



Tuberculosis of the Breast: A Review of the Literature

Anthony Kodzo-Grey Venyo^{1*}, Lucy Kodzo-Grey Venyo², Ali Nawaz Khan³

¹North Manchester General Hospital Department of Urology Delaunays Road Manchester United Kingdom

²Queen Elizabeth Hospital Critical Care Unit Division of Anaesthesia Gateshead United Kingdom

³North Manchester General Hospital Department of Radiology Delaunays Road Manchester United Kingdom

Abstract

Tuberculosis of the breast is uncommon globally and its diagnosis may not be straightforward. The disease may present as breast lump, abscess or sinus and it may sometimes mimic breast cancer. A history of previous or recent tuberculosis is helpful with regard to suspicion of the diagnosis. Radiological investigations including chest X-ray, mammography, ultrasound scan of the breast, computed tomography scan and magnetic resonance imaging scan are useful tools in the investigation of the disease. The diagnosis can be achieved by demonstration of AFB in the breast tissue by Ziehl-Neilson stain or culture but not in all cases. Incorporation of PCR can aid in the confirmation of the diagnosis early. The disease is curable with anti-tubercular drugs, and surgery may rarely be required. The disease can be encountered in all countries globally. Confirmation of the diagnosis may be obtained by the use of Ziehl Neilson stain demonstration of Acid fast bacillus or culture of biopsy or aspirate specimen from the breast lesion or by means of PCR technique. It is curable with anti-tubercular therapy.

Key Words: Tuberculosis of the breast; tuberculous mastitis;

*Corresponding Author: Dr Anthony Kodzo-Grey Venyo. MB ChB FRCS(Ed) FRCSI FGCS Urol LLM, North Manchester General Hospital, Department of Urology, Manchester, United Kingdom, Email: akodzogrey@yahoo.co.uk

Received: December 20, 2014, Accepted: April 20, 2015. Published: May 20, 2015. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Introduction

Tuberculosis is the most widespread and persistent human infection in the world. The infection can involve any organ and mimic other illness; hence, it is called the great mimicker. [1] Tuberculosis (TB) is a mycobacterial infection which can affect multiple organ systems. [2] Tuberculosis of the breast is an uncommon presentation of tuberculosis, even in countries where the incidence of pulmonary and extra-pulmonary tuberculosis is high. [3] Mastitis refers to inflammation of the breast tissue which may or may not be accompanied by infection. Inflammatory breast disorders can be classified as:

infectious, non-infectious, or mastitis associated with malignancy [5] [6].

Infectious mastitis includes simple mastitis for example lactational mastitis, and complicated mastitis for example with abscess formation. [6] Non-infectious mastitis does not necessarily occur during lactation, it is not always accompanied by microbial infections, and it may not resolve with antibiotics [6]. Inflammatory breast cancer, come do ductal carcinoma in situ, and locally advanced breast cancers can be confused with infection. Cancer should always be suspected if an apparent breast infection does not respond to appropriate treatment. [6] Skin disorders of the breast can cause confusion with true breast infections and should be considered when evaluating a patient with inflammation of the breast [6].

Throughout the world no country has ever been able to eradicate tuberculosis. [7] Even in tuberculosis endemic countries it is difficult to diagnose tuberculosis of the breast. It would be even more difficult to diagnose tuberculosis of the breast in non-tuberculosis endemic countries in the world. The ensuing paper contains a review of tuberculosis

of the breast which has been presented in two parts; the first part contains an overview of the disease and the second part contains narrations from some reported cases of tuberculosis of the breast to illustrate the biological behavior of the disease vividly.

Literature Review

Definition: Sir Astley Cooper in 1829 described tuberculosis of the breast or tuberculous mastitis as “scrofulous swelling” in the bosom of young women [8].

Terminology: It is also called tuberculous mastitis [9]

Types of tuberculosis of the breast

Breast tuberculosis (TB) is classified as either primary when no demonstrable tuberculous focus exists elsewhere in the body or secondary to a pre-existing lesion located elsewhere in the body.

Incidence / Epidemiology

Tuberculosis of the breast is rare in Western countries, but more common in India [10]. It typically tends to affect young lactating multi-parous women and it can manifest either as an abscess or as a painless breast mass. Primary tuberculosis of breast is a rare form of extra-pulmonary tuberculosis. Even though more than one billion people suffer from tuberculosis worldwide, tuberculosis of the breast is a relatively rare condition. [11] The prevalence of tuberculosis of the breast has been estimated to be 0.1% of breast lesions examined histologically. [12] Furthermore, the diagnosis of tuberculosis of the breast is not straightforward in view of its similarity to carcinoma and bacterial abscesses. It is rare to see breast tuberculosis in infra-mammary area especially in unmarried female [12]

Tuberculous mastitis (TM) is a rare extra-pulmonary presentation of tuberculosis accounting for less than 1% of all diseases of the breast in the industrialized world. [3]; [4]; [13]; [14]; [15]. The incidence of this disease is higher in countries endemic for tuberculosis, like the Indian subcontinent, where it may be as high as 4%. [4] In the Arabian Gulf, the frequency of the disease is reported to be between 0.4% and 0.5%. [16] [17]. TM may be part of a systemic disease or may be the only manifestation of tuberculosis. Tuberculosis of the breast occurs far more frequently in women,

especially in their reproductive age, and is uncommon in prepubescent and elderly women [18] [19]; “This” has been said to parallel the highest incidence of pulmonary tuberculosis. [20] It had been stated that this could be because the female breast undergoes frequent changes during the period of childbearing activity and is more susceptible to trauma and infection. [21]

Tuberculosis of the breast is very rare in males; in a review by Gupta *et al.* [22] which included 160 patients, only 6 were males. Some of the documented risk factors associated with tuberculosis of the breast include multi-parity, lactation, trauma, past history of suppurative mastitis, and AIDS.[22] [23] Some authors [21] [24] had stated that patients would frequently be symptomatic for at least a few months prior to diagnosis. Other authors [25] [26] had stated that it may be difficult to differentiate from carcinoma of the breast, a condition with which it may coexist. [25] [26]

Routes of Spread

The routes of spread of tuberculosis of the breast include:

- (a) Haematogeneous spread
- (b) Lymphatic spread
- (c) Direct spread.

