

Received: 2019.01.26
Accepted: 2019.02.13
Published: 2019.04.17

A Case of Locally Advanced Breast Cancer in a 59-Year-Old Man Requiring a Modified Approach to Management

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

ABCDEF 1 **Mohammed Yousef Aldossary**
BC 2 **Fatimah Alquraish**
ADEF 1 **Jamila Alazhri**

1 Department of General Surgery, Surgical Oncology Unit, King Fahad Specialist Hospital, Dammam, Saudi Arabia
2 Department of General Surgery, King Abdulaziz Air Base Hospital, Dhahran, Saudi Arabia

Corresponding Author: Mohammed Yousef Aldossary, e-mail: Dr.Mohd.Aldossary@gmail.com
Conflict of interest: None declared

Patient: Male, 59
Final Diagnosis: Invasive ductal carcinoma
Symptoms: Foul-smelling discharge • painful breast mass
Medication: —
Clinical Procedure: Modified radical mastectomy
Specialty: Surgery

Objective: Rare disease

Background: Male breast cancer is rare, accounting for approximately 1% of all malignancies in men. The lack of awareness of this rare cancer results in delayed diagnosis and its aggressive behavior can result in poor prognosis. This report is of a case of locally advanced, high-grade breast cancer in a 59-year-old man who was reluctant to undergo diagnostic procedures, and describes the approach to clinical management.

Case Report: A 59-year-old man presented with a large left breast mass with enlarged axillary lymph nodes. The patient had ignored the mass and declined all diagnostic procedures. After modifying the diagnostic workup and involving a psychiatrist, the patient agreed to undergo a modified radical mastectomy. Histopathology showed a high-grade invasive ductal carcinoma with lymph node metastasis. The breast cancer was triple-positive for human epidermal growth factor receptor 2 (HER2), estrogen receptor (ER), and progesterone receptor (PR). Adjuvant treatment included herceptin, tamoxifen, and radiation therapy.

Conclusions: This case demonstrates the importance of raising public awareness of breast cancer in men, and to assess and overcome the factors leading to delay in accessing medical attention. In challenging cases, modifying the diagnostic workup and the treatment approach with the least deviation from the standard of care, including counseling may be required.

MeSH Keywords: Anxiety • Breast Neoplasms, Male • Carcinoma, Ductal, Breast • Genes, erbB-2 • Mastectomy

Full-text PDF: <https://www.amjcaserep.com/abstract/index/idArt/915377>

2162 — 4 45



Background

Worldwide, male breast cancer is extremely rare, accounting for <1% of all breast tumors and <1% of all malignancies in men [1–3]. Recently, the incidence of male breast cancer has increased from 1.0 per 100,000 men in the late 1970s to 1.2 per 100,000 men from 2000 to 2004 [4–7]. The American Cancer Society reported a similar trend in the incidence of breast cancer in men from 1975–1979 to 2010–2014 [7,8]. However, the prevalence of male breast cancer differs between countries, with Tanzania and areas of Central Africa reporting >6% of all breast cancers in men [9]. More than 40% of men with breast cancer present with advanced disease (stage III or IV) [10], resulting in a delay in diagnosis and treatment [11–14]. Assessing the factors that lead to delay in seeking medical attention is crucial to avoid delays in consultation and diagnosis and to prevent metastasis. The anatomy of the breast differs between men and women and because male breast cancer is so rare, the clinical guidelines for the diagnosis and treatment of breast cancer in men are based on those for women [1].

The clinical presentation of breast cancer in men varies from occult cancer with palpable axillary nodes to visible breast lumps with changes in the overlying skin [15,16]. Histologically, all breast types of breast cancer can occur in men, with invasive ductal carcinoma not otherwise specified (or ductal carcinoma NOS) being the most common [10]. The prevalence of psychological distress among patients with breast cancer is high, leading to a higher risk of depression, mood disorders, and anxiety [17–19]. Therefore, counseling is an important component of patient management before and after treatment. Treatment for locally advanced breast cancer includes neoadjuvant systemic therapy followed by surgery [20]. This treatment approach is indicated in breast cancer that is triple-negative, or for human epidermal growth factor receptor 2 (HER2)-positive breast cancer [21,22].

