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MANAGEMENT OF BREAST CANCER IN THE ONCOLOGY DEPARTMENT OF UNIVERSITY HOSPITAL OF TAMBOHOBE FIANARANTSOA

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SUMMARY

Introduction: Breast cancer is a common cancer in Malagasy women but the diagnosis and treatment of cancer is insufficient. Our aim was to describe the diagnosis and treatment of breast cancer in the Oncology Department of the University Hospital Tambohobe Fianarantsoa Madagascar. **Methods:** This is a descriptive retrospective study at the Oncology Department in Fianarantsoa from 1st January, 2011 to 31st December, 2016. We have included all new cases of breast cancer confirmed by cytological and / or histological analysis. The data collected were: age, the patient delay, the staging, the diagnosis and therapeutic methods and the follow-up. **Results:** we included 52 patients. The mean patient delay was 12 +/- 17 months. Fine needle aspiration cytology confirmed the diagnosis in 73% of cases. Breast ultrasound was performed in 50% and mammography in 7.69% of cases. Chest X-ray was performed in 90.38% and abdominopelvic ultrasound in 75% of cases. After the diagnosis, 25% patients were lost to follow-up without specific treatment. Surgery and chemotherapy were performed in 61.54% and 92.31% respectively. Only 3 patients received hormone therapy. No patient underwent the radiation therapy. The radical mastectomy with axillary lymphadenectomy is the most surgical procedures (46.15%). Nineteen patients (48.72%) had completed the number of cycle of chemotherapy. At 6 months of diagnosis, 51.28% (n = 20) were lost to follow-up. **Conclusion:** The management of breast cancer is a challenge in Fianarantsoa. Prevention and

screening are important in low resources countries.

KEYWORDS: Breast cancer, diagnosis, surgery, chemotherapy, follow up.

INTRODUCTION

Breast cancer is the most commonly diagnosed cancer of women in the world and the leading cause of cancer death.[1] There will be an estimated 2.1 million new cases and 626 679 cancer deaths in 2018.[1]

In sub-Saharan Africa, breast cancer is diagnosed with advanced stage and the mortality rate increased whereas in developed countries, early detection allowed a curative treatment and better prognosis.[2]

In Madagascar, breast cancer is the most common cancer of women.[3-5] It affected a young and active population[3,6,7]; most presented with advanced stage at first consultation because of the lack of national screening program.[3,6,8] According to the National Cancer Control Policy in 2010, the diagnosis and therapeutic resources in cancer care are insufficient.[8]

Our aim was to describe the diagnosis and treatment of breast cancer in the Oncology Department of the University Hospital of Tambohobe Fianarantsoa. To our knowledge, this is the first data on the management of breast cancer performed in this department.

METHODS

This was a descriptive retrospective study conducted at the Oncology Department of the University Hospital of Tambohobe in Fianarantsoa from 1st January 2011 to 31st December 2016 (6 years). Until 2010, only one cancer centre existed in Madagascar localized in Antananarivo, capital of Madagascar. After, in 2011, our department is opened; so it was the second cancer centre in Madagascar and it was the only cancer centre in the south of Madagascar until August 2016. There was one medical oncologist, one general physician and three nurses.

We have included all new cases of breast cancer confirmed by cytological and / or histological analysis. We excluded recurrent breast cancers and benign breast tumours.

The data recorded included: age, patient delay defined by the interval between the date of the first symptoms and the date of the first medical consultation, diagnosis check-ups: breast

ultrasound and mammography, type of pathology analysis, the extension assessments: chest X-ray, abdominopelvic ultrasound, CT scan, bone scintigraphy, the staging and location of metastases. The treatment strategies were categorized as surgery, radiotherapy, chemotherapy, hormone therapy.

The staging was regrouped by:

- Localized stage: breast tumour without axillary lymph node extension, corresponding to stage I and IIA of TNM classification
- Locally advanced stage: breast tumour with involvement of regional nodes corresponding to IIB and III stages
- Metastatic stage: breast tumour with distance extension corresponding to IV stage of TNM classification.

The surgery was regrouped by: radical mastectomy, breast conserving surgery and axillary lymphadenectomy.

The chemotherapy was regrouped by: neoadjuvant chemotherapy, adjuvant chemotherapy, both neo and adjuvant chemotherapy and palliative chemotherapy. We collected the name of protocol and the number of cycle of chemotherapy.

The data was analysed on Microsoft Excel 2007.

