

Patterns of Malignant and Benign Breast Lesions in Hail Region: A Retrospective Study at King Khalid Hospital

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Abstract—Background and Objectives: Breast carcinoma is the most common cancer of females in Hail region, accounting for 31% of all diagnosed cancer cases followed by thyroid carcinoma (25%) and colorectal carcinoma (13%). Methods: In the present retrospective study, all cases of breast lesions received at the histopathology department in King Khalid Hospital, Hail, during the period from May 2011 to April 2016 have been retrieved from department files. For all cases, a trucut biopsy, lumpectomy, or modified radical mastectomy was available for histopathologic diagnosis, while 105/140 (75%) had, as well, preoperative fine needle aspirates (FNA). Results: 49 cases out of 140 (35%) breast lesions were carcinomas: 44/49 (89.75%) was invasive ductal, 2/49 (4.1%) invasive lobular carcinomas, 1/49 (2.05%) intracystic low grade papillary carcinoma and 2/49 (4.1%) ductal carcinoma in situ (DCIS). Mean age for malignant cases was 45.06 (+/-10.58): 32.6% were below the age of 40 and 30.6 below 50 years, 18.3% below 60 and 16.3% below 70 years. For the benign group, mean age was 32.52 (+/-10.5) years. Benign lesions were in order of frequency: 34 fibroadenomas, 14 fibrocystic disease, 12 chronic mastitis, five granulomatous mastitis, three intraductal papillomas, and three benign phyllodes tumor. Tubular adenoma, lipoma, skin nevus, pilomatrixoma, and breast reduction specimens constituted the remaining specimens. Conclusion: Breast lesions are common in our series and invasive carcinoma accounts for more than 1/3rd of the lumps, with 63.2% incidence in pre-menopausal ladies, below the age of 50 years. FNA as a non-invasive procedure, proved to be an effective tool in diagnosing both benign and malignant/suspicious breast lumps and should continue to be used as a first assessment line of palpable breast masses.

Keywords—Age incidence, breast carcinoma, fine needle aspiration, Hail Region

I. INTRODUCTION

BREAST carcinoma is the most commonly diagnosed female cancer in different parts of the world including Saudi Arabia and Hail region. It accounts for one third of newly diagnosed female cancers, coming in frequency more than thyroid and colorectal carcinomas [1]. The increased incidence worldwide and presentation at a younger age in developing countries [2]-[4] with poor resources has led to the adoption of simple, cost effective methods of early diagnosis [5]-[7]. FNA is one of the most widely used methods for

diagnosing and grading of breast carcinoma on cytological material [8], [9]. The efficiency of cytological grading adopted by Robinson and its concordance with histological grade on tissue biopsy, has been a subject of debate. Some authors suggested a core needle biopsy as the first measure where grading and hormone receptor status can be done, thus replacing FNA [10]-[13]. Others still preferred the FNA technique and performed cytological grading on scant material [14]-[16].

II. MATERIAL AND METHODS

Benign and malignant breast lesions retrieved from Histopathology files of King Khalid hospital during a 5-year period (from May 2011 up to April 2016) have been studied and relevant clinico pathological data have been recorded. Diagnosis was performed on tissue sections from surgical specimens (lumpectomies and/or modified radical mastectomies) as well as on needle core biopsies. Preoperative FNA cytology has been recorded whenever available.

All cytological specimens were air-dried and stained by Giemsa stain. Tissue specimens were formalin-fixed, paraffin embedded and stained by conventional H&E.

Robinson breast carcinoma grading system [4] was used for FNA grading where six parameters have been evaluated: cell dissociation, cell size, cell uniformity, nucleolus, nuclear membrane, and nuclear chromatin pattern (Table I). For each of the six criteria, a grade of 1-3 was given. Score from 6-11 was grade 1, from 12-16 grade 2, and from 17-18 grade 3.

The modified Bloom and Richardson grading [5] was used for histology. Score 3-5 was grade 1, from 6-7 grade 2, and from 8-9 grade 3 (Table II).

An IBM SPSS 16 was used to compare variants. A *p*-value less than 0.05 was considered significant.

III. RESULTS

Total number of breast lesions during a 5-year period was 140 biopsy specimens, out of which 105 (75%) had as well an initial FNA cytology. Malignant breast lesions constituted 35% of the cases (49 out of 140). Majority of carcinomas 44 out of 49 were invasive ductal carcinomas (IDC) Non-Otherwise Specified (NOS). Two cases were Invasive Lobular Carcinoma (ILC) subtype, one case of intracystic low grade papillary carcinoma and two cases ductal carcinoma in situ (DCIS) (Fig. 1). Lymphovascular invasion was present in four cases of IDC, lymph node metastasis in three cases, and a

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locally advanced fungating mass in one case.