This report is of a case of locally advanced breast cancer in a 59-year-old man who was reluctant to undergo diagnostic procedures and describes the approach to clinical management.

Case Report

History

A 59-year-old man presented to the surgical clinic with discharge from a left breast mass. The mass had been increasing in size for more than one year. The patient described several attempts at cauterizing the left breast, without benefit. The patient did not seek medical care until he was in pain and developed foul-smelling discharge from the tumor. His only significant medical history was poorly controlled diabetes mellitus.



Figure 1. Preoperative photograph of the left breast of a 59-year-old man. An ulcerating large left breast mass is shown with distortion of the left nipple but with no discharge.

The patient had received an elementary school education. He denied any history of psychiatric illness, the use of anabolic steroids, drug abuse, or alcohol consumption. He reported smoking about two packs of cigarettes each day for 30 years. There was no history of exposure to ionizing radiation or trauma. He had no family history of malignancy.

Clinical findings

The patient appeared to be generally well with a normal distribution of male body hair, no gynecomastia, and body mass index (BMI) of 36.9 kg/m². Physical examination of the left breast and axilla showed a hard, erythematous, ulcerating, mass measuring approximately 9x5 cm in the subareolar region (Figure 1). His left nipple was distorted by the mass with no discharge (Figure 1). His body temperature was normal. Examination of the ipsilateral axilla showed an enlarged mobile lymph node. The right breast and axilla were normal on examination.

Laboratory investigations

Liver function tests showed the following results: albumin, 28 g/L; total protein, 48 g/L; alanine aminotransferase (ALT), 38 units/L; aspartate transaminase (AST), 42 units/L; alkaline phosphatase (ALP), 87 IU; total bilirubin, 5.9 μmol/L; conjugated bilirubin, 2.3 μmol/L; amylase, 56 units/L; and lipase, 37 units/L. All results were within their respective normal range. Tumor markers were also within the normal range: cancer antigen 19-9, 7 IU/mL; cancer antigen 15-3, 14.7 U/mL; prostate-specific antigen (PSA), 1.9 ng/mL; and carcinoembryonic antigen (CEA), 2.2 ng/mL. Other laboratory results were also unremarkable.

