Concurrent Plasma Cell Mastitis and Metastatic Breast Cancer a Rare Presentation of a Bilateral Disease: Case Report and Literature Review

Joseph E. Udosen[1], John A. Ashindoitiang[1,*], Victor I.C. Nwagbara[1], Theophilus I. Ugbem[2], Joseph S. Ukam[3] and Maurice E. Asuquo[1]

[1]*Department of Surgery, University of Calabar/University of Calabar Teaching Hospital, Calabar, Nigeria*

[2]*Department of Pathology, University of Calabar/University of Calabar Teaching Hospital, Calabar, Nigeria*

[3]*Department of Surgery, University of Calabar Teaching Hospital, Calabar, Nigeria*

Abstract: The concurrent occurrence of plasma cell mastitis(PCM) and breast cancer is rare. Plasma cell mastitis(PCM) is a chronic inflammatory breast disease. Metastatic breast cancer(MBC) is breast cancer that has spread to another part of the body commonly the bones, lungs, liver or brain. Presented is a 28 year old woman who was seen at the emergency department with difficulty in breathing and abdominal swelling of one month and two weeks duration respectively. In the previous year, she was diagnosed with bilateral PCM but declined therapy. Clinical, imaging and laboratory evaluation revealed a definitive diagnosis of metastatic bilateral breast cancer. Reported is a bilateral PCM and a metastatic bilateral invasive ductal carcinoma(IDC). PCM should be regarded as a key alert for a persistent check for cancer. Timely diagnosis and prompt surgical removal is recommended for the best possible outcomes.

Keywords: Plasma cell mastitis, Benign disease, Breast cancer, Metastatic, Concurrent, Bilateral.

INTRODUCTION

Diseases of the breast constitute a wide spectrum of pathologies that ranged from non-neoplastic (inflammatory, traumatic, ductal and cystic lesions) to neoplastic (benign and malignant) lesions. Inflammatory, benign and malignant pathologies rarely present as concurrent diseases [1]. The concurrent occurrence of PCM and cancer in the same breast have been reported in literature [4]. Plasma cell mastitis(PCM) also known as granulomatous mastitis(GM) or mammary duct ectasia is a chronic inflammatory breast disease that rarely occurs with breast carcinoma [1,2]. Metastatic breast cancer(MBC) is breast cancer that has spread to another part of the body commonly the bones, lungs, liver or brain [3]. The link of chronic mastitis to malignancy was reported in 5 sisters of whom 3 developed cancer [5]. Malignancies have been reported to arise from benign diseases. These conditions may mask or mimic another thereby presenting the clinicians with diagnostic and therapeutic challemges [6]. The benefits of imaging are evolving with the use of advanced imaging. Histology is key to the diagnoses [1,7]. Differentiating between breast cancer and PCM can be daunting due to overlapping clinical features, but it is crucial in view of the significant difference in the treatment strategies [7]. The aim of treatment of MBC is palliative and it is associated with low survival in most patients [3]. The present report is a case of a patient who was initially diagnosed with bilateral PCM that was eventually proved to be masking an underlying bilateral, invasive ductal carcinoma(IDC) diagnosed after the disease had become metastatic. The aim of this case study is to highlight the challenges of late presentation of PCM, a benign disease associated with remarkable morbidity. The grave attributes of MBC are also highlighted to emphasize the need for alertness required to achieve early presentation and diagnosis in patients with PCM for improved outcomes.

CASE SUMMARY

A 28 year old woman presented to the Accident and Emergency with complaints of difficulty in breathing for a duration of one month and abdominal swelling of 3 weeks duration. Difficulty in breathing was insidious in onset. It progressively worsened from difficulty in breathing on mild exertion to difficulty in breathing at rest. There was associated history of orthopnea but no paroxysmal nocturnal dyspnoea. She had cough but no hemoptysis or chest pain. There was a history of weight loss. However, there was no history of fever or drenching night sweats. She was not a known asthmatic or diabetic with no history of allergies. Abdominal swelling was insidious in onset, progressively increased in size and was painless. There was no history of nausea, vomiting, constipation

