Case Report

Invasive Cribriform Carcinoma of the Male Breast

Abdulrazzak O. Lawal, Adekoyejo A. Phillips[1], Nnamdi O. Orah[1], Adetola O. Daramola[1], Fatimah B. Abdulkareem[1]

Departments of Surgery and [1]Anatomic and Molecular Pathology, College of Medicine, University of Lagos and Lagos University Teaching Hospital, Lagos, Nigeria

Abstract

Male breast cancer is rare and it accounts for about 1 % of all breast cancers. Men of African and Jewish descent have higher risk of developing breast cancer. Invasive cribriform carcinoma of the breast, which has a good prognosis, is rarer particularly in male patients and only few cases have been reported in the literature. A young adult male presented with a painless, left breast mass of one-year duration at the surgical out-patient department of the Lagos University Teaching Hospital. On examination, a 24x16x6 cm mass, involving all four quadrants, attached to the overlying skin and underlying structure, was palpated in the left breast. It was non-tender and there was no differential warmth. Imaging studies revealed a Breast Imaging Reporting and Data System (BIRADS) IV lesion. On histopathology examination, an infiltrating carcinoma which was disposed in a cribriform pattern was seen. The neoplasm comprised of fairly monomorphic cells that exhibited increased nucleocytoplasmic ratio, moderate eosinophilic cytoplasm, vesicular nuclei and prominent nucleoli. Immunohistochemistry for estrogen receptor, progesterone receptor and HER-2 revealed a luminal A tumour. A diagnosis of invasive cribriform carcinoma of the breast was made. We report the first known case of invasive cribriform carcinoma of the breast in a male patient from Nigeria.

Keywords: Breast, cancer, cribriform and male

Introduction

Male breast cancer is a rare entity that is becoming more common; it accounts for 1% of all breast cancers.[1] Different incidences have been reported depending on the study population, but it has been said to occur more commonly among men of African descent and Ashkenazi Jews having a risk that is 80% greater than other men because of Breast Cancer (BRCA)1 or 2 genetic mutations.[2] In Nigeria, the incidence varies between 1.9% and 9%.[3,4] One of the major prognostic factors in breast cancer is the histological subtype. Histological types with excellent prognosis include tubular carcinoma, cribriform carcinoma, and mucinous carcinoma.

Invasive cribriform carcinoma (ICC) of the breast is characterized microscopically by invasion of the breast stroma by malignant epithelial cells in predominantly cribriform growth pattern.[5] It was first described in 1983 by Page *et al*.[6] Pure and mixed variants of ICC have been described; when the cribriform architecture is >90% of the tumor, it is described as "pure ICC," while cases with other histological patterns, tubular pattern exclusive, involving up to 50% of the tumor are described as "mixed ICC."[5] In males, ICC accounts for between 0.13% and 6.7% cases of all breast cancers.[7,8]

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To the best of our knowledge, only a few cases of male ICC of the breast have been reported in the literature. This is a report of the first known case of ICC of the breast in a male patient from Nigeria.

Case Report

We report an adult male in the fifth decade of life, who noticed a rapidly enlarging mass in his left breast 1 year before presentation. It was painless and was associated with scanty bloody nipple discharge. He had no family history of any cancer, prior history of irradiation, or enlargement of the affected breast. He had no comorbid illness, and there was no prior history of consumption of alcohol or ingestion of tobacco.

On physical examination, his general condition was satisfactory with a body mass index of 27.6 kg/m^2. The breasts were asymmetrical with the left breast larger than

Address for correspondence: Prof. Adetola O. Daramola, Department of Anatomic and Molecular Pathology, College of Medicine, University of Lagos and Lagos University Teaching Hospital, Lagos, Nigeria.
E-mail: aodaramola@cmul.edu.ng

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the right. The right was essentially normal; however, the left breast was distorted with a widened nipple areolar complex; the nipple was displaced inferiorly and retracted. There were dilated superficial veins and peau d'orange but no ulcerations. There was a large, nontender mass involving the entire breast measuring 24 cm × 16 cm × 6 cm with ill-defined margins and heterogeneous in consistency. It was attached to the overlying skin and pectoralis muscle but not the bony chest wall. He also had matted ipsilateral axillary nodes but no supraclavicular or infraclavicular nodes. He had no clinical feature to suggest a distant metastasis.