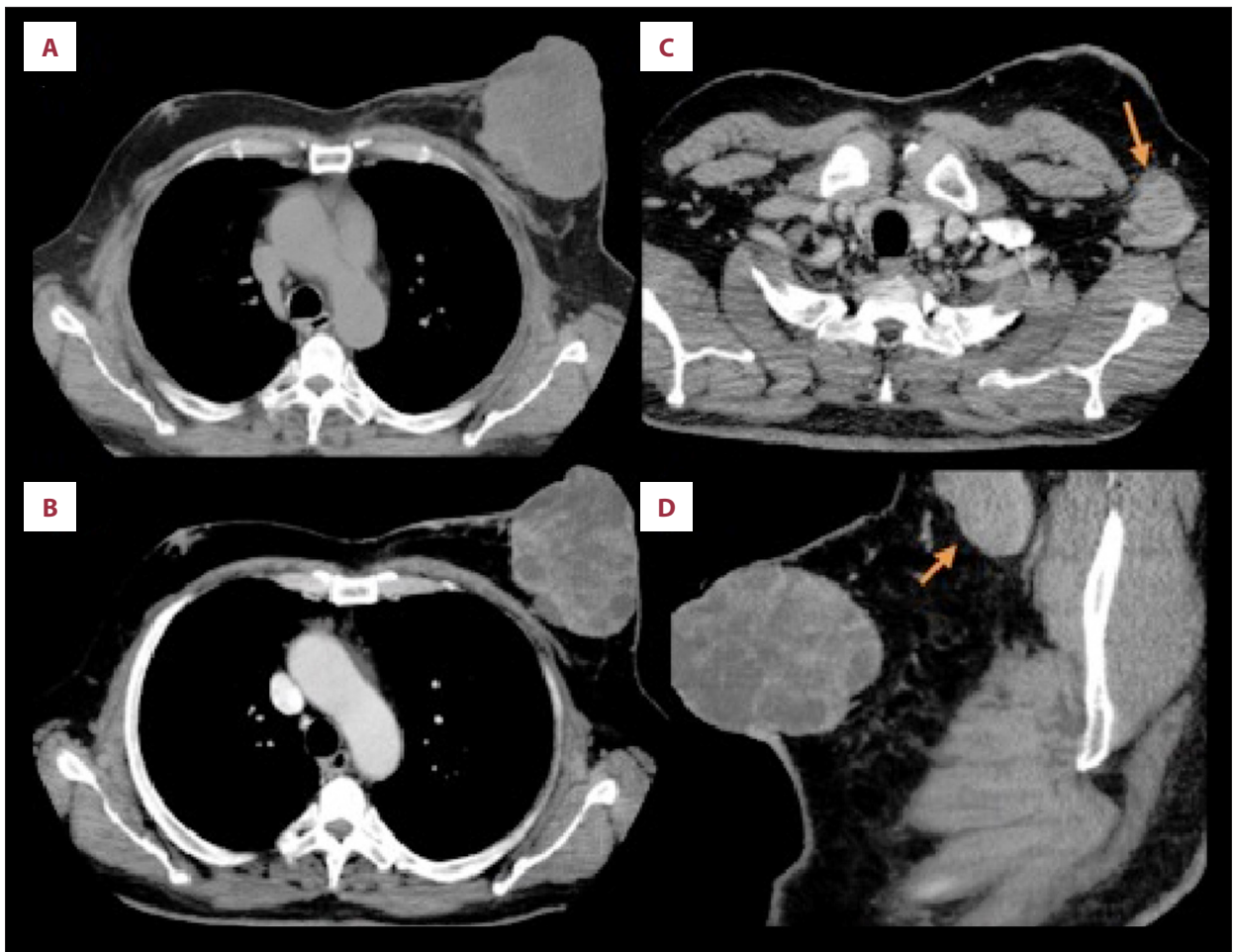


Figure 2. Computed tomography (CT) imaging of the left breast and axilla (A) Axial non-enhanced computed tomography (CT) imaging. (B) Axial enhanced computed tomography (CT) imaging shows a heterogeneous and necrotic exophytic mass in the left breast associated with thickening of the skin with a preserved fat plane between the mass and underlying pectoralis muscle. (C) Axial and (D) sagittal views show an enlarged ipsilateral axillary lymph node (arrows).

The patient refused core-needle biopsy or fine-needle aspiration cytology despite counseling regarding the importance of histopathological diagnosis and its impact on his treatment options, because of his fear of pain from these procedures.

Imaging

Ultrasound examination of the breast and mammography were not feasible due to pain and discomfort in the left breast. The patient refused these imaging studies despite being prescribed strong pain medication. The patient did not comply with the recommendation for diagnostic workup for metastases in the form of computed tomography (CT) of the chest, abdomen, and pelvis, and a bone scan.

A psychiatric consultation was requested. The patient was diagnosed with an anxiety disorder. His major concern came from his belief that the biopsies or any contact with the breast mass

during mammography or ultrasound examination might result in the spread of the disease and worsen his condition. He was treated with oral alprazolam 0.5 mg every six hours to relieve his anxiety. Also, counseling and psychotherapy were provided. Eventually, the patient agreed only to undergo imaging without any contact between the equipment and his breast lesion. Computed tomography (CT) of the chest, abdomen, and pelvis showed a heterogeneous necrotic exophytic mass in the left breast associated with thickening of the skin. CT also showed an enhancing ipsilateral axillary lymph node with cortical thickening (Figure 2A–2D) and no distant metastases were identified. A bone scan did not identify bone metastases.