*Address correspondence to this author at the Department of Surgery, University of Calabar Teaching Hospital, UNICAL Hotel Road, Calabar South, Calabar, 540281. Cross River State, Nigeria;
E-mail: ashindoitiang90@yahoo.com

ISSN: 1927-7210 / E-ISSN: 1927-7229/24

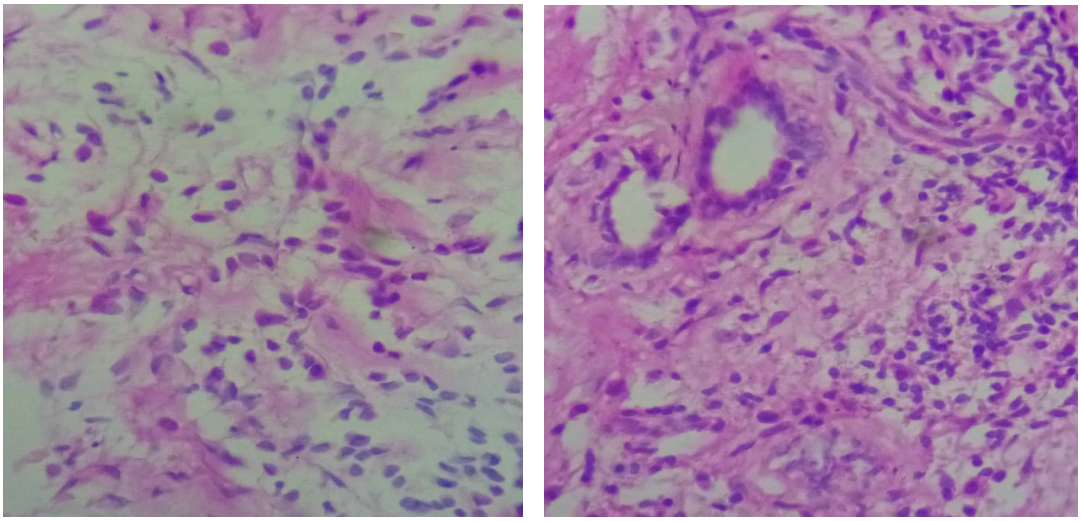

Figure 1: a(Right) and **b**(Left)- Photomicrographs of PCM showing granulomatous reaction mostly aggregates of plasma cells, histiocytes, lymphocytes an a few neutrophils. There was no proliferation.

or jaundice. She last opened bowel to stool two days prior to presentation and to flatus on the day of presentation. No history of headache, seizures or blurring of vision. She had no history of back or bone pain. Patient admitted to using herbal concoction for self-medication prior to presentation. She was para 2 with no comorbidities. There was no known family history of breast cancer. Two years ago in the same facility on account bilateral breast swellings and following clinical and histologic evaluation, she had a definitive diagnosis of bilateral plasma cell mastitis(PCM) following two separate biopsies, Figures (**1a** and **b**) [2]. She was counselled on the nature of the ailment and treatment with the assurance that disease was not cancer. Thereafter, she sought for alternative medical treatment to no avail.

Examination showed a young ill-looking woman, in respiratory distress, not pale, anicteric, acyanosed, afebrile, mildly dehydrated with bilateral axillary lymphadenopathy and left supraclavicular lymphadenopathy. There was no pedal edema. On chest examination, the respiratory rate was 36c/m, trachea was central, percussion note were dull, more on the right side. There were absent breath sounds more on the right side. On breast examination, the left breast showed the presence of peau d'orange, nipple retraction and the entire breast was hard in consistency. Right breast showed the presence of an ulcer around the nipple, it was hard consistency, Figure **2**. There were matted axillary lymphadenopathy bilaterally. Abdomen was distended, Figure **3**, with the presence of striae and moved with respiration. It was soft and there was no area of tenderness. Ascites was demonstrated by fluid thrill. Bowel sounds were present but distant. A clinical diagnosis of metastatic bilateral breast cancer (stage IV) was made.

