

Retrospective analysis of seven breast tuberculosis cases

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Abstract. The present study aimed to evaluate the demographic data, diagnostic methods, therapeutic regimens and duration of therapy in 7 breast tuberculosis (BTB) cases. The data of BTB cases treated between January 2006 and December 2013 were retrospectively evaluated, with a total of 648 tuberculosis (TB) cases recorded during the 8-year period. Among these cases, 296 patients (50%) suffered from pulmonary TB, 278 (43%) from non-pulmonary TB and 45 (7%) from PTB plus NPTB. In total, 7 BTB were diagnosed, which constituted 1.08% (7/648) of all TB cases and 2.51% (7/278) of all NPTB cases. The mean age of patients was 34±9.46 years, with no pregnant or lactating women. Bilateral breast involvement was detected in only 1 case, while all cases had a BCG scar, and obtained a mean tuberculin skin test (TST) result of 14.28±6.79 mm (range, 7-26 mm). The symptoms included presence of a mass, tenderness, pain, swelling and fluctuation in the breast, with or without discharging sinuses. In 1 case, history of contact with TB was found. All patients were newly-diagnosed BTB cases, with no other organ involvement. Upon histopathological examination of breast tissue, granulomatous inflammation with typical caseous necrosis was observed in 1 case, non-caseous necrosis inflammation was detected in 2 cases, granulomatous inflammation was observed in 3 cases, and mastitis and fat necrosis inflammation was observed in 1 case. Acid-fast bacilli (AFB) staining was positive in only 2 cases, and all patient were treated with anti-TB drugs with a successful outcome and no recurrence. In conclusion, BTB is a rare form of TB and the present retrospective study reported 7 cases of BTB along with the results of histopathological examination, microbiological examination and treatment. TB must be considered when there is presence of breast masses presenting with tenderness, pain, swelling and fluctuation, with or without discharging sinuses.

Introduction

Breast tuberculosis (BTB) is a rare type of extrapulmonary tuberculosis (TB). A BTB case was first described by Sir Astley Cooper in 1829 as a scrofulous swelling of the breast. Mammary gland tissues, skeletal muscles and the spleen are resistant to the multiplication and survival of the *tubercle bacillus*. It has been reported that the uncommon occurrence of BTB may be due to this feature (1). BTB commonly affects females of a reproductive age (range, 20-40 years), whereas it is rare in prepubescent females, elderly women and males. BTB lesions can mimic carcinoma in elderly patients, while it may be misdiagnosed as a pyogenic breast abscess in young patients. Thus, establishing an accurate diagnosis of BTB is often challenging. Breast tuberculosis has no specific clinical features and has been termed as a 'great masquerader' as a result of its different presentation. The history of the presenting symptoms in BTB is typically less than a year; however, it varies from a few months to several years (2). A lump in the central or upper outer quadrant of the breast is the most common form of presentation. Upon physical examination, common symptoms include a mass, tenderness, pain, swelling or fluctuation in abscess formation in the breast, presenting with or without discharging sinuses (2,3).

Radiological imaging is not diagnostic. Diagnosis is based on the identification of typical histological features or the tubercle bacilli under microscopy or culture (2-4). However, smear positivity for acid-fast bacilli by Ziehl-Neelsen staining is low, and in the majority of cases, the diagnosis can only be accurately diagnosed by histological identification of the typical necrotizing granulomatous lesion (5). It has been reported that, in endemic countries, the incidence is 3.0-4.5% of all breast lesions (6). BTB constitutes <1% of all diseases of the breast in developed countries. However, the incidence of the disease is higher in countries endemic for TB, such as the Indian subcontinent, where BTB may comprise up to 4.0% of breast diseases (4,7). In addition, tuberculosis constitutes 0.025-0.1% of all surgically treated diseases of the breast (8). The treatment of breast tuberculosis consists of anti-tubercular chemotherapy and surgery with specific indications (2).

In the present study, a retrospective analysis of 7 BTB cases was conducted, with the aim to evaluate the characteristics of this disease. The aims of the present study was to evaluate the clinical features, demographic data, diagnostic methods, therapeutic regimens and duration of therapy in BTB cases.

