



A case report of coexisting breast cancer with peritoneal, cutaneous tuberculosis, and potential Pott's disease: therapeutic and diagnostic challenges

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Introduction: Breast cancer affects one in eight women during their lifetime; it may coincide with other diseases due to its high prevalence. Different pathologies that occur simultaneously with breast cancer, or later during its course, lead to multiple interactions with cancer and have a significant impact on its management.

Presentation of case: A 58-year-old Syrian female was admitted to our hospital for complaint of abdominal distension. Following complete examination, obtained biopsies confirmed the diagnosis of peritoneal tuberculosis. At a subsequent time, she suffered back pain and the computed tomography showed vertebral lesion with breast mass that was diagnosed as invasive lobular carcinoma (ILC) of the left breast. Vertebral lesion that appeared on radiologic assessment was diagnosed as cancer metastasis. However, the interaction of this metastasis with the proposed management diverted the attention towards its non-cancerous entity. Five months after completing the chemotherapy, biopsies revealed the recurrence of triple-negative (ER – , PR – , HER2 – neu –) ILC of the breast. Ultimately, the patient was followed up for an overall duration of 4 years.

Discussion: Latent tuberculosis infections may be activated by chemotherapy regimens that suppress immunity. Therefore, initial management of tuberculous infection is preferred when it coexists with cancer.

Conclusion: Breast cancer is common and may co-present with other diseases, which, in some cases, produce mimicking lesions that alter its diagnosis. Pott's disease, albeit a rare entity, has shown a resurgence in developed countries and should be considered in the differential diagnosis of vertebral lesions in patients with breast cancer.

Keywords: breast cancer, extrapulmonary tuberculosis, invasive lobular carcinoma, Pott's disease, tuberculosis

Introduction

Breast cancer remains a predominant public health concern with an estimated 2.3 million incident cases in 2020. It also has exceeded lung cancer as the most diagnosed cancer and is the leading cause of cancer mortality in females^[1]. The disease disproportionately affects different populations due to differences in early diagnosis, management, and other health disparities^[2].

Tuberculosis (TB) is generally caused by a bacterium called *Mycobacterium tuberculosis*. The incidence of this disease has

HIGHLIGHTS

- Tuberculosis, including its extrapulmonary form, has shown a resurgence in many developed countries.
- Preferably, anti-tuberculous treatment should be administered prior to chemotherapy in cases of tuberculosis and cancer coexistence.
- The co-occurrence of diseases that coincide with breast cancer may produce imitative lesions that complicate its diagnosis, posing a challenging case for medical professionals.

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shown a new resurgence in developed countries, this re-emergence was attributed to immigration from countries where the disease is endemic^[3]. The most common type is pulmonary tuberculosis (PTB) whereas joint and bone tuberculosis, a subtype of extrapulmonary tuberculosis (EPTB), is extremely rare and constitutes only around 2% of total TB cases^[4].

The double coexistence of TB and cancer in one breast is infrequently reported and comprises a challenge in terms of treatment and diagnosis^[5]. Few previous literatures reported the coexistence of breast cancer with tuberculous mastitis^[6], breast cancer with tuberculous lymphadenitis^[5,7], or both^[5,6]. Although neither breast cancer nor tuberculosis are rare diseases, the association between breast cancer and tuberculous spondylitis (Pott's disease) is not previously reported. Furthermore, there is a substantial need in the clinical practice to understand how these

pathologies interact and thus affect the patient management and prognosis. Herein, we report a case of quadruple coexistence of breast cutaneous tuberculosis, peritoneal tuberculosis, Pott's disease and breast carcinoma in one patient. The case has been reported in accordance with the SCARE guidelines^[8].

Presentation of case

A 58-year-old middle eastern female was examined in the general surgery clinic in February 2018 for complaint of abdominal distension. The patient history was unremarkable. Additionally, physical examination revealed shifting dullness of 4 months' duration. Applied ultrasound (US) of the abdomen showed single asymptomatic cholecystic stone, in addition to accumulation of 500 ml ascitic fluid in the abdomen. Other intrabdominal structures were normal by US evaluation. Laboratory findings were unremarkable except for high erythrocyte sedimentation rate that measured 75 mm/h and c-reactive protein of 65 mg/l. Depending on the US and undistinguished patient history, a laparoscopic exploratory surgery was indicated to rule out malignancy and ascertain biopsies. Grossly, the operative field showed diffuse miliary lesions in the abdomen, subsequently, ascitic fluid sample, omental, and peritoneal biopsies were obtained. The biopsies showed necrotizing granulomatous inflammation containing epithelioid cells and Langhans cells (Fig. 1). The ascitic fluid contained lymphoid infiltrates, both biopsies and ascitic fluid were negative for neoplastic cells.

