

Association of Metastasis and Axillary Lymph Node Tuberculosis in Breast Cancer: Clinical Case and Review of the Literature

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Abstract

The coexistence of tuberculosis with axillary lymph node metastases in breast carcinoma is rare. Axillary lymph node metastasis is the most important factor in the staging of breast carcinoma, and the number of axillary lymph nodes metastasizing changes the stage. Since tuberculosis also produces lymph node enlargement, this can mimic or complicate the staging of a malignant disease. Dual organ pathology can lead to interpretation difficulties and inappropriate treatment of tuberculosis as well as breast carcinoma. Additionally, fine needle aspiration cytology (FNAC) of such cases can be misleading if only one of the diseases is detected. We report two cases of infiltrating carcinoma of the nonspecific type of the breast in two women aged 35 and 55 where tuberculosis was found in the axillary lymph nodes in addition to metastases. As the present case led to the fortuitous discovery of tuberculosis with tumor metastasis, it reinforces the possibility of a coexisting lesion in the minds of pathologists, especially in areas endemic to tuberculosis.

Keywords

Breast Carcinoma, Tuberculosis, Lymph Node, Association

1. Introduction

The coexistence of breast cancer and tuberculosis is very rare and less reported in the literature [1] [2] [3] [4]. The occurrence of metastasis from mammary carcinoma to a tuberculous axillary lymph node is an even more unusual association, with only a limited number of cases in the literature [5] [6]. The concomitant presence of two diseases in an organ is almost always a diagnostic and

therapeutic challenge [6] [7]. Tuberculosis (TB), cannot be ignored even if it is considered a coexisting lesion, especially in endemic areas like Mali. It is the histological examination which made it possible to make the differential diagnosis. We report two rare cases of invasive mammary carcinoma of the nonspecific type with metastatic ipsilateral lymph node associated with lymph node tuberculosis discovered incidentally during histological examination.

2. Summary of Case 1

A 35-year-old woman presented with a left breast mass in the upper outer quadrant for five months, without a personal medical and surgical history. G3P1A2V1.

On examination, a firm, hard, irregular mass, mobile in relation to the two planes, indole, measuring 4 cm was palpable in the upper outer quadrant of the left breast. A left axillary node was also palpable ranging from 2 cm in diameter. No mass was detected in the contralateral breast and armpit. There was no cervical or inguinal lymphadenopathy.

Mammography coupled with breast ultrasound revealed multiple para-axillary nodular opacities and the upper-external quadrant, the largest of which measures 29 mm long axis and 25 mm thickening of the peri areolar skin coating (**Figure 1(a)** and **Figure 1(a)**).

The thoraco-abdomino-pelvic scanner revealed a left breast mass of 27 × 25 mm. Homolateral axillary lymphadenopathy measuring 25.6 mm, 11.5 mm and 14.6 mm in small diameter. No mediastinal lymphadenopathy, pleuropericardial effusion and large vessels or cardiac chambers. Absence of liver metastasis.

Routine hematologic and biochemical examinations, Brain CT, and cardiac ultrasound were within normal limits. The micro-biopsy carried out of the tumor made it possible to demonstrate an invasive carcinoma of the nonspecific type of grade II according to Scarff Bloom Richardson (SBR) of the left breast.

The diagnosis of invasive grade II non-specific type carcinoma with axillary metastasis was made by microbiopsy. A left mastectomy was performed with axillary dissection (**Figure 2(a)** and **Figure 2(b)**). The raw sample showed a firm to hard gray white mass in the upper outer quadrant. During axillary dissection, 13 lymph nodes were isolated. Histological examination confirmed the diagnosis of infiltrating nonspecific type III carcinoma according to Scarff Bloom Richardson (SBR) with localization of lymph nodes (6N+/13N) associated with caseo-follicular adenitis of tuberculous origin (5N+/13N). There were vascular emboli. The deep resection limit is healthy, classified as pT3N2aMx.

Microscopy shows 11 mitosis/10 fields at magnification 400. SBR grade: differentiation: 2, pleomorphism: 3, mitoses: 2, total = 7 corresponding to grade II.

Immunohistochemical study carried out on dewaxed sections by immunoperoxidase technique coupled to streptavidin-biotin and revealed with the DAB substrate:

- Estrogen receptors (monoclonal, SP clone) ROCHE: negative with positive internal control



Figure 1. Left breast mammogram. (a) Face; (b) Profile.