Treatment

Although there was no preoperative diagnostic histopathology, the clinical presentation and the findings on CT scans were considered diagnostic for locally advanced breast cancer with

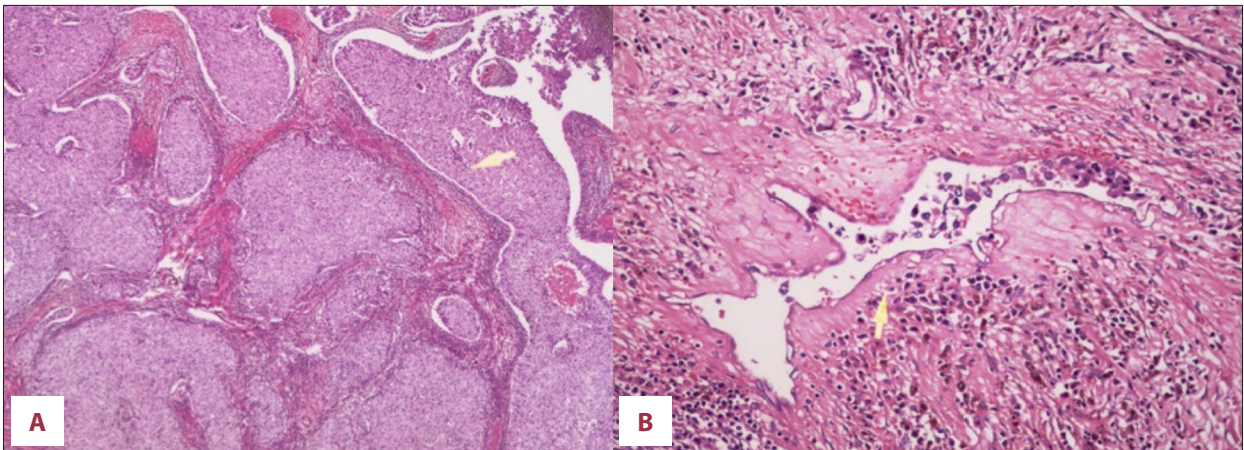


Figure 3. Photomicrographs of the histopathology of the ductal carcinoma of the breast. (A) Histopathology shows a high-grade (grade 3) invasive ductal carcinoma. Hematoxylin and eosin (H&E). Magnification, $\times 10$. (B) Histopathology shows intravascular emboli. Hematoxylin and eosin (H&E). Magnification, $\times 20$.

metastasis to ipsilateral axillary lymph node. However, the lack of histological type, grade, and receptor status, precluded neoadjuvant chemotherapy as a treatment option and the patient was offered mastectomy. Axillary dissection was proposed as the treatment for axillary metastasis. The patient underwent a modified radical mastectomy. Intraoperatively, the mass was not found to be attached to the pectoralis major muscle. Level I and II axillary dissection was performed, the wound was closed primarily without the need for a skin graft.

Postoperative histopathology

The histopathology of the surgical resection specimen of the breast showed invasive ductal carcinoma with dermal deposits and lymphovascular invasion. The tumor was grade 3, measuring 8×8×6 cm. All surgical resection margins were free from tumor. Dissection of the axillary lymph nodes showed metastatic deposits in one of 19 lymph nodes (Figure 3A, 3B). Biomarker analysis using immunohistochemistry showed strong estrogen receptor (ER) positivity (70%), progesterone receptor (PR) positivity (50%), and HER2 positivity (3+) (Figure 4). The breast cancer was stage IIIB (pT4b, N1, M0).

Adjuvant treatment

The patient was referred to the medical oncologist and radiation oncologist for adjuvant treatment. Postoperative treatment with herceptin and pertuzumab was planned followed by adjuvant radiation therapy to the chest wall and axilla, and adjuvant tamoxifen for at least five years. The patient was also referred to a genetic counselor for BRCA gene mutation testing.