RESULTS

We included 52 patients. Mean age at diagnosis was 52.83 ± 10.42 years. The mean patient delay was 12 +/- 17 months.

Fine needle aspiration cytology confirmed the diagnosis of malignancy in 73% of cases (n = 38) and histology in 27% of cases (n = 14). In all cases, the histological sample was performed by macrobiopsy. None of the patients received immunohistochemistry analysis.

Breast ultrasound was performed in 50% of cases (n = 26). Mammography was performed in 7.69% of cases (n = 4). Chest X-ray was performed in 90.38% (n = 47) and abdominopelvic ultrasound in 75% of cases (n = 39). The Computerized tomography (CT) scan wasn't performed in any patient.

Ten patients (19%) had localized stage, 28 patients (54%) had locally advanced stage and 14 patients (27%) metastatic stage. Eight patients (57%) had pulmonary metastases. Five patients (36%) had bone metastases. In one patient, there was both bone and pleuropulmonary metastasis.

Of the 52 patients enrolled in the study, 13 (25%) patients were lost to follow-up at diagnosis and they didn't undergo specific treatment. Thus, 39 patients received treatment.

Table I summarizes the therapeutic modalities. Of the 39 patients treated, 24 patients (61.54%) underwent surgery. Fourteen patients underwent lymph node dissection (35.90%). Thirty-six patients (92.31%) received chemotherapy. Three patients received hormone therapy with tamoxifen in combination with chemotherapy.

The drug combination Cyclophosphamide-Methotrexate-5 Fluoro-uracil (CMF) and 5 Fluoro-uracil-Adriblastine-Cyclophosphamide (FAC) were used in 10 patients respectivily (42%). The number of cycle of chemotherapy was completed in 48.72% of patients (n = 19).

At 6 months of diagnosis, 35.90% (n = 14) remained alive, 51.28% (n = 20) were lost to follow-up and 12.82% (n = 5) were died.

Competing interests

The authors declare that they have no competing interests.

Table I: Distribution of therapeutic modalities.

Therapeutic modalities	Stage			Number (%)
	Localized	Advanced	Metastatic	
Chemotherapy	**4**	**21**	**11**	**36 (92,31)**
Neoadjuvant chemotherapy	0	3	0	3 (7,69)
Adjuvant chemotherapy	4	11	0	15 (38,46)
Neo and adjuvant chemotherapy	0	3	0	3 (7,69)
Palliative chemotherapy	0	2	10	12 (30,77)
Chemotherapy and hormone therapy	0	2	1	3 (7,69)
Surgery	**6**	**18**	**0**	**24 (61,54)**
Radical mastectomy	3	15	0	18 (46,15)
Breast conserving surgery	3	3	0	6 (15,38)
Axillary lymph node dissection	-	-	-	14 (35,90)

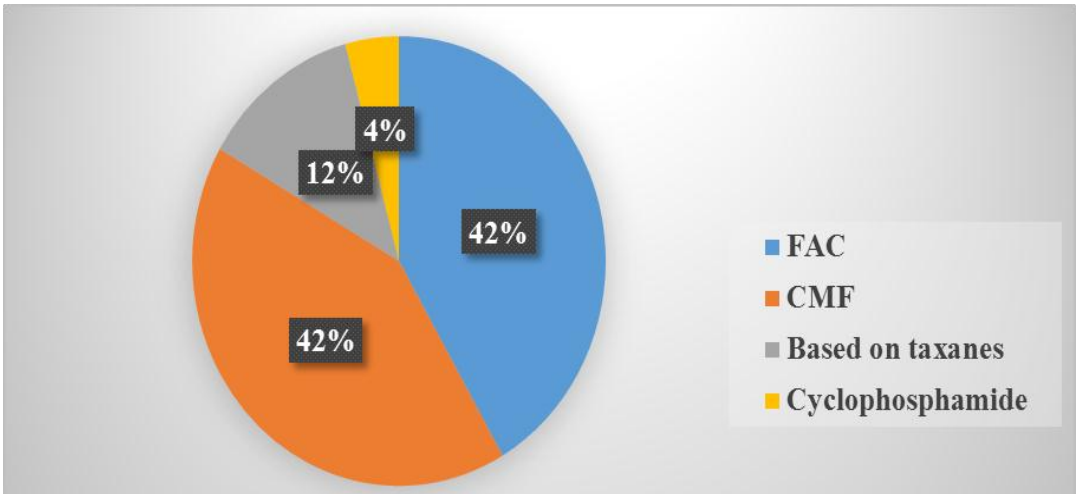

Figure 1: Protocol of chemotherapy

DISCUSSION

To our knowledge, this is the first data on the management of breast cancer in the Oncology Department since its creation in January 2011.

