

## **MAMMARY TUBERCULOSIS ABOUT A CASE AND REVIEW OF THE LITERATURE**

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### **SUMMARY**

Breast tuberculosis is a rare pathology, it ranks last among extra-pulmonary localizations but its incidence remains considerable since the resurgence of HIV infection. The profile of the woman carrying this disease is that of the young woman in period of reproductive activity, multiparous and of low socio-economic level. The most frequent form seems to be the primary form. The appearance of breast swelling is the most frequent mode of revelation and reason for consultation. Clinically, it is a single tumor, unilateral, firm, painless, irregular, mobile in both planes sitting in the outer quadrants +/- associated with ipsilateral axillary ADPs raising suspicion of carcinoma. General signs (fever, weight loss, sweating) are rarely found. On mammography, it appears in 3 forms: the nodular, diffuse, and sclerosing form. On ultrasound, it is most often a poorly delineated heterogeneous hypoechoic image with minimal posterior enhancement.

The diagnostic confirmation remains histological by the demonstration of an epithelioid-giganto-cellular granuloma with caseous necrosis. A favorable outcome under well-conducted anti-bacillary treatment for a sufficient duration; prevention remains very important and calls for BCG vaccination, treatment of all diagnosed cases.

**KEYWORDS:** Breasts; Koch's bacillus; Granulomatosis; Caseous necrosis; Anti-bacillary.

### **INTRODUCTION**

Breast tuberculosis is a rare form of tuberculosis extrapulmonary even in endemic countries; its frequency is 0.06-0.1% of all tuberculous localizations. It occurs mainly in young women in reproductive activity. Its diagnosis is difficult due to the multiplicity and non-specificity of

its clinical and radiological aspects, it is often taken for a cancerous lesion. Confirmation of tuberculous origin is based on isolation of BK or on histology. The treatment is mainly based on anti-tuberculosis drugs but sometimes surgical treatment is necessary. We report a clinical case diagnosed and treated at the obstetrics gynecology department of the Mohamed V Military Hospital in Rabat.

### **PATIENT AND COMPLIANCE**

This is a 35-year-old patient, single, nulliparous, with no notable pathological history, unfavorable socio-economic background, referred to our department for management of mastitis of the right breast with amenorrhea evolving for two months in a context of weight loss fever amounting to 6 kg in two months. On clinical examination; the right breast was enlarged with skin redness in the outer quadrants and under the nipple. Palpation revealed a rounded retroareolar mass of the right breast measuring 2cm long axis, firm consistency, regular contours. The lymph node areas were free. The remainder of the examination was unremarkable. Plasma B HCG assay was negative.

The mammography had shown: increased opacity involving the lower and outer quadrants of the right breast with diffuse cutaneous thickening.

The breast ultrasound revealed diffuse cutaneous thickening with the presence of retroareolar hypoechoic areas with a nodular formation involving the outer quadrants measuring 7x7 mm.

The study of the product the breast biopsy with tru-cut G 14 had shown, on a polymorphic inflammatory background, the presence of giganteo-cellular granulomas centered by caseous necrosis.

The tuberculin skin test was positive. The chest X-ray was normal.

The evolution under antibacillary treatment for six months was marked by clinical and radiological improvement with a follow-up of 48 years.



A- Right breast: Para and sub-areolar redness with skin thickening.

B- Mammography side view of the right breast: increased opacity affecting the lower quadrants.

C- Breast echography (7.5MHz probe): Retro areolar hypoechoic areas with diffuse cutaneous thickening.

## DISCUSSION

### Frequency

Breast tuberculosis is a pathology considered particularly rare, its frequency is estimated between 0.025% to 4.5% of all tumoral conditions of the breast. Since glandular tissue, such as the spleen and skeletal muscle, provide resistance to the survival and multiplication of the tubercle bacillus.<sup>[4,6]</sup>

It ranks last among extra-pulmonary tuberculous localizations, representing 0.06% of these.<sup>[4]</sup>

Breast tuberculosis is encountered in countries with high tuberculosis endemicity. For KHAIZ, out of a study of 215 cases, Asia comes first with 45.2% followed by black Africa 27.4%, North Africa 17.2%, Europe 16.2 % and finally America 4%.<sup>[1,3]</sup>

In Japan, during a 15-year period from 1982 to 1996, 28 cases of breast tuberculosis were reported.<sup>[4]</sup>

In Tunisia, over a period of 22 years from January 1980 to December 2002, the incidence of breast tuberculosis was 0.3% among the breast diseases collected at the Salah Azaiez Institute in Tunis.<sup>[1]</sup>

