



ISSN: 0067-2904

Elucidative Histopathological Study in Female Cancer Patients

Juveria Tarannum^{1*}, P. Manaswini¹, Ch. Deekshitha¹, B. Pratap Reddy², A. Shyam Sunder³

¹Pharm D, Department of Pharmacy Practice, Balaji Institute of Pharmaceutical Sciences, Narsampet, Warangal, Telangana, India

²Surgical Oncologist, MBBS, MS (General Surgery), Fellowship in Surgical Oncology, St. Ann's Cancer Hospital, Warangal, Telangana, India

^{3*} Head of the Department, Department of Pharmacy Practice, Balaji Institute of Pharmaceutical Sciences, Narsampet, Warangal, Telangana, India

Received: 26/7/ 2019

Accepted: 30/ 9/2019

Abstract

Aims: Because of the high incidence of cancer in females, we need to identify an accurate therapy to deal with the treatment of different types and stages of cancer. Histopathology acts as an important step to foresee the stage in which the cancer is present, its risk of metastasis, and the health outcomes after completion of treatment. Histopathology grading acts as an important criterion to determine the treatment pattern to be adopted, the prognosis in patients and other possible future risks. Hence conducting novel histopathological studies in major female cancers is necessary in determining the treatment plan to be chosen for the patient.

Study design: Retrospective Observational study

Place and Duration of Study: St. Ann's Cancer Hospital, Warangal, Telangana, India. The patient's histopathological reports were collected between March and August 2018.

Methodology: The study sample included 275 non-pregnant female patients aged above 20 years and diagnosed with different cancers based on histopathology. Histopathological observations were taken by collecting parameters that included specimen submitted, lymphadenopathy specimen, macroscopic appearance, macroscopic tumour site, coexistent pathology, histological tumour grade, lymphovascular invasion, and distant metastasis.

Results: The histopathological study concludes that regional lymph nodes (55.2%) were more common than other lymph nodes. Mostly, tumours demonstrated swollen and ulcerative appearance (48%), with grading as G0 stage (57.45%) having better prognosis and good quality of life. The most commonly observed types of tumours were as follows; In Breast Cancer: infiltrating ductal carcinoma (61.9%), in Cervix Cancer: squamous cell carcinoma (83.92%), in Ovarian Cancer: mucinous cystadenocarcinoma (53.84%), in Vaginal Cancer, and in Vulvar Cancer: squamous cell carcinoma (100%).

Conclusion: Knowing the type of tumour to develop, the threat it poses to health, and the mechanisms that mediate its development are important factors in the management of the disease. This detailed information may aid the implementation of more accurate preventive measures in a population by selecting the proper treatment plan and understanding the risk of future chances of reoccurrence and metastasis.

Keywords: Cancer, Carcinoma, Histopathology, Infiltrating Ductal carcinoma, Metastasis, Mucinous cystadenocarcinoma, squamous cell.

*Email: juveria5496@gmail.com

1. Introduction

Pathology is the cornerstone of cancer pathogenesis, diagnosis, prognosis, and treatment [1]. Epidemiological studies focusing on histopathology provide an insight on the molecular mechanisms of the disease from a population perspective. Major insights into the causes of cancer can be obtained by epidemiological studies that can relate to particular environmental, hereditary and cultural influences on occurrence of specific neoplasms [2]. The epithelial elements of tumour are used for grading and they are based on three histological factors; First, degree of: structural differentiation as shown by the presence of tubular arrangement of the cells. Second, variation in size, shape, and staining of the nuclei, thirdly frequency of hyper chromatic and mitotic figures. Having assessed each of these factors separately, the potential malignancy of the tumour is determined from the composite histological picture [3]. If the tumour cells and the organization of tumour tissue are close to normal, the tumour is called “well differentiated”, whereas if they tend to grow and spread at fast rate, the tumour is known as “undifferentiated” or “poorly differentiated”, with abnormal shape of cells and possible lack of normal tissue structure. The extent of tubule formation, nuclear size, pleomorphism, and mitotic rate are the parameters which are routinely measured, and each assigned with a score of 1 to 3, with the final grade is identified from the sum of each individual score [3]. Depending on the degree of differentiation, well differentiated tumour (grade I) scores 3 to 5, moderately differentiated tumour (grade II) scores 6 to 7, and poorly differentiated tumour (grade III) scores 8 to 9 [4]. Morphological assessment of the degree of differentiation was shown in numerous studies to provide useful prognostic information in cancer development [5], where survival is decreased with the advancement in grade. Within each stage, grading separates the case into three distinct subgroups. First, the regional stage cases are assigned as Grade 3, 4, 5 which have higher survival rates. Second, the localized stage cases are assigned as Grade 6, 7. Third, the distant and or metastised stage tumours are assigned Grade 8, 9. Thus, the pathological grading helps in the identification of high- and low-risk subgroups within each stage. Grading reflects the potential malignancy of the tumour and it is important due to two reasons. Firstly, it provides a measurement of the probable extent of tumour upon the initial examination and indicates the likelihood of occult metastases in regional lymph nodes and distant organs, which would not be detected by ordinary staging methods. Secondly, grading can propose the potential of persistent decline in survival rate, as in the case of Grade 1 tumours where the decline reaches up to 15 years for patients who may have incidence of distant metastases upon first diagnosis with low malignancy. This feature is supported by the fact that more than 50% of these patients had the axillary deposits which may had undergone metastases [3]. A more accurate grading will help to clarify the relative quality of the different approaches used for the operable cases [3].