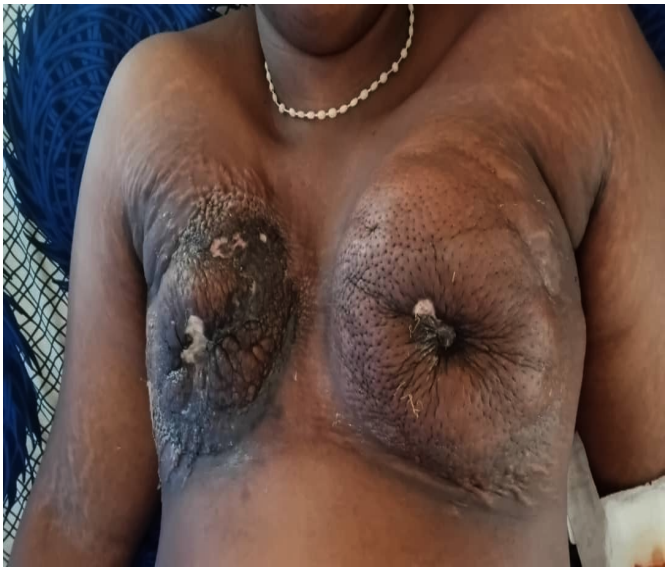

Figure 2: Clinical photograph of the breast.

Work up of the patient included: Full blood count (FBC), serum electrolytes, urea and creatinine that were normal, Table **1**. Abdominopelvic USS showed severe ascites. Chest X-ray was in keeping with right sided pleural effusion , Figure **4**. Pleural fluid Gene Xpert was negative. Pleural fluid protein and cholesterol showed: cholesterol- 1.3mmol/L; protein-23g/L. Cytology of the pleural aspirate was positive for malignancy. Ascitic fluid Gene Xpert was negative. Ascitic fluid MCS revealed: Pus cells +, Gram positive rods + Gram positive cocci + and no pathogen was isolated. Incision biopsy was reported as bilateral breast carcinoma- invasive ductal carcinoma, SBR

grade II, Figure (**5a**(Right) and **b**(Left)). Immunohistochemistry: ER- positive, PR- positive, HER 2/Neu-negative, Figure (**6 a**(Right) and **b**(Left)). A definitive diagnosis metastatic bilateral invasive ductal carcinoma was made.

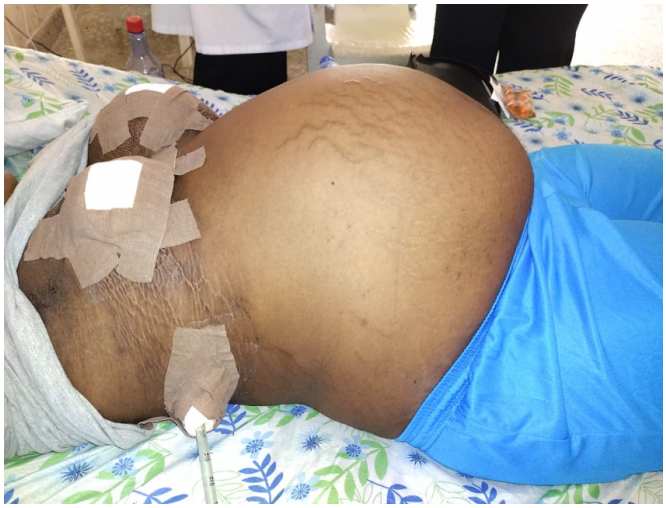

Figure 3: Clinical photograph showing a distended abdomen.

Table 1: Full Blood Count and Electrolytes/Urea/ Creatinine

Name	Result	Range	Unit
WBC	6.18	4.0-12.0	10^3/ul
Neutrophil	62.6	50.0-80.0	%
Lymphocyte	29.3	25.0-50.0	%
Monocytes	00	2.0-10.0	%
Basophil	00	0.0-2.0	%
Eosinophil	00	0.0-5.0	%
Hematocrit	33	35.0-55.0	%
Serum E/U/Cr			
Sodium	139.7	132-145	mmol/l
Potassium	4.63	3.2-5.0	mmol/l
Chloride	106.9	96-108	mmol/l
Bicarbonate	25.0	22-28	mmol/l
Urea	3.89	2.5-6.7	mmol/l
Creatinine	113.86	88.6-177.2	mmol/l

She had a right closed thoracostomy tube drainage (CTTD) done with drainage of serous fluid, Figure **7** and later intermittent therapeutic thoracocentesis. She had intermittent paracentesis and later the insertion of a peritoneal catheter. Patient eventually commenced neoadjuvant chemotherapy using IV Paclitaxel weekly. She received 5 doses with minimal improvement.