Tuberculosis of the breast is seen more frequently secondary to a tuberculous focus from the lungs, pleura or lymph nodes which may not be detected on radiology or clinically. [11]

Classification of types of tuberculosis of the breast:

A. McKeown *et al.* classification: [27]

McKeown *et al.*, [27] classified tuberculosis of the breast into 5 pathological varieties

- (a) the nodular form; (b) the diffuse or disseminated form; (c) the sclerosin form; (d) tuberculous mastitis obliterans; and (e) acute miliary tuberculous mastitis.

The nodular form is the most common variety and usually presents as a localized slowly growing mass that progresses to involve skin, may ulcerate, and can form sinuses. Histologically, this form is characterized by extensive caseation and little fibrosis. [21] [24] [28]

The diffuse or disseminated form is the second most common sub-type and this involves the

entire breast with multiple intercommunicating foci of tubercles within the breast, which caseate leading to ulceration and discharging sinuses. The overlying skin tends to be thickened with multiple ulcers. The ipsi-lateral axillary lymph nodes are usually enlarged and matted. This form is more common in older females and may be confused with malignancy. [29]

The third variety of tuberculosis of the breast described by Mckeown et al. [27] is the sclerosing form. This variety demonstrates extensive fibrosis rather than caseation, in which the entire breast is hard and the nipple is retracted. This form is often seen in involuting breasts of older females and may be also mistaken for carcinoma of the breast. [27]

The last two forms described by Mckeown et al [27] are tuberculous mastitis obliterans and acute miliary tuberculous mastitis. Tuberculous mastitis obliterans is characterized by duct infection which produces proliferation of the lining epithelium and marked epithelial and periductal fibrosis. The ducts

are occluded and cystic spaces are produced and these resemble ‘cystic mastitis.’ Acute miliary tuberculous mastitis occurs as a part of generalized miliary tuberculosis. Both forms have rarely been encountered in recent literature and they may be of historical importance only

B. Tewari and shukla classification [30]

Tewari and Shukla [30] recently classified tuberculosis of the breast into 3 groups:

- (a) nodulocaseous tubercular mastitis,
- (b) disseminated/confluent tubercular mastitis,
- (c) tuberculous breast abscess.

Clinical features

The clinical features of tuberculosis of breast include:

- Presentation with abscess, fistula or mass [31]
- The presentation is usually unilateral without pulmonary involvement [3] [32]
- Acid-fast bacilli are usually not identified

Fig 1a



Fig 1b



FIGURA 4
Paciente após início do tratamento demonstrando área de retração cutânea de fístulas cicatrizadas em quadrante infero lateral.

Figure 1a: illustrates a case of tuberculosis of the breast which visually resembles breast carcinoma.

Figure 1b: shows the breast of a patient who had tuberculosis of the breast which illustrates partially healed fistulas after initiation of treatment.

Figure 1c: Shows granulomatous inflammation of major lactiferous duct and epithelial necrosis.

Figure 1d: shows granulomatous inflammation with and Langhans giant cells

Figures 1a, b, c, and d: Reproduced from pathologyoutlines.com with permission from PathologyOutlines.com available from Hind Nassar Breast – non-malignant – Tuberculosis – Pathology Outlines 2012 September 2012:www.pathologyoutlines.com/topic/breastTB.html with permission from Pathology Outlines.com [Reference 9]