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Materials and methods

Cases. The medical files of BTB cases among TB patients registered and treated at the Ankara Tuberculosis Control Dispensary No. 7 (Ankara, Turkey) between January 2006 and December 2013 were retrospectively evaluated. The information gathered from the medical documents included the age, gender, occupation, marital status, gestation, lactation, number of children (as well as gender and child age upon admission of the patient), TB family contact history, symptoms, diagnostic duration, diagnostic methods, BCG vaccine scar, tuberculin skin test (TST) results, pathological results, chest X-ray scans, anti-TB treatment duration and existence of a TB type other than BTB. The cases were divided as PTB, NPTB and PTB plus NPTB cases. This retrospective study was approved by the Department of Tuberculosis Control at the Ministry of Health, No. 63519166/620/2840 (Ankara, Turkey).

X-ray, computed tomography and ultrasonography. The results of chest X-ray, computed tomography and ultrasonography were used for radiological investigation were obtained from patients files.

Histopathological examination. Histopathological analysis data was retrospectively analyzed. The samples were obtained by fine-needle aspiration in 2 cases, excisional biopsy in 2 cases, incisional biopsy in 1 case, tru-cut biopsy in 1 case and surgical resection in 1 case for histopathological examination. Both smear with Ziehl-Neelsen staining and Lowenstein Jensen culture were performed for a microbiological diagnosis.

TB treatment regimen. TB treatment was administered according to the Turkish national guidelines TB treatment consisted of 2 months of HRZE plus 4 to 7 months of HR (H, isoniazid, R, rifampin, E, ethambutol and Z, pyrazinamide). The duration and drugs may have been adapted according to the advice of a physician.

Results

TB cases. A total of 648 cases diagnosed TB were identified during 2006-2013. Among them, there were 296 cases (50%) of pulmonary TB (PTB), 278 cases (43%) of non-pulmonary TB (NPTB) and 45 cases (7%) PTB plus NPTB cases. In total, 7 of the NPTB cases involved the breast, constituting 1.08% (7/648) of all TB cases and 2.51% (7/278) of all NPTB. All the identified BTB patients were newly-diagnosed cases, with a time from symptom to definite diagnosis between 2 and 6 months.

Patient characteristics. The demographic and clinical features of study group are shown in Table I. The mean age of BTB patients was 34 ± 9.46 years (age range, 24-53 years). Unilateral breast involvement was observed in 6/7 cases, including involvement of the right breast in 3 cases, and of the left breast in another 3 cases). In addition, 1 case presented bilateral breast involvement. All the included BTB cases had one or two children, with the exception of 1 case that did not have any children. There were no pregnant or lactating women within the included cases. All cases had a scar from the BCG TB

vaccine, while a TST test indicated a mean size of induration of 14.28 ± 6.79 mm (size range, 7-26 mm). One patient had family history of contact with TB.

Common symptoms. The commonly observed symptoms among the BTB patients included presence of a mass, tenderness, pain, swelling and fluctuation in abscess formation in the breast, which presented with or without discharging sinuses. Nipple retraction or discharge were not observed in any of the included BTB patients. In addition, no respiratory symptoms were observed.

Examinations and diagnosis. Chest X-ray scans were normal in all the included BTB cases. The diagnostic methods included mammography, ultrasonography, thorax computed tomography (CT), fine needle aspiration cytology (FNAC), staining for acid-fast bacilli (AFB) in smear and culture tests, excisional or incisional biopsy, and excision (including mastectomy or lumpectomy). Representative examples of CT and ultrasonic examinations performed for the diagnosis of BTB are shown in Figs. 1 and 2, respectively. AFB testing was positive in 2/7 cases.

Histopathological examination. Upon histopathological examination of tissue samples, the following characteristics were observed: Granulomatous inflammation was observed in 3 cases; granulomatous inflammation with typical caseous necrosis was detected in 1 case; non-caseous necrosis inflammation was detected in 2 cases; and mastitis and fat necrosis inflammation was observed in 1 case.

Treatments. All cases were successfully treated with anti-TB drugs. The TB treatment consisted of 2 months of isoniazid + rifampin + ethambutol + pyrazinamide (HRZE regimen), followed by 4-7 months of isoniazid + rifampin (HR regimen). Recurrence was not observed in any of the cases.