In Morocco, over a period of 8 years from 2001 to 2008, ZEKRI et al. Found an incidence of breast tuberculosis of 0.4% among the breast diseases collected in the obstetrics gynecology

department "A" of the Ibn Rochd hospital in Casablanca, which represents an incidence close to those noted in studies carried out in South Africa. North.<sup>[6]</sup>

### Age

Breast tuberculosis occurs in young women of childbearing age, it is rare before puberty and after menopause. This is explained by the physiological activity of the breast.<sup>[8]</sup>

The "Age" setting varies by region. Indeed, in regions with high tuberculosis endemicity, the disease seems to affect young women; on the other hand, in developed countries, it mainly affects elderly women. FRAISSE P and col noted in Africa an age of 34.7%.<sup>[9]</sup>

Breast tuberculosis mainly affects women in the period of genital activity. However, extreme ages are not spared: AMMAR F reported the case of a male infant aged 06 months<sup>[5]</sup>, and El BIAZE. M reported a case of breast tuberculosis in an 84-year-old woman.<sup>[7]</sup>

### Favoring factors

Tuberculous mastitis seems to be favored by a certain number of factors.

The menstrual cycle: it appears during the last days of the cycle, mastodynia, or the exacerbation of a preexisting pain, an increase in the volume of a possible tuberculoma or a fistulous flow which dries up with the end of the rules.<sup>[5]</sup> Zekri.H, et Col. reported a case in a 23-year-old woman whose evolution was cyclical for several months.<sup>[2]</sup>

Multiparity: breast tuberculosis is more common in multiparous women.<sup>[7]</sup>

Zekri.H,<sup>[2]</sup> found that, of the 215 cases studied, 2.4% of women were nulliparous, 4.7% were primigravidae.

Pregnancy and lactation remain the most favorable factors since the vascularization of the mammary gland is very rich during this period, which explains its susceptibility to tuberculosis.<sup>[2,9,3]</sup>

During lactation, the milk ducts are ecstatic, favoring canalicular contamination.<sup>[3]</sup>

In 1992, SHARMA N<sup>[3]</sup> found that breast tuberculosis coincided with pregnancy in 8% of cases and was found in breastfeeding women in 11%.

Immunosuppression: Mammary tuberculosis can be indicative of hitherto unrecognized seropositivity. Indeed, Hartstein<sup>[35]</sup> reported a case of AIDS revealed by breast tuberculosis.

### Ways of contamination

Before, it was thought that mammary tuberculosis occurred in confirmed tuberculosis patients and constituted a secondary localization to pleuro-pulmonary involvement in more than 50%.

Currently, it is considered that tuberculous mastitis generally presents as a primary and isolated attack, or on the contrary associated with other bacillary manifestations, especially lymph node, pulmonary, osteo-articular or genito-urinary.

There are five pathways of bacillary extension.

The lymphatic route: this is the most frequent route of contamination. The extension is carried out by retrograde or anterograde route from intrathoracic, cervical, supraclavicular or axillary adenopathies.<sup>[6,7]</sup>

### Clinical Diagnosis

It is always difficult because breast tuberculosis can simulate a large number of conditions, particularly in elderly women where breast cancer remains the main concern and also because of the lack of specificity of its clinical and radiological signs. Only histological evidence can guarantee a certain diagnosis.<sup>[1]</sup>

However, some clinical criteria seem useful to draw attention to a tuberculous etiology, namely:

- The existence of a recurrent breast abscess after ordinary antibiotic therapy and correct surgical drainage.
- Fistulized axillary adenopathy associated with a breast nodule.
- Rarely a breast fistula with intermittent discharge punctuated by the menstrual cycle.

**Risk factors:** the risk factors classically reported in the literature are: pregnancy, lactation, history of trauma or breast abscess and immunosuppression.

History of tuberculosis.

It is necessary to look in the antecedents for another tuberculous focus, in particular pulmonary, and the notion of tuberculous contagion. A history of pulmonary or extra-pulmonary tuberculosis was observed in 25% of the cases studied<sup>[4]</sup> and in 44.2%.<sup>[9]</sup> The latter found the notion of tuberculosis contagion in 2.3% of cases.

**Functional signs:** breast tuberculosis can have different modes of revelation.

Breast swelling: The patient may present for a breast nodule which represents the most frequent mode of revelation.

Premenstrual mastodynia can be observed.

Purulent or bloody discharge may be present. The evolution is towards ulceration with a flow of serous or brownish appearance punctuated by menstruation.