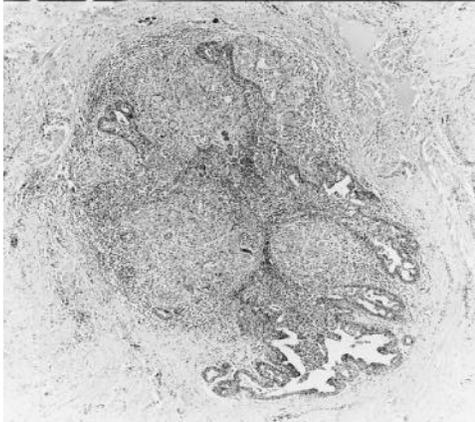


Fig 1c

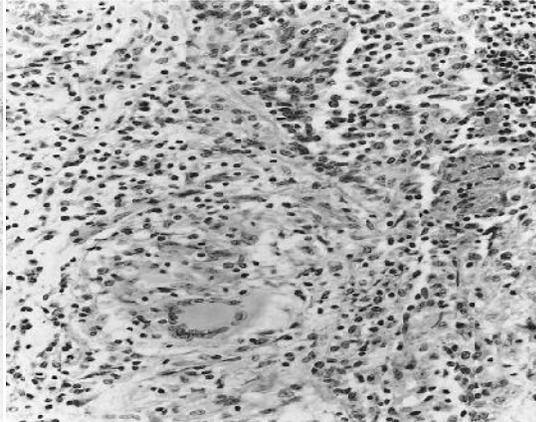


Fig 1d

Fig 2a

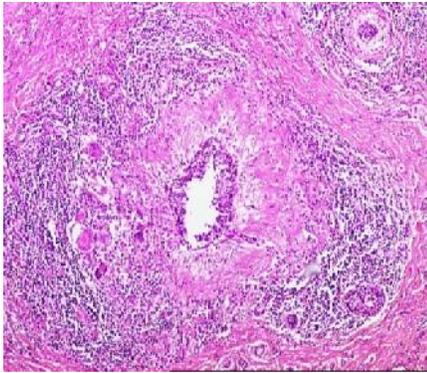


Fig 2b

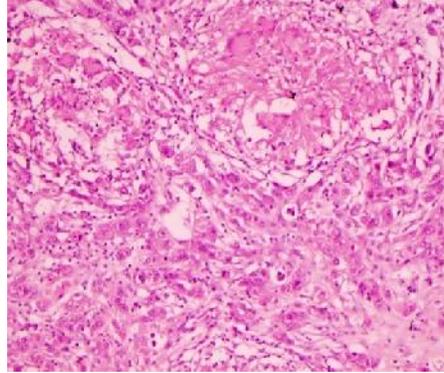


Fig 2c

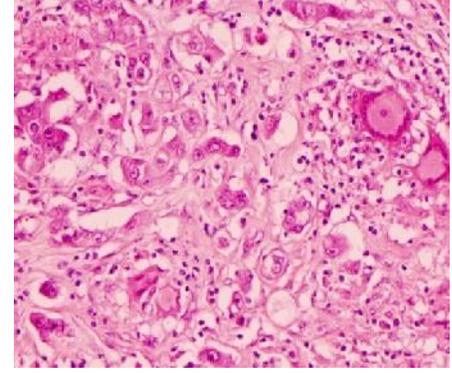


Figure 2a, 2b, 2c: Granuloma with central necrosis and epithelioid histiocytes. The histopathologic examination of the specimen revealed granulomas with central caseation necrosis, epithelioid histiocytes, Langhans' giant cells, and intense lymphocytic infiltration at the periphery of the granulomas (H&E, $\times 40$). Reproduced from *World J Surg Oncol*. 2007; 5: 67. Published online 2007 June 18. doi: [10.1186/1477-7819-5-67](https://doi.org/10.1186/1477-7819-5-67) PMID: PMC1910599 Mammary tuberculosis – importance of recognition and differentiation from that of a breast malignancy: report of three cases and review of the literature Müfide Nuran Akçay, Leyla Sa lam, Pınar Polat, Fazlı Erdo an, Yavuz Albayrak, and Stephen Povoski with permission from Bio Med Central on behalf of the journal. Figure 2b Infiltrating ductal carcinoma in the lower half of the field with two epithelioid granulomata containing multinucleated giant cells in the upper half of the field (H&E $10\times$). Alzaraa A, Dalal N. Coexistence of carcinoma and tuberculosis in one breast *World J Surg Oncol*. 2008; 6: 29 Published online 2008 March 4. doi: [10.1186/1477-7819-6-29](https://doi.org/10.1186/1477-7819-6-29) PMID: PMC2268920 www.ncbi.nlm.nih.gov/pmc/articles/PMC2268920/ with permission from Bio Med Central on behalf of the journal. Figure 2c Higher power view of infiltrating ductal carcinoma with an epithelioid granuloma containing Langhan's type giant cells in the upper right hand corner of the field (H&E $20\times$). Alzaraa A, Dalal N: Coexistence of carcinoma and tuberculosis in one breast. *World J Surg Oncol*. 2008; 6: 29 Published online 2008 March 4. doi: [10.1186/1477-7819-6-29](https://doi.org/10.1186/1477-7819-6-29) PMID: PMC2268920 www.ncbi.nlm.nih.gov/pmc/articles/PMC2268920/ with permission from Bio Med Central on behalf of the journal under The Creative Commons Attribution License.

Fig 3a

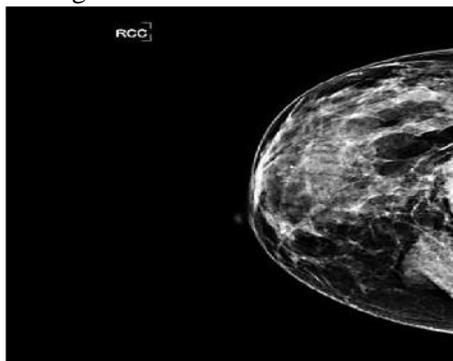


Fig 3b

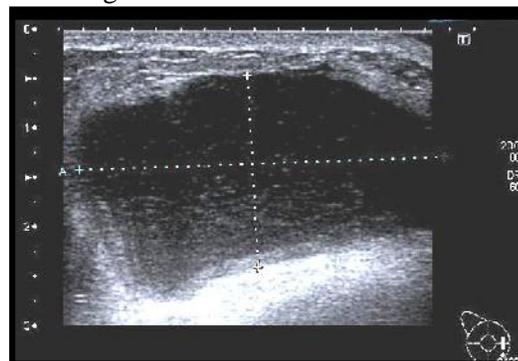


Figure 3a: Mammogram showing an infiltrative mass lesion with punctate coarse calcification. The mass is indistinguishable from a breast cancer.

Figure 3b: Ultrasound of the same lesion as in the mammogram shows an ill-defined cystic lesion with particulate intraluminal matter and ragged margins indistinguishable from an abscess or necrotic tumour.

Figure 3c: Ultrasound of the same lesion as in the mammogram shows an ill-defined cystic lesion with particulate intraluminal matter and ragged margins indistinguishable from an abscess or necrotic tumor. Note the intramural nodule.