TABLE I
ROBINSON CYTOLOGICAL GRADING FOR BREAST CANCER

Scoring	1	2	3
Cell dissociation	Mostly clusters	Mixture of single cells and clusters	Mostly discohesive single cells
Cell size	1-2 times size of an RBC	3-4 times size of an RBC	>or= 5times size of RBC
Cell uniformity	monomorphic	Mildly pleomorphic	pleomorphic
Nucleoli	inconspicuous	noticeable	prominent
Nuclear outlines	smooth	Slightly irregular /folds & grooves	Buds and Clefts
Chromatin pattern	Fine or vesicular	granular	Clumped and cleared

TABLE II
HISTOLOGICAL GRADING OF BREAST CARCINOMA (MODIFIED BLOOM AND RICHARDSON GRADING SYSTEM)

Score	1	2	3
Tubule formation	Tubular formation in > 75 % of the tumor	Tubular formation in 10 to 75 % of tumor	Tubular formation in < 10 % of the tumor
Nuclear Pleomorphism	Nuclei with minimal variation in size and shape	Nuclei with moderate variation in size and shape	Nuclei with marked variation in size and shape
Mitotic count per 10 high power fields	0-5/10 hpf	10/10 hpf	>11/10 hpf

Fibroadenomas constituted the majority of benign breast lumps (no. = 34), followed by fibrocystic disease, chronic mastitis, granulomatous mastitis, intraductal papilloma, benign phyllodes tumor, tubular adenoma and lipoma (Fig. 2). Intradermal nevus, pilomatrixoma, and breast reduction specimens constituted the remaining lesions.

For malignant cases mean age were 45.06(+/-10.58). The most affected age group was 40-49 years. For benign cases, mean age was 32.52(+/-10.5) and the age group from 20-29 years was the most affected (Fig. 3).

Out of 49 malignant histologically proven cases, FNA diagnosis was either suspicious for malignancy, atypical cells or malignant in 45/49 of cases. Four lesions were false negative, with a diagnosis of fat necrosis (DCIS), proliferative breast disease with atypia (IDC gr3), fluid cyst low grade intra ductal papillary carcinoma and acute mastitis (IDC gr3).

Both cytological and histological gradings were available in 26 malignant cases: 24 IDC and two IL. Two out of 24 IDC were grade1, 18/ 24 grade 2, and 4/24 were grade 3 (Figs. 4-6). In two cases of invasive lobular carcinoma (IL) grade was 1 (Fig. 7). Low grade ductal papillary carcinoma and ductal carcinoma in situ (DCIS) had only histological grading (Table III).

Concordance between cytological and histological grading was found in 18/24 (75%) of IDC, and in 2/2(100%) of IL carcinomas. Grade 2 tumors were all same grade on both cytology and histology. Grades 1 and 3 were not coinciding with each other in eight cases (Table IV). Using one way ANOVA, a borderline significance could be found between cytological and histological grading ($p=0.059$).

