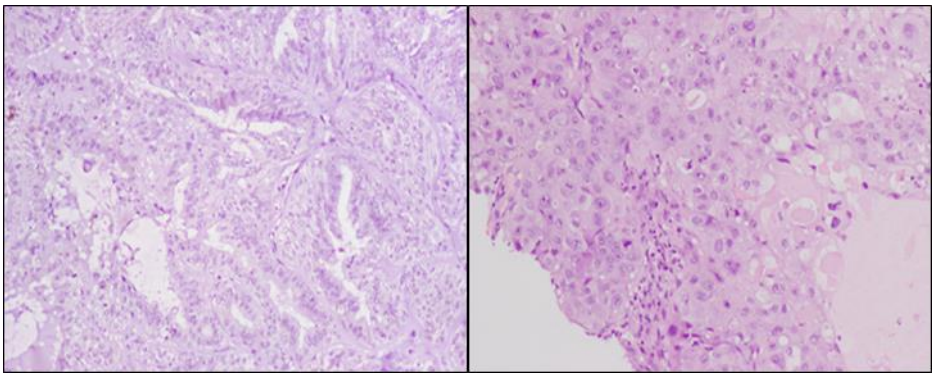

Fig 14: 44/19 Solid papillary carcinoma, showing negative expression of HER2 receptor, IHC: HER2,10X and 670/20, Metaplastic carcinoma, ER-Negative,IHC:ER, 400X

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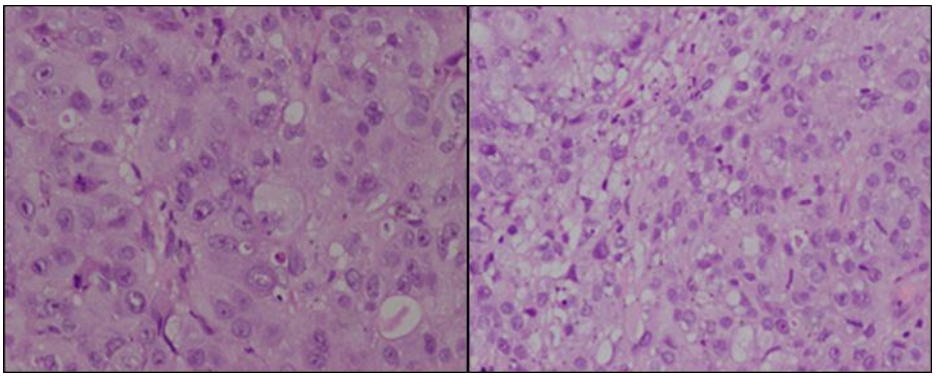

Fig 15: 670/20,Metaplastic carcinoma, PR-Negative,IHC: PR 400X and 670/20,Metaplastic carcinoma, HER2/neu-Negative,IHC:HER2,400X

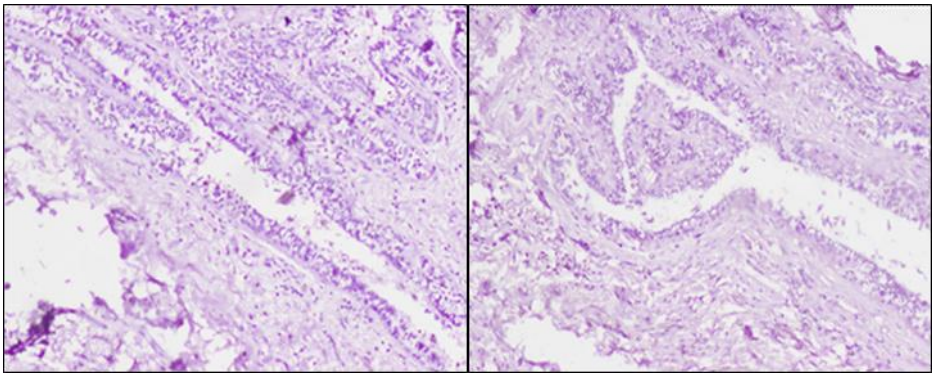

Fig 16: 655/19,Invasive Lobular carcinoma,ER-Negative,IHC:ER,100X.3655/19, Invasive Lobularcarcinoma, PR-Negative,IHC:PR, 100X

Discussion

Breast lesions may be accidentally found during a diagnostic technique or during a normal clinical evaluation. Differentiating between benign and malignant tumours is difficult. The most frequent breast lesions, which might be mistaken for invasiveductal carcinomas, are in situ and microinvasive carcinomas [1]. Tumor cells in traditional duct-cell carcinoma are structured in a variety of configurations, most prominently in uncommon varieties including cribriform type carcinoma and metaplastic carcinoma, among others[2].It is crucial to explain the diagnostic features and assess adjunctive immunohistochemistry in order to achieve a precise and fast diagnosis [6].