Figure 3d: Ultrasound of the same lesion as in the mammogram shows an ill-defined cystic lesion with particulate intraluminal matter and ragged margins indistinguishable from an abscess or necrotic tumour. Note the intramural nodule. **Volume 4, Issue 2**

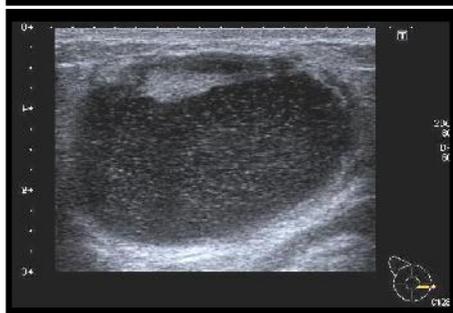


Fig 3c

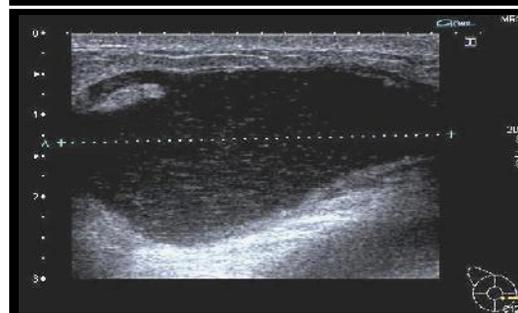


Fig 3d

Fig 4a



Fig 4b



Figure 4 a: PA chest radiograph of the same patient shown in figure 3 with an abnormal mammogram and ultrasound showing granulomatous disease left apical region suggestive of lung tuberculosis, confirmed on sputum culture. **Figure 4b:** Left lateral chest radiograph of the same patient shown in figure 3 showing active disease in the left upper lobe.

Diagnosis

It has been stated that the most reliable and definitive diagnostic studies include aspirate culture, polymerase chain reaction for mycobacterium, and histological examination of the tissue sample. [11] [33] Some authors, [34] had stated that fine needle aspiration cytology (FNAC) from the breast lesion can diagnose tuberculosis of the breast in as many as three quarters of cases when both epithelioid cell granulomas and necrosis are present. Nevertheless, failure to demonstrate necrosis on fine needle aspiration cytology (FNAC) does not exclude tuberculosis of the breast as often a spectrum of histological abnormalities can be found in tuberculosis of the breast specimens. [34]

Some authors [22] had stated that the gold standard for the diagnosis of tuberculosis of the breast is by bacteriological culture of breast tissue or by Ziehl-Neelsen (ZN) stain. Nevertheless, in tuberculosis of the breast the bacilli are isolated in only 25% of cases, and acid-fast bacilli (AFB) are identified only in 12% of the patients. Other authors [15], [30], [35] had stated that in view of this, the demonstration of caseating granulomas from the breast tissue and involved lymph nodes may be sufficient for the diagnosis. Some authors [15], [36] had stated that fine needle aspiration cytology (FNAC) has been the most widely used initial invasive method for diagnosis of breast tuberculosis and about 73% of the cases of tuberculosis of the breast can be diagnosed on FNAC when both epithelioid cell granulomas and necrosis are present.

Other authors [15], [37] had iterated that in tuberculosis-endemic countries, the finding of granuloma in fine needle aspiration warrants empirical treatment for tuberculosis even in the absence of positive acid fast bacilli (AFB) and without culture results. Nevertheless, a number of authors [25] [30] [35] [38] [39] had advocated an excision biopsy in order to rule out other differential diagnoses like sarcoidosis, fungal infections, ductular ectasia, and a co-existing malignancy. Some authors [36] had stated that adequate tissue samples are usually not possible with fine needle aspiration. It had also been stated that, the differentiation between idiopathic granulomatous mastitis and tuberculosis of the breast is extremely important as treatment options of the former may include steroids and that the administration of steroids may flare up tuberculosis; and in tuberculosis-endemic regions, empiric antituberculous therapy might be warranted prior to the consideration steroids therapy. [40]

The differentiation between idiopathic granulomatous mastitis and tuberculosis of the breast (tuberculous mastitis) could be intriguing; however, the differentiation between the two clinical entities could be elucidated by the ensuing clinical and histological features:

(a) Clinically, idiopathic granulomatous mastitis tends to appear after pregnancy but the appearance of tuberculosis of the breast (tuberculous mastitis) but there has not been relationship between tuberculosis of the breast and pregnancy; granulomatous mastitis is not associated with any constitutional symptoms however, tuberculosis of the breast is associated with

constitutional symptoms; idiopathic in cases of granulomatous mastitis there has not any relationship with breast feeding and similarly no relationship has been described between tuberculosis of the breast and breast feeding; idiopathic granulomatous mastitis has a possible relationship with oral pills but there has not been any relationship with oral pills; granulomatous mastitis tends to occur between the ages of 17 years and 42 years and on the other hand tuberculosis of the breast can occur in any age group; granulomatous mastitis tends to occur in the parous group of patients and tuberculosis of the breast can occur both in the parous and non-parous group; in granulomatous mastitis, a hard breast mass is found which can be located in any site of the breast but the sub-areolar region is spared and in tuberculosis of the breast a hard breast lump can be found anywhere in the breast; bilateral idiopathic granulomatous mastitis is un-common, however, bilateral tuberculosis of the breast is common; nipple discharge in idiopathic granulomatous mastitis is rare, and in tuberculosis of the breast there is occasional; there is tenderness in idiopathic granulomatous mastitis but in tuberculosis of the breast tenderness is rare; in idiopathic granulomatous mastitis axillary lymph node enlargement is rare and in tuberculosis of the breast axillary lymph node can be enlarged; in idiopathic granulomatous mastitis the size of the breast mass may vary from 1 cm to 8 cm and in tuberculosis of the breast the size of the breast mass may vary from 1 cm to 8 cm; idiopathic granulomatous mastitis clinically and radiologically mimics carcinoma and tuberculosis of the breast clinically and radiologically mimics carcinoma; the aetiology of idiopathic granulomatous mastitis is idiopathic but the cause of tuberculosis of the breast is tuberculosis. [40]

