Case Report

Invasive Breast Carcinoma with Osteoclast-Like Stromal Giant Cells and Triple-Negative Immunophenotype: A Case Report and Literature Review.

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Abstract

Breast carcinoma with osteoclast-like stromal giant cells (OGCs) is a rare variant of invasive ductal carcinoma of no special type. (NST). The unique stromal features of this tumour can be found in some other invasive breast carcinoma such as papillary carcinoma. lobular carcinoma, and metaplastic carcinoma. The origin of OGC have been shown to be derived from macrophages and the tumour biology showed variable immunophenotyping and prognosis. Thus, we report a case of a 43-year-old woman who had a painless lump in her left breast that had grown larger over a period of 2 months. The lump had specific histopathological characteristics that were consistent with invasive ductal carcinoma of no special type (NST) with osteoclast-like giant cells (OGC), Nottingham grade 3 and its pathological stage was $pT_4N_0M_x$ (clinical stage IVb). The tumour cells were not immunoreactive with human epidermal growth factor-2 (HER-2), progesterone receptor (PR), and oestrogen receptor (ER) antibodies. She underwent a left breast mastectomy, followed by conventional chemotherapy and was tumour-free for two years. The left mastectomy defect was subsequently repaired using a transverse thoracoepigastric flap. A crucial factor in the patient's mortality was a recurrence that showed up at the patient's follow-up appointment after eight months, along with accompanying bleeding from the mass lesion site with associated severe anaemia. The prognosis is unpredictable in IBC with OGC and triple-negative molecular subtypes. Our case offers information about the patient's characteristics and case presentation.

Keywords: Invasive Breast carcinomas (IBC), osteoclast-like giant cells (OGC), Triple-negative breast carcinoma (TNBC)

INTRODUCTION

The WHO classifies invasive breast carcinoma (IBC) with osteoclast-like stroma giant cells as an uncommon subtype of invasive breast carcinoma of no distinctive type.[1] There are about 2% of breast carcinomas with osteoclasts (Osteoclastic giant cells (OGCs).[2] Rosen published the first study in 1979

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Ann Trop Pathol 2023;14(2):103-106.

describing breast carcinoma with large cells and 200 cases have been reported.[2] The majority of cases have distinct masses with a characteristic inflammatory and hypervascular stroma, despite varied tumour histopathology.[2,3] There is general agreement that OGCs in invasive breast carcinoma are of histiocytic origin and are thought to come from macrophages.[4] which have both pro-tumour and anti-tumour function. [3,4,5] This case report will contribute to the expanding body of clinicopathological knowledge regarding the IBC with OGC and triple-negative immunophenotype.

CASE REPORT

This is the case of a 43-year-old woman who was referred from a private hospital due to a painless left breast lump that had first manifested itself over a period of 2 months. It had a starting size of roughly 2.0 cm, but it became bigger over time. The skin that covered the lump had not changed in the past, and there was no tumour in her armpit. There was no prior history of nipple discharge, and there was no family history of breast disease. She underwent an incisional biopsy (for histopathological evaluation) at a private hospital with a histopathologic diagnosis of invasive breast carcinoma possibly invasive ductal carcinoma of no special type (NST), and Nottingham grade 3 status. She was then referred to our facility for specialized cancer care.

She had a history of hypertension and had been on Aldomet and Moduretic four years prior to the presentation. There was no documented medical history of peptic ulcer disease, asthma, or diabetes mellitus. The painless left breast lump was firm to hard upon examination and measured 8.0cm × 8.0cm x 6.0cm in the upper outer and lower outer quadrants. This tumour was fixed to the pectoralis fascia and the overlying skin. However, axillary lymphadenopathy was absent.

The clinical examination showed that the patient had clinical-stage IVb left invasive breast carcinoma (with the pathological stage of $pT_4N_0M_x$). Investigations done include chest X-ray, which reveals no focal lesions and abdominal ultrasound scan (USS) showed no evidence of metastases. Unfortunately, further radiological evaluations of the patient using computed tomography [CT] scan and magnetic resonance imaging [MRI] was not done due to financial constraints. The investigation carried out prior to surgery and chemotherapy are: full blood count (FBC), white blood cells (WBC) of 5.2 x 10^9/L (Normal), platelets of 230 x 10^9/L (Normal), haemoglobin (Hb) of 11.6 g/dl (Normal); Electrolyte, urea, and creatinine (E/U/Cr), sodium (Na) of 140 mmol/l, Urea of 4.1 mmol/l, potassium (K) of 3.5 mmol/l, creatinine (Cr) of 82.0 mmol/l (Elevated). Thereafter, after 10 months of clinical presentation, she underwent a left breast mastectomy and subsequently commenced on six courses of adjuvant chemotherapy with oral Tamoxifen tablets 20 mg daily for one-month, intravenous Epiburin 50 mg/m^2 (100 mg), intravenous Cyclophosphamide 500 mg/m^2 (1000 mg) with Normal Saline infusion. More importantly, her pre-chemotherapy vital signs were stable.