Breast cancer is the most commonly diagnosed cancer and the second leading cause of death in women. Breast cancer is mostly comprised of the cases of infiltrating ductal cell carcinoma (IDC), ductal cell carcinoma [6]. Ovarian tumours are notorious for their large size and they have high incidence of invasive epithelial ovarian cancer [7]. Ovarian cancer is divided into two types of epithelial tumours based on morphological and clinical characteristics. Type I epithelial tumors include low grade serous, endometrioid, clear cell, mucinous, and transitional cell carcinomas. They are often present at an early stage, may arise from borderline ovarian tumours or endometriosis, and have better prognosis. Type II epithelial tumours comprise high- grade serous carcinoma, undifferentiated carcinomas, and malignant mixed mesodermal tumors, which are mostly at advanced stage and have poor prognosis [8]. Cervix cancer, being the third leading cancer in mortality among women worldwide, includes squamous cell carcinoma (SCC) that is the predominant histological type, as well as adenocarcinoma and adenosquamous cell carcinoma, which are identified by the link with human papilloma virus (HPV), poor prognosis, and the need for early detection [1, 9]. Endometrial cancer is predominantly observed in postmenopausal women, being mostly related with reproductive factors such as parity and age at birth, and is at increase in incidence worldwide. Endometrial type I cancer involves low grade endometrioid histology with hyperestrogenism and is observed at early age with good prognosis. Type II endometrial cancer involves hyper-estrogenic state, non- endometrioid serous, or clear cell carcinoma, which are mostly diagnosed at advanced stages [10]. Adenocarcinoma, squamous metaplasia, and mucinous cancers are the most detected histological features in endometrial cancer. Endometrial hyperplasia can be simple or complex based on the glandular framework. Simple hyperplasia is a proliferative lesion characterised by minimal glandular complexity and crowding with abundant stroma between lands. Complex hyperplasia represents a proliferative lesion with severe

glandular complexity and crowding [11, 12]. The incidence of primary vaginal cancer increases with age [13]. The precursors for vaginal cancer, vaginal intraepithelial neoplasia (VAIN) and invasive vaginal cancer, have a strong association with HPV infection and previous history of cervical neoplasia. Lymph nodes drainage is important as vaginal cancer involves lymph nodes even in early stage of disease. Mostly, inguinal lymph node involvement has aggressive tumour behaviour with lower rates of survival. The most common tumour of vagina occurs via metastasis. Primary histopathological types include squamous cell carcinoma, adenocarcinoma, and clear cell adenocarcinoma. Squamous cell carcinoma arises from vaginal mucosa composed of estrogen-sensitive stratified squamous epithelium, which is mostly observed in postmenopausal women. Adenocarcinoma, unlike squamous cell carcinoma, affects younger patients and has a high rate of metastasis [14]. Vulvar cancer is the fourth most common gynaecological cancer among the female genital tract malignancies. Vulva is comprised of female external genitalia, which includes labia majora, minoris, vestibule, vaginal introitus and urethral meatus. Vulvar cancer is distinguished into two separate diseases, the first type involves HPV infection that causes vulvar intraepithelial neoplasia (VIN), whereas the second includes vulvar neoplastic epithelial disorder (VNED), considering that advanced age leads to cellular atypia and eventually develops to cancer [15]. Squamous cell carcinoma accounts for most of the malignant vulvar cancers, which can be grouped into three main histological subtypes which are the warty, basaloid, and keratinizing subtypes. The most predominant keratinizing subtype is seen mostly in post menopausal women, while the warty and the basaloid subtypes are observed in premenopausal and perimenopausal women [15, 16].