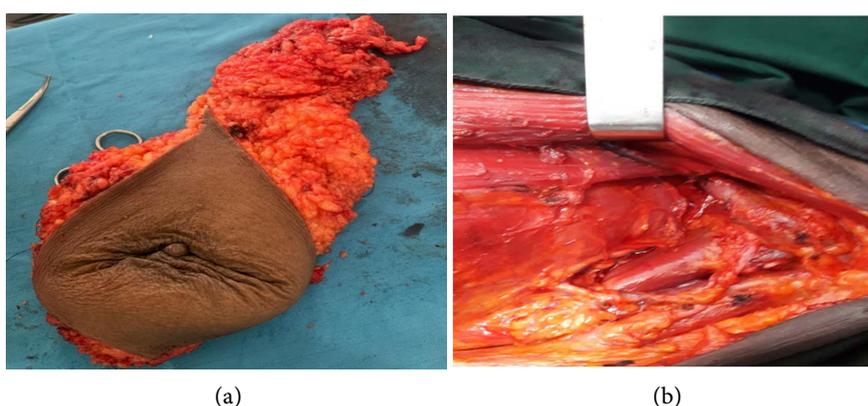


Figure 2. (a) The part of total mastectomy; (b) After axillary dissection with lymph node dissection.

- Progesterone receptors (monoclonal, clone 1E2) ROCHE: negative with positive internal control
- Anti HER2/neu (monoclonal, clone 4B5, rabbit) ROCHE: negative, score 0 (with positive external control)

It is a non-specific infiltrating carcinoma stage T3N2aMx, triple negative.

The patient received an anti-tuberculosis treatment combining Rifampicin (H), Isoniazid (I), Pyrazinamide (Z), Ethambutol (E) over 2 months and on the other hand a combination of Rifampicin and Isoniazid over 4 months (2RHZE/4RH). Antitumor chemotherapy used a protocol combining 4 AC60 + 3 Taxotere (A = Adriblastine[®], C = Cyclophosphamide). Radiation therapy of 35 gray was performed.

3. Summary of Case 2

A 55-year-old woman presented with a lump in her left breast in the lower outer quadrant for ten months, with no known medical or surgical history, having had two pregnancies and two abortions.

On examination, a firm, hard, irregular mass, mobile in relation to the two planes, indole, measuring 8 cm was palpable in the lower quadrant of the left

breast. A left axillary node was also palpable 1 cm in diameter. No mass was detected in the contralateral breast and armpit. There was no cervical or inguinal lymphadenopathy.

Mammography coupled with breast ultrasound revealed nodular opacity of the lower inner quadrant, the largest of which is 6 mm long, thickening of the skin coating.

The thoraco-abdomino-pelvic scanner revealed a scar lesion in the lower quadrant of the left breast. 8 mm homolateral axillary adenomegaly. 4 mm anterior right upper lobe micronodules. No mediastinal lymphadenopathy, pleuropericardial effusion and large vessels or chambers of the heart. Absence of liver metastasis.

Routine hematologic and biochemical examinations and cardiac ultrasound were within normal limits.

The diagnosis of invasive grade II non-specific type carcinoma with axillary metastasis was made by microbiopsy. And neoadjuvant chemotherapy was done. A left mastectomy was performed with axillary dissection (**Figure 3(a)** and **Figure 3(b)**). The raw sample measuring $23 \times 21 \times 4$ cm was covered by a flap, of whitish color. During axillary dissection, 8 lymph nodes were isolated. Histological examination revealed fibrosis strewn with residues of tumor casings in process of lysis with lymph node metastasis (1N+/8N) associated with caseo-follicular adenitis of tuberculous origin (4N+/8N). The presence of vascular embole and the limit of deep resection are healthy.

The microscopy is counted. SBR grade: differentiation: 2, proliferation made of tubes, layers of poly adenoids structures lined with atypical cells, numerous mitoses.

Immunohistochemical study carried out on dewaxed sections by immunoperoxidase technique coupled to streptavidin-biotin and revealed:

- Estrogen receptors absence of labeling of tumor cells with positive external control.
- Progesterone receptors absence of labeling of tumor cells with positive external control.
- HER2 absence of labeling of tumor cells with positive external control.
- Ki67: Mitotic index is 5%.

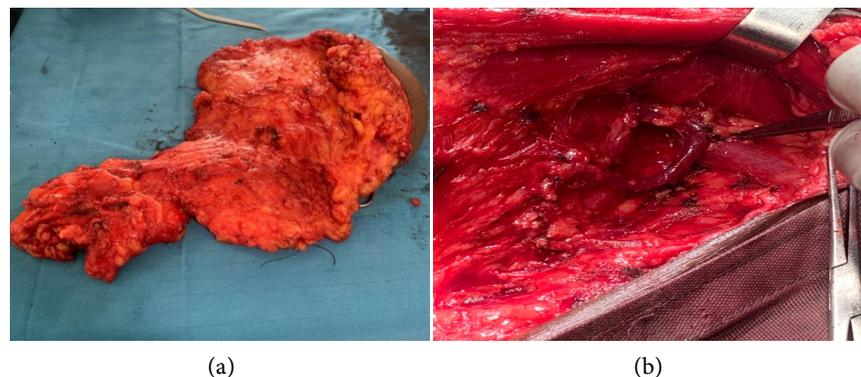


Figure 3. (a) The total mastectomy part; (b) After axillary dissection with lymph node dissection.