The mastectomy specimen was immersed in 10% neutral buffered formalin and submitted together with pathology request form at the Department of Anatomic Pathology, University of Ilorin Teaching Hospital. The specimen was registered at the reception of the department and subsequently examined by pathologist at the surgical cut up bench. The tumour was a clearly defined, reddish-brown mass with haemorrhage and haemorrhagic stroma on gross examination. (Figure 1A). The histologic section of the tumour is consistent with invasive ductal carcinoma of no special type with osteoclast like stroma giant cells.

Figure 1A: Gross photograph of specimen showing a relatively well-delineated tumour mass that has been serially sectioned to reveal a reddish-brown haemorrhagic cut surface.

The resection margins were free of the tumour and no lymph node were submitted for examination. Notably, serial dissection of the axillary tail of spence fat revealed no lymph nodes. The histology examination of this tumour showed osteoclast-like stroma giant cells admixed with malignant epithelial cells that were arranged in cords, sheets, and glandular patterns, against a background of a hypervascular stroma as illustrated in figure 2. These malignant epithelial cells range in shape from spherical to polygonal, are medium to large in size, and have an elevated nuclear-cytoplasmic ratio, a scattered chromatin pattern, conspicuous nucleoli, and sparse cytoplasm. The stroma was made up of fibrocollagenous tissue, numerous giant cells that resembled osteoclasts and were of different sizes, recent haemorrhages, and a large number of hemosiderin-rich macrophages. This giant cell (OGCs) feature varied from several small, uniform,

round to oval nuclei as well as an abundance of eosinophilic cytoplasm (Figures 1B, 2A – 2D).

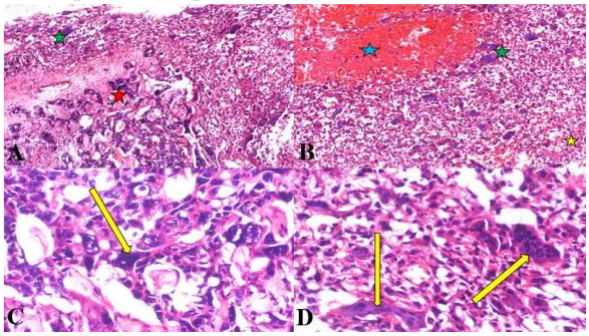

Figure 2 (A - D): Shows photomicrographs of (A) the tumour composed of sheets of malignant epithelial cells {***red star***} arranged in cords, sheets, and glandular patterns admixed with osteoclast-like giant cells {***green star***} in the background of the hypervascular stroma. The stroma is composed of fibrocollagenous tissue with numerous osteoclast-like giant cells of varying sizes and fresh haemorrhages as well as abundant hemosiderin-laden macrophages [H&E stain, x100 mag.]. (B) the tumour stroma composed of fibrocollagenous tissue {***yellow star***} with numerous osteoclast-like giant cells {***green star***} of varying sizes and fresh haemorrhages {***blue star***} [H&E stain, x100 mag.]. (C) the tumour composed of sheets of malignant epithelial cells {***thick yellow arrow***} arranged glandular pattern admixed with a few tumour giant cells [H&E stain, x400 mag.]. (D) the tumour stroma composed of fibrocollagenous tissue with numerous osteoclast-like giant cells of varying sizes. The osteoclast-like stroma giant cells {***thick yellow arrows***} are composed of multinucleated round-to-oval cells with hyperchromatic nuclei and abundant cytoplasm [H&E stain, x400 mag.].