The patient had no pulmonary symptoms and subsequent work up to rule out PTB included chest X-ray that was normal, and Ziehl-Neelsen stained smear of bronchial lavage that tested negative for mycobacterial cells. Classic manifestations of spinal tuberculosis such as back pain or kyphosis were not primarily present. The patient was commenced on an anti-tuberculosis regimen, which included isoniazid, rifampicin, pyrazinamide, and ethambutol.

Four months later, the patient suffered from moderate upper back pain and chest paraesthesia, her computed tomography (CT) scan showed destruction of the fifth thoracic vertebra (Fig. 2).

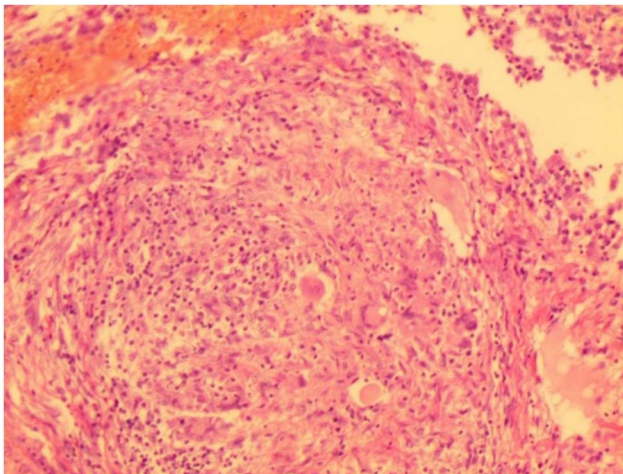


Figure 1. Histological findings of the peritoneal and omental specimens. numerous aggregates of chronic inflammatory cell infiltrate with epithelioid and Langhans cells surrounding small foci of necrosis, consistent with peritoneal tuberculosis.

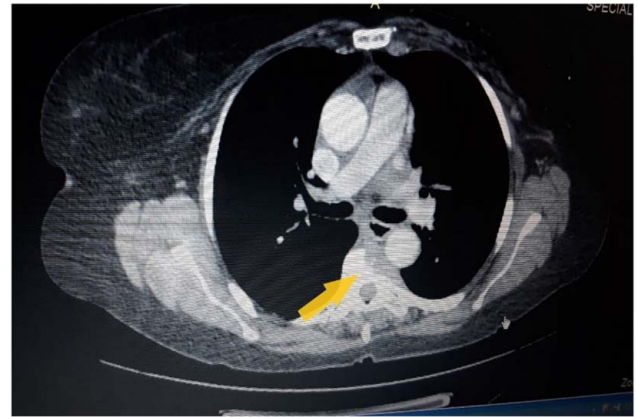


Figure 2. Findings from computed tomography. Computed tomography scan of the fifth thoracic vertebrae shows vertebral destruction with adjacent tissue formation (arrow).

Coincidentally, the CT also showed nodular formation in the left breast and the subsequent clinical examination of the breast revealed a firm ill-defined 3 × 2 cm mass with no abnormal skin appearance or nipple discharge. An excisional biopsy of the mass was carried out and evidenced a diagnosis of invasive lobular carcinoma (ILC) (Fig. 3) and mild skin thickening with granulomatous inflammation (cutaneous tuberculosis).

Immunohistochemistry of the breast carcinoma identified positive HER2 receptors and positive hormone receptors (HER2⁺, ER⁺, PR⁺). Wherefore, the patient underwent complete mastectomy of the left breast and axillary lymph nodes. Metastases of ILC were detected in 3 out of 15 resected lymph nodes (Grade II–stage pT1, pN1, pMx). The patient was started on chemotherapy lasting for 16 months, during which she had 29 sessions of chemotherapy. She also went through radiation therapy of the vertebral lesion. The treatment protocol included doxorubicin, cyclophosphamide, paclitaxel and trastuzumab. No detectable recurrences were noted by continual MRI and CT scan with contrast over the course of treatment.

