

Immuno-Histochemical Profile of Breast Cancers at the General Hospital of Douala-Cameroon

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Abstract

Introduction: The aim of the study was to describe the immunohistochemical aspects of breast cancers at Douala General Hospital, Cameroon. **Methodology:** This was a descriptive study with retrospective data collection, conducted from January 1st 2010 and December 31st 2019. It was focused on histologically proven breast cancers followed up at Douala General Hospital. **Results:** We collected 285 cases of breast cancer, all female, representing an annual frequency of 28.5 cases. The mean age of the patients was 48 ± 13 years. The most frequent histological form was infiltrating ductal carcinoma (83.9%), with grade II predominating (38.6%). Immunohistochemical analyses were performed on 89 patients (31.23%). The triple-negative subtype was the most common class (35.95%), followed by Luminal A (32.60); Human Epidermal Receptor 2-class and Luminal B tumors were observed at a frequency of 13.48% each. Treatment consisted mainly of surgery (78.60%) combined with chemotherapy (65.97%) and/or radiotherapy (63.16%). Hormonal treatment was used in only 10.18% of patients. Targeted therapy was exceptional (4%). **Conclusion:** Triple-negative phenotype is the most common. However, potentially hormone-sensitive tumors account for almost half of all patients, who are relatively young. Individualized treatments are rare. It is important to systematize these analyses for all breast cancers, with a view to appropriate management in our environment.

Keywords

Breast Cancer, Immunohistochemistry, Douala General Hospital of Cameroon

1. Introduction

Breast cancer is the most common cancer worldwide [1]. In fact, the World Health Organization estimates that there will be 2.3 million new cases in 2020. It also carries a high mortality rate, with 685,000 deaths worldwide in the same year [1] [2]. In Africa, the incidence of breast cancer has almost doubled in a decade [3] [4]. In Cameroon, 4170 new cases were diagnosed in 2020, compared with 3265 in 2018 [2] [4]. What's more, the continent has a singularly high mortality rate. Along with Polynesia, Africa has the highest breast cancer mortality rate: 85,800 women died of the disease in 2020, while 2108 died in Cameroon in the same year [1] [2]. However, the survival of breast cancer patients worldwide has improved markedly thanks to the introduction of new prognostic factors in the development of therapeutic strategies [5]. Indeed, several authors have demonstrated the role of tumor biology profiling, through immunohistochemistry, molecular biology and genomic studies, leading to personalized treatment for patients, which in turn guarantees better yields [5]-[9]. Immunohistochemical analysis of breast cancer is not yet widespread in Cameroon, and data on the subject remain limited. The aim of this study was to describe the immunohistochemical profile of breast cancer patients at the Douala General Hospital in Cameroon.

2. Participant and Method

2.1. Setting and Study Population

This was a descriptive study with retrospective data collection from January 1^{er} 2010 to December 31 2019, *i.e.* 9 years, at the Douala General Hospital. It concerned all patients followed in the obstetrics and gynecology department for histologically proven breast cancer. We excluded records of patients with primary cancer of another organ with metastasis to the breast and those with cancer other than gynecological or breast cancer.

2.2. Procedures

Records of patients treated for breast cancer were identified in the outpatient, inpatient and operating room registers of the obstetrics and gynecology departments, and in the oncology department. We selected those in which the diagnosis had been confirmed by histological study, either on biopsy samples or surgical specimens. The medical record was consulted to collect data on a survey form previously designed using Epi Infos 7.0 software, including:

- Epidemiological data: age, marital status.
- Clinical data: personal history: medical, gynecological and obstetrical, toxicological, family history of cancer, lesion location, lesion sites, evolutionary stage (FIGO International Federation of Gynecology and Obstetrics) histological type, scarff Bloom Richardson's histopronostic grade.
- Histological data.
- Immunohistochemical data.

We assessed estrogen receptor (ER) and progesterone receptor (PR) expression by the percentage of tumor cell nuclear labeling, estimated visually. A percentage greater than 1% was considered positive [10]. The results of RO and RP labeling were combined and analyzed jointly to define hormone receptor (HR) status. We defined RH-, any tumor with RO- and RP-status. HER (Human Epidermal Receptor) 2 expression was expressed as a score (0, 1+, 2+, 3+). A score of 0 or 1+ and a score of 3+ were considered HER2- and HER2-enriched, respectively. We considered 2+ scores as unclassifiable breast cancers. We proceeded to characterize molecular subtypes using the recommendations of the 13^{ème} St Gallen International Breast Cancer Conference 2011 [11]. Based on the expression of oestrogen receptor (OR), progesterone receptor (PR) genes, the level of proliferation index

$$\text{Ki67} < 14\% = \text{weak}; \text{Ki67} > 14\% = \text{strong}$$

and the expression of the proto-oncogene Human Epidermal Receptor 2 (HER2), patients were grouped into 4 subtypes:

Luminal type A Luminal type B HER 2 type.

