

## RESEARCH COMMUNICATION

# Preliminary Data about Female Malignant Breast Tumours in Cambodia

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### Abstract

**Background:** Breast cancer is the most frequent cancer among women and the most frequent cause of cancer death in women in both developing and developed countries. However, little is known about the situation in Cambodian women living in Cambodia. **Objectives:** To describe the different histological types of invasive breast cancer, their frequency, grade and stage and their surgical management in Cambodia. **Materials and Methods:** A retrospective study of female primary invasive malignant lesions processed during 2003 and 2004 in the pathology laboratory of the 'Institut Pasteur du Cambodge', in Phnom Penh, was carried out with conventional histology techniques. **Results:** A total of 102 patients were included, with an average age of 47. Most specimens were tumour excisions or mastectomies. Tumours were generally large (37.5 % at least T3), distributed into carcinomas (94.2 %), phyllodes tumours (3.9 %) and lymphomas (1.9 %). Most cases of carcinoma presented with histological grade III (76.6%) and were invasive ductal (82.3%) or medullary (11.4%) in type. Lymphadenectomy was not systematic but nodal metastases were observed in 26 of 31 (83.9%). **Conclusions:** Late diagnosis of the disease is due to absence of systematic breast cancer screening and awareness. Apparent rarity of lobular carcinoma and over frequency of medullary carcinoma and phyllodes tumours should be confirmed on a larger series of patients using immunohistochemistry. Its use for other markers to help oncologists to decide whether anti-hormone treatment is indicated is also recommended, together with more standardized surgery.

**Keywords:** Breast - malignant tumours - carcinoma - phyllodes tumours - Cambodia

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### Introduction

Breast cancer is the most frequent cancer among women both in developed and developing countries. Prognosis of breast cancer depends on many factors including histological type, grading, stage at the time of diagnosis and access to health care. In developed regions of the world, incidence rates are higher than in developing regions but survival is more favorable. As a result, breast cancer remains the most frequent cause of cancer death in women in both developing and developed countries (Mathers et al., 2006).

In Cambodia, there is no cancer registry but in 2008, the WHO estimated the age-standardized incidence rate of breast cancer at 20.7 per 100,000, which is lower than 99.7 per 100,000, in metropolitan France. However, estimated age-standardized mortality rates due to breast cancer in Cambodia and metropolitan France are not so different (respectively 8 and 17.6 per 100,000) (Ferlay et al., 2010).

In this context, our objective was to give more detailed background information of breast cancer, in Cambodian women living in Cambodia by giving a description of the malignant breast tumours diagnosed in

our pathology unit, with specific information of the age at the time of diagnosis, the different histological types observed, the stage of the disease and management from a surgical point of view.

### Materials and Methods

This is a retrospective study about female breast tissue specimens with malignant lesions that were processed during 2003 and 2004 in the pathology laboratory of the "Institut Pasteur du Cambodge", in Phnom Penh. This laboratory was at that time, one of the five existing pathology laboratories in Cambodia.

All specimens were fixed in 10% formalin solution. After 24h fixation, small biopsies (less than 1 cm) were totally embedded. Larger biopsies and surgical specimens were sampled by the pathologist after gross examination. Sections were obtained from paraffin embedded tissue then stained by the H&E technique. There were no extemporaneous frozen sections. Immuno-histochemistry was not available in the lab for detection and quantification of estrogens and progesterone receptors and for detection of the HER2 gene amplification associated with aggressive invasive tumours (Slamon

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et al., 1987). We could, however, exceptionally obtain immuno-staining for 2 cases for which paraffin blocks were sent to a French pathology laboratory.

Consideration was given only to cases classified as primary invasive malignant breast neoplasm. In situ carcinomas were not included in the study. Carcinomas were graded using the Nottingham modification of the Bloom-Richardson system (Elston et al., 1991) and staging was established at the time of diagnosis, according to the 2003 TNM classification (Singletary et al., 2003).

## Results

A total of 102 female patients were investigated. With exception to two cases, the geographical location was known for all patients of which 48 (47 %) came from Phnom Penh and 52 (51 %) from the provinces. Surgical operations were carried out in the two main cities, Phnom Penh, the centrally located capital city, and Battambang in the Northern area. Their average age was 47 within a range of 16 and 76 years.

Concerning the type of sampling, 12 women (11.8 %) had surgery post biopsy, whereas 77 (75.5 %) had surgery directly and for 13 (12.7 %) patients, only biopsy was carried out. All biopsies were performed surgically; there were no tru-cut needle biopsies. The lesions were distributed into 96 (94.2 %) invasive carcinomas, four (3.9 %) phyllodes tumours and two (1.9 %) lymphomas. The latter were confirmed by immuno-histo-chemistry performed in France. Tumour classification is detailed in Table 1. Most cases of carcinoma were classified as histological grade III (76.6%) rather than grade II (19.5 %) and I (3.9 %).