2. Methods

4.1. Study sample and design:

The study was conducted at St. Ann's Cancer Hospital. It is a retrospective observational study that included 275 female cancer patients above the age of 20 years. It was a 6 Months study (March 2018-August 2018). Based on reported data, the study population was divided on the basis of the pathogenesis involved. Based on reported data from the patients, data was entered in MS excel database using MS Excel graphs.

Histopathological Profile

The histopathological profile includes: Submitted specimen, Lymphadenopathy specimen, Macroscopic appearance, Macroscopic tumour site, co existent pathology, Histological tumour grade, Lymph vascular invasion, Distant Metastasis.

3. Results

Table 1-Lymph nodal involvement in different female cancers

TYPES OF LYMPH NODES INVOLVED	NUMBER OF LYMPH NODES INVOLVED
Regional lymph nodes	152
Axillary lymph nodes	118
Inguinal lymph nodes	2
Non regional lymph nodes	3

Table-1 Lymph nodes involvement in female cancers, the results of the present study demonstrated that the regional lymph nodes invasion is seen mostly.

Table 2-Macroscopic appearance of all tumours in female cancers

TYPES OF MACROSCOPIC APPEARANCE	NUMBER OF CASES
Swollen	132
Ulcerative	132
Palpable	9
Cauli Flower Growth	1
Mucinous	1

Table -2 Macroscopic appearance of carcinoma in female cancers, the macroscopic appearance of tumours was swollen and ulcerative mostly.

Table 3-Grading of tumours in female cancers according to their differentiation rate

TYPES OF GRADING	NUMBER OF CASES IN EACH GRADING
G0(not graded)	158
G1(well differentiated)	109
G2(moderately differentiated)	4
G3(poorly differentiated)	4

Table-3Histological tumour grading, this study shows that most tumours were in G0 and G1 phase when reported at the health care centre

Table 4-Types of tumours involved in breast cancer patients

PATHOLOGY OF BREAST CANCER	NUMBER OF CASES
Infiltrative ductal cell carcinoma	75
Squamous cell carcinoma	1
Medullary ductal cell carcinoma	1
Ductal cell carcinoma	10
Medullary carcinoma	2
Adenocarcinoma	1
Invasive ductal cell carcinoma	4
Infiltrative medullary carcinoma	8
Infiltrative tubular carcinoma	1
Mucinous ductal carcinoma	1
Invasive medullary carcinoma	3
Fibrocystic carcinoma	1
Mucinous variant carcinoma	1
Mucinous variant infiltrative ductal cell carcinoma	1
Total	121

Table-4Types of tumours in breast cancer patients, in this study, the types of tumours involved in breast cancer were Infiltrative ductal cell carcinoma mostly.

Table 5-Types of tumours involved in cervix cancer patients

PATHOLOGY OF CERVIX CANCER	NUMBER OF CASES
Squamous cell carcinoma	94
Stratified squamous cell carcinoma	1
Papillary squamous cell Carcinoma	1
Infiltrative squamous cell carcinoma	1
Adenocarcinoma	6
Adenosquamous cell carcinoma	1
Invasive squamous cell carcinoma	1
Keratinised squamous cell carcinoma	4
Invasive squamous small cell carcinoma	1
Squamous glassy carcinoma	1
Total	112

Table-5 Types of tumours in cervix cancer patients, in this study, the results show that squamous cell carcinoma was present mostly in cervix cancer patients.