And the basal like triple-negative type (see **Table 1**).

2.3. Statistical Analysis

Data was entered and analyzed using SPSS 20.0 software. Qualitative data were represented as numbers and proportions. Quantitative data was represented by mean and standard deviation.

2.4. Ethics

Ethical clearance was given by the institutional ethic committee of University of Douala. Total confidentiality was respected. All analyses were performed anonymously.

3. Results

During our study period, we recorded 285 cases of breast cancer, representing an annual frequency of 28.5 cases.

3.1. Epidemiological Data

All patients were female. The mean age of patients was 48 ± 13 years, with extremes of 19 and 84 years, and a median age of 47 years. The most represented age group was [40 - 50[(30.9%), followed by [30 - 40[(24.60%). Two-thirds of

Table 1. Molecular classification of breast cancers.

Criteria	Luminal A	Luminal B	HER 2	Basal-likeTriple negative
Immunohistochemistry	RO+/RP+/HER2-Ki67 < 14%	RO+/RP+/HER2+OR RO+/RP+/HER2-Ki67 > 14%	RO-/RP-HER2+	RO-RP-HER2-

patients were married (66.0%) (see **Table 2**).

3.2. Clinical Data

A family history of breast cancer was found in 7.02%. Nearly half the patients (48.77%) were grand multiparous. More than half the patients (54.04%) were non-menopausal. The average consultation time was 8.9 ± 12.7 months. The predominant tumour location was the upper-external quadrant (41.8%), with left breast involvement predominating (53.3%). Stages III (54.73%) and II (36.49%) were the most common (see **Table 3** and **Table 4**).

Table 2. Ages, sex, marital status of patients. N = 285.

Terms and condition	Features	Values
Gender	Female	285 (100)
	Male	0
Age	Average age	48 ± 13
	Median age	47
Age ranges	[10 - 20[1 (0.35)
	[20 - 30[10 (3.5)
	[30 - 40[70 (24.6)
	[40 - 50[88 (30.9)
	[50 - 60[64 (22.5)
	≥ 60	52 (18.2)
Marital status	Bride	188 (66.0)
	Single	57 (20.0)
	Widow	40 (14.0)

Table 3. Medical and surgical history of patients with breast cancer at Douala General Hospital. N = 285.

Terms and conditions	Features	Values
Notion of familial cancer	Breast	20 (7.02)
	Collar	3 (1.05)
	Ovary	3 (1.05)
	Horn	1 (0.35)
Parity	Parity not specified	9 (3.16)
	0 children	20 (7.02)
	1 to 2 children	30 (10.52)
	3 to 4 children	87 (30.53)
	≥ 5 children	139 (48.77)
Genital status	Non-menopausal	154 (54.04)
	Menopausal women	131 (45.96)

Table 4. Lesion location and stage of breast cancer on admission to Douala General Hospital. N = 285.

Terms and conditions	Features	Number (%)
Lesion location	Bilateral	5 (1.75)
	Law	128 (44.92)
	Left	152 (53.33)
Lesion site	Bifocal	3 (1.05)
	Lower External Quadrant (IEQ)	49 (17.20)
	Inferior-internal quadrant (QII)	25 (8.77)
	Upper-external quadrant (QSE)	119 (41.75)
	Superior-internal quadrant (QSI)	59 (20.70)
	Retroareolar Whole breast	10 (3.51)
Progressive stage on admission	Stage 1	20 (7.02)
	Stage 2	10 (3.51)
	Stage 3	104 (36.49)
	Stage 4	156 (54.74)
	<u>Undetermined</u>	10 (3.51)
	<u>Undetermined</u>	5 (1.75)

3.3. Data on Histological Type, Grade and Immunohistochemical Class

Infiltrating ductal carcinoma was the most common histological type (83.86%). These cancers were predominantly grade II (64.33%). Immunohistochemical analyses were carried out on 89 patients (31.23%); the majority of breast cancers were of triple-negative subtype (35.95%), followed by Luminal A (32.60); tumours of HER2 class and Luminal B were observed at a frequency of 13.48% each (Table 5).