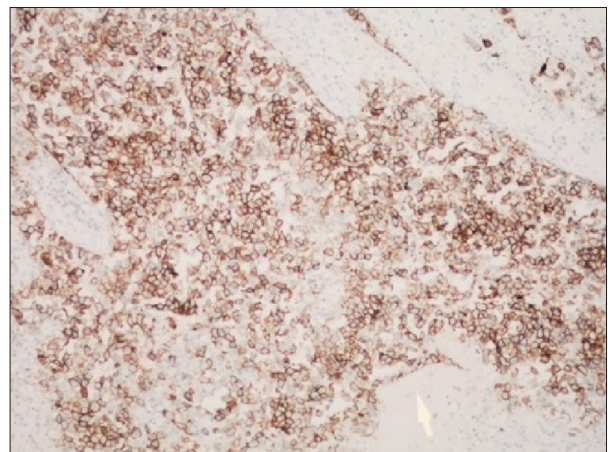


Figure 4. Photomicrograph of the immunohistochemical staining of the ductal carcinoma of the breast for human epidermal growth factor receptor 2 (HER2). Immunohistochemistry shows strong HER2 positivity (3+) of the breast carcinoma cells (brown). Magnification, $\times 10$.

Discussion

The American Cancer Society reported that the incidence of breast cancer in men increased from 1 per 100,000 men in 1975–1979 to 1.3 per 100,000 in 2010–2014 [7,8]. The number of new cases in the US was estimated to reach 2,550 in 2018, with patient mortality of 480 cases [7,8]. The mean age at diagnosis is 60–70 years [16,23], and the pattern of breast cancer in this age range tends to be similar to that in postmenopausal women [1,16,23]. However, cases have been reported in men as young as 10 years old [24]. While the risk factors for breast cancer in women are well-described, the risk factors for male breast cancer remain poorly understood due to its low incidence. However, Klinefelter's syndrome is a possible risk

factor for breast cancer in men, and other risk factors are similar to those for women, including acromegaly and neurofibromatosis [15]. In areas with a higher incidence of male breast cancer, including Central Africa and Eastern Africa, the etiology has been linked to hyperestrogenism resulting from endemic hepatic infection [25]. Supporting studies have confirmed that the combination of estrogen and progesterone is associated with an increased risk of breast cancer in postmenopausal women [26,27]. Breast cancer has also been reported in male to female transsexuals who use high doses of estrogen [28].

The delay in seeking medical attention will lead result in men presenting with advanced breast cancer. Al-Kahiry et al. [11] reported that 67% of their cohort of men with breast cancer presented with advanced disease. Clegg-Lamptey et al. reported that 57.6% of men presented with advanced stage breast cancer [29]. Bourhafour et al. [30] reported that 50.3% of male patients with breast cancer presented with stage III disease and 29% with stage IV breast cancer. Due to his late presentation, the patient in this report presented with stage IIIB locally advanced breast cancer that had already metastasized to the axillary lymph nodes. There are several factors that may lead to a delay in presentation, including lack of awareness about breast cancer, distance to the hospital, ignorance, fear of the consequences, a strong belief in traditional treatments, low educational level, ignorance, and poverty [13,31–35]. This patient had three factors that contributed to his late presentation, a strong belief in the benefits of traditional therapy, an elementary level of education, and being unaware of the condition.

The most common psychiatric co-morbidities in breast cancer patients are anxiety and depression [36,37]. Patients with breast cancer may experience anxiety and/or depression at any stage of the disease. Dastan and Buzlu [38] reported that 35% of female patients with breast cancer experienced anxiety. In this case, the support that the patient received from the psychiatrist, following his presentation to the hospital, encouraged him to cooperate to some extent with the clinical team. However, due to the late presentation, and the concern for disease progression, his psychotherapy session was brief.

