Clinical Case : Breast Cancer Associated with Early Pregnancy and Screening for BRCA 1 & 2 Mutations at the Panzi-Bukavu/Uea Hospital

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ABSTRACT

Introduction: Breast Cancer Associated with Pregnancy("BCAP") is one of the rare entities of breast tumor pathologies in senology. According to the literature, it has a low frequency. But it is characterized by a clinical picture often very severe.

The **objective** of this article is to illustrate the particularities of this type of cancer by the clinical cases diagnosed in 2022. In addition, to discuss and analyze the epidemio-clinical, histological, therapeutic aspects and short-term prognosis; consented genetic testing was initiated and justified by young age (less than 32 years).

Patients and methods: This is a 12-month cross-sectional study, for analytical purposes with prospective collection, conducted at the Department of Gynaecology and Anatomopathology of Panzi/UEA Hospital in 2022.

Two patients collected, after clinical examination, met the criteria for selecting BCAP definitions according to the "Journal of Gynaecological-Obstetrics" (36) [6]. Then, their biopsy and blood samples allowed histo-genetic diagnosis at the anatomopathology and molecular biology laboratories of the UEA with counter-expertise in Netherland-Amsterdam.

Results: Over a period of twelve months and in a sample of 28 patients with breast cancer, there were 2 cases of BCAP, or 7% incidence. The

patients were Bukavu residents from South Kivu, married, under 32 years of age and all with higher education. They consulted late; more than a year, after discovery of breast nodules by self-palpation. All have re-acknowledged having undergone exposure to potential ionizing irradiation.

Risk factors were analyzed. For patient (A): menarche at 17 years, ages of marriage and 1st pregnancy at 31 years, primiparity, no breastfeeding, history of breast tumors and local treatment with indigenous products. For (B), obesity, shortened breastfeeding and taking hormonal con-traceptions were noted.

The clinic noted in common, advanced cancer, large adherent mass; but, for the patient (A) were associated cachexia, infectious syndrome, anemia and fetal distress ended by fetal death in utero. Anatomical pathology has found a common type "advanced invasive ductal carcinoma"; grade SBR III for (A) and SBR I for (B). The extension assessment noted more peculiarities for (A) with hyperleukocytosis, low hemoglobin, radiopulmonary images in favor of metastases.

Genetic testing, looking for BRCA 1&2 mutations, suspected the BRCA1 mutation for both patients, after PCR by presence of amplification of primers 185 and 187 at the UEA/HGRPanzi laboratory. However, sequencing done at the MACROGEN - Netherland laboratory, confirmed the presence of mutations at exon 2 of the objectified BRCA1 gene in the patient (B). Due to lack of resources, genetic analysis of other exons of the BRCA1 and BRCA2 genes has not been performed to exclude associated muta-tions.

Conclusion: BCAP, being classically rare, had a very high frequency (7%) in our series. It has affected patients of young age (less than 32 years), diagnosed with late-stage invasive ductal carcinoma with at least 50 percent genetic factor positivity (BRCA 1 mutation). These elements suggest the prospect of undertaking a large-scale study to investigate the most common breast cancer risk factors in Bukavu.

Keywords: Breast Cancer, Epidemio-Clinical, Histopathology, BRCA Mutation Screening. Mass Awareness.

I. INTRODUCTION

The breast is a precious organ of the woman by its aesthetic, erotic and breastfeeding role. It is a frequent occurrence of benign and malignant tumor pathologies, of which cancer is a public health problem worldwide and in the DRC in particular.

Breast cancer has risk factors, modifiable or not. Among the non-modifiable factors, age, hormonal and genetic factors have a significant place. The

classic age of breast cancer is ≥ 50 years, less frequent before menopause and rare at a young age (less than 40 years) [1].

Several authors confirm: the lower the age of diagnosis, the more suspected and very likely the genetic factor is [4,5]. These two factors appear to be linked and intrinsic.

On the other hand, the hormonal factor can be extrinsic and become modifiable. Conventionally, it becomes either a protective factor (pregnancies before 30 years, multiparity ...), or a risk factor (prolonged exposure to hyperestrogenism ..).

