

Nipple Paget's Disease Revealing a CIS and an Underlying Infiltrating Carcinoma about a Case and Review of the Literature

Yacoubi Khebiza S^{1*}, Fdili A Fz¹, Jayi S¹, Chaara H¹, Melhouf My A¹

¹Department of Obstetrics Gynecology II CHU Hassan II of Fez

DOI: [10.36348/sijog.2023.v06i11.002](https://doi.org/10.36348/sijog.2023.v06i11.002)

Received: 14.08.2023 | Accepted: 20.09.2023 | Published: 08.11.2023

*Corresponding author: Yacoubi Khebiza S

Department of Obstetrics Gynecology II CHU Hassan II of Fez

Abstract

We report in this article the case of a patient treated for nipple Paget's disease and in whom clinical and radiological investigations found the association of Paget with carcinoma in situ and infiltrating carcinoma of the breast. Paget's disease of the nipple is a rare variant of CIS. It is associated with an underlying breast adenocarcinoma in more than 80% of cases. Its research must be systematic in imaging, namely MRI. The management of Paget's disease depends on whether or not it is associated with carcinoma in situ or invasive carcinoma. Through our case and in the light of the review of the literature, we insist on the particularity of the positive and differential diagnosis of this entity as well as the therapeutic side, the good knowledge of which allows practitioners to make the diagnosis in time and therefore to improve the prognosis of these young patients.

Keywords: Paget's disease, association with carcinoma in situ and invasive carcinoma, MRI.

Copyright © 2023 The Author(s): This is an open-access article distributed under the terms of the Creative Commons Attribution 4.0 International License (CC BY-NC 4.0) which permits unrestricted use, distribution, and reproduction in any medium for non-commercial use provided the original author and source are credited.

INTRODUCTION

Paget's disease is a rare variety of carcinoma that manifests as eczematiform or psoriasiform plaque of the nipple and areola. It is due to the extension to the epidermis of ductal adenocarcinoma of the breast. Paget's disease of the nipple can also have other localizations, most often the groin or perianal region (extra-mammary Paget's disease). Extramammary Paget's disease is a rare adenocarcinoma that can come from the apocrine glands of the skin or from cancer of the bladder, anus or rectum. Indeed Clinically: Redness, oozing and crusty appearance produce an appearance close to dermatitis, but it is advisable to suspect carcinoma because the lesion is strongly margined, unilateral, and does not respond to topical treatment but the biopsy shows a characteristic histological image. Diagnosis of paget disease is based on breast biopsy. Because this tumour is associated with an underlying cancer, systemic assessment (e.g., history and clinical examination, age-appropriate cancer screening, imaging) is required. Treatment of Paget's disease of the nipple involves appropriate breast cancer treatment for the discovered underlying tumors and includes wide excision of the nipple-areolar complex. If no underlying

breast cancer is detected, a mastectomy or resection of the areolo-nipple complex followed by radiation therapy may be performed. But you should know that it is recommended to perform a breast MRI before considering conservative surgery, in order to detect occult carcinoma as well as multifocality or multicentricity.

CLINICAL CASE

Patient aged 45 years, married, G1P1 (UC), still settled, without particular personal ATCD, without family ATCD of tumor of the breast. Follow-up 2 years, before her 1st consultation with us in dermatology for nipple pruritus with realization of an echo mammography (normal income) + skin biopsy returning in favor of Paget's disease put under local corticosteroid therapy treatment according to the patient then in front of the non-improvement she was referred to us for PEC. The clinical examination at his first consultation with us:

- General status and WHO life capacity at 0
- Senological examination: C cup breasts, slightly asymmetric

- Right breast: straight nipple skin thickening with ulcerations in places, otherwise no palpable nodule, no spontaneous or provoked discharge
- Left breast: serous nipple discharge at pressure, otherwise absence of palpable nodule or skin changes,
- Free lymph node areas
- CT 4b N 0 M X

Radiological assessment

Echo mammography

Right nipple clinically ulcerated and echo graphically very hypo echogenic and heterogeneous compared to the left nipple is it Paget's disease? Right axillary adenopathy of inflammatory appearance

Breast MRI

SD

Thickening of the right areolar plate arriving at 4 mm associated with a retro glandular linear enhancement classified BIRADS 4 (figure 2). More pronounced matrix enhancement at the level of the QSI classified BIRADS 3. 02 lesions at the level of the upper outer quadrant of the right breast near the outer quadrant junction, which may be with intramammary GG making 06 and 09 mm of major axis

SG

Linear enhancement of the left breast outer quadrant junction classified as BIRADS 4. Bilateral axillary GG formations measuring 12 mm small axis for the largest on the right. To be compared with the data of a mammography echo.