3.4. Therapeutic Modality

Surgery was performed on 224 patients (78.60%). Almost all surgeries were radical (93.75%). Chemotherapy was used in 65.97% of patients, and was generally neoadjuvant (90.4%). It was generally neoadjuvant (90.4%), and the most frequently used chemotherapy protocol was Paclitaxel combined with Cyclophosphamide and Doxorubicin (AC) (35.6%).

Radiotherapy was used in 180 patients (63.16%). Hormonal treatment was used in 29 patients (10.18%). Among our patients, 12 (4.21%) benefited from Trastuzumab-based targeted therapy (see Table 6).

4. Discussion

In the course of this study, we recorded 285 cases of breast cancer, all involving female subjects, a result similar to that of Atenguena and al [12]. In a multicentre study, Enbang and al. found 2.40% of cases in men [13].

The mean age of the patients was 48 ± 13 years. The age of the patients in our study is close to that reported by various African authors [13] [14] [15].

Table 5. Distribution of breast cancers by histological type, grade and immunohistochemical class at Douala General Hospital. N = 285.

	Modality	Number (%)
Histology	Invasive ductal carcinoma	239 (83.86)
	Invasive lobular carcinoma	15 (5.26)
	Medullary carcinoma	12 (4.21)
	Intracanal carcinoma	11 (3.86)
	Mucinous carcinoma	6 (2.11)
	Paget's disease	1 (0.35)
	Mesenchymal sarcoma	1 (0.35)
Grade	Evaluated	171 (60)
	Not rated	114 (40)
	Grade 1	17 (9.94)
Grade n = 171	Grade 2	110 (64.33)
	Grade 3	44 (25.73)
	Immunohistochemical class	Not done
Class n = 89	Fact	89 (31.23)
	Human Epidermal Receptor 2 (HER2)	12 (13.48)
	LUMINAL A	29 (32.60)
	LUMINAL B	12 (13.48)
	Triple negative basal like	32 (35.95)
	<u>Uncategorized</u>	4 (4.49)

HER2: Human Epidermal Receptor 2; ACR: American college of radiology.

More than half of our patients (54.03%) were non-menopausal, in line with various sub-Saharan authors [13]-[17]. Breast cancer therefore occurs in relatively young patients, still subject to sex hormone stimulation. This detail could prove decisive when faced with a hormone-sensitive tumour.

The vast majority of our patients were either grand multiparous (48.77%) or multiparous (31.52%), a fact found by various authors in our area, in contradiction with the risk factor status accorded to nulliparity in the literature [17] [18] [19] [20].

We observed 7.01% family history of breast cancer in our patients, indicating the possibility of genetic transmission mentioned in the literature (5% - 10%). Data similar to that of Tchente (7.14%) [21].

There is conflicting evidence in the literature as to the predominance of tumour location in one breast or the other [12] [13] [22] [23] [24] [25]. In our series, the left breast was the most frequently affected (53.33%). Bilateral involvement has been described in proportions ranging from 1% to 11.1% in our setting [13] [24] [25]. It is thought to be associated with mutation of the BRCA1 and

Table 6. Distribution of patients by type of treatment.

Terms and conditions	Variables	Number (%)
Surgery	Yes	224 (78.60)
	No	61 (21.40)
Type of surgery n = 224	Radicale	210 (93.75)
	Curator	14 (6.25)
Radiotherapy	Yes	180 (63.16)
	No	35 (12.28)
	Not specified	70 (24.56)
Chemotherapy	Yes	188 (65.97)
	No	97 (34.03)
Type of chemotherapy n = 188	Adjuvant	27 (9.6)
	Neoadjuvant	161 (90.4)
Protocol used	FAC	36 (17.6)
	AC+Paclitaxel	73 (35.6)
	AC	50 (24.4)
	FAC+Docetaxel	28 (13.7)
	Cisplatin	1 (0.5)
	Docetaxel	5 (2.4)
	FAC+Paclitaxel	3 (1.5)
	Paclitaxel	5 (2.4)
	Vinorelbine	2 (1.0)
	TC	1 (0.5)
	Doxorubicine + Docetaxel	1 (0.5)
Targeted therapy n = 12	Trastuzumab	12 (4.2)
	Tamoxifen	23 (79.2)
Hormonal treatment (29)	Anastrozole	5 (17.3)
	Radical castration	1 (3.5)

BRCA2 genes [26]. It was observed in 1.8% of patients in our series.

