

Tuberculosis in 7 Breast Cancer Cases: Diagnostic and Therapeutic Challenges

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Abstract

Objective: To review the challenges in treating patients with breast cancer and history of or co-existing tuberculosis [TB].

Method: A review of the data base of the breast unit at King Fahd General Hospital performed from 1998 till end of July, 2012. Records of all breast cancer patients seen in that period [221 patients] were reviewed for clinical, radiologic, pathologic data and disease outcome.

Results: In the study period, there were 7 cases with concurrent or past history of tuberculosis. Two cases had concurrent tuberculosis of axillary lymph nodes, one had contralateral calcified tuberculous axillary lymph nodes that were radiologically suspicious for malignancy and the other one had ipsi-lateral tuberculous axillary lymph nodes discovered during axillary dissection. Both were reluctant to receive the lengthy anti-tuberculous treatment for an asymptomatic disease. Three cases had past history of pulmonary tuberculosis, 2 of them presented with multiple lung nodules that were radiologically indistinguishable [whether tuberculous or metastatic nodules] and eventually they died of lung metastases. They had no radiologic evidence of skeletal or other metastatic sites. One case had past history of treated synovial [knee] and cerebral tuberculosis presented with lung metastases. She also had a thigh lesion that was suspicious for tuberculosis but proved histologically to be metastatic in nature. The last case had a past history of treated ovarian tuberculosis; she had multiple calcified pelvic nodules on computerized tomography. The last 2 cases received chemotherapy with no evidence of reactivation of tuberculosis.

Conclusion: The presence of tuberculosis with breast cancer cause clinical and radiologic diagnostic difficulties and requires extra invasive diagnostic procedures for differentiation. Fear of tuberculosis reactivation with chemotherapy may force clinicians to prescribe prophylactic anti tuberculous treatment unnecessarily. A well planned management with psycho-social support is mandatory to maximize patient compliance.

Keywords: Tuberculosis; Breast cancer; Cancer misdiagnosis; Metastases

Introduction

Tuberculosis [TB] is a worldwide major health problem. The world health organization [WHO] reported an estimated 8.8 million new cases of TB in 2010 [1]. In Saudi Arabia, the number of newly discovered cases of TB was 3,949 and 4,294 for years 2009 and 2010 respectively with an incidence rate of 15 cases per 100,000 population [2].

Breast cancer is the commonest female malignancy. In Saudi Arabia, it comprises 21% of female cancers of all ages [3].

The coexistence of TB and cancer has been described in many literatures. Malnutrition, deterioration of immunity resulting from local or systemic effects of cancer, and the administration of chemotherapy or radiotherapy are all likely to have a role in TB infection or re-activation [4,5].

We are presenting 7 cases of breast cancer that had concurrent or past history of TB to discuss the challenges faced during management of these cases.

Material and Method

A review of the data base of the breast unit at King Fahd General Hospital performed from 1998 till end of July, 2012. There were 221 documented cases of female breast cancer in that period; out of these 7 cases had past history or concurrently discovered to have tuberculosis. These patient's records were reviewed for clinical, radiologic and pathologic data.

Results

There were 221 documented cases of female breast cancer in the study period; out of them 7 cases had concurrent or past history of tuberculosis. In Table 1 we summarized the clinical presentation as well as the outcome of breast cancer and tuberculosis in these 7 cases.

All of them were Saudis; age range was 40- 75 years [average 55.7]. Two cases [No. 1 & 3] were diabetic, hypertensive and were previously treated from malignancy [colon and uterus respectively]. Breast cancer treatment was tailored for each case according to age, stage of disease and hormonal receptors status.

The first two cases were discovered to have concurrent tuberculous axillary lymph nodes involvement at the time of breast cancer surgery. They had no previous exposure or contact with tuberculous patients. One of them [Case No. 1] had enlarged contralateral axillary lymph nodes with microcalcifications seen on mammogram that were suspicious for malignancy (Figures 1A and 1B). The possibility of a