Data with regard to tumour size is reported in Table 2. More than 40 % of tumours were T3-T4. Concerning treatment, among the 82 patients with invasive carcinoma who had surgical treatment, 40 had tumour excision and 42 had a mastectomy. Lymphadenectomy was

performed in association with tumourectomy in 7 out of 40 patients, and mastectomy in 36 out of 42 patients. Among these 43 patients with invasive carcinoma who had lymphadenectomy, lymph node metastases were detected in 34 patients (79 %).

## Discussion

The high average age and high proportion of patients with T3 and T4 tumours at the time of diagnosis was observed in other low-resource countries such as the Sudan (Ahmed et al., 2010). Development of systematic breast cancer screening could improve earlier detection and care of cancer. But experience in developed countries demonstrated the importance of increasing awareness of breast cancer to those targeted for screening in order to optimize early diagnosis of the disease (Yi et al., 1996).

Classification into the different histological types was based exclusively on morphological analysis, except for the two lymphomas. For such a survey, the fact that no cases of lobular carcinoma were observed (normally less than 10 %) (Albrektsen et al., 2010), may have been due either to the reduced total number of patients or to confusion with invasive ductal carcinoma. Immuno-staining would have permitted the correction of the diagnosis, showing lack of expression of E-cadherin in most invasive lobular carcinoma cells (Rakha et al., 2010). For other types of carcinoma such as medullary carcinomas that generally have a typical histological pattern, immuno-histo-chemistry is not absolutely necessary for diagnosis. Medullary carcinomas usually represent about 1 % of breast invasive carcinomas (Anderson et al., 2006; Li et al., 2005). With reserves linked to lack of statistical power, our series shows a higher rate. The same observation was made with Malaysian women (Sheikh et al., 2009) but other studies did not confirm such inter ethnic differences (Fong et al., 2006). With a heavy inflammatory infiltrate, as observed in undifferentiated nasopharyngeal carcinomas, frequently found in Southeast Asia, one might suspect medullary carcinoma of having a viral origin, especially linked to the Epstein-Barr virus but this was not confirmed (Trabelsi et al., 2008).

Frequency of malignant phyllodes tumours in our series is much higher than the generally observed average of 1% in all breast tumours (Rosenfeld et al., 1981). A higher incidence rate of malignant cystosarcoma phyllodes was previously observed among Latina whites and Asians (Bernstein et al., 1993). Again, a statistical bias might explain these findings and further studies of larger series of patients are required.

No data is available with regard to complementary radiotherapy and chemotherapy for survival purposes, as patients were not located for follow-up from our pathology laboratory. Patients previously had to go abroad (mainly to Vietnam or Thailand) for further treatment, but in 2003-2004, an oncology unit started operation in Phnom Penh to the benefit of all patients.

With regard to surgical management, procedures should be standardized so that fine needle aspiration or tru-cut needle biopsy be performed before radical surgery.

**Table 1. Malignant Breast Carcinomas in Cambodian Women according to Tumour Histology**

Histological types	n	%	Average age (range)
Ductal	80	83.3	48.2 (23-76)
Medullary	10	10.4	46.3 (40-59)
Metaplastic	2	2.1	47.5 (43-52)
Papillary	2	2.1	48.0 (41-55)
Mixed	2	2.1	50.5 (43-58)
Lobular	0	0.0	-
All types	96	100	48.0 (23-76)

**Table 2. Malignant Breast Tumour Size According to Histological Type**

Histology	Tx*	T1	T2	T3	T4
Carcinoma (96)	18(18.7)	8 (8.3)	34 (35.5)	11 (11.5)	24.5 (26)
Phyllodes (4)	0	0	0	4	0
Lymphoma (2)	0	0	0	2	0
All types (102)	18 (17.7)	8 (7.8)	34 (33.3)	17 (16.7)	25 (25)

\*Unknown; T1< or = 2 cm; T2< or = 5 cm; T3> 5 cm; T4 Spread to chest wall or to skin or inflammatory carcinoma

On the one hand, it would avoid operating on patients with lymphomas who principally need chemotherapy and on the other hand, it would lead to a more adapted surgical treatment method including lymphadenectomy at the time of tumour excision, when necessary. As for medical treatment, it could benefit from improvement of pathology laboratories, as immuno-histo-chemistry results would help decide indications of adjuvant anti-hormonal and anti-her2 therapy.

According to these preliminary data, some histological types of tumours seem more frequent in Cambodia than on average, especially medullary carcinomas and malignant phyllodes tumours. This has to be confirmed with wider series and validated by immuno-staining. The setting up of immuno-histo-chemistry will improve diagnosis and also allow oncologists to decide whether anti-hormone and anti-her2 treatments are of interest. Earlier diagnosis by systematic screening should be encouraged. With regard to the surgical management of tumours, it should be standardized for an improved efficiency.

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