The tumor was located preferentially in the upper lateral quadrant (41.75%), in line with the literature [19] [21] [23]. On admission, stage III patients predominated (54.7%), followed by stage II (36.5%). Late diagnosis has been described in several African series [13] [16] [20] [21] [27].

Invasive ductal carcinoma was the most frequent histological type, accounting for 83.89% of all cases, in agreement with Atenguena and al. (90%) and other authors [12]-[25]. Sarcomas were rare (0.35%), in line with the work of Echi-mané *et al.* [28]. Lymphoma was not observed, contrary to the work of Engbang and al [13].

The predominant Scarff Bloom Richardson histopronostic grade was grade II (64.33%), followed by grade III (25.73%), data similar to those of Engbang *et al.*

(60% and 20%) [13].

The most common immunohistochemical class was the triple-negative subtype (35.95%). The predominance of this subtype was found by Atenguena and al. and Atangana and al. in two Cameroonian series at rates of 41.9% and 37.98% respectively [12] [14]. Other series have also found this predominance of triple-negative tumours in African patients [29] [30] [31]. However, Western and North African series found a preponderance of luminal A breast cancer [32] [33].

The second most frequent immunohistochemical class was the Luminal A subtype (32.60%). This is in agreement with the findings of Atangana and al. (36.06%) [14]. However, in the Atenguena and al. series, the HER2 subtype was more frequent than the 2 hormone-sensitive forms (Luminal A and Luminal B), at 25.3% versus 16.1% for both [12]. Engbang and al, in a series of 3044 cases involving 5 of the 10 regions of Cameroon, were only able to observe immunohistochemical analysis in 11 patients (0.36%) [13]. These aspects reflect the inadequate implementation of these analyses in our environment, probably due to the limited technical resources available. This could have a deleterious impact on the management of breast cancer in our environment, even increasing mortality. Indeed, several authors have demonstrated the decisive role of immunohistochemical profiling in therapeutic and prognostic terms, and its vital importance in improving the efficiency of breast cancer management [5]-[9].

More than 3/4 of patients (78.60%) underwent surgery, mostly radical, while virtually all 2/3 received courses of chemotherapy (65.97%) and/or radiotherapy (63.16%). Hormonal treatment was used in only 10, 18% of patients despite the relatively high proportion of potentially hormone-sensitive tumors in genitally active subjects in our series (luminal A = 32.60%); luminal B = 13.48%), *i.e.* almost half the cases. Targeted treatment was exceptional (4%). This shows that the results of immunohistochemical analysis had very little influence on treatment in this series. However, the successful management of breast cancer in the West seems to be based on matching the treatment to the patient's immunohistochemical class and hormonal situation, resulting in individualized treatments with reputable yield [5]. This is a step that needs to be taken in our field.

5. Conclusion

Breast cancer is the most common malignant tumour in our environment. It occurs mainly in women of childbearing age. The most common histological type is invasive ductal carcinoma. The triple-negative phenotype is the most frequent in our series. However, potentially hormone-sensitive tumors account for almost half of all patients. It is important to introduce systematic immunohistochemical analysis for all cases of breast cancer, possibly with the support of the state. Broader studies, including gene mutation research, will be carried out to guide and individualize treatment protocols, with a view to optimal management of this pathology in our environment.

6. Highlights

6.1. What Is Known

Breast cancer is the number one cancer in the world. It has a high mortality rate in Cameroon. There is very little data on immunohistochemical aspects in our environment.

6.2. The Issue

The aim of the study was to clarify the immunohistochemical aspects of breast cancers at Douala General Hospital.

6.3. Contribution of This Study

- Breast cancer occurs in relatively young patients. In most cases, it is diagnosed at an advanced stage;
- The triple-negative subtype is the most common in our sample; almost half of patients have a hormone-sensitive subtype.

6.4. The Implications

We need to systematize immunohistochemical analyses in Cameroon, and adapt treatment to the molecular profile.

Authors' Contributions

Study design: Nguefack Tchente. Data collection: Ekono Michel. Editor: Ekono Michel.

Reviewers: Ngaha Yaneu Junie, Neng Humphry Tatah, Messakop Yannick, Azoumbou Mefant Thérèse, Essome Henri, Essola Basile, Engbang Jean-Paul.

Supervision: Nguefack Tchente.

Conflicts of Interest

Authors declare no conflicts of interest.

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