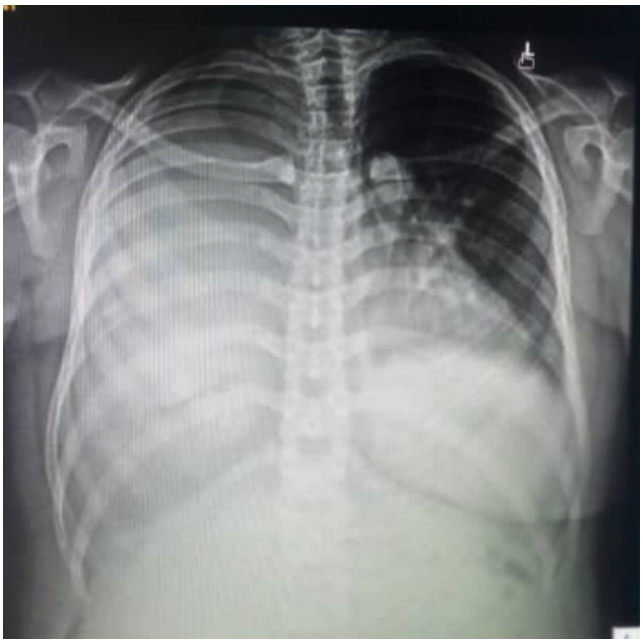

Figure 4: Chest X-ray showing right sided pleural effusion.

DISCUSSION

Plasma cell mastitis (PCM) is a rare chronic inflammatory condition of the breast with an unknown aetiology and estimated to occur in 2.4 per 100,000 women [1,9]. It is typically found in women in the 2nd and 4th decades of life [2]. Metastatic breast cancer also called stage IV breast cancer is cancer that has spread to another part of the body commonly to the lungs, liver, bones and brain [1]. Greater than 50% of histologically confirmed breast cancer patients presented with MBC in Nigeria. The menace MBC afflicting young women has been consistently reported among Africans including African Americans with a mean age of 45.9 years [3]. Recently, case reports have been described of the concurrence of granulomatous mastitis(GM) and malignancy in the same breast [10,11]. Evans *et al.* reported a 39 year old woman with concurrent granulomatous mastitis and invasive ductal cancer in the contralateral breasts [6]. Yoshida *et al.* reported a concurrent GM and ductal carcinoma in situ(DCIS) in a 34 year old woman [7]. A 30 year old lactating women earlier diagnosed with a recurrent GM that eventually proved to be masking an underlying DCIS was reported by Salih *et al*. [1]. We report this unique and rare occurrence in a young woman earlier diagnosed with bilateral PCM that presented with bilateral IDC diagnosed at presentation with metastatic breast disease in keeping with late presentation associated with advanced lesions typically seen in sub-Saharan Africa to highlight the need for early diagnosis and follow up of patients with PCM.