The **"Journal de Gynéco – obstétrique"** [6] defines the association of breast cancer and pregnancy as its occurrence either during pregnancy or 1 to 2 years after childbirth for some authors. In addition, the association is rare: 0.2 to 3, 8/100,000 breast cancers are associated with pregnancy.

According to **Andersson TM** [7], its incidence increases with the increase in the overall incidence of breast cancer and the postponement of the age of childbearing. In young women, being 3% of breast cancers, this incidence should not be neglected since it corresponds to 15% of breast cancers in women under 35 years of age.

Apart from these particularities, there are also difficulties of diagnosis (turgid pregnant breast!), therapeutic (adverse effects) and poor prognosis (severe forms often of inflammatory ductal carcinoma with lymph node invasion 60 to 70%) [11,12].

Certainly, these characteristics make patients with BCAPparticular areas of breast cancer in women. It is for this purpose to highlight the particular field of the association breast cancer and pregnancy. This article aims to report the clinical cases of BCAP diagnosed on the sidelines of the study on "the histo-clinical profile of breast tumors in Bukavu", conducted in two university clinics in Bukavu.

II. MATERIALS & METHODS

1. MATERIALS

1.1. Study framework

The study took place in Bukavu, the capital of South Kivu province in the Democratic Republic of the Congo; precisely, at the **HGRPanzi**and the HPGR of Bukavu.

A. **HGRPanzi**: This hospital began its activities as a dispensary in 1999 during the war period. In the same year, under the initiative of Prof. Dr Mukwege and the 8°CEPAC, the hospital was built. It is located in the commune of Ibanda, more precisely in the Panzi district, on Mushununu Avenue. It is 8 km from the city center, towards the road connecting Bukavu to Uvira.

This hospital is a University Hospital Center of the Evangelical University in Africa. It trains general and specialist doctors. It has a capacity of 650 beds, distributed among the four ordinary departments of a hospital and related services.

Currently, he is internationally recognized for his expertise in the holistic care of victims of sexual and gender-based violence as well as uro-gynecological surgery.

B. **HPR Bukavu.** Created in colonial times in 1929, it served as a Provincial Hospital of the former Kivu (Maniema-North and South Kivu). It was extended by the White Nuns and the SociétéChemin des Fer de l'Est before being put back under the direction of the colonial state. In 1995, it was ceded to theBukavu Archdiocese management until today.

Located towards the north-west of the Bukavu city, on the borders of the health zones of Kadutu and Ibanda, it is 500 metres from Independence Square, on the road to Bagira and Kavumu Airport. According to the provincial health division, it is currently the health reference for the South Kivu province.

This hospital is the CHU of the Catholic University of Bukavu which trains general practitioners and specialists. It has a capacity of 500 beds, distributed among the four ordinary departments of a general referral hospital and their related services. They are

organised into two main services: "medical" and "support".

Its choice is consistent with the presence of well-equipped gynaecology and pathology departments as well as its rank as a university clinic, the best academic research environment.

1.2. Study period

It was twelve months, from January 1st, 2022 to December 31st, 2022.It proceeded in two stages: the first in a hospital setting for the collection of clinical and paraclinical data, followed by the laboratory one for the detection of BRCA mutations.

1.3. Study population

All patients who consulted in gynaecology of the Panzi Hospital and the HPGR of Bukavu, during the study period; in whom the clinical diagnosis of breast cancer has been made and clarified in the AnatomopathologyService.

1.4. Sample type

(a) **The sampling technique**is*probabilistic of convenience*.

(b) **Inclusion criterion**: Any patient of any age with pregnancy, with clinical and histological diagnoses of breast cancer, who "**consents to genetic testing**" for BRCA 1&2 mutations.

(c) **Exclusion criteria:** Any patient who does not meet this criterion above.

2. METHODS

2.1 **Type of study:** This is a **cross-sectional analytical study with prospective collection**.

2.2 **Data collection techniques and tools**

The data were collected by:

- "**use of a pre-established collection form (see annexes)**" of clinical (subjective and objective) as well as paraclinical information (echography, mammography, biopsy and genetic test as well as NFS and radiography depending on the particularity of the case).