Five months after completion of the chemotherapy course, the patient was followed up by ⁹⁹Tc-MDP bone scan that showed increased uptake in the mandible of the sternum and the anterior end of the first left rib, consecutive CT showed abnormal growth in the anterior mediastinum adjacent to the aortic arch and sternum. The manubrial and sternal biopsies revealed the recurrence of triple-negative (ER⁻, PR⁻, HER2⁻ neu) ILC restarting the chemotherapy (Fig. 4).

The patient was last seen in December, 2021, and was responding well to chemotherapy on radiologic evaluation. after an overall follow-up duration of 4 years at our centre, she changed her place of residence and pursued the therapy in another hospital. A timeline of the patient's case can be seen in Fig. 5.

Discussion

Overview

Bone tuberculosis is an ancient disease dating back to the Iron age and was also detected in Egyptian mummies^[4]. Multiple risk groups associate with a higher incidence of this disease, such as AIDS patients, transplant recipients, and immigrants from

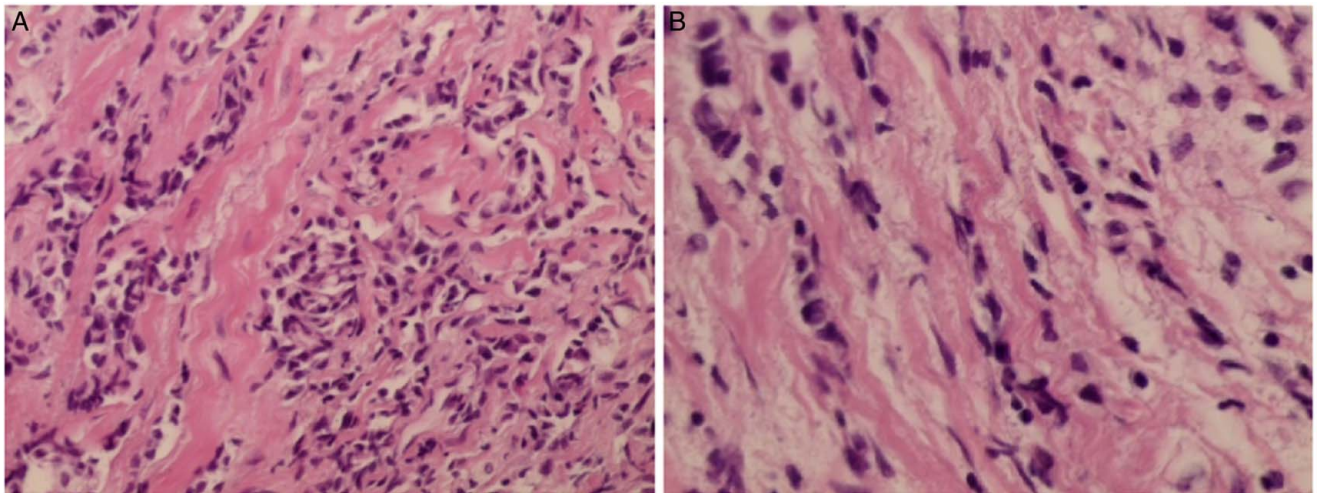


Figure 3. Pathological examination of the excisional biopsy of the breast mass. Anaplastic small and medium-sized cells occurring predominantly in lobular formation with hyperchromatic nuclei, basophilic cytoplasm and occasional bizarre mitotic figures surrounded by desmoplastic reaction of the stroma. Low magnification (A). High magnification (B).

populations where HIV or TB infections are endemic^[9,10]. This risk group classification aids in early disease suspicion and better management plans.

Diagnostic challenges

The role of different diagnostic investigations in confirming a diagnosis of tuberculous spondylitis is limited. TB is usually described as a paucibacillary disease, explaining the low sensitivity of direct detecting of mycobacterium by culture or Ziehl-Neelsen staining in only 25% of cases^[9,11]. The published literature reported negativity of TB tests despite presence of Pott's disease (negative acid-fast bacilli smear^[9,12,13], negative culture and polymerase chain reaction^[13]) and the diagnosis of TB was made despite those findings with marked improvement after therapy^[9,13].