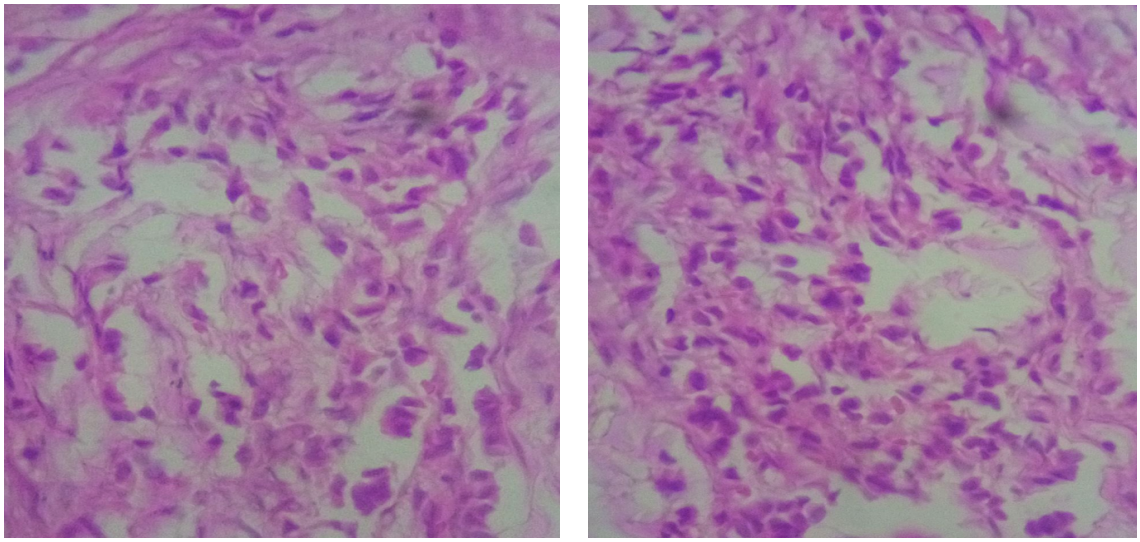

Figure 5: a(Right) and **b**(Left)- Photomicrograph, H&E x100- shows malignant epithelial tumor. Bilateral invasive ductal carcinoma(IDC), SBR Grade II.

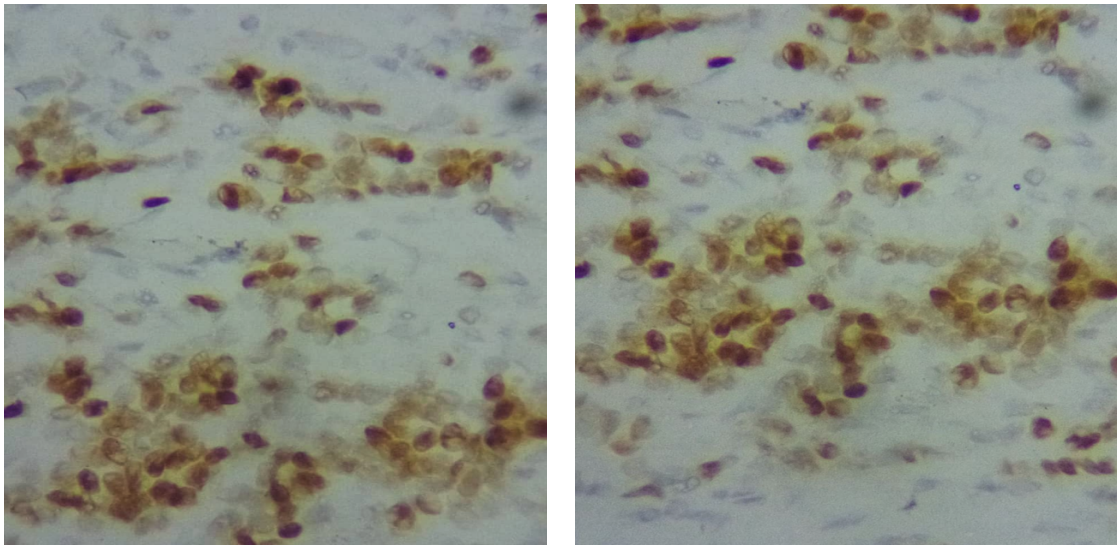

Figure 6: a(Right) and **b**(Left), Photomicrograph IHC- ER^+, PR^+.

It has been suggested that mastitis may be a precancerous lesion, however, this remains unclear [7]. Handley WS [5] reported the earliest link between mastitis and malignancy in 5 sisters with chronic mastitis, 3 of whom developed breast cancer. Chen *et al.* reported that women with mastitis have an increased risk of developing breast cancer [12]. Furthermore, they suggested that women >40 years could reduce breast cancer by taking precaution to prevent mastitis. Several reports have reflected the association between inflammation at a young age especially among lactating women and cancer. The biological link between PCM and malignant lesions remains unclear due the limited number of cases [1]. It is possible that breast cancer and PCM coexisted incidentally [7]. However, the occurrence in both breast in our patient increases the potential relationship between the two conditions and cannot be disregarded.