- "**samples**": (a) In the operating room, **tissues** for anatomopathology **biopsies**, (b) In the laboratory, **whole blood for genetic testing** in EDTA tubes; for BRCA mutation screening. This investigation was conducted in 2 molecular biology laboratories:

(1) from UEA in Bukavu, DRC to extract DNA purified and amplified by PCR with the use of BRCA 1 and 2 gene primers.

(2) Amsterdam, the Netherlands, for purification and sequencing of extracted DNA for analysis of mutations specific to the amplified fragment in accordance with the corresponding nitrogenous base pairs.

2.3 Processing of statistical data and study variables

Qualitative methods were used for data processing.

Study variables included (see summary table in appendix):

- Socio-demographic data

- Clinical and paraclinical data

- Therapeutic and clinical evolution data.

3. ETHICAL CONSIDERATIONS

This study was carried out respecting the principles of human dignity and confidentiality of the information collected. Informed consent was given by all participants in this study, registered with the ethics committee under number 0016-4125001-118-2022.

III. RESULTS AND COMMENTS

During the study period of breast cancer at Panzi Hospital and HPGR in Bukavu, 28 new cases of breast cancer were diagnosed and collected. Of this sample, only two cases met the criteria for cancer and pregnancy association, i.e. 7%.

Table I summarises (see annexes) all the sociodemographic, clinical and paraclinic characteristics as well as therapeutic data and short-term clinical evolution (study period limits) of these pregnant women.

Some salient points common to both clinical cases:

1) All the inhabitants of Bukavu are from South Kivu, from the village of Kabare and tribe of Mushi for (A) and from the village of Kalehe and tribe of Muhavu for (B).

2) The two patients were too young in age: 32 years old for (A) and 30 years old for (B).

3) The two pregnant women being married.

4) They have done higher education and practiced self-examination as the mode of discovery of breast mass for both.

5) As for the risk factors for breast cancer, the only common ones are: exposure to suspicious radiation and delay in consultation for breast tumor for both.

6) As for the clinical variables, both pregnant women showed unilateral involvement, orange peel skin, warm, sensitive swelling with a large adherent nodular mass.

7) The pathologist found a common type, the advanced stage infiltrating ductal carcinoma, despite the difference in the degree of cell differentiation [**SBR III** for (A) and **SBR I** for (B)] which influences the prognosis more than the treatment remaining identical.

8) Genetic screening confirmed a BRCA1 mutation by primer 185 amplification. And sequencing in Netherland, the Netherlands specified the type of BRCA1 mutations knowing that BRCA2 was unremarkable; knowing that associated mutations would not be excluded.

IV. DISCUSSION OF COMMON AREAS AND RISK FACTORS

1. SOCIODEMOGRAPHIC PROFILE

These patients having similar ethnic backgrounds, their age of diagnosis is also less than 32 years.

Researchers have found that the age of the patient seems to be a more determining factor in survival than the association with pregnancy or postpartum.

These breast cancers occurring in young women are characterized by the greatest frequency of lesions with unfavorable prognostic factors [6,12].

2. CLINICAL AND PARACLINICAL PROFILE

2.1 Time limits and reason for consultation

The two patients consulted late: More than a year of mass self-discovery and previous treatments; with patient's confession (A) of an indigenous treatment. The latter "probably precipitated" ulcero-necrotic complications, superinfections or even metastases within a shorter period of time than that of (B) which did not present severe complications.

According to **Tshimpi's** article, in the DRC, poverty and retrograde cultures (Prejudices! Witchcraft!) are among the obstacles to early consultations and even cancer screening [13].

This is also the case in Mali where **Baba Traoré** found 60 percent of patients who presented after more than eight months of discovery of the breast mass [14].

BOUZAKRAOUI HICHAM [15] also found that the diagnosis of CSAG is made later than outside of pregnancy. This partly explains the high frequency of more advanced and evolving forms in proportion to the delay time. The risk of axillary lymph node metastases increases by 0.9% for a delay of 1 month and increases by 5.1% for a consultation delay of 6 months after discovery by self-examination.

As a result, several authors have considered the delay in consultation as a risk factor favoring the severity and difficulty of late diagnosis which delay treatment and make it less effective [16].

BOUZAKRAOUI HICHAM [15] in his study found that the average duration between the first symptoms and the start of treatment is 9 months for breast cancers outside pregnancy and 15 months during pregnancy.