He was referred with a breast ultrasound report of a breast imaging reporting and data system IV lesion. Histology of the core needle biopsy revealed findings of tumor cells disposed in solid sheets and ducts within a fibrocollagenous stroma. The cells had abundant eosinophilic cytoplasm, fairly regular nuclei with hyperchromasia, and indistinct nucleolus. There was brisk mitotic activity as well as areas of calcification. The conclusion was a B5 (malignant) lesion.

Other investigations revealed no feature suggestive of metastasis. He had modified radical mastectomy which revealed matted Level I and Level II axillary nodes in addition to the previously described mass. The postoperative period was uneventful.

The histological findings showed irregularly shaped nests of malignant epithelial cells with a cribriform pattern haphazardly infiltrating the stroma. Punched out areas with foci of necrosis were seen within the nests. The malignant cells were fairly monomorphic with increased nucleocytoplasmic ratios and vesicular nuclei. Mitotic figures were frequent. Areas of cribriform ductal carcinoma *in situ* and calcification were also seen. No areas of tubular carcinoma or high-grade carcinoma components were observed. A diagnosis of ICC was made [Figure 1]. Immunohistochemistry for estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2) using Thermo-Scientific SP1 – ER, Thermo-Scientific SP2 – PR, and Thermo-Scientific SP3 – HER2 revealed a Luminal A tumor (ER positive-Quick Score of 5; PR positive-Quick Score of 6; HER2 negative [score 1]) – Figure 2.

The patient was referred for radiotherapy and discharged on tamoxifen 20 mg daily. The patient was disease free for 1 year postoperative and had no complaints. He, unfortunately, stopped attending the clinic.

Discussion

Breast cancer is a rare entity in men. ICC of the breast is even a much rarer histologic subtype, particularly in male patients. In a review of male breast cancer in Ile Ife, Nigeria, over a 19-year period, there was no case of cribriform breast cancer in all the 10 cases seen.[3] Over a 20-year period in Benin, there was no case of cribriform breast carcinoma in all the 16 male patients reviewed.[9] Other studies of male breast cancer from Zaria,[10] Ibadan,[11] Maiduguri,[12] and Ilorin[13] in Nigeria did not document any case of cribriform breast carcinoma. This goes to corroborate the rarity of this histological type of breast carcinoma in males.

This patient who had histologically confirmed breast carcinoma of the invasive cribriform type presented late (1 year after onset of symptoms). Late presentation is a common occurrence among cancer patients in Nigeria and has been observed more in men.[8] However, with increase in medical knowledge and availability of medical facilities, men apparently have begun to present earlier. For example, a more recent study from Zaria in Nigeria had only 29% of the patients presenting after 12 months, though the median duration of the presentation was 11 months.[9]

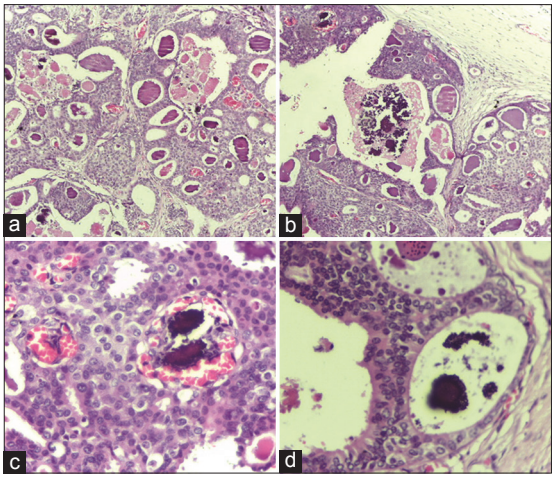

Figure 1: Microscopic appearance of the lesion showing cribriform architecture and calcifications. (a) Cribriform architecture H and E, ×40, (b) with calcifications H and E, ×40, (c) calcifications H and E, ×100, (d) calcifications H and E, ×100