With regard to histological findings: in idiopathic granulomatous mastitis the lobules of the breast are affected but in tuberculosis of the breast any component of the breast is affected (the lobules, the ducts, and the fat); in idiopathic granulomatous mastitis granulomas as found in the lobules but in tuberculosis of the breast the granulomas are found anywhere in the breast; in idiopathic granulomatous mastitis the granulomas are composed of histiocytes, Langhans giant cells, lymphocytes, plasma cells, and occasional eosinophils, and in tuberculosis of the breast the granulomas are composed of histiocytes, Langhans giant cells, lymphocytes, rare plasma cells and eosinophils. in idiopathic granulomatous mastitis caseation necrosis is absent and in tuberculosis of the

breast caseation necrosis is present; in idiopathic granulomatous mastitis there is fat necrosis and in tuberculosis of the breast there is fat necrosis; in idiopathic granulomatous mastitis there is fibrosis and in tuberculosis of breast there is fibrosis; abscess formation is common in idiopathic granulomatous mastitis but in tuberculosis of the breast abscess is un-common. [40]

It has been stated that: [40]

- In view of the fact that the detection of acid fast bacillus (AFB) in a smear requires more than 10,000 organisms / mL, nucleic acid amplification test could be very helpful in establishing the diagnosis of tuberculosis in smear-negative samples.
- With the use of amplification systems, nucleic acid sequences unique to *Mycobacterium tuberculosis* (*M. tuberculosis*) can be detected directly from clinical samples, offering better accuracy than acid fast bacilli (AFB) smear and greater speed than culture.
- Two direct amplification tests (DATs) have been approved by the FDA, the *M. tuberculosis* direct test (MTD; Gen-Probe, San Diego, CA) and the AmpliCor *M. tuberculosis* test (AMPLICOR MTB Test; Roche Diagnostic Systems, Branchburg, NJ). Both tests amplify and detect *M. tuberculosis* 16S ribosomal RNA. [41], [42]

Some authors [43] [44], iterated that the appropriate use of these DATs in diagnosis of tuberculosis has yet to be completely determined. Other authors [45], [46] had also stated that the specificity of DAT approaches 100% and sensitivity is about 96% in acid fast bacillus (AFB) smear-positive specimens, and diagnosis of pulmonary TB can be established if the two are present. Nevertheless, it had been observed that in acid fast bacillus (AFB) smear-negative samples, the specificity, sensitivity, and positive predictive value had varied significantly with the pretest probability of the disease. [46]

Some authors, [42] had observed that the positive predictive value of *Mycobacterium. Tuberculosis* direct test in a pulmonary sample approaches 100% if pulmonary tuberculosis is strongly clinically suspected but is only 59% with low clinical suspicion. They also found that the negative predictive value, however, of a negative PCR was about 91% even if pulmonary TB was

strongly suspected, in contrast to a value of 37% for AFB stain in the same clinical setting. Other authors [47] found similar results and they reported a sensitivity of 53% and a specificity of 93% of DAT versus culture when the Amplicor assay was applied to smear-negative specimens. The same authors [47] stated that a positive DAT result may still be valuable in the early detection of the approximately 50% of active tuberculosis cases which are smear negative. For breast cancer patients with granulomatous axillary lymphadenitis, PCR may be required to rule out TB in endemic regions [48]

Macroscopic features

Macroscopic examination of a tuberculous mastitis may reveal multiple sinuses or fistulas; and there may be focal discoloration or mass (see figures 1 a and b for examples of photographs taken of breasts of patients with tuberculosis of the breast) [9].

Histopathological features

Histological examination of tuberculosis of the breast may reveal granulomas with Langhans giant cells and caseous necrosis (often) [9] (see figure 1 c, d, 2 a, b, c for examples).

Cytological features

In cases of tuberculosis of the breast cytological examination may reveal foamy histiocytes, neutrophils, necrotic debris [9]

Radiological features

On the whole radiological tools like mammography, computed tomography (CT scan), and magnetic resonance imaging (MRI) of the breast have all been utilized in diagnostic work-up of breast lumps. Either mammography or ultrasound of the breast may reveal a dense sinus tract connecting an ill-defined breast mass to a localized skin thickening. This 'sinus tract sign,' which was originally described by Makanjuola, may be strongly suggestive of tuberculous breast abscess but it is found in only a small percentage of patients. [49] [50]

Radiological tools are generally helpful in defining the extent of the lesion but not very helpful in differentiating tuberculosis from other differential diagnoses, for example, malignancy [3] [51].

Mammography

Tuberculous abscess can be diagnosed on mammography as a dense sinus tract connecting an ill-defined breast mass with a localized skin thickening but Khanna reported these findings in less

number of cases (see figure 3 a, which illustrates a mammogram of a woman who had tuberculosis of the breast). [50], [52]

Ultrasound scan

There are no specific ultrasound scan findings to diagnose lesions due to tuberculosis. [52] However, there may be heterogeneous, hypo-echoic, irregularly bordered mass with internal echoes or thick-walled cystic lesions on ultrasonography.[52] In certain cases, there may be fistula formation and thickening of Cooper's ligaments and subcutaneous tissues [52] (see figures 3 b, c, and d) which illustrate the ultrasound scan findings of a woman who had tuberculosis of the breast).