Table 6-Types of tumours involved in ovarian cancer patients

PATHOLOGY OF OVARIAN CANCER	NUMBER OF CASES
Mucinous cystadenocarcinoma	14
Adenocarcinoma	1
Serous cystadenocarcinoma	5
Mucinous papillary cystadenocarcinoma	1
Dysgerminoma	1
Papillary mucinous adenocarcinoma	1
Papillary cystadenocarcinoma	1
Mucinous adenocarcinoma	1
Mucinous carcinoma	1
Total	26

Table-6 Types of tumours in ovarian cancer patients, in this study for ovarian cancers, mucinous cystadenocarcinoma was observed mostly

Table 7-Types of tumours involved in vaginal cancer patients

PATHOLOGY OF VAGINAL CANCER PATIENTS	NUMBER OF CASES
Squamous Cell Carcinoma	2
Total	2

Table -7 Types of tumours in vaginal cancer patients, in Vulva cancers Histopathology it included squamous cell carcinoma in examined cases.

Table 8-Types of tumours in vulvar cancer patients

PATHOLOGY OF VULVAR CANCER PATIENTS	NUMBER OF CASES
Squamous Cell Carcinoma	2
Total	2

Table -8 Types of tumours in vulvar cancer patients, in the examined Vagina cancers histopathology it included squamous cell carcinoma.

Table 9-Type of tumours involved in endometrium cancer patients

PATHOLOGY OF ENDOMETRIUM CANCER PATIENTS	NUMBER OF CASES
Squamous Cell Carcinoma	2
Adenocarcinoma	7
Signet Ring Cell Carcinoma	1
Total	10

Table-9 Types of tumours in endometrium cancer patients, in the examined endometrium cancer histopathology adenocarcinoma was seen mostly.

Discussion

The results of the present study demonstrated that the lymph nodes invasion types mostly included regional lymph nodes 152 and axillary lymph nodes 118 in accordance with Bloom and Richardson [3]. The macroscopic appearance of tumours was swollen in 132 cases. The histopathological tumour grading showed that 158 cases (57.45%) which according to reflects the potential malignancy of the tumour and indicates which cases are likely to have distant metastases and may produce symptoms lately and may cause death in accordance with Bloom and Richardson [3]. Also, the types of tumours

involved in breast cancer were the infiltrative ductal cell in 75 cases (61.9%). These results are in concordance with Shereen S *et al.*, which states infiltrative ductal cell carcinoma is mostly seen histologic type [6]. As related to the type of tumours involved in cervix cancer, the results showed that squamous cell carcinoma was present in 94 cases (83.92%) in accordance with Okoye showing the most predominant histologic type in cervix cancer patients [9]. For ovarian cancer mucinous cystadenocarcinoma was observed in 14 cases (53.846%) and serous cystadenocarcinoma in 5 cases (19.2%) which has not come in accordance with Matz et al [8]. For vaginal and vulvar cancers, Squamous cell carcinoma was recorded as 2 cases (100%) in concordance with N. Murakami et al and CS Gardner et al [13, 14]. For endometrium cancer, Adenocarcinoma was in 7 cases (70%) which is in accordance with Chen et al [11].

Conclusions

- Our Histopathological study concludes that regional lymph nodes invasion was more commonly recorded in the patients, followed by non-regional lymph nodes. Most tumours appeared macroscopically as swollen and ulcerated. In breast cancer, infiltrating ductal cell carcinoma was mostly detected, followed by ductal cell carcinoma and then other types. In cervical cancer, squamous cell carcinomas were mostly seen, followed by adenocarcinoma and the other types. In ovarian cancer, Mucinous cystadenocarcinoma were mainly observed, followed by Serous cystadenocarcinoma. In both vaginal and vulvar cancers, Squamous cell carcinoma was seen primarily, while Adenocarcinoma was mostly seen in endometrium cancer. Squamous cell carcinoma, Mucinous and Serous cystadenocarcinoma, as well as Ductal carcinoma were observed in undifferentiated state with higher rate of spread of tumors to adjacent tissue. Performing histopathological studies allows the determination of pathogenesis patterns of a specific cancer. Histopathological examination has been the golden standard for diagnosis in cancer and its role includes the elucidation of etiology, pathogenesis, clinicopathological correlation, and prognosis. Since the foreseeable future will likely witness the introduction of histology- based treatment options, this will require histology reports. In this study, 95% of the female cancers mentioned above had the final diagnosis based on pathology as a guide for identifying the major pathologies. Each of the identified histopathology groups has a distinct molecular pathway that influences the chemosensitivity, the pattern of metastasis, and the probability of survival.