These cancers occur in young women, and were discovered at an advanced stage joining data from Malagasy and African literature.[3,4,7,9,10,11,12]

The duration of symptoms before consultation to physician was long with a mean patient delay of 11.95 months in our study. In Antananarivo, patient delay was shorter with a mean of 9.4 months[3] and in Nigeria, it was 11.2 months.[10] In Ghana, mean delay was longer with mean of 13.8 months.[9] Compared with data in developed countries, our delay is very long; in United Kingdom, the mean patient delay was 40.4 days.[13] Our results could be related to the lack of national screening program in Madagascar.[8] The only recommendation is to use breast self-examination because many public hospitals don't have mammography.[8] So, it is important to teach women how breast self-examination is performed and sensitive them to come for consultation as soon as breast palpable mass appears.

Concerning diagnosis management, the most commonly used diagnosis method in our study was fine needle aspiration cytology examination in 73% while the histology was performed in 27% of cases. None of the patients received immunohistochemistry analysis. In Antananarivo, the histological analysis is the most diagnosis method for breast cancer; among the 259 breast cancer patients, fine needle aspiration cytology was performed in 21 patients and the biopsy in 238 patients.[3] In Ghana, fine needle aspiration cytology examination was

done in 12% of patients, histological analysis was performed in 80.6% of cases.[9] In Nigeria, the diagnosis was obtained in 79.3% by fine needle aspiration cytology.[10] Cytological analysis would be the most diagnosis method of breast cancer in the majority of countries in sub-Saharan Africa because of the insufficiency of pathologist and pathology laboratory.[14] But cytology requires an experienced cytologist and is only valuable if it is positive.[14] In our study, the high rate of fine needle aspiration cytology could be related to its accessibility because it is performed in the same hospital; for histological analysis, it is necessary to send the biopsy sample to Antananarivo before 2016. Indeed, in Madagascar, all pathology laboratories were in the capital.[8] Cytological analysis would also be less expensive than histology and would allow diagnosis more quickly.[14] The use of cytology could also be explained by the fact that our cases were discovered at an advanced stage limiting the possibility of an excisional biopsy and the equipment for a microbiopsy is not available in Fianarantsoa. With the establishment of a pathology laboratory in Fianarantsoa in 2016, the practice of histological analysis should be increased.

In our study, no patient received an immunohistochemistry testing similar to the results reported by Rafaramino and Balekouzou in the Central African Republic.[3,12] In Ghana, of the 330 breast cancer patients, only 68 patients had a hormone receptor assay and 54 patients had HER2.[9] Our results could be related to the absence of a public laboratory for immunohistochemistry testing in our country. Brandao reported that less than 20% of countries in sub-Saharan Africa have these immunohistochemistry and molecular pathology; also, hormone receptor studies are not widely available in these countries.[14] In Madagascar, a private laboratory sends the sample abroad to immunochemistry testing since 2009.[15] But its cost is expensive; use of immunohistochemistry is limited. A first study of hormone receptors in Madagascar found that only 43.4% of patients had hormone receptor positive.[15]

In our study, 50% of patients had breast ultrasound and 7.69% had a mammography. According to Rafaramino, from 1996 to 1998, mammography was used in a limited number of patients; among the 259 patients, only 4 patients underwent mammography.[3] In Fianarantsoa, the low rate of use of mammography could be explained by the absence of this method at the public hospitals. In addition, the majority of breast cancers were already at an advanced stage limiting the practice of mammography. So, for diagnosis, the most common imaging used is the breast ultrasound.

In our study, 90.38% had a chest X-ray and 75% had an abdominopelvic ultrasound; no patient performed a CT scan. Rafaramino also found that the only tools used for staging were chest X-ray and abdominal ultrasound.[3] According to Turpin in France, thoraco-abdomino-pelvic CT scan and bone scintigraphy are the standard to evaluate the risk assessment for breast cancer.[16] In developed countries, CT scan, PET scan, and MRI are available, while in low-income countries, clinical examination, chest X-ray, and ultrasound are used.[17] Our results could be explained by the absence of CT scan and scintigraphy in Fianarantsoa during the study period. With the installation of the CT scan in Fianarantsoa in 2016, the practices of this exam will become more common.