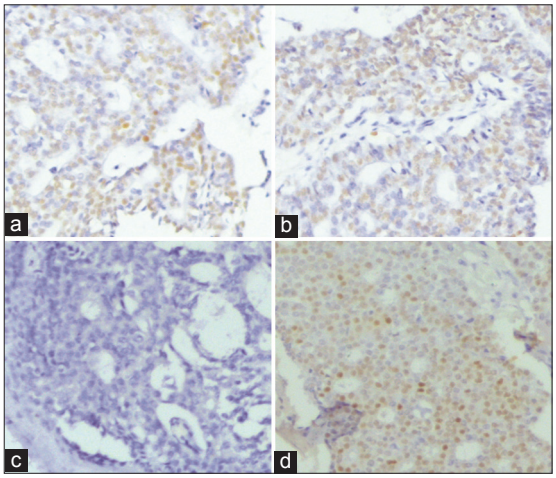

Figure 2: Microscopic appearance of the lesion showing immunohistochemical reactions to estrogen receptor, progesterone receptor, and human epidermal growth factor receptor 2 antibodies. (a) Estrogen receptor, ×40; (b) estrogen receptor, ×40, (c) human epidermal growth factor receptor 2, ×40, (d) progesterone receptor, ×40

Only a few cases of ICC have been reported to have extensive microcalcifications. Shousha *et al*. reported a case of extensive microcalcifications in a woman with ICC who had a 20-year history of silicon augmentation.[14] They thought this to be due to an active secretory process by the tumor cells, with the relationship between the secretions and the silicon being unclear. Nishimura *et al*. have reported a case of ICC with extensive microcalcifications.[15] They attributed the microcalcifications to the secretions from the epithelial cells. Microcalcifications are said to be unique for ICC because they are more common in *in situ* types of breast carcinoma.[15]

This patient had a breast large tumor (24 cm × 15 cm × 6 cm) with no clinical evidence of distant metastasis. This is unusual because tumors >5 cm are at increased risk of distant metastasis. The histology of ICC can largely account for the lack of evidence of distant metastasis. Most studies believe that ICC confers better prognosis in patients with breast cancer.[14,15] In contrast to this, a 40-year retrospective single-institution review of practice by Meattini *et al*. found that ICC was an independent predictor of death in male patients with breast cancer.[7]

The findings on ER and PR analysis in this study are similar to those observed in other studies, showing that over 90% of metastatic breast cancer (MBC) are ER positive while 80%–96% are PR positive. The retrospective study of MBC in the USA by Ge *et al*. showed that ER positivity was 100%, while PR positivity was 64%.[16] Similar results were obtained in Singapore where all the cases of MBC seen were ER positive and 86% were PR positive.[17] At the Lagos University Teaching Hospital (LUTH), Orah *et al*. showed that over 10 years, 17 of 18 male breast cancer were ER positive while 16 were PR positive. HER2 results were consistently negative in the LUTH series and so the HER2 profile of this patient is not surprising.[18] Overexpression of HER2 in these patients has been shown to be associated with shortened survival.[19] The negative result seen on HER2 overexpression analysis seen in this study may point to better survival rates for male breast cancer in our environment.

Conclusion

Male breast cancer is rare and the invasive cribriform subtype is even rarer. It shows characteristic histologic features, and on immunohistochemistry, most are hormone receptor positive and HER2 negative. Histologic diagnosis of this subtype of male breast cancer is important as it is relevant in prognostication.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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