ORIGINAL ARTICLE

Histopathological Characteristics of Female Breast Carcinomas Seen at the University of Port Harcourt Teaching Hospital, Port Harcourt Nigeria

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ABSTRACT

Background: *Breast carcinoma is an unpredictable disease in the sense that some patients may present with relatively early disease and die of widespread metastases within six months to one year, while others present with fairy advanced disease and yet survive longer. The aim of this study was to characterize breast carcinomas into prognostic groups using histological features.*

Methodology: *A total of 269 breast carcinomas in females received during a five-year period (January 1991 to December 1995 inclusive) were analyzed. Archive records (request forms and microscopic slides) of all breast malignancies diagnosed in the department of Anatomical Pathology of University of Port Harcourt Teaching Hospital were retrieved and evaluated with respect to histological type, histological grades, and mononuclear cell infiltration within the primary tumour. The modified Bloom-Richardson system of microscopic grading of breast carcinoma was used.*

Results: *The majority of carcinomas showed scanty or absent tubule formation (43.1%) and 59% of cases showed numerous mitotic figures. Forty-nine percent of carcinomas show poorly differentiated or anaplastic nuclei. The final tumour grade (FG) which is the summation of tubular pattern, nuclear pleomorphism and mitotic grades of each of the tumours reveals that 53% fall in FG3, 26% in FG2while only 21% fall in FG1. The majority of the breast carcinomas in this study, 58%, show scanty or absent mononuclear infiltration.*

Conclusion: *The majority of breast carcinomas in this study are poorly differentiated invasive ductal carcinoma, "not otherwise specified" which exhibit high proliferation ratio and are associated with poor host cellular immune reaction. These attributes translate to poor prognosis.*

KEY WORDS: *Breast carcinoma; tumour grade; prognosis.*

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INTRODUCTION

Breast carcinoma is an unpredictable disease in the sense that some patients come with relatively early disease and die of widespread metastases within six months to one year, while others present with fairly advanced disease and yet survive longer[1].

The clinical behaviour of breast carcinoma in individual patients reflects complex interactions between the biological properties of the neoplastic cells and the host tissue response.

There are numerous known social and biological determinants of patients' survival. Some of the parameters which could be used in determining the prognosis of breast carcinoma include: socioeconomic class, age at presentation, duration of tumour, primary tumour size, axillary lymph node involvement, histological type, tumor malignancy grade, host immune response, hormone receptor studies, vascular invasion, oncogene expression and ploidy analysis[2]. This work is limited to the study of three of the pathological characteristics of breast carcinomas namely histological type, tumour grade and host immune response.

Histological Type

Survival is generally related to specific histological types of breast cancer. The relatively uncommon histological types of breast cancer: medullary, colloid, tubular and adenoid cystic carcinomas tend to be prognostically more favourable than the infiltrating ductal carcinoma also referred to as not otherwise specified (NOS)[3,4].

Tumour Grading

Grading of a cancer is based on the degree of differentiation of the tumour cells and the number of mitoses within the tumour, as

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presumed correlates of the aggressiveness of the neoplasm[1]. In general, the better the differentiation or grade, the better the prognosis of the cancer[5-11].

Several authors have criticized grading of cancer as being too subjective and prone to intraobserver and interobserver variation[12,13].

However, analysis of tumour grading data from the population-based registry of the SEER [Surveillance, Epidemiology and End Results] program of the NCI [National Cancer Institute], covering about 12% of the US population, showed positive prognostic correlation. Significantly the grading was done by hundreds of pathologists working from different geographic areas[14].

Inflammatory Cell Infiltrate/Mononuclear Cell Reaction

Mononuclear cell reaction is a specific manifestation of humoral and cell-mediated immune response evoked by the tumour cells per se. While tumour malignancy grading may be prognostically helpful, it does not guarantee uniform behaviour within a particular grade[5]. Heterogeneous behaviour persists even among patients grouped according to grade and stage[6]. In such cases the survival characteristics have been shown to be correlated with microscopically demonstrable lympho-reticuloendothelial responses associated with the primary tumour, and reactive changes in the regional lymph nodes[15-24].

Histopathologists have the primary responsibility of establishing the histological diagnosis of the cancer. The pathology report should also provide additional information as to which subsets of patients (with different outlook) may be considered for appropriate additional treatment modalities, apart from surgical procedures.

MATERIALS AND METHODS

This study was done at the department of Anatomical Pathology of the University of Port Harcourt Teaching Hospital (UPTH), Port Harcourt, Rivers State of Nigeria.

A total of 269 breast carcinomas in females, received during a five-year period (January 1991 to December 1995 inclusive) were analyzed. Archival records (request forms and microscopic slides) of all breast malignancies diagnosed in the department were retrieved and re-evaluated. Fresh sections were re-cut from paraffin blocks of faded or unavailable slides, and stained by the H & E method. Pathological variables of widely accepted prognostic significance evaluated included histological type, histological grade, nuclear grade, mitotic grade, and mononuclear cell infiltrate within the primary tumour.

Histological Types

The typing and nomenclature of the histological patterns was classified according to the WHO guidelines on the classification of breast tumours[25].

Grading

The tumors were graded according to a modification of the method of Bloom and Richardons[8] summarized by Russo, and his co workers, of the Michigan Cancer Foundation, Detroit, USA[26]. Essentially, this method separately evaluates each of the three grading components (degree of tubule formation; size, shape and chromatism of the nuclei; and number of mitotic figures). For each breast carcinoma assessed, point scores were assigned for each grading component, and then the total points for all 3 grading components were summed.

