A malignancy Mimicker in an unusual location: Pseudotumoral malakoplakia of the breast

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Abstract

Malakoplakia is an uncommon granulomatous disease that occurs in immunocompromised individuals. It's thought to be caused by macrophagic bactericidial defect. We report a rare case of breast malakoplakia in a pregnant 35 ears-old woman that mimicked malignancy.

TITLE

A malignancy Mimicker in an unusual location: Pseudotumoral malakoplakia of the breast

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ABSTRACT

Malakoplakia is an uncommon granulomatous disease characterized by macrophagic bactericidal defect, affecting mostly immunocompromised individuals. Its breast localization is extremely rare.

We report a rare case of breast malakoplakia in a 35 year-old pregnant woman mimicking malignancy. In our knowledge, our case is the sixth described in the literature.

INTRODUCTION:

Malakoplakia is an uncommon, granulomatous disease that occurs in immunocompromised individuals. It's thought to be caused by a defect in macrophages functioning against bacterial agents (1).

Breast is extremely rare as a site of occurrence (1).

We report the case of breast malakoplakia (BM) in a 35-year-old pregnant woman, that mimicked a malignant tumor and we aim to discuss its clinicopathological characteristics in this uncommon location.

CASE REPORT:

The patient was a 35 year-old pregnant woman who presented with a nodule of the right breast. This nodule was discovered incidentally on a PT-scan performed to explore respiratory problems at the time of SARS-COV2 pandemics. The patients had a negative SARS-COV2 PCR and CT-Scan didn't show any SARS-COV2 associated lesions. At clinical examination, the nodule was not palpable.

Mammography X-rays showed a speculated lesion that measured 8 mm in size. This suspicious aspect was confirmed by ultrasounds. Microbiopsies have been performed.

Pathological examination revealed a circumscribed lesion of the breast parenchyma. It was composed of an infiltrate of inflammatory cells within a myxoïd background. The predominant component of this inflammatory infiltrate was represented by a large number of foamy histiocytes with granular cytoplasm. These PAS positive granules are Michaelis and Gutmann bodies. In view of these histological aspects, we concluded to "breast pseudotumoral malakoplakia".

DISCUSSION:

Historical aspects and terminology:

Malkoplakia or Von Hannsemman disease has been originally decribed in the early 1900s by Michaelis and Gutmann (2). The name Malakoplakia has been attributed to this condition by Hannsemman, in 1903, from the Greek *malakos* (soft) and *plakos* (plaque) that represents its clinical aspect: friable soft plaques (3).

Etiology and pathophysiology:

Malakoplakia typically affects immunocompromised individuals. Its etiology is poorly understood.

It's thought to be caused by macrophagic bactericidal defect. In fact, deficiencies in beta-glucuronidase and intracellular cGMP lead to impaired phagolysosomal activity and the accumulation of partially digested bacteria in macrophages, recognized microscopically as Michaelis-Gutmann bodies.

Organisms implicated in malakoplakia are gram-negative rods and Escherichia Coli is the most common organism associated with this condition.

Less frequent associations are with Klebsielle, Pseudomonas, Proteus, Enterococcus, Mycobacterium and Salmonelle (3)(4)(5)(6).

Localization:

Malakoplakia occurs mainly in the genito-urinary tract, especially in the bladder (7). Other localizations may be seen like the skin, gastro-intestinal tract, lungs, etc…

The first extra-urinary localization has been described in 1983 (8).

Breast localization is extremely rare. Few studies have reported breast malakoplakia (BM). In our knowledge, our case is the sixth described in the literature (9) (10) (11) (12).

Other granulomatous lesions of the breast have been described but in these cases no particular investigations have been performed to confirm or rule out malakoplakia (13)(14).

Epidemiology:

The peak incidence of malakoplakia is in patients over fifty (7).

In our case, the patient was 35 years old. BM has also been described in young female adults in two italian case reports (9,10). In El Kataibi case report, the patient was 52 years-old (11).

In the urinary tract, there is a female predilection with a female to male sex ratio of 4:1. However, there is no gender predilection in extra-urinary localizations (15).

In the breast, it seems to be a female predominance of malakoplakia since in all the published cases of breast malakoplakia and in our case, the patient was a female.

Patient predispostition:

In the literature, it is established that malakoplakia occurs mainly in immunocompromised individuals (15). Repeated infection should raise suspicion of immunodeficiency.

In the two italian reports of Di Léo (9,10), BM was related to the puerperal period. In our case, it was a pregnant woman. This can be explained by the weakened immune system during pregnancy and puerperal period.

Clinical presentation:

Clinical presentation of malakoplakia differs according to the localization.

In the skin, all spectrums of lesions may be seen: nodules, ulceration, papules.

In internal organs, it often presents as a mass or nodule (15).

In the breast, malakoplakia manifests itself frequently as a diffuse mastitis. In El Kataibi report (11) as in our case, the lesion presented as a breast nodule suspicious of malignancy.

In this same report of El Kataibi (11), the “orange skin” aspect and ulceration raised suspicion of malignancy.

In our case, in which the nodule was discovered incidentally, radiologic aspects as spicules and ill-defined margins were suspicious of malignancy (**Figure 1**).

Diagnosis:

Histological examination is the main diagnosis tool. Malakoplakia can be self-limited or diffuse.

Its histological features don’t differ according to the localization.