Idiopathic granulomatous mastitis(IGM) is an uncommon form of chronic inflammatory disease. It is a benign disease; however, it may be difficult to distinguish it from breast cancer [13]. Kessler and Welloch in 1972 [14], reported the first case of GM and stated that it can be confused with breast cancer as the diseases share similarities in clinical signs and presentation such as lumps, pain, swelling, skin changes, abscesses, ulcerations, sinus tracts and fistulas. They are sometimes associated axillary lymphadenopathy. In some instances, patients have

been clinically diagnosed with breast cancer resulting in complete mastectomy and axillary lymph node dissection, only to later be discovered through histology

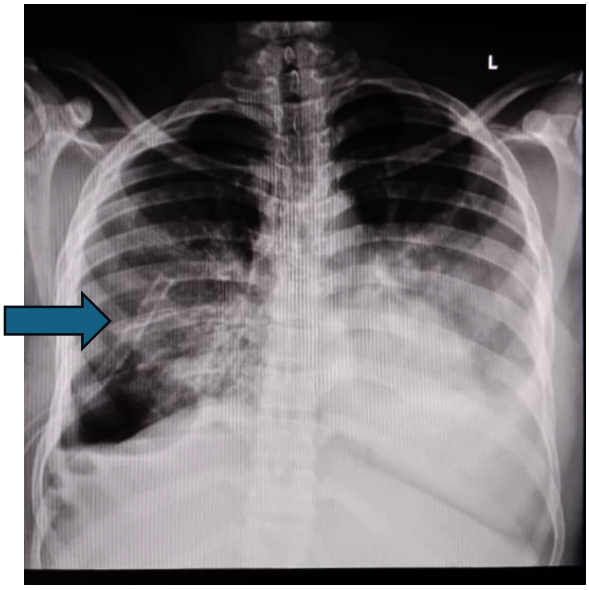

Figure 7: Chest X-ray showing right, CTTD, blue arrow with expansion of the lung.

to be GM [1]. Conversely, there are reports of patients initially diagnosed with PCM and treated conservatively who were later found to have breast carcinoma following surgery due to lack of improvement [15]. MBC symptoms vary depending on the metastatic cancer location. Chest metastasis may present with constant dry cough, difficulty in breathing and chest pain. Intraabdominal location may present with jaundice and ascites. Other locations include the bones that may present as back, bone or joint pain. These may in addition present with numbness or weakness of the limbs. Metastasis to the brain may present as severe headaches, confusion and seizures. We report this peculiar scenario, our patient initially diagnosed with bilateral PCM, was lost to follow up and represented as an emergency with MBC(difficulty in breathing and abdominal distension diagnosed with right sided pleural effusion and ascites) from bilateral IDC.

The clinical and radiology features of PCM and IDC are very similar. Tumor markers for breast cancer include AFP, CEA, CA15-3, CA 125, CA199. These are important for clinical diagnosis. Zhu *et al.* in their study illustrated the possible genetic relationship between GM and breast cancer in support of the symptom similarity [16]. The finding from gene sequencing technology to unravel the genetic mechanism of GM may have potential value in the diagnosis of GM(identification of biomarkers) and provide potential drug targets for PCM therapy [16]. To distinguish between PCM and IDC, it has been suggested that inflammatory markers(IL-33) or circulating tumor factors miR-155, let-7c, phosphatase and tensin homolog(PTEN) may act as future diagnostic markers [17]. Imaging- USS, mammographic and MRI findings are generally nonspecific, only serving to confirm the mass, parenchymal irregularity and multiplicity [6]. Some of the multiparametric MRI features of PCM and IDC were different. An integrated analysis of these multiparametric MRI features can assist in the differential diagnosis of PCM and IDC lesions thereby improving diagnosis [18]. In MBC evaluation, X-ray of the chest may reveal lung metastasis, pleural or pericardial effusion. Abdominal USS may detect liver metastasis and ascites. Pleural and abdominal tap for fluid analysis may assist in the diagnosis. The cytology of our patient from the pleural aspirate was reported as positive for malignancy. There is need for follow up with imaging in patients with PCM to prevent delayed diagnosis of cancer. The regular follow up investigations with tumor markers at the first presentation and during follow up in patients with PCN to facilitate early diagnosis of malignancy are highlighted. The Gold standard investigation remains histology aiming at the biopsy of all areas [3,6]. PCM, chronic granulomatous inflammation showing granulomatous reaction mostly aggregates of plasma cells, histiocytes, lymphocytes an a few neutrophils. There was no proliferation, Figure **1a** and **b**. Malignancy can be delineated from PCM if it's within the analyzed specimen, Figures **5a** and **b**. The biomarkers (Immunohistochemistry-IHC) for breast cancer are ER, PR, Her2. Luminal A- ER^+, PR^+, Her2 neg, Luminal B- ER^+, PR^+, $HER2^+$. Basal-like- Triple Neg and ER^+, PR^-, $Her2^+$. IHC of our patient was Luminal A- hormone receptor positive, Figure **6a** and **b**. The general poor outcome of MBC confirms the suspicion that biological aggressive form of breast cancer is predominant among African patients, Basal like(Triple negative) is found in 46% of patients compared to 12% among European patients [3].