2.2 Risk factors

2.2.1 Personal health history

1) Three risk factors for breast cancer were common to the patients: Exposure to suspicious

radiation and self-medication by frequent hormonal therapy for contraceptive purposes at a young age. This third factor seems very preponderant.

Some authors **Ronckers CM** [17] and **Hendrick RE** [18] demonstrated the effects of ionizing radiation on the occurrence of breast cancer. It is "dose dependent", "cumulative doses" and a function of the age of onset of exposure; especially for exposures beginning with nulliparas of young age (before 30 years).

Overall, the majority of recent literature does not highlight a significant link between oral contraception and breast cancer. But taking into account the age of exposure to the factor, a relative risk of around 1.5 was found for women who used OCs (oral contraceptives) very young for at least 5 years and before a first pregnancy. [19]

2) In patient (A), six risk factors for breast cancer were identified: Late age (at 31 years) of marriage and first pregnancy, nulliparity, no breast-feeding, history of breast tumors treated without biopsy precision and prolonged local treatment of mammary mass with indigenous products.

Classically, it is known that multiparity is an important protective factor [15,20,21]: gravid hormonal biology promotes the differentiation of epithelial cells by reducing undifferentiated cells being potentially very susceptible to the initiation of carcinogenic alterations of the mammary gland .

What influences more is the age of onset of the first pregnancy. Thus, for a woman who has carried a pregnancy to term at a young age (there are almost no undifferentiated cells yet, nor initiated into carcinogenesis!), she sees her risk reduced.

According to Marc ESPIE [22], pregnancy before age 19 lowers the risk by 50% compared to a nullipara. However, this risk is significantly increased (relative risk: 1.72) in women who had used oral contraception for at least four years before the first full-term pregnancy. Meta-analysis of 47 studies states that the risk decreases by 7% for each birth (apart from the risk reduction linked to breastfeeding). The younger the woman during her pregnancies, the lower the risk (3% per year younger).

Many authors [23] have shown that certain benign mastopathies increase the risk of breast cancer by two to three; varying according to the degree of atypia of the cells. The highest risk (RR= 5) corresponds to fibrocystic diseases associated with proliferative hyperplasia and a high degree of cellular atypia. Isolated fibroadenoma does not seem to constitute a risk factor; the relative risk increases from 1 to 5 when breast density is high on mammography.

3) In patient (B), two risk factors for breast cancer were identified: Obesity and lack of prolonged regular breastfeeding.

The literature confirms the beneficial effect of breastfeeding as a protective factor against breast cancer; without depending on the age of the first pregnancy [15].

As for obesity, a study in Tunisia [24] analyzed the relative risk of breast cancer mortality. It is proportionally increased with the degree of excess weight going from "1" for a body mass index (BMI) below 25 "to 1.34" in case of overweight, "to 1.63" in case of obesity moderate, "to 1.70" in the event of severe obesity and "2.12" for massive obesity (morbid). In familial forms, an excessive BMI also increases the risk of cancer twice.

4) No particular medical and surgical history has been identified, nor factors related to smoking or alcoholism, although they are major risk factors. No notion of menstrual disorders or abortion was declared in the gynaeco-obstetric history.

A meta-analysis of 53 studies involving 4805 patients confirmed that there is no increased risk of breast cancer associated with abortion or spontaneous miscarriages [22].

5) A reflection remains on the composition and the unknown effect of most indigenous products of frequent use in the "poor" environments to try to treat cancers.

Isn't it a factor favouring the severity of cancer complications? As was the case with patient (A)!! Such reflection would require an in-depth study to find out more in detail.

2.2.2 Familyhealth history

The notions of family cancers and the elements of the metabolic syndrome (of Lynch) were not identified with the relatives of the patients in this study. This is a fact contrary to what is known classically.

2.3 Objective signs

2.3.1 General objective signs

=>The general condition of patient (B) seemed preserved; for (A), it was altered by infectious syndrome and anaemia on a gravid state with a poor prognosis because foetal vitality was also threatened by a picture of foetal distress (Cfr table N°I).

Classically, the symmetrical relationship between these two entities attaches to the pejorative reciprocal influence between pregnancy and cancer, which is based on immunosuppression. In addition, to the cases of BCAP described, is added the young age which predisposes to the aggravation of the clinical picture.