Figure 4. Findings from computed tomography. Computed tomography scan at the level of sternum mandible shows the cancerous lesion in the superior and anterior mediastinum with lateral pleural thickening at the left side (arrow).

In our case, the vertebral lesion was primarily thought to be metastatic from breast cancer, however, multiple observations during the follow-up period raised the suspicion of spinal tuberculosis. First, the vertebral lesion was solitary and no other distant metastases were detected despite cancer recurrence through 4 years of follow-up. Second, the structure of the lesion remained constant without changes or further deterioration by chemotherapy during follow-up. Third, radiation therapy of the vertebra did not result in any changes in the lesion dimensions or symptoms relief.

The follow-up by ^{99m}Tc-MDP bone scintigraphy showed normal uptake in the vertebral lesion despite cancer recurrence in the primary site of diagnosis that was indicated by higher intake. Normal or low uptake in bone scintigraphy could be seen in osteolytic metastases or healed inflammation processes, in such cases, PET scan is more sensitive than gamma camera in detecting osteolytic metastases because it depends on tissue metabolism. PET scan was not accessible in our under-resourced settings, however, lesion responsiveness to anti-tuberculous treatment (ATT) and refractoriness towards chemotherapy and radiation supports its tuberculous nature.

Therapeutic challenges

The chronological order of treatment of tuberculosis and breast cancer upon simultaneous diagnosis remains controversial. Chemotherapy protocols that contribute to an immunocompromised status^[14] may activate latent TB infections or worsen the symptomatic infections^[7]. Tulasi *et al.*^[5] argue that treatment should be concomitant for both diseases. By contrast, Akbulut and colleagues suggested that ATT should be started first in cases of TB accompanying malignant entities that require chemotherapy, and ATT should last for at least 3 weeks prior to chemotherapy and continues along with chemotherapy for an overall duration of 9 months. This is justified by the immunocompromising effects of cancer therapy^[7].

In our case, there was a temporal window between TB and cancer diagnoses, and the patient had already been started on