The standard of care for the evaluation of patients with breast carcinoma is mammogram and ultrasound of the breast and axilla [20]. The strong misbelief that the patient had about the possibility of the spread of breast cancer from biopsy or contact with any equipment, initially prevented the standard diagnostic approach. However, due to the advanced tumor stage and the presence of a large ulcerating breast tumor and an enlarged ipsilateral axillary lymph node, and in addition to the clear requirement for mastectomy, mammography and ultrasound were not performed and computed tomography (CT) imaging was used, which showed the extent of the breast cancer and involvement of the axilla.

Invasive ductal carcinoma is the most common type of breast cancer in men [10]. Because the male breast is usually small, local and occult invasion by cancer cells tend to involve the pectoralis major. Mastectomy and radiotherapy is the recommended combined approach to achieve a complete tumor resection [39]. This patient did not have involvement of the pectoralis muscle on CT scan or by intra-operative clinical assessment. Histological assessment of the mastectomy specimen also showed negative deep margins.

Systemic treatment for breast cancer is determined by the hormonal and biological status of the tumor. A study by Avisar et al. [40] showed that 56% of cases of male breast cancer showed overexpression of HER2 [40]. This patient had a HER2-positive invasive ductal carcinoma of the breast (3+). In HER2-positive breast cancer, the standard of care is to start with herceptin-based neoadjuvant chemotherapy, which is associated with a 40% increase in the rate of pathological complete response [41]. Studies have shown that the inhibition of HER2 using the combination of herceptin and pertuzumab in the neoadjuvant setting can increase the complete response rate by 60% [42–44]. The longterm benefit of this treatment approach in terms of improved overall survival has also been shown [45]. However, this patient refused a preoperative diagnostic biopsy and it was not possible to identify the histological type of the tumor or the receptor status prior to surgery. Therefore, the treatment approach was changed for this patient and he was offered first-line surgical treatment followed by HER2-based chemotherapy in the adjuvant setting.

Conclusions

Male breast cancer is a rare but challenging malignancy for the clinician to manage, due to lack of patient awareness and the increased presentation at an advanced stage. Increasing public awareness of male breast cancer is essential to avoid the delay in clinical consultation, prevent axillary and distant metastases, and ensure diagnosis at a treatable stage. Assessing and modifying the factors that lead to a delay in seeking medical attention is crucial to improving patient prognosis. It is important for the treating physician to recognize the advantage of obtaining psychiatrist assistance as early as possible in the clinical management of patients with denial or who have misunderstandings of the condition, which may affect their ability to make decisions. In challenging scenarios, it is important for the treatment plan to be flexible to overcome difficult circumstances. As this case has shown, the diagnostic workup and the treatment approach can be safely modified with the least possible deviation from the standard of care guidelines to obtain the best outcome for the patient.

References:

1. Korde LA, Zujewski JA, Kamin L et al: Multidisciplinary meeting on male breast cancer: Summary and research recommendations. *J Clin Oncol*, 2010; 28: 2114–22
2. Speirs V, Shaaban AM: The rising incidence of male breast cancer. *Breast Cancer Res Treat*, 2009; 115: 429–30
3. Yoney A, Kucuk A, Unsal M: Male breast cancer: A retrospective analysis. *Cancer Radiother*, 2009; 13: 103–7
4. Anderson WF, Jatoi I, Tse J, Rosenberg PS: Male breast cancer: A population based comparison with female breast cancer. *J Clin Oncol*, 2010; 28: 232–39
5. Anderson WF, Althuis MD, Brinton LA, Devesa SS: Is male breast cancer similar or different than female breast cancer? *Breast Cancer Res Treat*, 2004; 83: 77–86
6. Hill TD, Khamis HJ, Tyczynski JE, Berkel HJ: Comparison of male and female breast cancer incidence trends, tumor characteristics, and survival. *Ann Epidemiol*, 2005; 15: 773–80
7. Stang A, Thomssen C: Decline in breast cancer incidence in the United States: What about male breast cancer? *Breast Cancer Res Treat*, 2008; 112: 595–96
8. American Cancer Society. *Breast Cancer Facts & Figures 2017–2018*. Atlanta: American Cancer Society, Inc. 2017. Available at: <https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/breast-cancer-facts-and-figures/breast-cancer-facts-and-figures-2017-2018.pdf>
9. Sasco AJ, Lowenfels AB, Pasker-de Jong P: Review article: Epidemiology of male breast cancer. A meta-analysis of published case-control studies and discussion of selected aetiological factors. *Int J Cancer*, 1993; 53: 538–49
10. Fentiman IS, Fourquet A, Hortobagyi GN: Male breast cancer. *Lancet*, 2006; 367: 595–604
11. Al-Kahiry W, Omer HH, Saeed NM, Hamid GA: Late presentation of breast cancer in Aden, Yemen. *Gulf J Oncolog*, 2011; 9: 7–11
12. Richards MA, Westcombe AM, Love SB et al: Influence of delay on survival in patients with breast cancer: A systematic review. *Lancet*, 1999; 353: 1119–25
13. Espina C, McKenzie F, Dos-Santos-Silva I: Delayed presentation and diagnosis of breast cancer in African women: a systematic review. *Ann Epidemiol*, 2017; 27: 659–71.e7
14. Joshi MG, Lee AK, Loda M et al: Male breast carcinoma: An evaluation of prognostic factors contributing to a poorer outcome. *Cancer*, 1996; 77: 490–98
15. Xu R, Li J, Zhang Y et al: Male occult breast cancer with axillary lymph node metastasis as the first manifestation: A case report and literature review. *Medicine (Baltimore)*, 2017; 96: e9312
16. PDQ Adult Treatment Editorial Board. *Male Breast Cancer Treatment (PDQ®): Health Professional Version*. 2002 (online). Available at: <https://www.ncbi.nlm.nih.gov/books/NBK65792/>
17. Mehnert A, Koch U: Psychological comorbidity and health-related quality of life and its association with awareness, utilization, and need for psychosocial support in a cancer register-based sample of long-term breast cancer survivors. *J Psychosom Res*, 2008; 64: 383–91
18. Deshields D, Tibbs T, Fan MY, Taylor M: Differences in patterns of depression after treatment for breast cancer. *Psychooncology*, 2006; 15: 398–406
19. Burgess C, Cornelius V, Love S et al: Depression and anxiety in women with early breast cancer: five year observational cohort study. *BMJ*, 2005; 330: 702
20. Gradishar W, Salerno KE: NCCN guidelines update: Breast cancer. *J Natl Compr Canc Netw*, 2016; 14(5 Suppl): 641–44
21. Wahba HA, El-Hadaad HA: Current approaches in treatment of triple-negative breast cancer. *Cancer Biol Med*, 2015; 12: 106–16
22. Callahan R, Hurvitz S: Human epidermal growth factor receptor-2-positive breast cancer: Current management of early, advanced, and recurrent disease. *Curr Opin Obstet Gynecol*, 2011; 23: 37–43
23. Abdelwahab Yusef AJ: Male breast cancer: Epidemiology and risk factors. *Semin Oncol*, 2017; 44(4): 267–72
24. Giordano SH, Cohen DS, Buzdar AU et al: Breast carcinoma in men: A population-based study. *Cancer*, 2004; 101: 51–57
25. Rudlowski C: Male breast cancer. *Breast Care (Basel)*, 2008; 3: 183–89