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Case Number	Age (Years)	Breast Cancer			Tuberculosis (TB)				
		Stage	Year of Diagnosis	Pathology	Site	Year of Diagnosis	Tissue Diagnosis	Treatment†	Contact
1	75	Stage III	2011	IDC, grade II	Concurrent, (Contralateral) Axillary Lymph Nodes	2011	Axillary Lymph Node Excision	Nil	Alive/Free 1.5 Year
2	55	Stage III	2012	IDC, grade II	Concurrent (Ipsi-lateral) Axillary Lymph Nodes	2012	Axillary Lymph Node Dissection	Nil	Alive/Free 6 months
3	72	Stage II	2005	IDC, grade III	Pulmonary	1972	Not available	Completely treated	Alive/Free 7 Years
4	51	Stage IV (multiple right lung nodules)	2004	IDC, grade II	Pulmonary	Unknown	Not available	Inadequate treatment	Death of Cancer
5	40	Stage IV (multiple bilateral lung nodules)	2003	Adenoid Cystic Carcinoma	Pulmonary	1993	Not available	Inadequate treatment (persistent cough)	Death of Cancer
6	43	Stage IV (multiple right lung nodules)*	2011	Metaplastic carcinoma (Spindle cell type)	Right Knee Cerebral Left Thigh	2007	Arthroscopy with Synovial Tissue Biopsy	Completely treated	Death of Cancer
7	54	Stage II	2002	IDC, grade II	Right Ovary	1982	Oophorectomy	Completely treated	Alive/ Free 10 Years

IDC: Invasive ductal Carcinoma.

*Metastases in abdominal lymph nodes also were found by CT scan.

†TB treatment history was obtained from the patient and/or her relatives.

Table 1: Breast Cancer Cases, their state of tuberculosis and outcome.

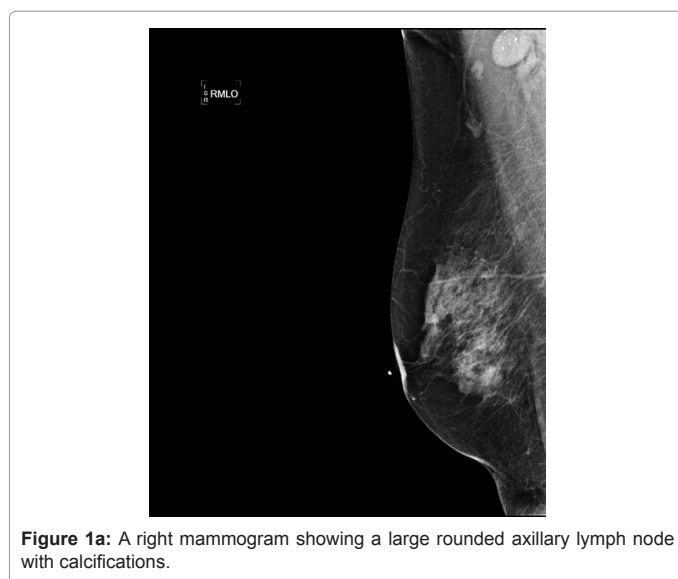


Figure 1a: A right mammogram showing a large rounded axillary lymph node with calcifications.

contralateral breast cancer was excluded by a breast magnetic resonant imaging [MRI]. Ultrasound guided fine needle aspiration of the calcified axillary lymph node was insufficient for diagnosis. Both cases were stage III breast cancer and were offered modified radical mastectomy. Case No. 1 underwent contralateral axillary lymph node excision biopsy as well and final histopathology showed calcified tuberculous lymph nodes (Figure 2). Case No. 2 had ipsilateral tuberculous axillary lymph nodes that were different than the malignant ones. There was no evidence of mammary TB in both cases. They received hormonal treatment for breast cancer. They were reluctant to receive anti TB treatment since they were asymptomatic and the treatment is lengthy.

Five cases had past history of TB; 3 were pulmonary [Cases No. 3, 4 and 5] and 2 were extra-pulmonary TB [Cases No. 6 and 7]. The details of TB diagnosis and treatment were obtained from the patients and their relatives; medical documentation was not available since they

were treated in other centers. Case No. 3 had past history of treated pulmonary TB; she received chemotherapy and she is alive for 7 years with no clinical or radiologic evidence of any disease. Cases No. 4 and 5 had past history of inadequately treated pulmonary TB. They presented with dyspnea and cough and computerized tomography [CT] scan of the chest showed multiple pulmonary nodules that were highly suspicious for metastases however tuberculous lesions were not totally excluded. Both cases had no radiologic evidence of skeletal or other visceral metastases. They were started on chemotherapy but unfortunately they died of breast cancer with lung metastasis at a relatively young age [40 and 51 years].

Case No. 6 presented with metaplastic carcinoma of the breast associated with lung nodules and intra-abdominal lymph nodes that were suggestive of metastases (Figure 3). She had history of treated synovial [knee] and cerebral TB. She also had a thigh lesion that was suspicious for tuberculosis but proved histologically to be metastatic in nature (Figure 4). Case No. 7 had history of treated ovarian TB [Oophorectomy and anti TB medications]. CT scan showed multiple calcified pelvic nodules that could be related to the previous TB. The last 2 cases received chemotherapy for breast cancer with no evidence of reactivation of TB.