**Clinical examination:** the general state of the patients is generally preserved. In 20% of cases, there are general signs such as weight loss, fever, night sweats.<sup>[9]</sup> This in the absence of any other concomitant bacillary localization, particularly in the lungs, where the signs of tuberculous impregnation are usually found.

**Inspection:** at this stage, morphological changes in the breast are often found. But, the breast can be completely normal. The affected breast as a whole is slightly larger than the opposite breast and has collateral venous circulation. But it can be reduced in volume, especially in sclerotic forms. The nipple is usually little affected. It can be retracted, but it is a sign that remains non-specific because it is found in any chronic and infiltrating breast lesion. This retraction may appear long before the other signs. A crusty eczematous ulceration may also be found. The skin next to the breast is either normal or the site of an inflammatory process giving the appearance of a fistulising orange peel skin at the end of its evolution. But often, it is breast ulcers that appear. And finally, the chronic fistula, which is a rare aspect but a little more evocative, it can be breast with intermittent flow or lymph node with a large breast.

**Breast palpation:** It will also specify the local heat of the breast.

In the presence of a tumour, it is necessary to specify its characteristics, namely.

The shape: is often rounded in cases of tuberculosis.<sup>[1]</sup>

The size: is variable ranging from 01 to 10cm.<sup>[1]</sup>

The site: The tumor is frequently located in the upper outer quadrant of the breast, perhaps because of the proximity of the axillary lymph node areas. But the other quadrants can also be affected.<sup>[2,7]</sup> Indeed, El BIAZE. M<sup>[9]</sup> noted damage to the upper outer quadrant in 63% of cases; the other quadrants were affected in equal proportions. Breast tuberculosis is often unilateral, bilateral involvement is observed in 3% of cases; the boundaries are usually irregular.<sup>[2]</sup>; **firm or hard, sometimes** stony consistency simulating breast cancer.<sup>[2,3,4,9]</sup> The tumor is painless in 75% of cases; sometimes it is painful and can take on the appearance of a breast abscess or a frankly inflammatory mastitis. This aspect is seen in young women.<sup>[4, 8]</sup>

The mass is often mobile and not adherent to the skin or to the deep plane. It is sometimes adherent evoking breast cancer.<sup>[43,44]</sup> It is often single; multiple nodules are less common.<sup>[5]</sup>

Indeed, El BIAZE. M described a case of breast tuberculosis with two nodules sitting in the same breast.<sup>[9]</sup> The palpation will also look for a possible nipple discharge by concentric pressure of the breast and by an expression of the nipple. It is necessary to specify the uni or pluriorificial and uni or bilateral character of the flow, the aspect, the quantity and to take a sample for a cytological and bacteriological study.

Adenopathies are present in 75% of cases according to the majority of authors. They are homolateral, contralateral or even bilateral axillary, or supraclavicular, or homolateral cervical. They often have no particular character, mobile and without peri-adenitis. However, they are often larger and more numerous than they would be for a neoplasm of the same volume. These lymph nodes evolve over time towards fistulization.<sup>[2, 6, 7]</sup>

Radiologically, there are no specific mammographic signs of breast tuberculosis. The mammogram instead shows suspicious images that may suggest a malignant lesion. Given this lack of specificity, mammography presents only an element of diagnostic orientation. Apart from inflammatory signs or purulent collection, several views can be performed (face, profile, additional views).<sup>[4]</sup> Breast tuberculosis has 4 appearances on mammography.<sup>[5]</sup>

A well-defined, dense mass of variable size and shape without skin thickening.

A dense oval area with blurred contours with cutaneous retraction suggestive of malignancy: BOUFETTAL H<sup>[4]</sup> found this appearance in 50% of cases. Djibril. A. M.<sup>[1]</sup> performed mammography in 05 patients and it evoked a suspicious process of malignancy in 02 cases.

Stellar dense opacity with skin retraction and thickening.

Thickened, irregular spans with loss of normal architecture and a micronodular appearance of the breast, often associated with significant skin thickening giving the appearance of tuberculous milia of the breast. Apart from the telling clinical forms (recurrent abscesses with multiple fistulous orifices), three radio-clinical forms have been individualized by Djibril. A.M.<sup>[1]</sup>

*A nodular form:* which corresponds to an insensitive and very slowly growing tumor mass, producing a dense round or oval shadow with blurred contours.

*A diffuse form:* which presents as an inflammatory, painful tumor mass with skin ulceration and nipple discharge. The mammographic appearance is that of a dense mass with thickening of the skin next to the lesion.