Computed tomography scan

In doubtful cases computed tomography scanning may be useful for the differentiation of primary and secondary lesions by detecting continuity with the thoracic wall or pleura, and associated lesions of the lungs. [33]

Magnetic Resonance Imaging

Magnetic Resonance Imaging may reveal parenchymal asymmetry with enhancement, micro-abscesses, and peripherally enhanced masses. [52]

Chest X-ray

In a number of cases chest X-ray may show evidence of tuberculosis of the breast (see figures 4 a and b for example) which illustrate evidence of tuberculosis of the lung in a patient with tuberculosis of the breast

Treatment

Treatment of tuberculosis of the breast is by means of antibiotics; [53] however, excision of the mass may also be necessary [54]. The treatment of tuberculosis of the breast with standard anti-tuberculosis therapy for 6 months usually results in good clinical response. [11] [52] [55] The regimen consists of a 2 month intensive phase (isoniazid, rifampicin, pyrazinamide, and ethambutol) followed by a 4 month continuation phase (isoniazid and rifampicin) [11]. Nevertheless, there are no specific available guidelines for chemotherapy of tuberculosis of the breast, and the therapy generally follows guidelines that are used for pulmonary tuberculosis. Most series have reported a success rate of medical therapy to be approximates 95% with 6 months of anti-tubercular therapy (2 months of Isoniazid, Rifampicin, Pyrazinamide, and Ethambutol / 4 months of Isoniazid and Rifampicin). [18], [56]. Other authors favor the 9-month regimen

(2 months of Isoniazid, Rifampicin, Pyrazinamide, and Ethambutol / 7 months of Isoniazid and Rifampicin) in view of lower relapse rate in general. Infection with multidrug-resistant tuberculosis (MDR) has been reported. Other authors have utilized therapy with a combination of first-line and second-line drugs which include kanamycin, ofloxacin, ethionamide, para-amino salicylic acid (PAS), pyrazinamide, and isoniazid. [57]

Surgical intervention is reserved for draining cold abscesses or excision of residual lumps. Surgical intervention was required in up to 14% of the patients in some reported case series, as a result of lack of response to chemotherapy or large painful ulcerative lesions involving the entire breast.[30] [51] Drainage of cold abscess in the axilla and breast to prevent sinus formation is mandatory. Axillary dissection may be required in patients with large ulcerated nodes [40]. Simple mastectomy is rarely needed nowadays and is reserved for patients with extensive disease comprising large painful ulcerated masses involving the entire breast and drainage of axillary lymph nodes. [40]

Discussion and miscellaneous narrations from reported cases

Marinopoulos et al. [58] reported an 80-year-old Caucasian female who underwent left breast lumpectomy and frozen section biopsy of the suspicious lump. Histopathological evaluation of the mammary gland revealed epithelioid abscesses with Langhans' giant cells and central caseous necrosis. The same histopathology was present in two out of seven excised axillary lymph nodes. Ziehl-Neelsen staining detected *Mycobacterium tuberculosis*, which gave the diagnosis of tuberculosis of the breast. She was treated with oral anti-tuberculosis therapy for 6 months postoperatively. No active breast or pulmonary disease was present one year after surgery in chest computerized tomography scan.

Peiris et al [59] reported a case of a 57-year-old female from Ghana who was found to have tuberculosis of the right breast masquerading as a fungating breast cancer. On initial presentation to the local breast unit in her home country, this was presumed to be breast cancer and was treated empirically with chemotherapy. Subsequent core biopsy had shown this to be a caseating granuloma in keeping with Tuberculosis infection. She was commenced on anti-tuberculosis treatment; Rifampicin 600mg, Isoniazid 300mg, Pyrazinamide 2g and Ethambutol 900mg daily. After she had

received this anti-tuberculosis regimen for two months, the skin and soft tissue infection in her right breast resolved completely. Peiris et al. [59] stated that:

- The 'triple assessment' of any breast lump is a well-established process to aid in the effective diagnosis of breast cancer.
- It is only after having assessed a patient clinically, imaging the lump appropriately and subjecting it to cytological or histological analysis that one can confidently diagnose or exclude breast cancer.
- Furthermore, in the era of endocrine treatment of breast cancer, characteristics of tumour biology can also be learned this way.
- Failure to achieve histopathological diagnosis and 'presumptive diagnosis' can lead to the mismanagement of potentially life threatening conditions and amounts to medical negligence.

Kao et al. [60] reported a Chinese woman who was admitted because of fever with chills and a mass in the upper quadrant of her left breast. She had suffered from a left-sided mastitis that had been incised and drained at another institution prior to her presentation. An echo-guided core needle aspiration biopsy of her left breast was also performed which revealed a mastitis with granulation tissue. A core needle biopsy tissue of her left breast was sent for a PCR test for *M. tuberculosis* which revealed the presence of *Mycobacterium tuberculosis* complex DNA. Kao et al [60] stated that their final diagnosis depended upon histopathological tissue findings and on the molecular detection of *Mycobacterium tuberculosis* and that their patient was then treated with anti-tubercular medication after her PCR results were made available. After undergoing four months of anti-tubercular treatment, the patient's left breast mass had gradually reduced, but a new small mass appeared from the medial side of the initial mass. Excisional biopsy was done which revealed the presence of chronic granulomatous inflammation composed of epithelioid cells with Langhans giant cells, as well as small foci of necrosis. Although acid-fast stain and culture showed no tubercle bacilli, her anti-tubercular therapy was continued. Her left breast mass gradually became smaller and then regressed. She was treated for 18 months without any further complication. She had been regularly followed up for another 18 months and no evidence of recurrence of her disease was noted.