198 patients from the current study were examined over the course of three years. Nine (4.55%) of the 198 patients were non-neoplastic, whereas 189 (95.4%) were, including one incidence of carcinoma in situ. We discovered 89 (46.35%) malignant cases and 100 (52.08%) benign cases. Our research was comparable to that done by Desai *et al*., who looked at 212 patients over the course of seven years. 81.13 percent of the lesions she described were benign, while 18.87 percent were malignant. In their analysis of 1724 instances over a 20-year period, Malik *et al*. found that 72.97% of the lesions were benign and 27.03% were malignant, which is consistent with our findings.

A female patient in her 27s has an adenomyoepithelioma, a second uncommon benign tumour. On histopathology, epithelial and myoepithelial cells both exhibit biphasic growth. Epithelial cells typically form glandular gaps; they might exhibit papillary epithelial growth or apocrine, sebaceous, or squamous metaplasia.

Two cases of male breast carcinomas were identified in the malignant group. Patients came in with clearly visible breast masses. About half of patients with male breast carcinomas typically have stage 3 or stage 4 illness. However, the patient in our situation had a rather unusual clinical appearance. The characteristics of benign breast disease were identified on mammography. However, a grade III breast cancer diagnosis was made after a histological examination revealed nests of epithelial cells with a high N/C ratio, nuclear pleomorphism, sparse cytoplasm, and elevated mitosis. Carcinoma in men manifests as a bigger, less well-defined tumour with areas of necrosis and bleeding. The outlook is worse than it is for women. There have been numerous instances like this in the literature [5, 6].

In our analysis, invasive cribriform carcinoma was the other uncommon cancer. 0.8% to 3.5% of breast carcinomas are caused by it. It is almost totally (>90%) an invasive cribriform pattern on histology. The tumour is structured as invasive islands that are frequently angulated, with well-defined voids created by apical snouts and arches of cells (a sieve-like or cribriform structure). Tiny and exhibiting little to moderate nuclear pleomorphism, the tumour cells are small [2, 6].Mitoses are uncommon. Cribriform carcinomas typically manifest at an advanced stage and have a bad prognosis. They test ER positive on

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IHC in all cases and PR positive in 69%.

Apocrine cancer was the other uncommon variation that our research found. It is a well-defined tumour made up of apocrine cell sheets. A 51-year-old woman who had a tumour in her left breast was found to have apocrine cancer. More than 90% of the tumour cells exhibit histological and immunohistochemical characteristics of apocrine cells. The tumour cells must exhibit defined cell borders, an abundance of acidophilic cytoplasm with eosinophilic granules, and central to eccentric vesicular nuclei with conspicuous nucleoli in order to meet the diagnostic criteria. They might have apocrine snouts and glandular differentiation. There is just a 0.3-4% occurrence.

0.1% of all mammary neoplasms are inflammatory breast carcinomas, an uncommon histological subtype of breast cancer7. In a 38-year-old woman who arrived with a painless tumour in her right breast, we found a case of inflammatory carcinoma. A tumour with neoplastic cells mixed in with a substantial inflammatory infiltration was visible under the microscope. Given its dismal prognosis, an accurate and timely identification of an inflammatory carcinoma in histopathology is therefore always desired.In our case, ER and PR were positive in the tumour cells, with Her-2 negativity.

A unusual variation of breast carcinoma known as invasive lobular carcinoma has a mixture of invasive tubules and lobule-like cells. It causes 1% of cases of breast cancer. A 60-year-old woman who had a lump in her right breast that had been there for four months participated in our study. A 4x3x2 cm grayish-white tumour with an infiltrating border was found on the sliced portion by MRM. A tumour with neoplastic cells arranged in sheets, cords, tubules, cribriforms, lobules, and a solid pattern was visible under light microscopy. Infiltrating the duct in the fibrous stroma, the tumour cells show an intermixed pattern of tiny, spherical tubules and solitary cells that resemble lobules. Due to the case's rarity and distinct variety with a good prognosis, we decided to report it.

Most pathologists have very little experience with some breast lesions, such as cribriform, metaplastic, mucinous, and apocrine carcinomas. Such lesions could go unnoticed or unidentified, which could lead to an inaccurate diagnosis and poor patient care. Therefore, the goal of this course is to familiarise patients with a variety of breast lesions in order to enable accurate identification and diagnosis of these lesions. Over the course of three years, we have compiled a list of unique breast lesions with a variety of benign and malignant aetiologies, behaviours, and prognoses. For identifying a diagnosis and gauging prognosis, histopathology and Immunohistochemistry have long been regarded as the gold standards.

Conclusion

Complete knowledge of common breast masses with unusual histological variants, as well as their accompanying clinical and imaging characteristics, can help with accurate diagnosis and prompt treatment. This study summarises the history, imaging, and histology of rare breast tumours in order to provide support for choosing the best surgical technique. We record these breast lesions because of their rarity in terms of clinical presentation and histological type, both of which were supported by immunohistochemistry. Despite the fact that breast cancer has imaging characteristics that are easily identifiable, it is usually difficult to diagnose cancer accurately merely only on imaging, necessitating a biopsy. The prevalence of benign breast illnesses that mimic cancer suggests a careful link between the radiologic and pathologic findings.

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