=>BMI (Body Mass Index) is abnormal for patients at two extremes: cachexia for (A) and obesity for (B). The cachexia would be explained by the advanced stage of the cancer. Obesity, one of the main risk and prognostic factors for breast cancer, also predisposes patient (B) to a severe picture.

A Moroccan study published in 2019 suggests that a risk of breast cancer is positively associated with abdominal adiposity [25]. Some authors [26,27] give nuances: In the pre-menopausal period, overweight and weight gain tend to reduce the risk of breast cancer; In the post-menopausal period, excess adiposity and weight gain increase the risk of breast cancer.

Currently, it is proven that being overweight increases the risk of cancer and its metastases as well as their dissemination. In turn, the cancer modifies the phenotype of the peritumoral adipocytes which will produce metastatic pro-inflammatory factors; especially in postmenopausal women under the effect of the serum increase in free estradiol [28,29].

In a meta-analysis combining 25 studies, Renehan et al. showed that a 5 kg/m2 increase in body mass index (BMI) led to a 12% increase in the risk of breast cancer in postmenopausal patients [30]. Other studies have shown an association between obesity and the appearance of more aggressive tumors [31].

In 2014, a meta-analysis of 79 publications including 213,075 patients concluded that a relative risk for mortality of 1.41 (95% CI 1.29–1.53) for obese patients compared to patients of normal weight, as well as than a 17% increase in total mortality and 18% in specific breast cancer mortality for each increase in BMI per 5 kg/m2 step [32].

2.3.2 Characteristics of the affected breast

A. **Five were common**: Many of these features were specific to advanced stage cancer.

The literature describes the high frequency of severe presentation and unfavorable prognosis in cases of cancer associated with pregnancy in young women [8,33].

1) Laterality of involvement: Both patients had unilateral breast involvement.

2) Orange peel skin is also a sign of invasive cancer by skin infiltration and inflammatory phenomenon.

3) Increased breast volume: nodular intra glandular mass beyond 5cm.

4) Indurated and non-mobile mass: This consistency and adhesion of the mass testify to the invasion of the peritumoral tissues.

5) Thillaux maneuver: Being present, it confirms the previous characteristic.

6)   Adenopathies were present.

B.   Two were different depending on the patient, but all did not exclude the severity of the pathology.

1)   Side reached: Right for (B) and left for (A).

2)   Ulceration + pus secretion were more marked for (A).

2.3.3 Cardiopulmonary effect: For patient (B), it was absent; for (A), there were complications (tachycardia, polypnea and subcrepitating rales) probably effects of metastases.

2.3.4 Peculiarities of pregnancy.

Both pregnant had no signs of threatened premature delivery. A poor condition of the foetus was objectified on examination of the patient (A) in whom the cancer was more inflammatory than for (B).

Several authors [8,33] explain the seriousness of the CSAG table by this pejorative reciprocal impact "pregnancy and cancer": In addition to the mechanism of reciprocally aggravated immunosuppression; the hormonal factor also plays a significant role.

Pregnancy is a period of estrogen and progestogen inflation. If a pregnancy occurs in a woman whose undifferentiated epithelial cells are already initiated (have genetic alterations favoring malignant transformation), these initiated cells will be stimulated by these hormones, multiply and acquire other genetic alterations which will lead to their uncontrolled division.

In addition to these two mechanisms (hormonal and immune) worsening the clinic and the prognosis, vascular mechanisms stimulated during pregnancy are also mentioned by some authors. Tumor angiogenesis and lymphangiogenesis are validated prognostic factors for lymph node involvement and poor survival [34,35]. **Genin A.S., Antoine M et al** found that

angiogenesis is more accentuated in BCAPs than in cancers not associated with pregnancy [12].

2.4   Presumptive diagnosis

"Advanced stage breast neoplasia in pregnancy at a young age" complicated for (A) (Cfr Table N°I) at stage IV (T4dN3M1) in pregnancy of 33 WA according to DDR with foetal distress and decompensated anaemia.

2.5   Paraclinical

1)   **Haematology**:Anaemia was noted of inflammatory origin in the patient (A). It is one of the main complications in patients with BCAP. It leads to a high risk of IUGR and in-utero foetal death. **Charlotte** found anaemia in 90% of pregnant women with breast cancer [36].