Of the 52 patients in our study, 13 patients (25%) were lost to follow-up before any treatment. According to the study by Rafaramino, 30% of patients had refused the proposed initial treatment because of poverty and fear of side effects of chemotherapy and of dying far from their village.[3] Finally, some people expected immediate and radical treatment in the specialized centre.[3] With the opening of our centre in 2011, the patients with breast cancer in Fianarantsoa didn't need to come to the capital for treatment, however, 25% of our patients did not benefit from treatment. Also, it would be interesting to explore causes of abandon of the treatment to improve cancer care.

In our study, 24 patients (61.54%) had breast surgery. In Antananarivo, all the patients had breast surgery.[3] In African studies, the proportion of patients who had breast surgery was higher, ranging from 95.4 to 99.2%.[11,12] In Cameroon, the importance of surgery is linked to the fact that no patient was metastatic.[12] In our study, all metastatic stages had not undergone surgery, so the low rate of breast surgery was observed. Radical mastectomy was the most commonly used surgical method (46.15%) compared to breast conservative surgery (15.38%). These results are consistent with data from Malagasy and African literature.[3,6,9,10,12] Radical mastectomy with axillary lymphadenectomy was used in 53.1% to 93.94% while breast conservative surgery was used in 7.14% to 39.9% of cases.[6,9,12,18] In Antananarivo, all patients had breast surgery; and of the 182 patients treated, 89 had partial surgery and 94 had total mastectomy.[3] Radical mastectomy is the most widely used surgical procedure in Africa, unlike in developed countries where breast conservative surgery is the most used.[18] The choice of radical mastectomy is explained by the fact that cancers in Africa are seen at an advanced stage, whereas in developed countries, the screening found tumours smaller than 2 cm allowing conservative treatment.[19] The lack of radiotherapy in most

African countries, the financial impossibility for neoadjuvant chemotherapy, lack of sentinel node staging and the lack of follow-up after conservative surgery contribute to the strong practice of mastectomy versus breast conservative surgery.[17,20,21] In our study, the absence of radiation therapy in Fianarantsoa and the advanced stage of the disease could explain the high rate of radical surgery. We also found that the majority of patients with advanced stage didn't receive neoadjuvant chemotherapy to allow breast conservative surgery. Of the 21 advanced cases receiving chemotherapy, only 6 patients had neoadjuvant chemotherapy.

Of the 24 patients who had breast surgery, 14 (35.90%) patients underwent lymph node dissection. According to Rafaramino, lymph node dissection was performed in 94 of the 182 patients who underwent surgery.[3] The practice of lymph node dissection is more important in African studies constituting 81.4% to 88.09%.[12,21] The clinical absence of axillary adenopathy may encourage surgeons not to perform a lymph node dissection. In addition, breast conservative surgery is often done during biopsy for diagnosis and patients are not referred for lymph node dissection. The lack of training in surgical oncology is also a major problem in our country. In France, surgeons who wish to practice cancer surgery must continue training in surgical oncology.[22]

In our study, 36 patients (92.31%) received chemotherapy. At the Military Hospital in Antananarivo, all patients received chemotherapy.[6] In the Central African Republic, 91.4% of cases received chemotherapy.[11] In other studies, the use of chemotherapy is lower; according to the Rafaramino study, of the 182 patients treated, 86 received chemotherapy[3] and in Cameroon, 56.5% of patients with non-metastatic breast cancer received chemotherapy.[12] Chemotherapy is widely used in the management of breast cancer in sub-Saharan Africa. In our study, the high use of chemotherapy would be related to the advanced stage of majority of our cases (of our 39 patients, 32 were locally advanced or metastatic). With the presence of the Oncology Centre in Fianarantsoa, patients no longer needed to go to the capital for treatment, this may also have contributed to this high rate of chemotherapy. However, number of medical oncologists should be increased.