*A sclerosing form:* pseudo-neoplastic with a predominance of fibrosis. It results in an accentuation of the density and homogeneity of the mammary gland: an increase in opacity with glandular retraction, which may or may not be associated with an architectural distortion.

**Breast Ultrasound:** an essential complement to mammography, it allows the exploration of inaccessible lesions and completes the mammography data, both in terms of their density and their location. It is indicated for women who are breastfeeding, pregnant and have dense breasts. In case of breast tuberculosis, it shows heterogeneity suggestive of mastitis. The most common aspect is that of a hypoechoic, heterogeneous, poorly delineated image with minimal posterior enhancement. Several other ultrasound aspects have been described in cases of breast tuberculosis.<sup>[1]</sup>

. Well-defined heterogeneous hypoechoic mass with moderate posterior enhancement and sometimes calcifications that may suggest a complicated and altered adenofibroma.

. Well-limited thick-walled fluid lesion with a finely sloping echogenic content.

. A dilation of the milk ducts with echogenic content.

These different aspects are non-specific, however the demonstration of an extensive sinus trajectory from the mass to the chest wall or the pleura seems to be very suggestive of the diagnosis.

As with any collection, ultrasound has a major role.

- By guiding the puncture, when the palpable plaque is difficult to delineate clinically.
- By monitoring the evolution under medical treatment, allowing to judge its effectiveness.

The combination of mammography and breast ultrasound increases the sensitivity and specificity of these two examinations.

**Breast MRI:** the aspects described on MRI are.

Intense and early contrast enhancement.

Irregular peripheral enhancement

Circumscribed Nodules.

These aspects are non-specific and can be found in carcinomas and other abscesses. However, MRI is especially useful for establishing the locoregional extension assessment, particularly on the chest wall.

**Pulmonary X-rays** are systematic in breast tuberculosis since active or dormant pleuro-pulmonary localization of tuberculosis is frequently found.<sup>[2;8]</sup> Breast tuberculosis can reveal pleuropulmonary involvement.

It can show mediastinal lymphadenopathy, osteitis of the chest wall or pericardial or pleural calcifications.<sup>[2]</sup> Sometimes, it shows sequelae of old tuberculosis, often unnoticed in the form of primary tuberculosis infection, leaving hilar calcifications.<sup>[5]</sup>

### **Biology**

**NFS:** it can highlight an anemia of the inflammatory type.

Lymphocytosis is found in 40% of cases.

Sometimes the complete blood count shows hyperleukocytosis with neutrophilic predominance.<sup>[5]</sup>

**VS:** often accelerated, rarely exceeds 100 mm, especially in cases with a diffuse inflammatory form.<sup>[4]</sup>

**The Tuberculin intradermal reaction**, or Mantoux test, is an interesting examination for diagnostic orientation while taking into account the vaccine and immune profile of the subject.

The test consists of the intradermal injection, just under the surface of the skin, at the level of the anterior surface of the forearm, of 0.1 ml of the purified tuberculin solution, at 10 international units.<sup>[6]</sup> The reading is done on the 72nd hour. The limits of induration are determined by palpation and measured in millimeters without taking into account any associated erythematous reaction.<sup>[6]</sup>

<5 mm: negative reaction.

5-10mm: weakly positive reaction.

>10mm: positive reaction.

The tuberculin TST is often positive in mammary tuberculosis.<sup>[2]</sup> Indeed, EL MANSOURI<sup>[8]</sup> found a positive IDR in 83.3% of cases; and Djibril. A.M.<sup>[1]</sup>, in his series, observed this in 100% of cases. However, FRAISSE only found a positive IDR in 50% of cases.<sup>[7]</sup>

### **Withdrawals**

In the case of breast tuberculosis, the search for the tubercle bacillus is done in the product of a cytopuncture, a biopsy or in the secretions coming from a breast fistula.

The search for another associated tuberculosis focus must be systematic.

Samples such as tissues, cytopuncture liquids and pus must be kept at +4°C, thus avoiding excessive bacterial proliferation.<sup>[7]</sup>

### **Direct Examination**

It is done using Ziehl-Neelson staining: This is the reference technique for staining mycobacteria, which appear as thin, more or less regular, pink rods on a blue, blue-green background. These pink rods are the bacilli that resist discoloration by acid and alcohol, hence their name: acid-alcohol-fast bacilli (AFB), which is a characteristic common to all mycobacteria.

Direct examination is considered positive if at least 3 AFB per 100 microscopic fields are observed after Ziehl-Neelson staining and/or 10 bacilli per 100 microscopic fields after auramine staining.