26. Schairer C, Lubin J, Troisi R et al: Menopausal estrogen and estrogen-progestin replacement therapy and breast cancer risk. *JAMA*, 2000; 283: 485–91
27. Ross RK, Paganini-Hill A, Wan PC, Pike MC: Effect of hormone replacement therapy on breast cancer risk: Estrogen versus estrogen plus progestin. *J Natl Cancer Inst*, 2000; 92: 328–32
28. Maglione KD, Margolies L, Jaffer S et al: Breast cancer in male-to-female transsexuals: Use of breast imaging for detection. *Am J Roentgenol*, 2014; 203: W735–40
29. Clegg-Lampsey J, Hodasi W: A study of breast cancer in Korle Bu Teaching Hospital: Assessing the impact of health education. *Ghana Med J*, 2007; 41: 72–77
30. Bourhafour M, Belbaraka R, Souadka A et al: Male breast cancer: A report of 127 cases at a Moroccan institution. *BMC Res Notes*, 2011; 4: 219
31. Benbakhta B, Tazi M, Benjaafar N et al: Determinants of patient and health system delays for women with breast cancer in Morocco, 2013. *Rev Epidemiol Sante Publique*, 2015; 63: 191–201
32. Clegg-Lampsey J, Dakubo J, Attobra YN: Why do breast cancer patients report late or abscond during treatment in Ghana? A pilot study. *Ghana Med J*, 2009; 43: 127–31
33. Ahmed AA: Clinicopathological profile of female Sudanese patients with locally advanced breast cancer. *Breast Dis*, 2014; 34: 131–34
34. Aloulou S, El Mahfoudi A, El Omrani A, Khouchani M: [Factors related to late diagnosis of breast cancer: Experience of CHU Mohammed VI Marrakech.] *Pan Afr Med J*, 2015; 21: 162 [in French].
35. Pace LE, Mpunga T, Hategekimana V et al: Delays in breast cancer presentation and diagnosis at two rural cancer referral centers in Rwanda. *Oncologist*, 2015; 20: 780–88
36. Baumeister H, Kriston L, Bengel J, Härter M: High agreement of self-report and physician-diagnosed somatic conditions yields limited bias in examining mental-physical comorbidity. *J Clin Epidemiol*, 2010; 63: 558–65
37. Härter M, Reuter K, Aschenbrenner A et al: Psychiatric disorders and associated factors in cancer: Results of an interview study with patients in inpatient, rehabilitation and outpatient treatment. *Eur J Cancer*, 2001; 37: 1385–93
38. Dastan NB, Buzlu S: Depression and anxiety levels in early stage Turkish breast cancer patients and related factors. *Asian Pacific J Cancer Prev*, 2011; 12: 137–41
39. Patten DK, Sharifi LK, Fazel M: New approaches in the management of male breast cancer. *Clin Breast Cancer*, 2013; 13: 309–14
40. Avisar E, McParland E, Dicostanzo D, Axelrod D: Prognostic factors in node-negative male breast cancer. *Clin Breast Cancer*, 2006; 7: 331–35
41. Buzdar AU, Ibrahim NK, Francis D et al: Significantly higher pathologic complete remission rate after neoadjuvant therapy with trastuzumab, paclitaxel, and epirubicin chemotherapy: Results of a randomized trial in human epidermal growth factor receptor 2-positive operable breast cancer. *J Clin Oncol*, 2005; 23: 3676–85
42. Gianni L, Pienkowski T, Im YH et al: Efficacy and safety of neoadjuvant pertuzumab and trastuzumab in women with locally advanced, inflammatory, or early HER2-positive breast cancer (NeoSphere): A randomised multicentre, open-label, phase 2 trial. *Lancet Oncol*, 2012; 13: 25–32
43. Gianni L, Eiermann W, Semiglazov V et al: Neoadjuvant and adjuvant trastuzumab in patients with HER2-positive locally advanced breast cancer (NOAH): Follow-up of a randomised controlled superiority trial with a parallel HER2-negative cohort. *Lancet Oncol*, 2014; 15: 640–47
44. Untch M, Fasching PA, Konecny GE et al: Pathologic complete response after neoadjuvant chemotherapy plus trastuzumab predicts favorable survival in human epidermal growth factor receptor 2-overexpressing breast cancer: Results from the TECHNO trial of the AGO and GBG study groups. *J Clin Oncol*, 2011; 29: 3351–57
45. Rastogi P, Anderson SJ, Bear HD et al: Preoperative chemotherapy: Updates of National Surgical Adjuvant Breast and Bowel Project Protocols B-18 and B-27. *J Clin Oncol*, 2008; 26: 778–85