2)   **Obstetric echography**highlighted the elements of foetal distress for (A) and good vitality of the foetus for (B).

3)   **Abdomino-pelvic ultrasound**of (B) noted no particularities.

4)   **Echography-mammography pair** confirmed BIRADS III malignant lesions.

5)   **Anatomopathology**proved the "infiltrating ductal carcinoma" despite the difference in the degree of cell differentiation.

6)   **Immunohistochemistry not done** (Refusal, it is expensive!).

7)   **Radiothorax**revealed lung images suggestive of lung metastases absent for (B).

8)   **Screening for BRCA 1&2 mutations**: This test is justified by the literature which attests that breast cancer associated with pregnancy, which manifests at a young age, always raises suspicion of a genetic predisposition, indicating an oncogenetic consultation [4,8, 9].

=> As for the results of the genetic test, the BRCA1 mutation was positive for the patient (A) and inconclusive for the patient (B): Two primers 185 and

187 of the BRCA1 gene, subjected to the extracted purified DNA, amplified at PCR on a range of 4 primers tested in the UEA laboratory. A counter-expertise at the MACROGEN laboratory in Netherland / Netherlands allowed sequencing which confirmed the presence of mutations at exon 2 of the BRCA1 gene and the absence at BRCA2. The available BRCA2 primer was not amplified by PCR to allow sequencing and genetic analysis.

This result agrees with OthmaneYddoussalah who observed in Rabat: Women carrying a BRCA1 mutation have a significantly higher risk of CSAG [OR: 3.9; 95% CI: 1.4–10.8] than patients with a BRCA2 mutation (OR: 1.9; 95% CI: 0.5–7.0) [37]

=>On clinical examination of our cases described in this work, patient (A) BRCA1 positive presented a severe clinical picture.

This severity would probably be explained by the data of different authors found in the literature. Patients with BRCA1/2 mutation have a high risk of developing, at a young age (< 40 years), a severe picture of an aggressive cancer associated with pregnancy [4,38,39].

Additionally, **Cullinane CA, Lubinski J et al**. found that these BRCA mutated patients have a breast cancer risk that increases with parity (OR = 1.37; 0.93–2.03) compared to nulliparas, with an increase in breast cancer risk of 15 % at each new birth [40,41].

V. CARE AND EVOLUTION

3.1 Treatment of infiltrating ductal carcinoma and its complications

According to the treatment protocol, these types and grades of cancer cases described in this work required surgical decision: **Neoadjuvant** treatment for (A) before "mastectomy + lymphadenectomy" and for (B) "**adjuvant** treatment" after surgery.

Recalling that (A) was at a very advanced stage (SBRIII) with severe systemic complications (Ca-chexia, pulmonary metastasis, anemia…), counseling

for specialized treatment in gynecological oncology was indicated.

3.2 Obstetric treatment

For patient (A), there was fetal death in utero expelled after taking cytotec. (B) refused surgery and followed up at Panzi, she had gone to Kigali for surgery and vaginal delivery which gave a normal and mature newborn.

VI. CONCLUSION

This "case report" is a scientific presentation, on the sidelines of the study carried out in Bukavu in 2022, on the "histoclinical profile of breast tumors and screening for BRCA genetic mutations in these patients". The analysis of the most frequent risk factors for breast cancer in these patients led to the particular finding of two cases of breast cancer associated with pregnancy out of the 28 cases of breast cancer diagnosed in two university clinics. selected, HGRpanzi and HPGR of Bukavu.

This particularity of cancers was associated with the particular terrain of young age, less than 32 years for all CSAGs. Thus, the suspicion of genetic defect was justified, which was investigated by genetic analysis until obtaining the result of the positivity of BRCA1 mutations at 50%.

The presence of BRCA 1 mutation coincided with severe clinical, paraclinical, biological and prognostic characteristics for the patient diagnosed positive. This finding agrees with the literature to substantiate the severity of breast cancer disease during pregnancy at a young age.

In addition, in all these patients, late consultation, previous use of indigenous treatments, late diagnosis and late treatment were observed, which would also justify their poor condition.