Representative BTB case. In the case presenting with mastitis and fat necrosis inflammation (case no. 7, Table I), right mastitis was developed while the patient was lactating 4 years prior to TBT diagnosis. The disease improved following nonspecific antibiotherapy; however, mastitis was again developed (1 year later), which was not resolved after further nonspecific antibiotherapy. Subsequent to biopsy and further investigation, the patient was diagnosed with TB and received anti-TB drugs, which resulted in successful treatment. The patient in this case received 6 months anti TB drugs (2 months of HRZE plus 4 months of HR) (H: 300 mgr, R: 600 mgr, Z :2,000 mgr, E: 1,500 mgr) This case has been reported in further detail as an exact diagnosis was not established

Discussion

BTB is a rare form of extrapulmonary TB that is associated with risk factors including past history of suppurative mastitis, trauma, lactation, multiparity and acquired immune deficiency syndrome. Lactation has been demonstrated to increase the susceptibility of the breast to TB. During lactation, the increased vascularity of the breast may facilitate infection and dissemination of the bacilli. However, there were no pregnant

Table I. Demographic and clinical features of study group.

Patient no.	Date	Age (years)/ gender	Contact with TB	TST size, mm	Number of children (age/gender)	Characteristics and symptoms	Diagnosis method	Histopathological results	Treatment duration, months ^a
1	2006	53/F	Yes	12	0	4x3x3-cm painful swelling in the upper-inner quarter of the right breast at right parasternal border	Fine-needle aspiration biopsy	Granulomatous inflammation with typical caseous necrosis, positive AFB smear	9
2	2009	30/F	No	20	2 (8/M, 13/F)	6x10-mm discharging sinus in the upper outer quadrant of right breast; 8x11-mm solid mass in the left breast	Fine-needle aspiration biopsy	Granulomatous inflammation, negative AFB smears	9
3	2010	38/F	No	26	2 (8/M, 6/M)	Discharging sinus invading the pectoral muscle and rib in the lower outer quadrant of the right breast	Excisional biopsy	Granulomatous inflammation; positive AFB DNA	9
4	2012	34/F	No	7	2 (15/M, 7/M)	Firm and tender breast; painful swelling and erythema of the breast skin; acne-like lesion in border of the left nipple	Incisional biopsy	Non-caseous necrosis, inflammation; positive AFB smear	6
5	2012	24/F	No	9	2 (5/F, 2/M)	Two solid masses in the upper outer quadrant of the left breast	Left segmental mastectomy + total excision	Non-caseous necrosis, inflammation	6
6	2013	31/F	No	16	2 (14/M, 5/M)	2x3-cm lump with fluctuation border areola of the right breast	True-cut biopsy + total excision (lumpectomy)	Granulomatous inflammation	9
7	2013	28/F	No	10	1 (4/F)	Painful swelling, discharging sinus in the left breast	Excisional biopsy	Mastitis and fat necrosis; negative AFB smears	6

^aTB treatment consisted of two months of HRZE plus 4 to 7 months of HR (H isovit, R rifampicin, E ethambutol, Z pyrazinamide). All patients were unemployed (housewives), and all presented a BCG vaccine scar, with patient no. 6 receiving two vaccinations. F, female; M, male; TST, tuberculin skin test; AFB, acid-fast bacteria.

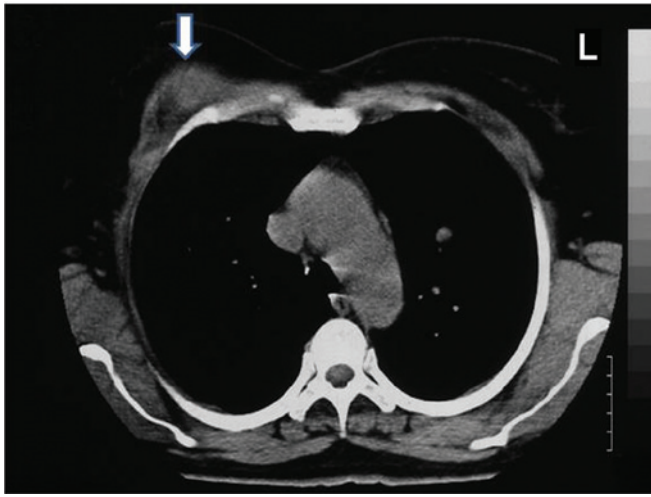


Figure 1. A representative spiral thorax computed tomography scan from a breast tuberculosis patient (patient 1). The mass was shown to be 4x3x3 cm in size, with clear margins and mild hypodensity on the right anterior paracostal muscle near the sternum in the right breast tissue (white arrow). No pathological findings were observed in the lung parenchyma and mediastinum.