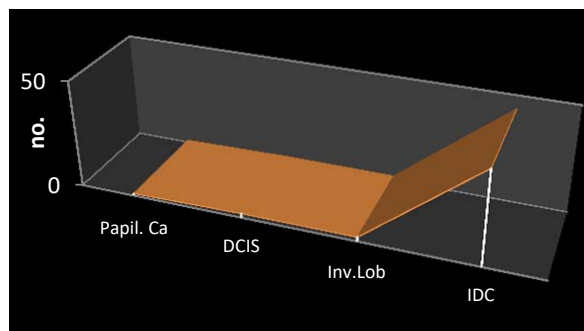


Fig. 1 Types of Malignant Breast Lesions in our Series

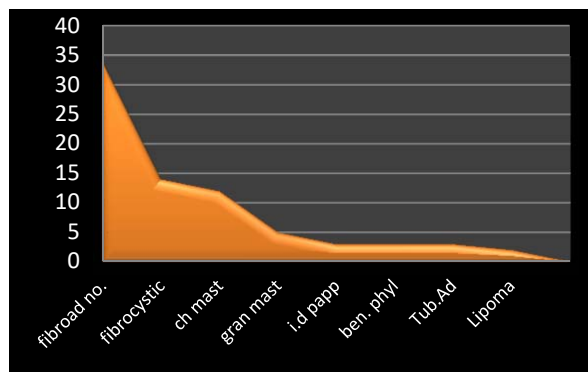


Fig. 2 Types of Benign Breast Lesions in Our Series

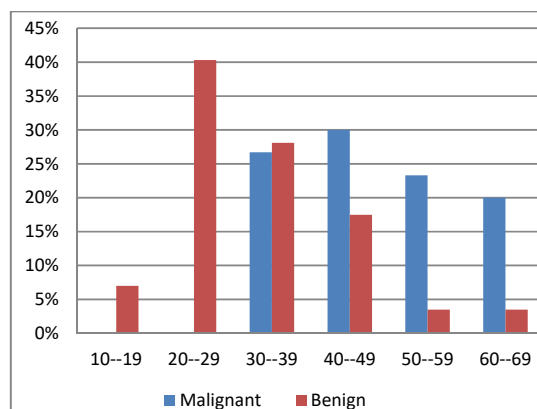


Fig. 3 Age Groups in Benign and Malignant Lesions Studied

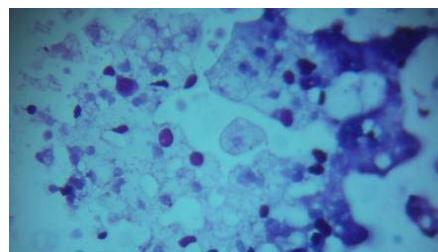


Fig. 4 IDC cytological score "2" grade "2" showing discohesive cells & clusters. Giemsa stain.x400

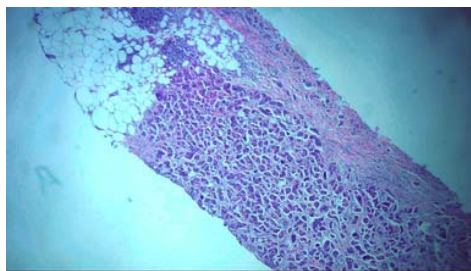


Fig. 5 IDC histological grade "2" in Needle core biopsy. H&E x100

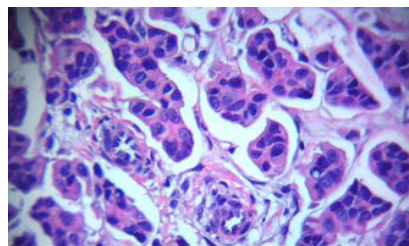


Fig. 6 IDC showing moderate pleomorphism and irregular nuclear outline score "6", grade "2". H&E x400

TABLE III
CYTOLOGICAL AND HISTOLOGICAL SCORING AND GRADING OF BREAST CARCINOMAS

No.	Diagnosis	Discoh. 1-3	Pleom 1-3	Nucleo 1-3	Nucl.irr 1-3	Chromatin 1-3	Nu.size1- 3	Scor /12	Gr.Cy	Tubules	pleomo rphism	mitosis	Score /9	Gr.H
1.	IDC	2	2	2	2	1	2	11	1	3	2	1	6	2
2	IDC	2	2	2	2	2	2	12	2	3	3	1	7	2
3	IDC	3	2	2	2	2	2	13	2	2	2	2	6	2
4	IDC	2	2	2	2	2	2	12	2	3	2	2	7	2
5	IDC	2	2	2	2	2	2	12	2	3	2	1	6	2
6	IDC	3	3	2	2	2	3	15	2	3	3	3	9	3
7	Papillary Carc.	Non	Non	Non	Non	Non	Non	Non	Non	Non	Non	Non	Non	Non
8	IDC	2	2	2	2	2	2	12	2	3	3	1	7	2
9	IDC	2	1	2	2	2	1	10	1	3	2	1	6	1
10	IDC	2	2	2	2	2	2	12	2	2	2	2	6	1
11	IDC	2	2	2	2	2	2	12	2	3	2	1	6	2
12	IDC	2	2	2	2	2	2	12	2	3	2	1	6	2
13	DCIS	Non	Non	Non	Non	Non	Non	Non	Non	Non	Non	Non	Non	Non
14	IDC	3	3	2	2	2	3	15	2	3	3	3	9	3
15	IDC	2	1	2	2	2	2	11	2	3	3	1	7	2
16	Inv. Lobular	2	1	1	1	2	2	9	1	1	2	1	4	1
17	IDC	1	1	2	2	2	2	11	1	3	2	1	6	2
18	IDC	2	2	2	2	2	2	12	2	3	2	1	6	2
19	Inv. Lobular	3	1	2	2	2	1	11	1	1	2	1	4	1
20	IDC	2	1	2	2	2	2	12	1	3	2	1	6	2
21	IDC	3	3	2	2	2	2	15	2	3	3	3	9	3
22	IDC	1	2	2	2	1	1	9	1	3	3	2	8	3
23	IDC	2	2	2	2	2	2	12	2	1	3	2	6	2
24	IDC	2	2	2	2	2	2	12	2	3	2	2	7	2
25	IDC	2	2	2	2	2	2	12	2	3	2	1	6	2
26	IDC	2	2	2	2	2	2	12	2	2	2	2	6	2
27	IDC	2	2	2	2	2	2	12	2	1	2	3	6	2
28	IDC	2	2	2	2	2	2	12	2	3	2	1	6	2