Mononuclear Cellular Infiltrate

The components of the cellular reaction around and within the tumour include lymphocytes, plasma cells and macrophages. The content was assessed according to the method of Black[6] which is confirmed by other studies[15,27] and classified into three;

Dense lymphoid infiltrate,
Moderate lymphoid infiltrate, and
Scanty or absent lymphoid infiltrate

RESULTS

Histological Types Of Female Breast Carcinoma

The most common histological type of breast carcinoma was the invasive ductal carcinoma (Table I). The next common types seen were papillary carcinoma, medullary carcinoma, and infiltrating ductal carcinoma with a predominant intraductal component, in that order. In four cases, the invasive

carcinoma was associated with a pagetoid spread to the skin of the nipple.

Tumour Grades

Fourteen point seven percent of the carcinomas showed a well-differentiated tubular pattern. In 43.1% of the carcinomas there was scanty or absent tubule formation. Nine point three percent of the carcinomas showed well-differentiated nuclei. The majority of the carcinomas (49.3%) showed poorly differentiated or anaplastic nuclei. Nineteen percent of the carcinomas in this study showed no mitosis, the majority (59%) showed numerous (frequent) mitoses per defined area of cancer tissue. Table II shows the distribution of the Final Grades (combined tubular pattern, nuclear pleomorphism and mitotic grades) of the female breast carcinomas in the study. Fifty-three percent of the carcinomas in this study were poorly differentiated; only 21% of the patients showed well-differentiated tumours.

Mononuclear cellular Infiltrate

The majority of the breast carcinomas in this study (58%) showed a scanty or absent mononuclear cellular infiltrate. Only 15% of tumours showed a dense mononuclear cellular reaction to the carcinoma cells.

Table I. Distribution of Histological types of Breast Carcinoma

Histological Type	No. of Patients	%
Non invasive		
Intraductal carcinoma	3	1.1
Invasive		
Invasive ductal (NOS)	219	81.4
Papillary	19	7.1
Medullary	11	4.1
Invasive ductal (with a predominant intraductal component)	10	3.7
Mucinous	3	1.1
Invasive lobular	2	0.7
Adenoid cystic	1	0.4
Apocrine	1	0.4
Total	269	100

Table II. Histological (Final Tumour) grade (FG) and number of cases

FG	No. of cases	Percentage
1	57	21
2	69	26
3	143	53
Total	269	100

DISCUSSION

Invasive ductal carcinoma, not otherwise specified, (NOS) is by far the most common type (81.4%) of breast carcinoma seen in this study. Comparable rates ranging from 66 to 80% have been reported from other studies in Nigeria[28-30] as in other parts of the world[1]. Only 3 patients (1.1%) presented with non-invasive intraduct carcinoma. In contrast, intraduct carcinoma constitutes about 20 to 30% of carcinomas in western countries[1]. This maybe partly due to early presentation and partly to the increasing use of mammographic screening, which detects smaller tumours in those countries.

Furthermore, the more prognostically favourable types of breast carcinoma (medullary, mucinous, adenoid cystic, apocrine, and invasive ductal with predominant intraductal component) together comprise only 9.7% of the invasive carcinomas in the study. It is concluded that the vast majority (over 90%) of invasive breast carcinomas seen in this hospital are of the worst prognostic types.

About 15% of the carcinomas seen in this study showed a well-differentiated glandular pattern. In contrast, only about 1% of carcinomas in western countries show well-differentiated glandular patterns[26, 31]. Furthermore, in the western cases, about 90% show very scanty or absent tubule formation. Several studies[6,27,31] have reported a significant positive correlation between increasing histological grade (degree of glandular de-differentiation) and tumour recurrence rates as well as a more rapid onset to death.

Only 21 out of 221 carcinomas (9.3%) showed well-differentiated nuclei which corresponds to the report from Detroit[26] where majority 99.7%) of carcinomas show moderately to poorly differentiated nuclei. There is a definite correlation between tumour recurrence or patient survival and the degree of nuclear pleomorphism as denoted by the

nuclear grade. Therefore the expected recurrence rate or survival rates of patients with breast carcinoma, based on the degree of nuclear pleomorphism alone is not likely to differ much from that of western countries. Nineteen percent of the carcinomas in this study showed absent or scanty mitoses as against the vast majority (59%) with a high mitotic rate. This is in complete contrast with figures from the Detroit study[26] in which only 11% showed a high mitotic rate. This finding suggests that carcinomas seen in this study have a higher proliferative rate. Indeed several investigators[26,32-34] have demonstrated that the higher the mitotic rate the higher the recurrence rate or the shorter the overall survival time.

Combination of the histological, nuclear and mitotic grades into a final grade showed that over half (53%) of all the female breast carcinomas in the study were poorly differentiated. Moderately differentiated tumours constituted 26% and well-differentiated tumours were the least frequent (21%). In contrast poorly differentiated tumours constituted only abut 18.5 to 20% of breast carcinomas studied in developed countries[26, 35].

In this study also, only 15% of carcinomas showed a dense mononuclear cellular reaction to the cancer cells. The vast majority of carcinomas showed scanty or absent mononuclear cellular infiltrate. Several investigators[5, 6, 15, 16, 19-24] have reported that the survival of patients with breast carcinoma is positively correlated with microscopically demonstrable lympho-reticulo-endothelial responses associated with the primary tumour. This relationship between mononuclear cells, nuclear atypia and tumour grade is exemplified by medulary carcinoma of the breast. The observed scarcity of mononuclear cellular reaction in this study, in addition to poor tumour cell differentiation is a manifestation of unfavourable host immunological mechanism. This could play an enhancing role in the growth and dissemination of breast carcinoma.

CONCLUSION

Majority of carcinomas in this study are poorly differentiated invasive ductal carcinoma, NOS. They exhibit high proliferative rates and are associated with poor host cellular immune resistance.

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