Discussion

TB and breast cancer presenting simultaneously or one after the other creates clinical and radiologic diagnostic difficulties as well as therapeutic challenges.

Kaplan et al reported 201 cancer patients with concomitant TB. They found that TB was most prevalent in patients with Hodgkin's disease, lung cancer, lympho-sarcoma, and reticulum cell sarcoma, whereas it was least prevalent in patients with carcinoma of the colon, bladder, uterus, breast, prostate, and kidney [6]. Tubercle bacillus can exist in a state of microbial persistence within the macrophage of the granulomas for the lifetime of the individual and leave the host with persistent immunity in the form of cell-mediated tuberculin sensitivity. Factors that disturb host immunity can allow the tubercle



Figure 1b: A left mammogram showing a stellate lesion in the retro-areolar area with skin involvement and nipple retraction.

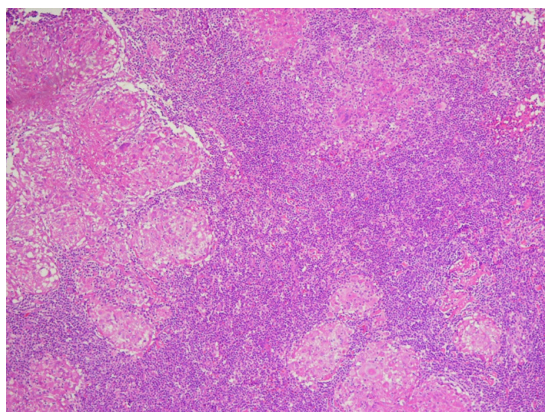


Figure 2: A lymph node containing multiple well defined granulomas with central caseation containing giant cell (Haematoxylin and Eosin stain, 10 x).



Figure 3: A CT scan showing multiple lung nodules consistent with metastases.

bacillus to cause endogenous reinfection [7,8]. Breast cancer patients may suffer reactivation of their TB during their treatment. Not only this will disturb the treatment protocol but the clinical and radiologic findings will also confuse the follow up process since a malignant and a tuberculous lesion may be indistinguishable.

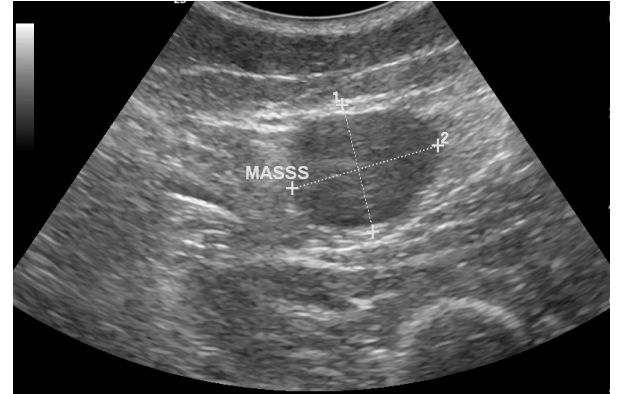


Figure 4: A thigh ultrasound showing a hypo-echoic well defined lesion that was suspicious for TB but proved histologically to be metastasis from the primary breast metastatic carcinoma.

The commonest site of tuberculous lymph node involvement is the cervical nodes. Other frequent sites include supraclavicular, inguinal and mediastinal nodes; axillary lymph node TB is not common [9,10]. In the literature, there were many reports of breast cancer cases with coexisting TB and metastases in axillary lymph nodes [9-14]. Case No. 1 had a locally advanced left breast cancer and right enlarged calcified axillary lymph nodes seen on mammogram and raised the possibility of a contralateral breast cancer. Breast MRI was required to exclude the presence of another primary cancer in the right breast. She underwent left modified radical mastectomy and at the same time right axillary lymph node excision biopsy that confirmed the tuberculous process. The patient required extra radiologic and interventional procedures in order to properly stage her cancer. Case No. 2 had locally advanced right breast cancer for which she underwent modified radical mastectomy and final pathology showed 2 malignant and 7 tuberculous axillary lymph nodes. Both cases had no evidence of mammary TB or other sites of lymph node involvement and had no prior history or exposure to TB. Lymph node TB should be suspected when lymph node swelling is noted and x-ray shows clustered calcifications in axillary lymph nodes [9]. In spite of that, malignant and inflammatory lymph nodes cannot often be definitely distinguished based on mammographic criteria, Computerized Tomography [CT], or Positron Emission Tomography [PET] scans [15,16]. In most of the reported cases tuberculous lymph nodes were incidentally discovered after the patient had undergone axillary dissection for breast cancer especially that a calcified tuberculous lymph node is not a common phenomenon. In these reports, anti TB treatment was prescribed for asymptomatic patients. Both of our cases were asymptomatic and were reluctant to receive anti TB treatment. Although there are no clear recommendations for treating incidental TB, there seems to be no conflict to prescribe anti TB treatment for such cases since the diagnosis was based on solid bacteriologic and/or histologic base. Prophylaxis anti TB treatment is recommended for patients with hematological malignancies or head and neck cancer and positive tuberculin skin test [4]. Tuberculin skin test has to be interpreted with caution in countries like Saudi Arabia where tuberculin skin test might be positive secondary to the mandatory TB vaccination. In these cases, Interferon gamma release assays [IGRAs] are the preferred method of TB infection testing [17]. In similar situations anti TB treatment may be considered if the patient is planned to receive chemotherapy, if there is contact with a case of open TB or if a chest X-ray showed suspicious TB changes.