TABLE IV
COMPARISON BETWEEN CYTOLOGICAL AND HISTOLOGICAL GRADING IN
BREAST CARCINOMA

Cytological score	Cytological Grade	No. (%)	Histological score	Histological Grade	No. (%)	p- value
6-11	1	6	3-5	1	4	0.0598
12-16	2	20	6-7	2	18	
17-18	3	0	8-9	3	4	
Total no.		26			26	

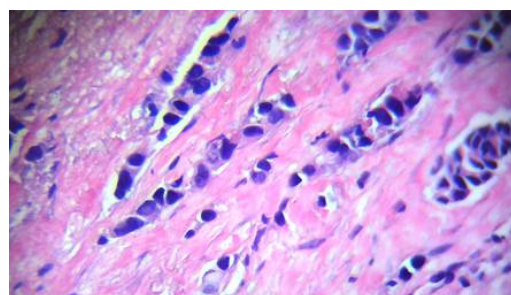


Fig. 7 Invasive lobular carcinoma, score "4" Grade "1" showing rows of single monomorphic malignant cells. H&E x400

IV. DISCUSSION

Breast cancer has comprised 22.9% of female cancers

world-wide [17], [18] causing 13.7% of cancer deaths in women in 2008 [19], [20]. Several studies in Arab world, Middle East, and Africa have documented a mean age below 50 years [21], [22] with an older age at diagnosis in Western and Asian countries [23], [24]. In the present study, the mean age was 45.06 (+/-10.58), 32.6% were below the age of 40 and 30.6% below 50 years, which makes altogether 63.2% below the age of 50, 18.3% below 60, and 16.3% below 70 years. This was in accordance with other regions in Saudi Arabia and Middle East countries [18]-[20], [24].

FNA cytology has long been used as a first diagnostic procedure for breast lumps, being simple, non-invasive and gives rapid, reliable results. However, recently, its replacement by needle core biopsy was recommended in several centers as a method for assessment of breast cancer preoperatively [24].

In the present study, diagnosis and grading of invasive ductal as well as invasive lobular carcinomas was efficiently done by FNA cytology. Both histologic and cytological gradings were in agreement in 75% of carcinomas, and there was a border-line significance ($p=0.0598$) (Table IV). However, lesions like intra ductal papillary carcinoma presenting as a cystic mass and DCIS failed to be correctly diagnosed. Cytological criteria set by Robinson et al. [4] especially discohesiveness, nuclear membrane irregularity, size of nucleus and pleomorphism were useful both in diagnosis and grading of malignancy in IDC and differentiating it from ILC (Table III). This was in accordance with other studies too [25].

V. CONCLUSION

Breast carcinoma in Hail region is the most common cancer among females and it occurred at a younger age, which was in accordance with other parts in Saudi Arabia and Middle East countries.

FNA cytology as a non-invasive, rapid, and inexpensive procedure proved to be an effective initial diagnostic tool in both benign and malignant/suspicious breast lumps. It is recommended to be used as a first assessment line of palpable breast masses, as it also allows immediate reporting. However, final grading of breast cancer is recommended to be done on histological sections, which would also allow assessment of hormone receptors and prognostic markers.

