Fungating breast cancer: How long are we going to see this stage of the disease? Case report and literature review.

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Introduction
Locally advanced breast cancer constitutes approximately 10%-20% of the newly diagnosed breast cancers and up to 75% of breast cancers in developing countries. Fungating breast cancer is considered as an entity of locally advanced breast cancer which remains a clinical challenge as the majority of patients with this diagnosis develop distant metastases despite appropriate therapy. We report a case of fungating breast cancer and review the literature with special reference to the management to this stage of the disease.

Case Presentation
A 65-year-old Eritrean lady presented to the surgical outpatient department at KFMC, Riyadh, because of a large fungating lump in her left breast. She stated that the lump had started as small nodule which had grown gradually in size and ulcerated through the skin over a period of one year. This was associated with a significant loss of weight over the last 3 months. She had no family history of breast cancer and did not seek medical advice because she used to live in a remote area in Eritrea which was lacking medical services. There was a striking foul smell when the patient entered the examination room. On clinical examination she looked emaciated, depressed and distracted. There was a fungating ulcerating lesion about 10cm in diameter involving the lower inner quadrant and the central part of the left breast (figures 1 & 2).
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Figure 2
Figure 2: Photograph of the tumor showing elevated margins, multiple areas of necrosis and hemorrhage.

There were neither clinically palpable axillary lymph nodes nor was there oedema of the left arm. The right breast was normal.

Blood investigation revealed a hemoglobin of 8.2g%. Urea & electrolytes, liver function test and coagulation screen were within normal limits.

The mammogram of the right breast showed moderate fatty replacement of the glandular tissue with residual fibroglandular densities but there was no evidence of dominant masses, speculated lesions, clusters of suspicious micro-calcification or skin changes (figure 3).

Figure 3
Figure 3: Mammogram of the right breast (contralateral breast) showing moderate fatty replacement of the glandular tissue and fibroglandular densities without evidence of malignancy.

A contrasted CT scan of the chest, abdomen and pelvis showed a large fungating mass in the left breast with the largest anteroposterior and transverse diameter of 9.1 x 6.6cm. There was one lymph node seen in the left axilla measuring 1.7 x 1.2cm. There were no liver or lung metastasis (Figures 4, 5 & 6).

Figure 4
Figure 4: CT scan showing a large fungating enhancing mass of the left breast (arrow), with significant central necrosis.

Figure 5
Figure 5: CT scan showing the elevated edges and the invagination of the centre of the tumor (arrow).

The pre-operative tissue biopsy showed invasive high-grade ductal carcinoma with focal necrosis.
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Figure 6
Figure 6: Chest CT scan showing an enlarged left axillary lymph node (arrow).

The bone scan showed no evidence of cortical bone metastasis. There was increased left-breast soft-tissue uptake consistent with breast carcinoma (figure 7).

Figure 7
Figure 7: Bone scan showing no evidence of cortical bone metastasis. There was increased left-breast soft-tissue uptake (arrow), consistent with breast carcinoma.

The patient was treated initially with metronidazole in the form of intravenous infusion and topical gel together with occlusive dressing to treat the infection and eliminate the foul smell. After screening for metastasis the patient underwent surgery in the form of radical mastectomy with removal of all involved skin, pectoralis muscle and axillary lymph nodes (Figure 8 & 9).

Figure 9
Figure 9: Photograph showing the closed wound and the drains at the end of the operation.

Figure 10
Figure 10: A histology slide of the mass showing infiltrative ductal carcinoma (Hematoxylin & Eosin, x10)

The histopathology of the mastectomy specimen showed a mass of 12 x 10 x 4cm in maximum dimension with fungating invasive intraductal carcinoma (Bloom Richardson Grade 3). The nipple was free from tumor as well as the resection margins. Thirteen out of thirteen lymph nodes were also free from tumor. ER and PR were negative while HER 2 neu was weak positive (figures 10 & 11).
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**Figure 11**
Figure 11: A histology slide of the tumor highlighting the high nuclear features, loss of ductal architecture and increased mitotic figures (grade 3) (Hematoxylin & Eosin, x40)

**Figure 12**
Figure 12: MRI of the spine showing heterogeneous abnormal uptake of contrast medium at the bone marrow of vertebra L1 (arrow) which could represent a possibility of metastatic deposits

Post-operatively, the patient received 6 cycles of chemotherapy. After a year of follow-up she started to complain of severe back pain. MRI of the spine showed heterogeneous abnormal uptake of contrast medium at the bone marrow of vertebra L1 which could represent a possibility of metastatic deposits. The enhancement was extending slightly anteriorly but there was no posterior extension and no evidence of cord compression (figure 12).

The patient was last seen in the outpatient clinic 3 months ago (2 years after the initial diagnosis). Follow-up CT scan showed no signs of metastasis in chest, abdomen and pelvis.

**DISCUSSION**
Breast cancer is the second leading cause of cancer deaths in women today (after lung cancer) and is the most common cancer among women, excluding non-melanoma skin cancers. According to the American Cancer Society, about 1.3 million women will be diagnosed with breast cancer annually worldwide and about 465,000 will die from the disease.

The National Cancer Institute defines a fungating skin lesion as a type of skin lesion that is marked by ulcerations and necrosis and that usually has a bad smell. This kind of lesion may occur in many types of cancer, including breast cancer, melanoma, and squamous cell carcinoma, and especially in advanced disease.

Fungating breast cancer is considered as one of the entities of locally advanced breast cancer which remain a clinical challenge as the majority of patients with this diagnosis develop distant metastases despite appropriate therapy (1).