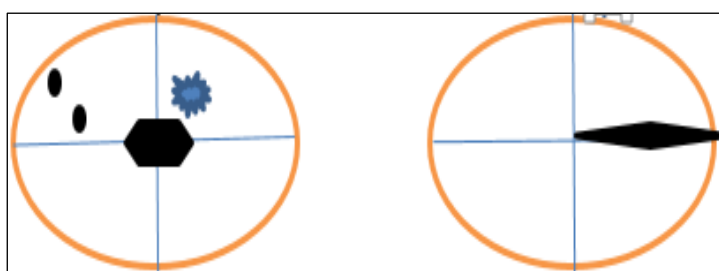


Figure 1: lesion diagram of our patient

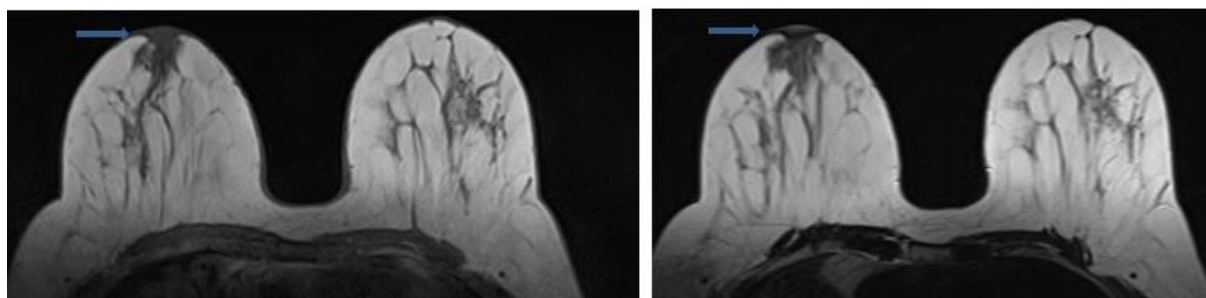


Figure 2: MRI T1 sequences: thickening of the right areolar plate arriving at 04 mm

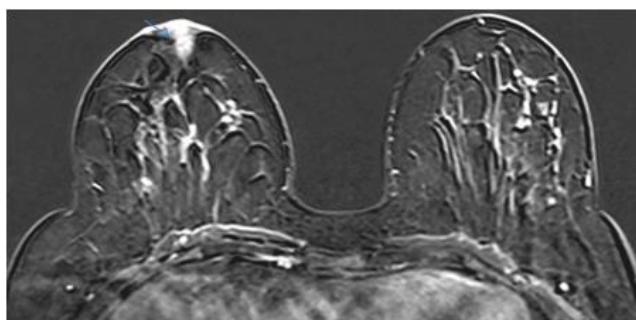


Figure 3: dynamic sequences injected: thickening of the right areolar plate reaching 04 mm, associated with retro glandular linear enhancement classified BIRADS 4

Complement Echo mammography

02 tissue lesions of the right breast in the upper outer quadrant near the outer quadrant junction each classified BIRADS 4b measuring 7 mm. Bilateral retro

nipple ductal dilation and at the level of the left breast in the outer junction quadrant with echogenic content. Tissue infiltrate of upper interne quadrant classified BIRADS 4a.