Identification of PCM and IDC remain essential as the treatment modalities between the two differ significantly representing a benign and malignant diseases respectively. The primary treatment for PCM is pharmacological with anti-inflammatory and antibiotics. The malignancy often require multimodal treatments (surgery, hormonal treatment, chemotherapy, targeted therapy and radiotherapy) [3,6]. The aim of treatment of MBC is usually palliative with the specific objectives of

the improvement of the quality of life, symptoms control and prolongation of survival [3]. The challenges of identifying and the diagnosis of breast cancer in patients with PCM is highlighted, this is further compounded by poor attitude of patients to treatment occasioned by ignorance, socioeconomic and cultural factors that favour traditional medical treatment [1,3]. MBC is associated with poor prognosis and a severe burden both to the patient and the health care delivery system [3].

CONCLUSION

Concurrent occurrence of PCM and malignancy(IDC) can occur as a bilateral disease. PCM should be regarded as a key alert for a persistent check for cancer. There is need for vigilance with imaging in patients with PCM to prevent delayed diagnosis of cancer. Regular follow up investigations for tumor markers at the first presentation and during follow up in patients with PCM to facilitate early diagnosis of malignancy are recommended. Timely diagnosis and prompt surgical removal are recommended for good outcomes.

ACKNOWLEDGEMENTS

We acknowledge the patient and all the participating author for their contribution to the paper.

DECLARATION OF CONFLICT OF INTEREST

The authors declare no conflict of interest with respect to the research, authorship and/or publication of this article.

FUNDING

This research received no specific grant from any funding agency in the public, commercial, or not for profit sectors.

CONTRIBUTORSHIP

All authors contributed to different aspect of the report.

ETHICAL STATEMENT

The requirement for ethics approval was waived because this study was a case report of a patient managed by our team, not an interventional study(i.e., no intervention or experimentation was carried out on the patient for the purpose of this study).

INFORMED CONSENT

The patient provided both verbal and written informed consent for the publication of this case and all accompanying images.

REFERENCES

[1] Salih AM, Pshtiwan LR, Abdullah AM, Dhahir HM, Ali HO, Muhiaiden AS, Hussein BO, Hassan SH, Kakamab FH. Granulomatous mastitis masking ductal carcinoma in situ: A case report with literature review. Biomedical Reports 2024; 20: 17. https://doi.org/10.3892/br.2023.1705

[2] Ashindoitiang J, Nwagbara V, Ugbem T, Ukam J, Asuquo M. Bilateral plasma cell mastitis simulating breast cancer: a case report and literature review. Journal of International Medical Research 2024; 52(3): 1-6. https://doi.org/10.1177/03000605241233167

[3] Adisa AO, Arowolo OA, Akinkuolie AA, Titiloye NA, Alatise OI, Lawal OO, Adesillonwo ARK. Metastatic breast cancer in a Nigerian tertiary hospital. African Health Science 2011; 11(2): 279-284.