Direct examination is unfortunately not very specific and not very sensitive, especially when the tuberculosis is extra-pulmonary (this is the case for mammary tuberculosis).<sup>[7]</sup>

### **Culture on specific medium**

The definitive diagnosis of tuberculosis, and of mycobacteriosis in general, is based on the isolation and identification of the etiological agent.

The medium of LÖWENSTEIN-JOHNSON (LJ), is the most used medium. Culture is slow, requiring 3 to 4 weeks for *Mycobacterium Tuberculosis* and 45 to 60 days for *Mycobacterium Bovis* and *Africanum*. The generation time is approximately 20 hours on the culture media.

The culture is declared positive as soon as bacterial colonies of characteristic morphology appear: The colonies are usually eugonic (when they are separated, the diameter is 5 to 10mm), with dry, warty, "cauliflower" appearance. , cream-beige in color and opaque in case of *Mycobacterium Tuberculosis*.<sup>[7]</sup>

### **New identification methods**

#### **Quantiferon gamma test**

Positive tests indirectly indicate the presence of latent or active tuberculosis infection.

Due to their higher specificity, they are less often positive than tuberculin tests.

Rapid detection of growth: this is radiometric respirometry or also called the "Bactec System". This technique is based on the measurement of carbon dioxide labeled with carbon 14 (C14) which is released by mycobacteria during their multiplication in a liquid culture medium. This method makes it possible to confirm the presence of *Mycobacterium*

Tuberculosis in just 10 to 12 days, whatever the sample, with good sensitivity and good reliability. This technique also makes it possible to carry out an antibiogram, but it is more delicate to carry out.

Clinical diagnosis by genetic amplification or PCR<sup>[7]</sup>

It is a technique that uses gene amplification to detect *Mycobacterium Tuberculosis* in biological fluids (ascites, pleural fluid, blood, cerebrospinal fluid) and tissues. The results are obtained in 24 to 48 hours and the specificity is excellent, approaching 100%.

In the presence of a sample with a positive microscopic examination, the sensitivity of PCR is always close to or greater than 95% for a specificity of 98-99%. But when taking a sample with a negative microscopic examination, this sensitivity varies between 40 and 77%.

The PCR technique is currently the fastest means of diagnosis and can be of some use, but its result must always be compared with other disease data and its high cost limits its routine use.

Tuberculosis serology.

It constitutes a true serodiagnosis of extra pulmonary tuberculosis by the detection of anti-antigen monoclonal antibodies to *Mycobacterium Tuberculosis*. It is currently widely used with a sensitivity that varies from 50 to 90% and specificity from 70 to 100%.<sup>[8]</sup>

## **Anatomo-pathological study**

### **The macroscopic study**

Breast tuberculosis presents as a reddish or yellowish-gray lesion, sometimes with ulcerated areas suggestive of cancer. The size of the nodule is variable (2 to 10cm). The consistency is initially firm then becomes soft in the presence of tonsil stones. When cut, the nodule appears dotted with whitish granulations or necrotic in the center leaving a dull yellowish granular pus.

Different forms are described in the literature.

**The nodular form:** 81.4% represented by a tuberculoma. This is the common form according to the majority of authors. It is in this form that the attack of the breast begins. The lesion extends slowly, becomes caseified, it can open and give a chronic fistula. Of firm or hard consistency, sometimes limited, sometimes diffuse, being able to adhere to the superficial or deep planes.

**The sclerosing form or scirrhous:** 12.2% non-abscessed, pseudo-neoplastic, simulating cancer in every way, characterized by excess fibrosis. The growth of the lesion is long. This scirrhous can retract the breast against the costal grill.

**Banal cold abscess type form:** 5.6%

The destructive form: 1.4%, it is tuberculous mastitis: There is an attack of the galactophores, it carries out a form around the nipple, badly limited, retracting the nipple with sometimes fistulous flow punctuated by menstruation.

### **Other rarer forms**

Warm abscess-like form;

Intra-mammary tuberculous lymphadenopathy

### **The microscopic aspect**

The histological criteria evoking breast tuberculosis are the presence of epithelioid follicles and Langerhans-type giant cells, associated or not with caseous necrosis.

### **IV-Treatment**

The therapeutic management of our patient is based on 2 components: Medical and surgical treatment.

### **V- CONCLUSION**

Breast tuberculosis is rare, mainly affecting young women in the period of reproductive activity. Breast contamination is often secondary. Its diagnosis is made difficult by the multiplicity and non-specificity of its clinical and radiological aspects. Confirmation of tuberculous origin is based on isolation of BK or on histology. The evolution is generally favorable under antibacillary treatment associated or not with surgery.

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