Locally advanced breast cancer constitutes approximately 10%-20% of the newly diagnosed breast cancers (2) and up to 75% of breast cancers in developing countries (3).

The true incidence of fungating breast cancer is difficult to estimate. There are numerous large prospective studies on patients with locally advanced breast cancer in the literature; however, little is reported on ulcerative breast cancer (4).

Fungating breast cancer, being an entity of locally advanced cancer, is presumably more common in developing countries than in developed countries. In developing countries, lack of public education and awareness, together with lack of screening programs especially in poor and politically unstable countries, are associated with delayed presentation of the disease. Unfortunately, many of these countries have no tumor registry and most of the data in cancer is collected from sporadic publications.

In searching the English literature for fungating breast cancer it was obvious that most of the studies including large numbers of patients are coming from developing countries.

In one study coming from Nigeria, Adesunkanmi et al., in their investigation of the challenges, severity, outcome and factors influencing the outcome of the management of breast cancer...
cancer in a Nigerian Teaching Hospital, found that the tumor was fungating in 83 out of 212 patients they studied (39%) (5). Another study from India included 30 patients of fungating breast cancer (6).

Diagnosis of fungating breast cancer is straightforward. Tissue diagnosis should be obtained in all cases and all patients should be screened for metastasis and involvement of the other breast. Estimation of tumor markers helps in predicting patient prognosis.

Management of patients with fungating breast cancer is difficult; disseminated cancer, physical deformity, foul odor, bleeding and infection, as well as associated psychosocial factors contribute to the complexity of caring for these patients (7).

The primary goals of the management of advanced breast cancer are to improve the length and quality of life. As the majority of patients with fungating breast cancer develop distant metastases despite appropriate therapy the disease may not be curable. Nevertheless, it is amenable to treatment, and this is an important distinction to make.

The main objective in treating patients with fungating breast cancer is to relieve the symptoms. Intolerable malodor emanating from ulcerated tumors is a serious problem in the management of advanced and recurrent breast cancer and probably the most distressing symptom for patients (8). It is caused by bacterial infection in devitalized tissue within the wound. The presence of a pervasive malodor can lead to embarrassment, disgust, depression and social isolation and may have a detrimental effect on sexual expression causing relationship problems (9, 10, 11 & 12).

Antibiotic therapy can be effective if it destroys the bacteria responsible for malodour (13, 14 & 15), the most common treatment being metronidazole. This may be given systemically, but side effects such as nausea, neuropathy and alcohol intolerance may affect patient acceptability (16). The topical use of metronidazole in a gel form was proved to improve the quality of life for patients with malodorous ulcerated tumors and to facilitate intensive treatment of the underlying disease (17).

Intra-arterial drug delivery may be appropriate in carefully selected cases of locally advanced, fungating breast cancers. The infusion of chemotherapy into arteries that feed locally advanced tumors, has theoretical appeal, since the tumor mass may be exposed to high drug concentrations with administration of reduced or conventional doses of chemotherapy.

Kumar et al. treated thirty cases of fungating breast cancer (stages III and IV) preoperatively by combination chemotherapy using cyclophosphamide (Endoxan), methotrexate, 5-fluorouracil, and prednisone. Mastectomy was performed after 2 cycles of preoperative chemotherapy followed by 6 more cycles postoperatively. They reported that, of 30 patients, 25 (83.3%) were made operable and had better disease-free survival (6).

Many studies from Japan revealed promising results of intra-arterial infusion chemotherapy in management of locally advanced breast cancer (18, 19 & 20).

Bufill et al. report a case of fungating breast cancer that was effectively palliated with intra-arterial administration of mitomycin, fluorouracil, cisplatin, and mitozantrone. The rapidity of the patient’s response using this approach supports the observations of other investigators. Experience in applying this technique to patients with breast cancer in the United States is limited and further study of intra-arterial chemotherapy in carefully selected patients with locally advanced and fungating breast cancers is warranted (21).

Stephens et al. report treating a patient with a huge fungating breast carcinoma which was bleeding and foul-smelling with intra-arterial infusion chemotherapy as basal treatment and with subsequent definitive radiotherapy. Local tumor regression was achieved and there was no evidence of residual carcinoma in the breast or axilla 12 months after treatment. They suggested that further investigation of this treatment seems worthwhile, since it may be effective not only in the management of large breast cancers but also in patients with less advanced disease who refuse mastectomy or wish to avoid it (22).

Surgery may be indicated for selected patients with locally advanced breast cancer, examples including patients who need mastectomies for fungating/painful breast lesions. As advanced carcinoma of the breast can make the last few months of life miserable, surgery can greatly assist in the amelioration of appearance, smell, and discharge from the ulcer (23).

The extent of surgery depends on the extent of the disease and the aim of surgery is to clear the breast and the axilla from the disease. This usually is achieved with a radical mastectomy.
Radiofrequency ablation for breast carcinoma is limited. Reports in the literature have focused on preoperative radiofrequency ablation followed by resection as feasibility studies (24, 25).

Vansonnenberg et al. reported palliative radiofrequency ablation of a case of fungating breast cancer (that failed to respond to chemotherapy) because of local discomfort, frequent bleeding, and oozing from the large, fungating tumor. Although this is a single case, and only palliation was achieved rather than cure, the patient’s and family’s satisfaction, the amelioration of symptoms and signs, and the lack of complications in this patient encourage further exploration of the use of radiofrequency for problematic breast cancer (26).

References
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