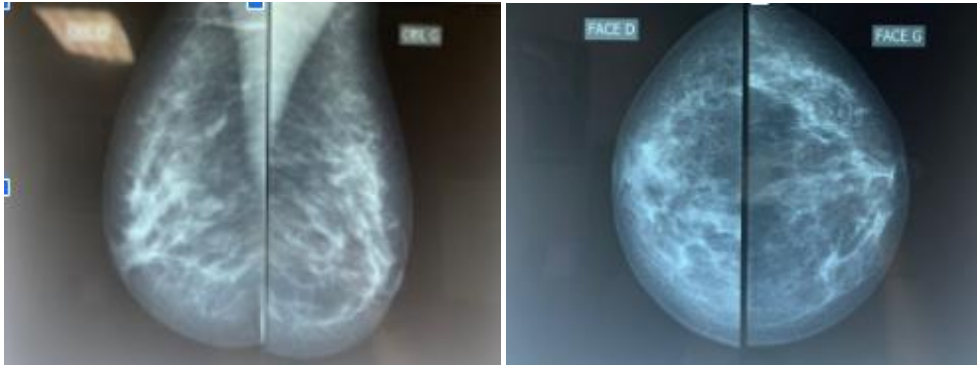


Figure 4: Complement Echo mammography

Histological assessment

1/Type of sample: nipple biopsy done by dermatologists. Histological aspect in favor of paget disease.

2/ other biopsies requested by us

Biopsy of the retro nipple tissue infiltrate of the SD: cystic fibro mastopathy. Biopsy of the 2 tissue lesions of the right breast BIRADS 4b: breast infiltrate carcinoma, grade II of SBR (RO 10%, RP 2 %, HER 2: score 3). Biopsy of the tissue infiltrate of the right breast: in situ carcinoma of high guard of architecture cri biform, absence of necrosis. Biopsy of the retro nipple dilation of the left breast: cystic fibromapathy. So she received chemotherapy first, then mastectomy + axillary dissection.

Definitive pathological examination of the operating room: mastectomy + axillary dissection:

Complete therapeutic response, without tumor residue. Grade 1 of Chevallier, TANB stadium of Sataloff. Resection limits are healthy. Presence of paget disease. Lymph node dissection: 23N-/23N. Stage: ypTON0.

DISCUSSION

Paget's disease of the nipple is a rare carcinoma manifested by eczema or psoriasiform plaque surrounding the nipple: it is a skin manifestation of an underlying ductal adenocarcinoma of the breast. It actually corresponds to the invasion of the nipple epidermis by ductal carcinoma in situ (DCIS) [1-2]. 2 theories have been developed about histogenesis:

- The most widespread is the epidermotropic theory: it is the migration of Paget cells from an underlying mammary carcinoma.
- The second is the malignant transformation of nipple keratinocytes independent of any underlying breast pathology.

Clinically

Paget disease presents as an erosive lesion sometimes in the form of hemorrhagic ulceration. Paget's disease of the breast causes the following symptoms: crusting, peeling or peeling skin, redness of the nipple and areola, burning or itching, bleeding or discharge, inverted nipple (which points inward), flattened nipple, mass in the breast, often near or below the nipple, we can describe 3 evolutionary stages.

- At the initial stage: pruritus, then red and shiny areolo-nipple plate
- In the intermediate stage: thickened and rough nipple, scales
- In the late stage: erosion, oozing ulceration, hardened crust with clear boundaries. Progressive loss of nipple relief.

Very slow, centrifugal extension from the nipple to the areola. Transient improvements are described and should not cause the diagnosis to be eliminated. Pigmented forms can simulate malignant melanoma, sometimes vulvar Paget disease is associated with it. There is generally a progressive loss of the relief of the nipple. The extension is very slow with a centrifuge from the nipple to the areola [4].



Figure 6: 3 evolutionary stages of paget's disease with mammary localization

In terms of imaging

In mammography, the nipple areolo plate is difficult to study, it is performed in order to locate an

underlying cancer. Mostly associated with micro calcifications, no visible abnormalities in 50% of cases in the absence of palpable mass. Thickening of MPA,

skin thickening, nipple retraction. Masses, distortion, asymmetries. Underestimation of extension by mammography in more than 40% of cases. Ultrasound examination allows for better analysis of the central galactophore ducts of MPA and retromamelon [5]. Breast MRI: is useful in case of Negativity of mammography and ultrasound, it can identify 78% of

underlying cancers, When considering conservative treatment.