On immunohistochemical evaluation, the tumour cells were negative for oestrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor type 2 (HER-2) immunostains respectively. The OGCs were not immunohistochemically evaluated (however, they are known to be positive for CD68, MMP12, TRAP, and Cathepsin K immunostains). Furthermore, in view of the haematoxylin and eosin (H&E) and ancillary immunohistochemical evaluations, an histopathological diagnosis of invasive ductal carcinoma with osteoclast-like stromal giant cells with triple-negative immunophenotype was made in accordance with the 2012 WHO classification of breast tumours.[1]

She was subsequently referred for radiotherapy but defaulted due to financial constraints. Her health was stable till January 2019 when she had transverse thoraco-epigastric flap reconstruction to repair the left mastectomy defect. She was subsequently discharged for follow-up visits. The follow-up was irregular until she re-presented to the Accident and Emergency (A&E) Unit with a fungating bleeding lump on the surgical scar of her left breast and Packed Cell Volume (PCV) of 16 percent. A diagnosis of recurrent left breast carcinoma with symptomatic anaemia was made. She was subsequently transfused with 4 units of blood until a post-transfusion PCV was 32%. Thereafter, she was discharged and was scheduled to re-commence the Taxane-based chemotherapy on her next clinic visit. However, she reported at a private facility a few days after being discharged, with continued bleeding from the surgical scar lesional mass and the unexpected commencement of a fainting spell. It was considered to be recurrent left breast carcinoma with symptomatic anaemia. After receiving a unit of blood through transfusion, she started having trouble breathing during her treatment and eventually stopped breathing. She was subsequently declared dead after 27 months from the date of first clinical presentation at the private hospital.

Ethical Issue

This case report was conducted in compliance with the guidelines of the Helsinki Declaration on biomedical research in human subjects. Confidentiality of the patient and personal health information was maintained.

DISCUSSION

This article gives an insight into a rare type of breast carcinoma that is classified by WHO as invasive ductal carcinoma with osteoclast-like stroma giant cells. Notably, the patient in our case report, a 43-year-old woman with invasive breast carcinoma with osteoclast like stroma giant cells (OGC) despite having no lymph node metastasis, had a poor prognosis (having passed away less than five years after her initial cancer diagnosis). The poor prognostic factors in this case included late stage at diagnosis (Stage IVb) and the triple negative immunophenotype of the tumour. The age of occurrence of this case in the 5th decade is consistent with similar reports by other authors.[6-9] However, a 64-year-old woman was reported to have invasive ductal carcinoma with OGC in one case.[11] In addition, a few of the reports showed infiltrating lobular carcinoma, pleomorphic lobular carcinoma and metaplastic carcinoma to co-exist with OGC respectively.[6,7,8,10]

It's interesting to note that this patient's initial histopathological diagnosis, following incisional biopsy, was invasive ductal carcinoma of no special type (NST) with Nottingham grade 3 (without reference to the presence of the osteoclast-like stromal giant cells). She then underwent a modified radical mastectomy, with the upper and lower

outside quadrants showing an 8 cm wide, reddish brown, soft to firm tumour mass that was well-circumscribed. The tumour was 1.5 cm away from the deep resection margin. More importantly, this case exemplifies the need to subject her previous incisional biopsy as well as mastectomy tissue to thorough histopathological examination which led to the discovery of IDC with OGCs, which could have resulted in a false-negative diagnosis, subsequently culminated into underdiagnosis and under-reporting. Therefore, the histopathological report from mastectomy tissue clarified the final histopathological classification of this tumour as invasive ductal carcinoma (IDC) of no specific type (NST) with osteoclasts-like giant cells (OGCs).

Although, the literature reports showed a variable prognosis for this type of tumour which range from 5 months to 2 years, the index patient lived for three years from the time of tumour appearance to the time of her death. Generally, this subtype of cancer has a 5-year survival rate of about 70%, which is comparable to patients with typical invasive ductal carcinomas (NST).[1]

Finally, it is important to note that the triple negative immunohistochemical phenotype, particularly common in women of African descent, together with additional comorbidities like hypertension in this index patient, and the fundamental biological behaviour of this tumour (presence of OGCs) are all relevant to the prognosis of this lesion. In contrast, a comprehensive clinicopathologic and molecular review of 27 cases showed luminal A molecular subtype and similar findings were reported from a case report.[6,8,12] A minority of cases have been reported to be luminal B.[12]

CONCLUSION

Invasive ductal carcinoma (IDC) with OGCs is a tumour with varied immunophenotyping and prognosis. The impact of OGCs on a patient's prognosis is still debatable. Thus, our case report with literature review offers insight into both the profile of our patient and this uncommon case presentation of IDC with OGCs. We advise additional molecular biological research on the prognostic significance of OGCs in IBCs.

Conflict of Interest: The authors declare that they do not have anything to disclose regarding conflict of interest with respect to this manuscript.

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