Neoadjuvant chemotherapy is indicated in locally advanced breast cancer before surgery.[17] However, in our study, we observed that only 11.53% of patients with advanced stage had used neoadjuvant chemotherapy. According to Nzeangung, only 27.2% had also performed neoadjuvant chemotherapy whereas in 65.2% of cases the tumors were classified as T3 T4.[12] For Rafaramino, none of her patients had received neoadjuvant chemotherapy.[3] According to

Adesunkanmi, of the 212 patients enrolled, 178 had adjuvant chemotherapy, including 65 patients with neoadjuvant chemotherapy.[10] The use of neoadjuvant chemotherapy is therefore rarely practiced. In our study, the low use of neoadjuvant chemotherapy could be explained by the distance of the Oncology Department from all health facilities that practice breast surgery in southern Madagascar. In addition, there is no multidisciplinary meeting between surgeons and medical oncologists and no continuing medical training in oncology. Also, we suggest a close collaboration between the two specialties and the development of a framework for the management of breast cancer in Fianarantsoa.

In our study, the most used protocols were CMF and FAC. According to Rafaramino, these two protocols are also the most used.[3] These two protocols are also the most used in African studies.[10,12,21] The most used molecules are therefore CMF and FAC in Africa. Indeed, these molecules are the most accessible in sub-Saharan Africa while other molecules such as taxanes, are available only in patients with a financial possibility.[17] In our study, the choice of chemotherapy was related to financial resources and availability of drugs at hospital pharmacy. In addition, there is a lack of a supportive treatment such as granulocyte growth factors to limit side effects of chemotherapy.

In our study, 48.72% completed their cycle of chemotherapy. In the Central African Republic, only 12.1% had completed their treatment despite that 91.4% did chemotherapy.[11] Despite the frequent use of chemotherapy, few patients can complete their treatment probably because of the limited financial resources. But other studies should also be carried out to search all causes of these discontinuations.

We found that 3 patients had hormone therapy with tamoxifen. As in Malagasy and African's studies, the prescription of hormone therapy is done without knowledge of the hormonal status.[3,10] And the type of hormone therapy is tamoxifen.[3,10,12] In Antananarivo, 108 of the 182 patients had tamoxifen hormone therapy.[3] In Nigeria, all patients received tamoxifen without knowledge of the hormonal status of their patients.[10] In Cameroon, 49.8% of patients received hormonal therapy, 94.6% of whom received tamoxifen.[12] In our study, the low use of hormone therapy would be related to the lack of immunohistochemistry test for determination of hormone receptors status in Fianarantsoa. In Madagascar, only a private laboratory sends immunohistochemistry test abroad to determine hormone receptor status.[15] However, hormone therapy is among the least expensive drugs among the therapeutic arsenal of cancer.[17] According to a study of hormone receptors in Madagascar, hormonal status is

often negative in Malagasy women with breast cancer.[15] So, the determination of hormone receptor status is important before giving hormone therapy. The establishment of public immunohistochemistry laboratory is essential to optimize the treatment.

Radiation therapy was not used for the treatment of breast cancer in our study. During 1996-1998, when Madagascar still had a radiation therapy device, all breast cancer patients underwent this type of treatment.[3] The rate of utilization of radiation therapy is also low in Nigeria and in the Central African Republic where the radiation therapy was performed in 30.4 to 33.2% of patients.[10,11] In Cameroon, radiation therapy was frequently performed in 77.3% of cases.[12] In our study, the absence of radiation therapy could be explained by the absence of this treatment in Madagascar since 2009. Currently, a centre of radiation therapy exists in a private clinic in the capital but the cost of treatment remains high; few patients can benefit of this radiation therapy.[23] The relocation of a public radiation therapy centre in Madagascar is currently being implemented.[23]

In our study, 20 women (51.28%) were lost to follow-up at 6 months of diagnosis. In Antananarivo, 18% of patients were lost to follow-up immediately after the treatment.[3] In Nigeria, among 212 patients with breast cancer, 102 patients were lost to follow-up.[10] The reason for this strong loss of view in our study would be related to the lack of correspondence between the general and the specialist physicians; so, we haven't news about the health status of patients when they return at home.

CONCLUSION

Breast cancer is often at an advanced stage in presentation and the duration between the first symptoms and the first consultation is very long. The diagnosis method is performed by fine needle aspiration cytology in the majority of cases. For the extension assessment, chest X-ray, breast ultrasound and abdominopelvic ultrasound are practiced. One quarter of women didn't benefit from specific treatment. This treatment consists mainly of surgery and chemotherapy. Few women underwent an optimal treatment and many women were lost to follow up after treatment.

Many progress were performed in Fianarantsoa with establishment of our cancer centre, implementation of CT scan centre and pathology laboratory. However, the management of breast cancer is proving to be a challenge. Also, prevention should be a priority in regions with limited financial and material resources.

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