Acknowledgements:

This study would not have been possible without the support of the female cancer patients at St. Ann's Cancer Hospital, Warangal, Telangana. We are thankful to Dr. B. Pratap Reddy, Surgical Oncologist, with whose support this study was moulded at each step. We are also grateful for the immense support of Dr. A. Shyam Sunder for reviewing decisions made by the authors.

Competing interests: Authors declare that no competing interests exist.

Author's contributions: Authors ¹ identified the need for this study, designed its criteria, performed data collection, performed the literature review, wrote the protocol and the manuscript, and performed the analysis. Author ², and Author ^{3*} managed the editing, corrections and directing the pathway of study. All authors have read and approved the final manuscript.

4. References

1. Bloom, H.J.G. and Richardson, W.W. **1957**. Histological Grading and Prognosis in Breast Cancer, A study of 1409 Cases of which 359 have been Followed for 15 years. *British Journal of Cancer*; **XI**(3): 359-377.
2. Pathak R., Jha A., Neupane PR., Chalise S., Basnyat AS. **2016**. Histopathological evaluation of carcinoma of breast. *Journal of PATHOLOGY of Nepal*, **6**:922-927.
3. Elston CW. and Ellis I. **1991**. Pathological prognostic factors in breast cancer. The value of histological grade in breast cancer: experience from a large study with long-term follow –up. *Histopathology*; **19**(5):403-410.
4. Shazima Sh., Flora D., Lobo, Waseemoddin Patel, Shamama Sheereen, Abhishek Singh Nayyar, Mubeen Khan.2018. *Cancer Translational Medicine*. **4**(4): 89- 94.
5. Geeta P., Uday Singh M., Ravi Kant S., Pramendra P., Nanik J., Tushar B. **2016**. Histopathological study of Ovarian tumors in Ajmer region. *International Journal of Medical Science and Public Health*. **5**(7):1400-1403.

6. Melissa M., Michel P., Milena S., Maria Dolores Ch., Otto V., Martin G. **2017**. The Histology of Ovarian Cancer: Worldwide Distribution and Implications for International Survival Comparisons (CONCORD-2). *Gynecol Oncol*; **144**(2):405- 413.
7. Vincent V., Claire B., Georges V., Gabor C., Mark De R. and Guy S. **2007**. Therese Vlastos. Prognostic value of histopathology and trends in cervical cancer: a SEER population study. *BMC Cancer*; **7**:164.
8. Chukwuemeka Asouzu O. **2014**. Histopathological pattern of cervical cancer in Benin City, Nigeria. *Journal of Medical Investigations and Practice*; **9**(4):147-150.
9. Emre G., Zeliha A., Mustafa A., Yuksel K., Gulcin G. **2018**. Endometrial histopathology results and evaluation of endometrial cancer risk in geriatric women. *Menopause Rev*, **17**(1):18- 21.
10. Tianhui C., Lina J., Adam G., Meike R., Bernd H., Alexander K., Hermann B. **2012**. Survival of endometrial cancer patients in Germany in the early 21st century: a period of analysis by age, histology and stage. *BMC Cancer*, **12**:128.
11. Mohamed O., Joanna F., Jckie R., Hizbullah Sh., Jemma J. **2015**. Endometrial pathology in the postmenopausal woman-an evidence based approach to management. *The Obstetrician & Gynaecologist*, **17**:29- 38.
12. Murakami, N., Kasamatsu, T., Sumi, M., Yoshimura, R. and Takahashi, K. **2013**. Radiation therapy for primary Vaginal carcinoma. *Journal of Radiation Research*, **54**:931-937.
13. Gardner, C.S., Sunil, J., H Klopp, A., Devine, C.E., Sagebiel, T., Viswanathan C. and Bhosale, P.R. **2015**. Primary vaginal cancer: role of MRI in diagnosis, staging and treatment. *British Journal of Radiology*, **88**:20150033.
14. Ibrahim A., Melanie S., Nele G., Marion Tina W., Walter J., Christoph M., Veronika G. **2015**. Vulvar cancer: epidemiology, clinical presentation and management options. *International Journal of Women's Health*; **7**:305-313.
15. Linda J. and Mauricio A. **2015**. Cuello. *International Journal of Gynecology and Obstetrics*; **143**(2): 4-13.
16. Vinay K., Abul k., Abbas, J. and Aster, C. **2006**. *Robbins Basic Pathology*. 9th Edition. Elsevier Press. Page No: 170.