Figure 2. Representative ultrasonography scan showing a mass in the right breast (patient 1). The scan was obtained during ultrasonography-guided fine-needle aspiration biopsy.

or lactating women in the patient cohort of the present study. The majority of cases had an age between 20 and 40 years. It has been previously shown that unilateral involvement is common in BTB. In the current study, unilateral involvement was observed in 6/7 cases, which is consistent with previous reports.

BTB commonly presents with the following clinical characteristics: Ill-defined, solitary, unilateral solid lump located in central or upper outer quadrant of the breast. The mass may be solid, irregular and occasionally fixed to the muscle, skin or chest wall. Bilateral involvement and presence of multiple lumps are rarely reported (in <3% of cases) (9). In the cases reported in the current study, the symptoms included presence of a mass, tenderness, pain, swelling and fluctuation in abscess formation in the breast, with or without discharging sinuses, while the lesions were generally located in the upper outer quadrant of the breast.

The main routes through which TB lesions spread and the breast may become infected with TB bacilli includes by haematogenous routes, lymphatic extension from primary foci of disease in the lymph nodes of the mediastinum, axilla and parasternal and cervical regions, direct inoculation and by ductal infection (10). The disease presents in two forms, primary and secondary BTB. Primary BTB is rarely reported, and the breast is the only affected area in this form of the disease. By contrast, secondary BTB is more frequently reported, and a prior history of TB is common in these cases (4,7,9). In the present study, the only organ involved was the breast, and thus all cases presented primary BTB.

No specific features of BTB are observed in mammography and ultrasonography examinations. Mammography can be used to identify the three different patterns of TB, which include the nodular, disseminated and sclerosing lesions. The nodular pattern is indicated by the presence of slow-growing, painless and well-circumscribed lesions. At an advanced stage, retraction and sinus formation may be observed through involvement of the skin. In addition, the disseminated pattern presents as interconnected focal lesions, sinus formation and skin thickening. Finally, the sclerosing pattern commonly occurs in older females and presents as slow-growing, dense fibrous tissue. Generally, no microcalcification or nipple retraction are observed. According to radiological findings, the nodular pattern may be misdiagnosed as fibroadenoma. Thorax computed tomography is important for evaluating chest wall, musculoskeletal and other involvement, and can also be used as a guide for obtaining tissue samples for diagnosis (4).

A suspicion of BTB is essential for diagnosis. The gold standard for diagnosis of BTB is the detection of the etiologic agent using Ziehl-Neelsen staining or culturing; however, AFB test is rarely positive. Histopathological examination, FNAC, true-cut biopsy or open biopsy are also important for diagnosis, with FNAC being the most widely used initial invasive diagnostic method. In order to establish a diagnosis, the present study, FNAC was used in 2 cases, excisional biopsy in another 2 cases, incisional biopsy in 1 case and total excision in 2 cases. Granulomas may be detected anywhere in breast tissue and granuloma is often composed of histiocytes, Langhans giant cells, lymphocytes, rare plasma cell and eosinophilic caseous necrosis. In the case with mastitis and fat necrosis inflammation presented in the current study, no improvement was observed following nonspecific antibiotherapy and the patient was then successfully treated with anti-TB drugs. In past years, mastectomy was the common treatment of BTB; however, in recent years, the success of antituberculous drug therapy is high and surgical intervention is rare (10-12).