REFERENCES

- [1] Seada LS, Al Rashid F, Negm A: A Four-Year Study of Thyroid Carcinoma in Hail Region: Increased Incidence. *International Journal of Medical, Health, Biochemical, Bioengineering and Pharmaceutical Engineering*, Vol 10 no.12, 2016.
- [2] Parkin DM, Bray F, Ferlay J, Pisani P. Global cancer statistics, 2002. *CA Cancer J Clin*. 2005;55(2):74-108
- [3] Anderson BO, Jakesz R. Breast cancer issues in developing countries: an overview of the Breast Health Global Initiative. *World J Surg*. 2008; 32(12):2578-85.
- [4] Robinson IA, McKee G, Kissin MW. Typing and grading breast carcinoma on fine needle aspiration: is this clinically useful information? *Diagn Cytopathol*. 1995; 13(3):260-5.
- [5] Fisher ER, Redmond C, Fisher B. Histologic grading of breast cancer. *Pathol Annu*. 1980; 15(Pt 1): 239-51.
- [6] Morgan D, Sibbering D, Galea M, Ellis I, Elston C, Blamey R. Selection for adjuvant therapy using the Nottingham prognostic index. *Breast*. 1993; 2:187.
- [7] Shyyan R, Masood S, Badwe RA, et al. Breast cancer in limited-resource countries: diagnosis and pathology. *Breast J*. 2006;12 Suppl 1:S27-37.
- [8] Vargas HI, Masood S. Implementation of a minimally invasive breast biopsy program in countries with limited resources. *Breast J*. 2003;9 Suppl 2:S81-5.
- [9] Feoli F, Paesmans M, Van Eeckhout P. Fine needle aspiration cytology of the breast: impact of experience on accuracy, using standardized cytologic criteria. *Acta Cytol*. 2008;52(2):145-51.
- [10] Howell LP. Equivocal diagnoses in breast aspiration biopsy cytology: sources of uncertainty and the role of "atypical/indeterminate" terminology. *Diagn Cytopathol*. 1999;21(3):217-22.
- [11] Hussain MT. Comparison of fine needle aspiration cytology with excision biopsy of breast lump. *J Coll Physicians Surg Pak*. 2005;15(4):211-4.
- [12] Elston CW, Ellis IO. Pathological prognostic factors in breast cancer. I. The value of histological grade in breast cancer: experience from a large study with long-term follow-up. *Histopathology*. 1991;19:403-10.
- [13] Ruibal A, Arias JJ, Del Rio MC, Lapeña G, Schneider J, Tejerina A. Histological grade in breast cancer: association with clinical and biological features in a series of 229 patients. *Int J Biol Markers*. 2001;16:56-61.
- [14] Al-Rikabi A and Husain S: Increasing prevalence of breast cancer among Saudi patients attending a tertiary referral hospital: a retrospective epidemiologic study. *Croat Med J*. 2012 Jun; 53(3): 239-243
- [15] Amin TT, Al-Mulhim AR, Chopra R. Histopathological patterns of female breast lesions at secondary level care in Saudi Arabia. *Asian Pac J Cancer Prev*. 2009;10:1121-6.
- [16] Najjar H, Easson A. Age at diagnosis of breast cancer in Arab nations. *Int J Surg*. 2010;8:448-52
- [17] Akhtar SS, Nadrah HM, Al-Habdan MA, El-Gabbani SA, El-Farouk GM, Abdelgadir MH, et al. First organized screening mammography programme in Saudi Arabia: preliminary analysis of pilot round. *East Mediterr Health J*. 2010;16:1025-31.
- [18] Sait WA, Al-Amoudi SM, Tawtai DA, Abduljabbar HS. The knowledge of breast cancer among young Saudi females. *Saudi Med J*. 2010;31:1242-4.
- [19] Westlake S, Cooper N. Cancer incidence and mortality trend in the United Kingdom and constituent countries 1993 to 2004. *Health Stat Q*. 2008;(38):33-46
- [20] Ezzat N, Hafez N: The validity of immunocytochemical expression of cyclin D1 in fine needle aspiration cytology of breast carcinoma. *Journal of the Egyptian National Cancer Institute*, Volume 24, Issue 3, September 2012: 145-150.
- [21] Elidrissi Errahhali M, Elidrissi Errahhali M, Ouarzane M, El Harroudi T, Afqir S, Bellaoui M. First report on molecular breast cancer subtypes and their clinico-pathological characteristics in Eastern Morocco: series of 2260 cases. *BMC Womens Health*. 2017 Jan 9;17(1):3.
- [22] B Lieske, I D Ravichandran, I* and D Wright I : Role of fine-needle aspiration cytology and core biopsy in the preoperative diagnosis of screen-detected breast carcinoma . *Br J Cancer*. 2006 Jul 3; 95(1): 62-66.
- [23] Blamey R, Hornmark-Stenstam B, Ball G, Blichert-Toft M, Cataliotti L, Fourquet A, et al. ONCOPOOL—a European database for 16,944 cases of breast cancer. *Eur J Cancer*. 2010;46(1):56-71.
- [24] Moschetta M, Telegrafo M, Carluccio DA, Jablonska JP, Rella L, Serio G, et al. Comparison between fine needle aspiration cytology (FNAC) and core needle biopsy (CNB) in the diagnosis of breast lesions. *G Chir*. 2014;35:171-6.
- [25] Tham TM, Iyengar KR, Taib NA, Yip CH. Fine needle aspiration biopsy, core needle biopsy or excision biopsy to diagnose breast cancer – Which is the ideal method? *Asian Pac J Cancer Prev* 2009;10:155-8.