De Sousa and Patil [61] reported a 46-years-old HIV negative woman who presented with a lump in her left breast. She had completed 6 cycles of palliative Cisplatin chemotherapy and radiotherapy for stage IV carcinoma of the maxilla two months earlier. She was found on examination to have an ulcer on the left breast in the upper inner quadrant, with purulent discharge and nipple retraction towards the ulcer. She underwent simple toilet mastectomy. Histological examination of the specimen was reported as showing chronic granulomatous mastitis with the presence of macrophages and Langhan giant cells. Periodic Acid-Schiff (PAS) and Gomori methenamine silver (GMS) staining of blocks of breast specimen were negative. Gram stain and Ziehl-Neelson stain were negative. She was diagnosed as having granulomatous mastitis and she was discharged on a course of cephalosporin. At four weeks following her operation she re-presented with a discharging sinus at the same site of the previous ulcer. She underwent local excision of the sinus. As a result of her profile, clinical features and non-response to antibiotic treatment, she was started on a six month course of four-drug anti-tuberculosis therapy (Isoniazid, Rifampicin, Ethambutol, and Pyrazinamide). After completion of the course of treatment, there was no evidence of a palpable mass and the wound had completely healed.

Sriram et al [34] reported a 34-year old HIV negative woman who presented with an abscess in her right breast. She had migrated to Australia from Bangladesh 6 years earlier. She had a firm mass in the upper quadrant of her right breast. She had ultrasound scan of the right breast lump which showed a diffuse hypo-echoic abnormality in the upper central aspect. She had mammogram which showed increased density and coarsened trabeculation. She underwent excision biopsy of the breast mass and histological examination of the specimen showed granulomatous inflammation in a mixed inflammatory cell background consisting of lymphocytes, plasma cells and polymorphs. Gram stain, Z-N stain, PAS-D stain were negative but bacteriological cultures grew *Corynebacterium kroppenstedtii*. She was treated with doxycycline for suspected granulomatous mastitis abscess. During her six weeks course of antibiotic therapy she developed sinus formation and discharge of purulent material from the breast. In view of the patient profile, histological findings and non-clinical response to antibiotic therapy, *Mycobacterium tuberculosis* was considered the most likely causative pathogen for the

breast abscess. Standard 6-month anti tuberculosis therapy was started with good clinical response. After she had completed two months of anti-tuberculosis therapy, there was no evidence of palpable breast mass. She had mammogram and ultra-sound scan which confirmed resolution of the mass lesion with residual scar tissue only. Two years after she had completed her anti-tuberculosis treatment she remained asymptomatic with no recurrence of abscess.

Wani et al. [62] reported a 21-year-old female from hilly area of Kashmir, who presented with discharge of pus from two openings on her right breast for a period of 6 years. She had already taken anti-tuberculosis therapy (ATT) thrice but had defaulted and she was reluctant to have further anti-tuberculosis therapy (ATT). There was no palpable swelling. Her chest X-ray revealed an osteolytic lesion in the anterior part of her fifth rib. She had computed tomography scan of chest as well as ultrasound scan which revealed only two sinus tracts in the breast tissue and a necrosed rib. The purulent aspirate was sterile for tubercle bacilli. She underwent excision of the fibrous tract and resection of the involved rib. Histological examination of the specimen revealed chronic inflammatory cell infiltrate, with areas of caseous necrosis, and giant cells. She had anti-tuberculosis therapy (ATT) for 9 months. She did not develop any recurrence over two years of follow-up.

Sen et al [32] reported 3 cases of tuberculosis of the breast in a 26-year-old female, a 30-year-old female and a 43 year-old woman who presented with painful swelling / lump in their breasts. Their tuberculin skin test results (Mantoux) were 16, 13 and 14 mm for cases 1, 2 and 3, respectively. Their sputum smears and discharge materials from the breast were found to be negative for acid-fast bacilli (AFB), both in culture and by PCR. They had both trucut and fine needle biopsies of their breast lesions. Pathological examination of the specimens revealed chronic granulomatous inflammation with areas of central necrosis, epithelioid granulomas with Langhans giant cells and lymphohistocytic aggregates suggestive of tuberculosis. The patients were all diagnosed as having tuberculosis of the breast. They were treated with anti-tuberculosis drugs for 6 months. With treatment, their breast lesions and tenderness steadily improved. Cures were obtained for all patients at the end of the sixth month period.

Alzaraa and Dalal [63] reported a 47-years-old Asian lady who presented with a rapidly increasing lump in the right breast and a palpable lymph node in her right axilla. She had mammogram which showed asymmetrically increased density in the right retro-areolar area and foci of fine calcification in both breasts. She also had ultrasound scan of the right breast which showed widespread hypo-dense irregular areas with some distal shadowing, which raised the suspicion of infiltrating ductal carcinoma and a lymph node with some cortical thickening at its distal pole. A tru-cut biopsy confirmed an invasive ductal carcinoma of no specific type along with evidence of non-necrotising granulomatous inflammation containing multinucleated Langhans type giant cells. Subsequent Ziehl-Neelsen staining for acid-fast bacilli showed multiple bacilli within macrophages, confirming a tuberculous aetiology. She underwent a right mastectomy with axillary node sampling and histological examination of this showed multifocal grade-II invasive ductal cell carcinoma. There was granulomatous inflammation. The TNM classification was pT3, pN3a, pMx. Special stains for acid fast bacilli were negative in this specimen. The patient received adjuvant eight courses of chemotherapy, and a course of radiotherapy (40 Gy in 15 Fractions). Subsequently, she had wide spread metastases with pleural and pericardial effusion which were drained. She was commenced on weekly Paclitaxel with three weekly Herceptin. She died before finishing the treatment. Alzaraa and Dalal [63] stated that:

The coexistence of carcinoma and tuberculosis (TB) of the breast and the axillary lymph nodes is rare and this was first reported by Pilliet and Piatot in 1897 [64] [65] [66]

Tuberculous mastitis (TM) is rare even in countries where tuberculosis is still common, accounting for only 0.1% of all cases [12] [64]. This is probably due to increased breast tissue resistance to the survival and multiplication of Mycobacterium bacilli, anti-tubercular treatment, and under-diagnosis of TM [12]