Three stages are described: an initial inflammatory stage, a classic stage with abundant Michaelis-Gutmann bodies and a latest stage with progressive fibrous tissue and scarring.

The lesion is composed of foamy epithelioid histiocytes with PAS+ granular eosinophilic cytoplasm. These granules are Michaelis-Gutmann bodies which can be mineralized (16).

It’s important to explore the entire speciman to rule out any associated malignancy.

In our case (**Figures 2**, **Figure 3**), the limitation of the lesion and the use of PAS stain allowed to diagnose a benign lesion and not to report an « inadequacy » of the sample.

For this purpose, pathologists should be careful in examining inflammatory granulomatous lesions and rule out malakoplakia in order to prevent mutilant treatment while considering the absence of a malignant component of a suspicious mammographic lesion as a « non diagnostic » in the breast biopsy sample.

Although BM may be suspicious of malignancy clinically and radiologically, one should keep in mind these cancer mimickers. A well conducted questioning of the patient looking for infectious history, as well as a history of immunosuppressor treatment or of repeated infections may help diagnose this lesion early.

Management:

There are no standardized treatment guidelines in malakoplakia. In fact, large clinical trials are lacking. Three treatment modalities may be applied including systemic antibiotherapy, surgical excision and immunity boosting (15).

Medical treatment is the standard treatment modality. It is based on antibiotics such as fluoroquinolones, trimethoprim/sulfamedazole, and rifampin for a long period (15). There is no standard for the duration of treatment.

Immunosuppressor treatment of connective disease or as a part of transplantation process is incriminated in the development of malakoplakia.

Some studies have shown that decreasing or discontinuing Prednisone and Azathioprine in such situations allowed a recovery from malakoplakia (15).

Surgery depends on affected site and is recommended in case of medical treatment failure.

In case of aggressive lesions as it is mainly the case in the urinary system, a surgical treatment have to be considered (17, 18, 19).

In our case, the patient received antibiotherapy by fluoroquinolones with ultrasonographic improvement after a 3 month-follow-up.

Prognosis:

The outcome of malakoplakia depends on the localization, the extend of the lesion and, also on the immune status of the patient.

If not treated, malakoplakia may lead to chronic disease, but can rarely lead to death (20).

In breast location, a well-established diagnosis is necessary to avoid excessive mutilating treatment and psychological consequences.

CONCLUSIONS:

Malakoplakia is a very rare granulomatous condition that typically occurs in immunocompromised individuals.

Breast location is seldom and may mimic malignancy, leading to excessive mutilant treatment and psychological complications.

BM should be managed by an interprofessional team approach since no clear treatment guidelines are established.

Large clinical trials should be conducted to best characterize therapeutic strategies.

DECLARATIONS:

AUTHOR CONTRIBUTIONS

All authors have made substantial contributions in developing the research idea. All authors also declare that they have read and approved the final version of the manuscript.

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CONFLICT OF INTEREST

The authors have no conflict of interest to declare.

DATA AVAILABILITY STATEMENT

Data will be made available on request.

ETHICAL APPROVAL

This is an observational study. Research Ethics Committee of the military hospital of Tunis has confirmed that this work does not transgress ethics.

CONSENT STATEMENT:

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy..

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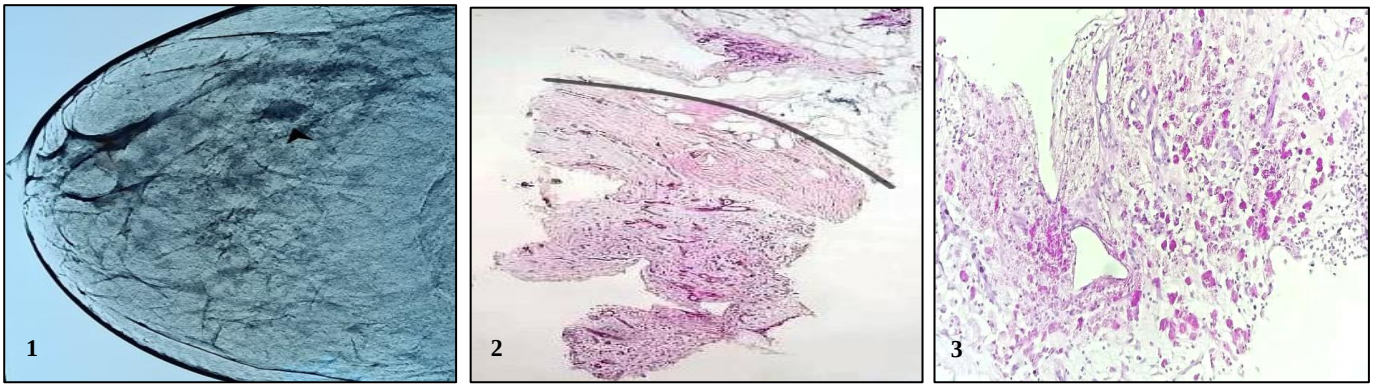

Figure_1: Mammography. A speculated lesion suspicious of malignancy is observed in the inner upper quadrant of the breast (arrow head). **Figure_2**: Biopsy. HEx100. The lesion is well defined by a fibrous rim giving a pseudotumoral aspect (black line). **Figure_3**: Biopsy. HEx200. In a myxoid background, Foamy histiocytes show PAS positive granules in their cytoplasms.