Kaplan et al reviewed patients with longstanding TB who

developed breast cancer to determine whether radiation exposure could be documented. They reported 7 women who had treated TB, three of these were subjected to repeated fluoroscopy and subsequently developed breast cancer [6]. We had 3 cases of breast cancer with prior history of treated pulmonary TB [Cases No. 3, 4 and 5]. Unfortunately we had no medical documentation of their TB treatment since it was carried out in other centers but we expect that they were exposed to frequent fluoroscopy as part of the disease assessment and follow up of response to treatment. Case No. 3 was adequately treated and she is alive with no evidence of disease for 7 years. Cases No. 4 & 5 had history of inadequately treated pulmonary TB; they died of breast cancer with lung metastases. They had no clinical or radiologic evidence of skeletal or other visceral metastases. There were different reports describing how the TB tissue repair process leads to a fibrous scar and ultimately extensive pulmonary fibrosis and scarring that can cause cancer in the same lung [18,19]. It is difficult to postulate that prior pulmonary TB played a role in the development of lung metastatic nodules and we don't have a document that the metastatic nodules were at the same site as the old TB focus. These cases may have been suffering from their inadequately treated pulmonary TB and the radiologic findings were actually for both TB and metastases. We recommend that in similar situations anti TB treatment should be initiated early before proceeding with cancer treatment in order to reduce the morbidity and prevent TB reactivation.

Case No. 6 presented with metaplastic carcinoma of the breast associated with lung nodules and intra-abdominal lymph nodes that were radiologically suggestive of metastases. She had history of treated synovial [knee] and cerebral TB 4 years ago. She also had a left thigh lesion that was suspicious for TB but proved histologically to be metastatic in nature. The fact that she had prior multiple sites of TB involvement created a dilemma in radiologic interpretation of lesions seen in the metastatic work up. Moreover, metaplastic carcinomas of the breast are rare and have an unpredictable behavior in terms of metastatic sites as well as response to chemotherapy [20]. She received different chemotherapeutic regimens with no evidence of disease regression neither in the breast nor at the metastatic sites. In spite of the fear of reactivation of her TB during chemotherapy, prophylaxis anti TB treatment was not initiated. Prior lengthy TB treatment followed by aggressive multiple courses of cancer treatment required extensive psycho-social support. The patient passed through multiple stages of depression and treatment compliance was a major concern. Thorough patient and family education and support is mandatory before and during the treatment journey.

Case No. 7 had history of treated ovarian TB 20 years ago [oophorectomy followed by anti TB treatment]. CT scan of chest, abdomen and pelvis showed mild lung base atelectasis and multiple calcified pelvic nodules which could be related to the previous TB. Such findings make radiologic Interpretation in cancer patients difficult. She received chemotherapy with no evidence of TB reactivation.

Conclusion

The simultaneous occurrence of tuberculosis and cancer can lead to diagnostic as well as therapeutic challenges. The difficulty in interpretation of diagnostic work up may lead to over-staging of the malignant disease as well as the need for extra diagnostic invasive procedures. Fear of TB reactivation due to the immunosuppressive state associated with cancer and chemotherapy may lead to unnecessary prescription of anti TB treatment; however it is recommended to start patients with cancer on anti TB treatment before initiating

chemotherapy. The compliance of patients to receive anti TB and chemotherapy with the associated side effects is not guaranteed. A thorough organized patient and family education and follow-up is required for a successful outcome.

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