It highlights: Abnormal nipple enhancement, Thickening and upgrading of the MAP, Evidence of tumor lesions with unilateral suspicious enhancement, Better highlighting of multicentricity and multifocality [6-7].

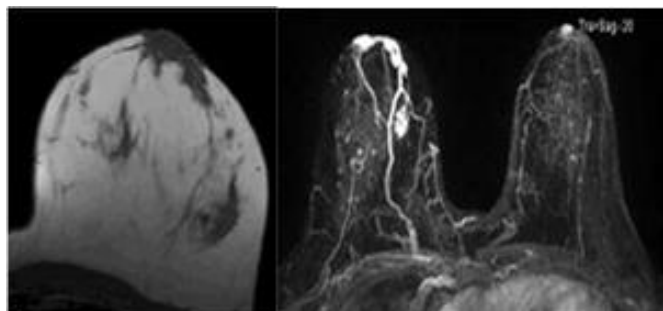


Figure 7: MRI aspect during paget's disease: the nipple is abraded, the plate is thickened different areas of enhancement of the lower inner quadrant of the breast and the right nipple

Diagnosis

The diagnosis is made by cytological scraping of the nipple or biopsy of the skin of the nipple ("punch"). Pathological examination of the skin biopsy

shows in the epidermis large clear glandular cells with abundant cytoplasm, wide nucleated nucleus (Paget cells). They predominate at the basal layers, but can invade the epidermis over its entire height.

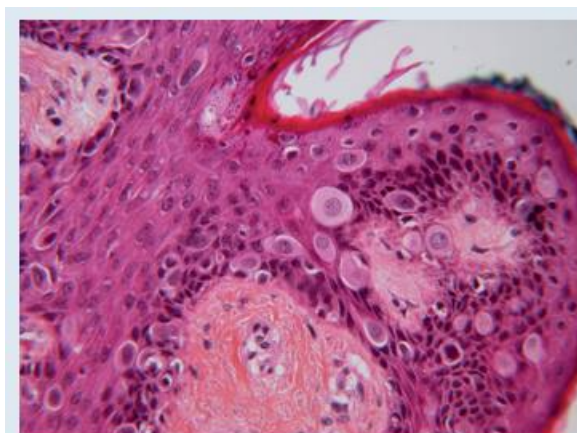


Figure 8: pathological appearance of paget's disease of the nipple

In immunohistochemistry, the expression of glandular cytokeratins, membrane epithelial antigen (EMA), carcinoembryonic antigen (CEA) and the negativity of high molecular weight epidermal cytokeratins point to the glandular nature of Paget's cell.

Differential diagnostics

Erosive nipple adenoma (MEA)

This benign tumor, developed at the expense of the nipple's galactophore ducts, also called Florida papillomatosis of the nipples, is the main differential diagnosis of Paget's disease.

Clinic

Unilateral swelling of the nipple which is thickened and indurated, ulceration well limited, oozing

or even bloody discharge (60%), sometimes palpable nodule under the nipple.

Treatment

The risk of breast carcinoma does not appear to be increased. The EMA is a conservative treatment with complete excision of the lesion by conventional or micrographic surgery, or even cryotherapy with spray. The prognosis is excellent but recurrences are possible in case of incomplete excision. Breastfeeding is then discouraged because of the risk of engorgement [3].

Nipple eczema

Eczema of the areolo-nipple region is mainly related to atopy. Treatment is based on intermittent local corticosteroid therapy, which should rapidly

regress symptoms. Faced with unilateral and chronic damage, Paget's disease must be eliminated by a

biopsy [3].