If the diagnosis were early and precise, these tumors would have a favorable prognosis after surgical treatment, easy and available. However, the monitoring and early detection of malignancy poses a

serious problem there due to the lack of organization of in-depth and effective strategies for the fight against breast cancer in our communities.

These are from very resource-limited settings; poverty preventing the diagnosis would be early and precise as well as access to quality care to expect a better prognosis with ideal follow-up.

Hence the illustration described above, **malignant tumors especially at the advanced stage**, admitted to hospital after a long journey in the hands of non-health professionals causing a diagnosis, often late:

- either out of ignorance: lack of government policy or institutional community awareness measures for screening for breast cancer and other cancers,
- either by patient vulnerability: lack of financial means,
- or following indicated therapies not available in our settings.

These results argue the reason for initiating future in-depth and large-scale studies to arrive at the evidence supporting the "**more preventive than curative**" approach in these settings lacking sufficient means.

Recommendations also result from these reflections:

(1) Encourage awareness raising by the State and/or partners to obtain overall (efficient) support for care, as well as well-trained health care providers to carry out a correct clinical screening examination,

(2) Support good training initiatives in oncology to capacitate gynecologists in the management of breast cancer,

(3) Educate the population to understand the usefulness of breast cancer screening, starting with daily self-examination, before considering in-depth screening investigations by echo-mammography or even genetics.

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ANNEXES
1. Table N°I

VARIABLES	PATIENT (A)	PATIENT (B)
I. SOCIO-DEMOGRAPHIC		
Adress (home)	Mushununu-panzi	Kadutu-IDR
Ethnicity (village +tribe)	Kalehe Muhavu	Kabare Mushi
Education level	Graduate Degree in Social Sciences	Undergraduate Degree in Nursing Sciences
Profession	Merchant	Nurse in the Radiology Service
Civil status	Married	Married
II. CLINICAL		
II.1.COMPLAINTS/REASON FOR CONSULTATION		
Timelines and discovery mode	One year per self-examination	Three years by self-examination
Features associated with the main symptom.	Ulcerative and purulent sensitive indurated mass of the left breast; with fever and cough for ≥ 3 months.	Painful nodule without discharge or wound located on the right breast; without fever or cough.
II.2. HEALTH HISTORY		
II.2.1.Personalhistory		
II.2.1.1. Gynaeco-obstetrichistory		
Age	32 years	30 years
Menarcheage	17 years	14 years
Marriageage	31years	23 years
1st pregnancyage	31 years	24 years
Currentpregnancyage	33 weeks of amenorrhea.	6 months (without specifying dates of last menstrual period)
Pregnancy	1	3
Parity	1	3
Abortion	0	0
Duration and injury complications of breastfeeding	Never breastfed	Breastfeeds without complications, but durations in decrecendo with parity 2 years = >1 years = >3 months.
Perioddisorders	No	No
Hormonotherapy	Never	Contraceptive (2-year microgynon from 2020 to 2021)
Breasttumours	Operated in early 2021	No

	(without doing histological study)	
II.2.1.2. Medical and surgical history		
High blood pressure	No	No
Diabetes	No	No
Colorectal cancer	No	No
II.2.1.3. Lifestyle		
Sport	No	No
Smoking	No	No
Alcoholism	No	No
Exposure to suspected radiation	Professional (Nurse in the radiology service)	Profession of the husband handling irradiating minerals, without accepting if he kept them at home
Local treatment with indigenous products	Yes	No
II.2.2.Familyhistory		
Family cancers	No	No
Lynch syndrome - metabolic in family	No	No
II.3.OBJECTIVE SIGNS		
II.3.1.General objective signs		
BMI (Body Mass Index)	13,85(Cachexia)	31,61(Obesity)
General condition	Altered by fever, asthenia and pallor of the conjunctiva	Preserved
II.3.1.Particularities of examination of the affected breast		
Laterality of achievement	Unilateral	Unilateral
Side	Left	Right
Orange peel	Present	Present
Ulceration + secretion of pus	Present	Absent
Increased volume + groove	Present	Present
Sensitivity + Heat	Present	Present
Indurated and non-mobile mass	Present	Present
Number of nodules, dimensions and quadrants occupied.	One measuring more than 25 cm in diameter and occupying the entire breast.	One occupying two upper and lower quadrants.
Lymphadenopathy (seat, number, mobility, laterality and consistency)	Bilateral, axillary, warm, firm and sensitive.	Absent
Thillauxmanoeuvre	Positive	Positive