Bani-Hani et al. [12] believed that immigration from endemic areas, and the increasing prevalence of immunosuppressive disorders, including HIV infection, might be responsible for increasing the incidence of TM in Western countries in the future. Therefore, a high index of suspicion might be justified in immigrants from regions with a high prevalence of tuberculosis, for example, or atypical clinical or radiological presentations. The

breast can be involved by a penetrating wound of the skin of the breast; the lactiferous ducts via the nipple; direct extension from the lungs and the chest wall; the blood stream and the lymphatics [65]

It is generally believed that tuberculous infection of the breast is usually secondary to a pre-existing tuberculous focus located elsewhere in the body. Such a pre-existing focus could be of pulmonary origin or could be a lymph node within the para-tracheal, internal mammary, or axillary nodal basin [67]. The clinical situations that arise are the presence of carcinoma and tuberculous mastitis, carcinoma in the breast with axillary tuberculous adenitis or both [65]. There does not appear to be a causal link between mammary tuberculosis and breast cancer, and there is no evidence that TB is carcinogenic at any site [68].

The simultaneous occurrence of carcinoma and tuberculosis can lead to many problems regarding diagnosis and treatment as there are no pathognomonic symptoms or signs to distinguish breast tuberculosis from breast cancer, especially if the upper outer quadrant is involved [12] [65] [66].

An isolated breast mass without an associated sinus tract can commonly mimic the presentation of breast cancer, since the clinically palpable breast mass is usually firm, ill-defined, irregular, and can be associated with fixation to the skin [67]. The radiological features of tuberculous mastitis (TM) are non-specific, mimicking those of many diseases including breast cancer. Ultrasound scan usually reveals homogenous, irregular hypo-echoic lesions with focal posterior shadowing, or multiple circumscribed heterogenous hypo-echoic lesions associated with a large mass [69]

A unique finding strongly suggestive of TM is the presence of a dense sinus tract connecting an ill-defined breast mass to localised skin thickening and bulge [12]. Most decisions in the management of breast cancer are taken based on TNM staging of the tumours. This can lead to overestimation of the tumour size, therefore, these patients lose the opportunity for breast conservation due to this [65]. The key to proper treatment is biopsy of the lesion [70]. In cases where the breast cancer is clinically operable, radical mastectomy is indicated, followed by postoperative anti-tuberculous chemotherapy for 18 months, and if the cancer is incurable palliative measures combined with anti-tuberculous drugs are indicated. [70]

Da Silva et al. [31] in 2009 reported their retrospective analysis of 20 women with tuberculosis of the breast who had received treatment in their hospital between 1994 and 2007. They analysed the clinical presentation of the disease, the diagnosis and the response to specific treatment. Da Silva et al. [31] reported that:

Most of the patients were of reproductive age, with the disease affecting the right breast in eleven patients (55%) and the left breast in nine patients (45%).

Palpable nodules were present in five patients (25%) and fistulae in 15 (75%).

The mean time between onset of symptoms and diagnosis was 7.7 months (range 3–12 months). Skin testing with purified protein derivative of tuberculin was strongly reactive in all patients, six (30%) of whom were breastfeeding. Diagnosis was confirmed by histopathology and all patients were satisfactorily treated with a combination of rifampicin, isoniazid and pyrazinamide. In their study, tuberculosis of the breast presented predominantly as breast abscesses and fistulae and responded satisfactorily to treatment with anti-TB drugs.

Summary

Tuberculosis of the breast is an extremely rare disease. It was first described by Sir Astley Cooper in 1829 as, "scrofulous swelling in the bosom of young women" TB of the breast can be primary, which is extremely rare. Secondary TB of the breast co-exists with TB elsewhere in the body. Typically the patient is a young woman with a fluctuant breast abscess or a firm mass, which is a poorly defined mass associated with skin or nipple retraction, suggestive of carcinoma. Purulent discharge from the nipple is common. Fistulous tracts or discharging sinus may occur. The disease is often diagnosed as a breast abscess or breast cancer. Mammography or ultrasonography of the breast, are unreliable. Diagnosis can be achieved by demonstration of AFB in the breast tissue by Ziehl-Neilson stain or culture. However, the bacilli are isolated in only 25% of cases therefore demonstration of caseating granulomas from the breast tissue and involved lymph nodes is usually sufficient for the diagnosis. Figures 3 a, b, c, and d and figures 4 a and b illustrate radiographic images and ultrasound scan images of a woman who had tuberculosis of the breast that was encountered by one of the authors.

Conclusions

Tuberculosis of the breast is not common even in countries where the incidence of pulmonary and extra-pulmonary tuberculosis is high.

The diagnosis of tuberculosis of the breast can pose a diagnostic problem on radiological and microbiological investigations hence a high index of suspicion is required.

The disease is often diagnosed as a breast abscess or breast cancer. Mammography or ultrasonography of the breast, are not always reliable. The diagnosis can be achieved by demonstration of AFB in the breast tissue by Ziehl-Neilson stain or culture but not in all cases.

The incorporation of a highly sensitive technique like PCR may be helpful in the establishment of the usefulness of such technology and can aid in confirming the diagnosis early.

The disease is curable with anti-tubercular drugs, but surgery may rarely be required.

Conflict of interest: Authors declare no conflict of interest.

Acknowledgements: To Dr Nat Pernick and Pathology Outlines.com for granting us permission to reproduce figures from their website. To The Editorial staff of World Journal of Surgical Oncology and Bio Med Central whose copy right and licence agreement states that any one is free to: Share – copy and distribute the material in any medium or format. Adapt – remix, transform and build upon the material. This information is available at: <http://www.biomedcentral.com/authors/license>. The authors are grateful to World journal of Surgical Oncology and Bio Med Central for making their figures available to be reproduced with acknowledgement of the source.

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