Tanrikulu *et al* (13) reported 27 BTB cases between 2004 and 2008, with all cases being newly-diagnosed patients with a mean age of 31.5 ± 8.4 years. The study reported that cases presented with breast swelling (48.1%), mass and fluctuation in abscess formation (40.7% each) and painful breasts (18.5%) (13). Of the included patients, 1 case had previous TB lymphadenitis in the cervical region, while the remaining cases had no history of TB; thus, 26/27 cases were diagnosed with primary BTB, and ~73.0% of cases were diagnosed using FNAC (13). In addition, Kalaç *et al* (8) presented 5 BTB cases with a mean age between 20 and 63 years. All the reported cases had children and were breast-feeding, while all lesions

were found to be unilateral and AFB testing revealed negative results. One of the cases had received anti-TB treatment for pulmonary TB 10 years earlier (8). Diagnosis was established histopathologically from the excisional biopsy material. Caseating granulomatosis was also identified in the axillary lymph nodes of 3 patients (8). Furthermore, Khanna *et al* (14) reported 52 cases of BTB within a 15-year period, which accounted for 3% of all breast lesions reported at their hospital. The authors reported presence of a breast mass with associated sinus in 39% of cases, isolated breast lump in 23% of cases, sinus with absence of a lump in 12% of cases and tender nodules in 23% of cases, with associated axillary lymphadenopathy reported in 41% of cases. The BTB diagnosis was confirmed using FNAC or histological examination in all the patients, and the main treatment administered was anti-TB therapy (14). Another study by Al-Marri *et al* (6) reported 13 multiparous women with BTB within a 10-year period, who were diagnosed based on histological examination. All patients presented with a mass, while 2 patients had symptoms of nipple discharge and 1 presented a palpable axillary node on the same side (6). Ben Hassouna *et al* (15) reported 65 BTB cases, which represented 0.2% of the tubercular localizations and 0.3% of the breast pathologies reported at their clinic within the investigated time period. The initial suspected diagnosis was malignant tumor in 60% of the BTB cases, benign nodule in 24.6% of patients and presence of an abscess in 16.4% of patients (15). Based on mammography examination, a malignant lesion was suspected in 49% of cases, while FNAC was performed in 8 patients, showing a negative result in 6 of these (15). Eventually, the BTB diagnosis was established using histological examination following identification of typical TB lesions on tumorectomy or biopsy samples, and all patients received anti-TB treatment (15). A study by Harris *et al* (16) evaluated 38 patients with BTB reported over a 5-year period, with a mean age of 29 years. Of these, 10 patients (26%) experienced breast pain with or without increased breast nodularity, while 14 patients (36%) presented axillary lymph node involvement (16). Associated pulmonary TB was only identified in 5/38 patients, with the remaining presenting isolated involvement of the breast (16). Patients were mainly treated with anti-TB drugs for 6-9 months (16).

In an earlier study by Sharma *et al* (17), 7 females with BTB were diagnosed between 1980-1988, with an age range of 17-50 years. The clinical features included lumps, ulcers, multiple discharging sinuses and recurring abscess of the breast. Diagnosis was established based on histological examination results, while AFB positivity was found in only 1 samples and positive culture in 1 other patient. Patients received anti-TB treatment along with removal of the infected breast tissue (17). Fukuoka *et al* (18) reported 12 BTB cases within a 10-year period, with a mean age of 42.8 years (range, 28-84 years). Only 1 case had past history of TB contact and in the remaining cases TB of the breast was considered to be a primary disease. Axillary lymph node involvement and formation of pyogenic breast abscess occurred in 7 cases. The histological findings revealed epithelioid cell granulomas with caseous necrosis in 11/12 cases, and 7/11 cases were treated with a combination of surgery and anti-TB chemotherapy (18). Furthermore, Morsad *et al* (19) treated 14 BTB cases at their hospital over a 16-year period, with patient ages of 16-65 years. Contact with

TB was reported in 2 cases, and axillary nodes were observed in 10 cases. The diagnosis of BTB was based on pathological findings in 14 cases (including 2 biopsies and 12 perioperative specimens) and isolation of bacilli from pus in 1 case. Medical treatment was provided, as well as surgery when required, for abscess drainage or treatment of residual lesions (19).

In conclusion, BTB is a rare form of TB and the present retrospective study reported 7 cases of BTB along with the results of histopathological examination, microbiological examination and treatment. TB must be considered when there is presence of breast masses presenting with tenderness, pain, swelling and fluctuation in abscess formation, with or without discharging sinuses.

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