In total, invasive type nonspecific grade II carcinoma according to SBR, cTxN0M0, triple negative and Ki67 at 5%.

The patient received an anti-tuberculosis treatment combining Rifampicin (H), Isoniazid (I), Pyrazinamide (Z), Ethambutol (E) over 2 months and on the other hand a combination of Rifampicin and Isoniazid over 4 months (2RHZE/4 RH). Antitumor chemotherapy used a protocol combining 4 AC60 + 4 Taxotere (A = Adriblastine[®], C = Cyclophosphamide). Then 4 Capecitabine.

35 gray radiotherapy was performed.

Conclusion: This coexistence is rare, of accidental discovery and requires multidisciplinary management.

4. Discussion

Tuberculosis (TB) is a major public health problem because it is very common in developed countries and developing countries like Mali. Tuberculous lymphadenopathy is the most common form of extrapulmonary tuberculosis and affects the cervical lymph nodes, axillary or inguinal. Primary tuberculous axillary lymphadenopathy (after exclusion of clinical disease in other body) is extremely rare in adults. Tuberculous lymphadenitis isolated axillary can be explained either by retrograde spread of mediastinal lymph nodes, or by hematogenous spread of a subclinical home, not detected by routine tests. Another explanation for the co-occurrence of tuberculosis and metastasis could be activating the silent infection with *Mycobacterium tuberculosis* due to an immunocompromised condition in cancer patients [1] [8]. In our patients we think of a previously undetected tuberculosis count, clinical and paraclinical, because of their strong immunity. The development of cancer is an immunodeficient factor. The coexistence of breast cancer and tuberculosis is very rare and less reported in the literature. This coexistence raises difficulties in diagnostic and therapeutic management [2] [9]. The discovery was fortuitous as a result of pathological and immunohistochemical examinations. The first case was described in 1899 by Wharti, followed later by others. The prevalence is estimated at 19/10,000 according to the literature [6] [10]. Histological examination of lymph nodes removed revealed a non-specific invasive carcinoma associated adenitis caseo-follicular to tuberculosis. Histology was determined conventional prognostic factors, including the score of Nottingham (SBR grade II), the number of invaded lymph nodes relative to the total number of lymph nodes removed ($N+ = 16/7$) and the presence of vascular embolisms. Other prognostic and therapeutic factors are determined by immunohistochemistry with the dosage of estrogen receptors (RO) and progesterone (PR), HER2 oncoprotein. These elements have established a molecular classification of tumor luminal B TNBC (RO, RP, HER2) [11]. We conducted our patients histology, with node location (6N+/13N) associated adenitis caseo-follicular tuberculous (5N+/13N) associated with vascular emboli in a patient and lymph node metastasis (1N+/8N) associated adenitis caseo-follicular tuberculous (4N+/8N). There were vascular emboli. The elements

immunohistochemistry showed triple negative cancer.

Kaplan *et al.* [12], the concomitant presence of TB and malignancy has been reported most often in the follow—Hodgkin lymphoma sarcoma, leukemia and lung cancer. Rarely, it has been reported in colon cancer, uterus, bladder, breast and prostate.

There is no evidence that tuberculosis is carcinogenic at any place whatsoever [3] [13] [14]. There are no signs and symptoms pathognomic to distinguish breast tuberculosis of breast cancer, especially if the upper quadrant is reached. It is necessary to multiply further actions to demonstrate the carcinogenic effect of TB and the appropriate symptoms.

The coexistence of tuberculosis and carcinoma requires concomitant treatment of both diseases and counseling to patients to ensure adherence [14] [15] [16].

Patients underwent TB treatment associated with a chemotherapy regimen. TB protocol is based on multidrug therapy. There are five first-line drugs used by the National Program against Tuberculosis (NTP) of Mali: isoniazid (H), Rifampicin (R), streptomycin (S), ethambutol (E), pyrazinamide (Z) [17] [18]. The treatment consists of two phases. An initial phase of treatment or intensive phase includes four drugs that are ethambutol (E), rifampin (R), isoniazid (H) and pyrazinamide (Z). The advantage of this phase is that it is very effective in reducing the bacilli and drug resistance. It takes two or three months. The continuation phase is necessary in the patient's final recovery. It helps to prevent the recurrence of tuberculosis treatment discontinuation. He needed two medications over a period of four months.

The safety and adherence were good. They were regularly assessed using the Direct Observed Therapy Strategy (DOT). This strategy is recommended by WHO and consists of giving the drugs under control or to check at least 3 times a week if they are actually taken. Chemotherapy is used by adjuvant and involves the 3 AC + 3 docetaxel protocol. It is currently recommended to administer it before radiotherapy. Treatment usually lasts six months [8] [12] [15].

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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