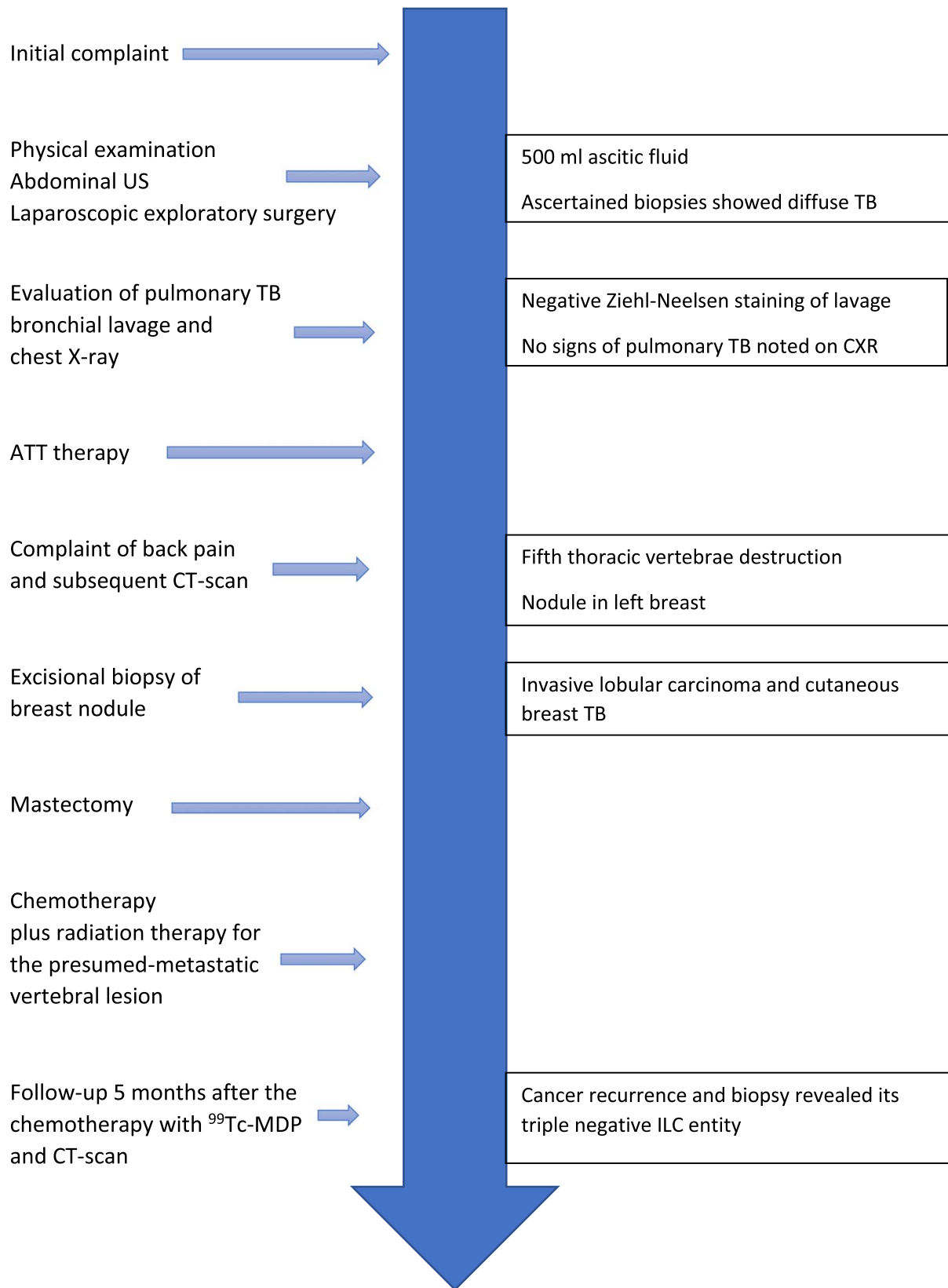


Figure 5. Disease course of a 58-year-old middle-eastern female with systemic tuberculosis (TB) and breast cancer starting at the initial complaint. ATT, anti-tuberculous treatment; CXR, Chest X-Ray; CT, computed tomography; ILC, invasive lobular carcinoma; US, ultrasound.

ATT when the cancer was diagnosed. In cases with simultaneous diagnosis of TB and cancer, we suggest that ATT should be started prior to cancer treatment, giving the fact that tuberculous infection (e.g., lymph nodes tuberculosis or tuberculous osteomyelitis) may lead to an overestimation of the cancer stage^[5], and prognosis^[7]. Additionally, some chemotherapy drugs that negatively affect the immune system may lead to deterioration in TB infections and compromise the efficacy of ATT treatment.

The recommended treatment of EPTB is usually similar to PTB and should minimally last for 6 months. However, due to the difficulties in confirming disease elimination by microbiologic assessment, experts often prolong the treatment for 12 months^[11]. Radiological assertion of disease regression is also difficult and posttreatment sequelae develop in around 25% of cases^[15]. The protocol of tuberculosis treatment usually includes isoniazid, rifampicin, pyrazinamide and ethambutol for the first 2 months, and isoniazid and rifampicin for 6 months.

Conclusion

First, Pott's disease should not be forgotten as a differential diagnosis in cancer-mimicking lesions, early suspicion of this disease is crucial for the right diagnosis, as diagnostic modalities may reveal negative results after initiating the treatment. Second, diagnosing this disease at early stages may alter the management of both tuberculosis and cancer and provides more favourable outcomes to the patient. Finally, in cases of late suspicion, a systematic approach to the history of treatment aids in establishing a therapeutic diagnosis.

Ethical approval

Ethical approval is not required for case reports according to the local institutional review board.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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Author contribution

B.H.: drafted the manuscript, collected and interpreted the patient data, critically revised and approved the final manuscript. Z.A.: evaluated the histopathological findings, revised and approved the final manuscript.

Conflicts of interest disclosure

The authors declare that they have no competing interests.

Research registration unique identifying number (UIN)

Not applicable.

Guarantor

Dr Zuheir Alshehabi.

Data availability statement

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Provenance and peer review

Not commissioned, externally peer-reviewed.

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