II.3.1.Peculiarities of examination of other parts of the body		
Thorax	Tachycardia, polypnea and crackling rails	Normal
Abdomen	Large by pregnant uterus. Abnormal BCF (Very high at 168 to 170b/minute). Uterine contractions absent.	Large by pregnant uterus. Normal BCF (135 to 150b/min). Uterine contractions absent.
Gynaeco-obstetricexamination	Featureless	Featureless
II.4.PRESUMPTIVE DIAGNOSIS	Neoplasia of the left breast [stage IV (T4dN3M1)] on pregnancy of 33 SA according to DDR with fetal distress and decompensated anemia.	Neoplasia of the left breast [stage III (T3N1Mx)] on pregnancy of unknown term with clinically normal fetal state.
III.PARACLINICAL		
Haematology	Hyperleukocytosis, hemoglobin 5g/dl and normal platelets.	Withoutparticularities
Obstetricultrasound	Abnormal (intra-uterine growth retardation, weight 1Kg, oligohydramnios at 20mm) because offoetal suffering	Normal (AG26 SA, weight 894Kg, amniotic fluid 36 mm) because of viable fœtuswithout particularity
Abdominopelvicultrasonography/echography	Not done	Done without particularity to the intraperitoneal organs onthe 16th/09/2022 at"Rwanda Military Hospital"
Breastechography/ ultrasonography + mammography	Abstinence (cfr very fulminent and purulent ulcero-necrotizing lesions)	Tissue formation, heterogeneous, irregular contour, Posterior attenuation, QSI and 25x15 mm in dimensions. Lesion classified SBR3 in different hospitals (HPGR ofBukavu, on the 18th /7/2022, HGRPanzion the 28th /8/ 2022 and at Rwanda Military Hospital, on the 16th /9/2022).
Anatomopathology	SBR3 infiltrating ductal carcinoma of 21/9/2022	SBR1 infiltrating ductal carcinoma of 6/9/2022

Immunohistochemis- try	Not done (Refusal by vulnerability)	Not done (Refusal by vulnerability)
Radiothorax	Images in favour of pulmonary metastases	Not done
Genetic Test for BRCA mutations	--"Suspected positive" to PCR (by presence of amplification of BRCA1 primers 185 and 187) at the UEA/Panzi lab.- Positive result confirmed (on exon 2 of the BRCA 1 gene) after sequencing at the Macrogen-Netherland lab.	- "Suspected positive" to PCR (by presence of amplification of primers 185 and 187 of BRCA1) -Unconfirmed positive result (on exon 2 of the BRCA 1 gene) after sequencing at the Macrogen-Netherland lab.
V. FINAL DIAGNOSIS	Invasive ductal carcinoma SBR3 / 27 weeks pregnancy with IUGR + Oligohydramnios (Manning score 6/10) + positive BRCA1 mutation	Invasive ductal carcinoma SBR1/ Pregnancy of 26 weeks of amenorrhea (Manning score 10/10) without BRCA mutation precision.
VI. CARE AND EVOLUTION		
VI.1. MANAGEMENT OF INFILTRATING DUTICAL CARCINOMA AND ITS COMPLICATIONS	-Anaemia improvement by transfusion, -Dressing of ulcerations bleeding on contact -Double antibiotherapy, -Counselling follow-up due to lack of oncology for neo-adjuvant treatment (Cfr inflammatory and metastatic cancer = stage IV)	Surgical counselling (Madden's mastectomy) before postpartum chemotherapy. She refused to undergo anoperation inPanzi in order to have it in Rwanda at the end of 2022.
VI. 2. OBSTETRICAL TREATMENT	-Cytotec induction for pregnancy stopped during the 1st transfusion. -Oestradiol benzoate injectable for three days to inhibit milky rise.	The delivery was at the end of 2022 with newborn without objectified particularity.

2. Pictorial illustration: Breast of patient (A) being an inflamed cancerous breast. That of patient (B) appears normal despite the swelling associated with the intraparenchymaltumour.

Cite this Article