[4] Tavacol M, Alvand S, Azmoadeh AF, Ardalan A, Assavian A. Idiopathic granulomatous mastitis with incidental lobular carcinoma in situ: A case report. Arch Breast 2022; 9: 315-319. https://doi.org/10.32768/abc.202293SI315-319

[5] Handley WS. Chronic mastitis and breast cancer. Br Med J 1938; 2: 113-138. https://doi.org/10.1136/bmj.2.4045.113

[6] Salih AM, Pshtiwan LR, Abdullah AM, Qaradakhy AJ, Kadamad FH, Ali HO, Salih KM, Rahim HM, Abdalla BA, Hassan MN, Mohammed SH. Carcinoma arising from fibroadenoma: presentation and management: a case series. Barw Med J 2023; 1: 1-28.

[7] Evans J, Sisk L, Chi K, Brown S, To H. Concurrent granulomatous mastitis and invasive ductal cancer in contralateral breasts- a case report and review. J Surg Case Reps 2021; 11: 1-3. https://doi.org/10.1093/jscr/rjab519

[8] Yoshida N, Nakatsubo M, Yoshino R, Ho A, Ujiie N, Yazawa S, Kitoda M. Concurrent granulomatous mastitis and ductal carcinoma in situ. Cureus 2023; 15(5): e38377. https://doi.org/10.7759/cureus.38377

[9] Bacon DR, Ngeve SM, Jordan SG. Granulomatous mastitis. An undiagnosed inflammatory disease afflicting minority of women. Radiol Care Rep 2021; 16: 3990-3994. https://doi.org/10.1016/j.radcr.2021.09.044

[10] Cahs H, Kihtei A. Granulomatous mastitis concurrence with breast cancer. Eur J Breast Health 2018; 14: 58-60. https://doi.org/10.5152/ejbh.2017.3804

[11] Oddo D, Dominguez F, Gomez N, Mendez GP, Navarro ME. Granulomatous lobular mastitis associated with ductal carcinoma in situ of the breast. SAGE Open Med Case Rep 2019; 7: 2050313x19836583. https://doi.org/10.1177/2050313X19836583

[12] Chen Y, Chan C, Lim Y, Yang S, Yeh L, Wang Y, Chou M, Yeh C. Risk of breast cancer in women with mastitis: A retrospective population based cohort study. Medicina 2020; 56: 372. https://doi.org/10.3390/medicina56080372

[13] Yin Y, Liu X, Mang G, Han X, Zhang H, Lv Y. Idiopathic granulomatous mastitis: etiology, clinical manifestations, diagnosis and treatment. J Invest Surg 2022; 35(3): 709-720. https://doi.org/10.1080/08941939.2021.1894516

[14] Kessler E, Welloch Y, Granulomatous mastitis: A lesion clinically simulating cancer. Am J Clin Pathol 1972: 58: 642-646. https://doi.org/10.1093/ajcp/58.6.642

[15] Waraya M, Inukai M. A case report of triple negative breast cancer diagnosed as GM. J Cancer Chemother 2020; 47: 1854-1856.

[16] Zhu Q, Wang L, Wang P. The identification of gene expression profiles associated with granulomatous mastitis. Breast Care 2021; 16: 319-326. https://doi.org/10.1159/000507474

[17] Aksan H, Kundaktepe BP, Sayili U, Validedeoglu M, Simell G, Koksal S *et al*. Circulating miR-155, let-7c, miR-21 and PTEN levels in differential diagnosis and prognosis of idiopathic granulomatous mastitis and breast cancer. Biofactors 2020; 46: 955-962. https://doi.org/10.1002/biof.1676

[18] Chen R, Hu B, Zhang Y, Liu C, Zhao L, Jiang Y, Xu Y. Differential diagnosis of plasma cell mastitis and invasive ductal carcinoma using multiparametric MRI. Gland Surg 2020; 9(2): 278-290. https://doi.org/10.21037/gs.2020.03.30

Received on 10-10-2024 Accepted on 06-11-2024 Published on 02-12-2024

https://doi.org/10.30683/1927-7229.2024.13.05