Figure 9: picture showing nipple eczema

Skin extension of invasive mammary adenocarcinoma

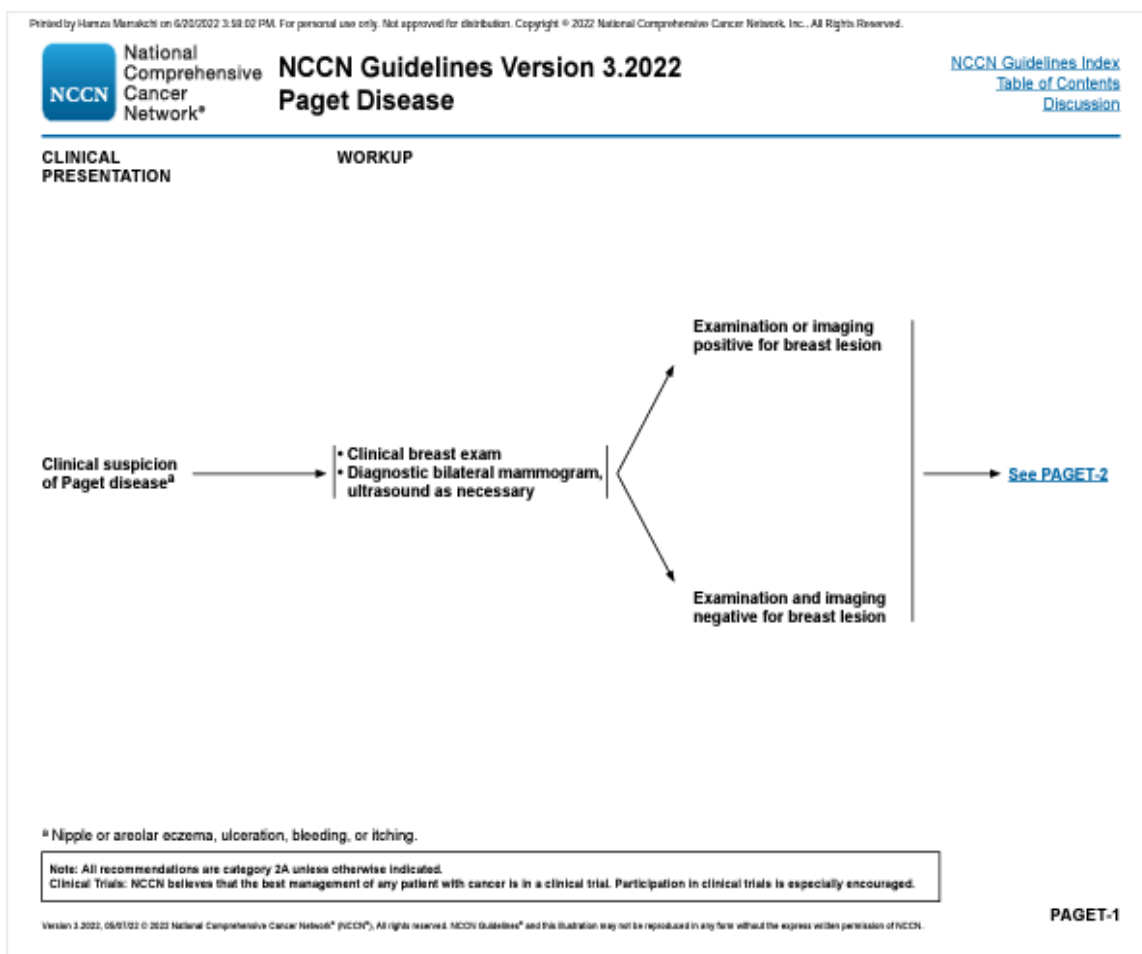
Other differential diagnoses (rarer)

Tumor disorders. Benign tumor disorders: Syringomatous tumor of the nipple, benign cutaneous lymphocytoma, neurofibroma, solitary leiomyoma of the nipple. Specific dermatoses of the areolo-nipple plaque: Neuroid hyperkeratosis of the nipple, Fox-Fordyce disease, galactophoric ectasia.

Treatment

The standard surgical treatment for Paget's disease was for many years total mastectomy. However,

conservative surgery (pamectomy), combined with radiation therapy, appears as an alternative to mastectomy. In any case, when Paget's disease will be associated with carcinoma in situ or invasive carcinoma or both, treatment will be based on the management of the most pejorative pathology [8]. In case of isolated Paget's disease, and after performing an MRI to eliminate any associated pathology the most appropriate treatment according to the most recent standards would be to carry out. Pamectomy including areolo-nipple complex followed by radiation therapy or. Mastectomy +/- sentinel lymph node with or without breast reconstruction.



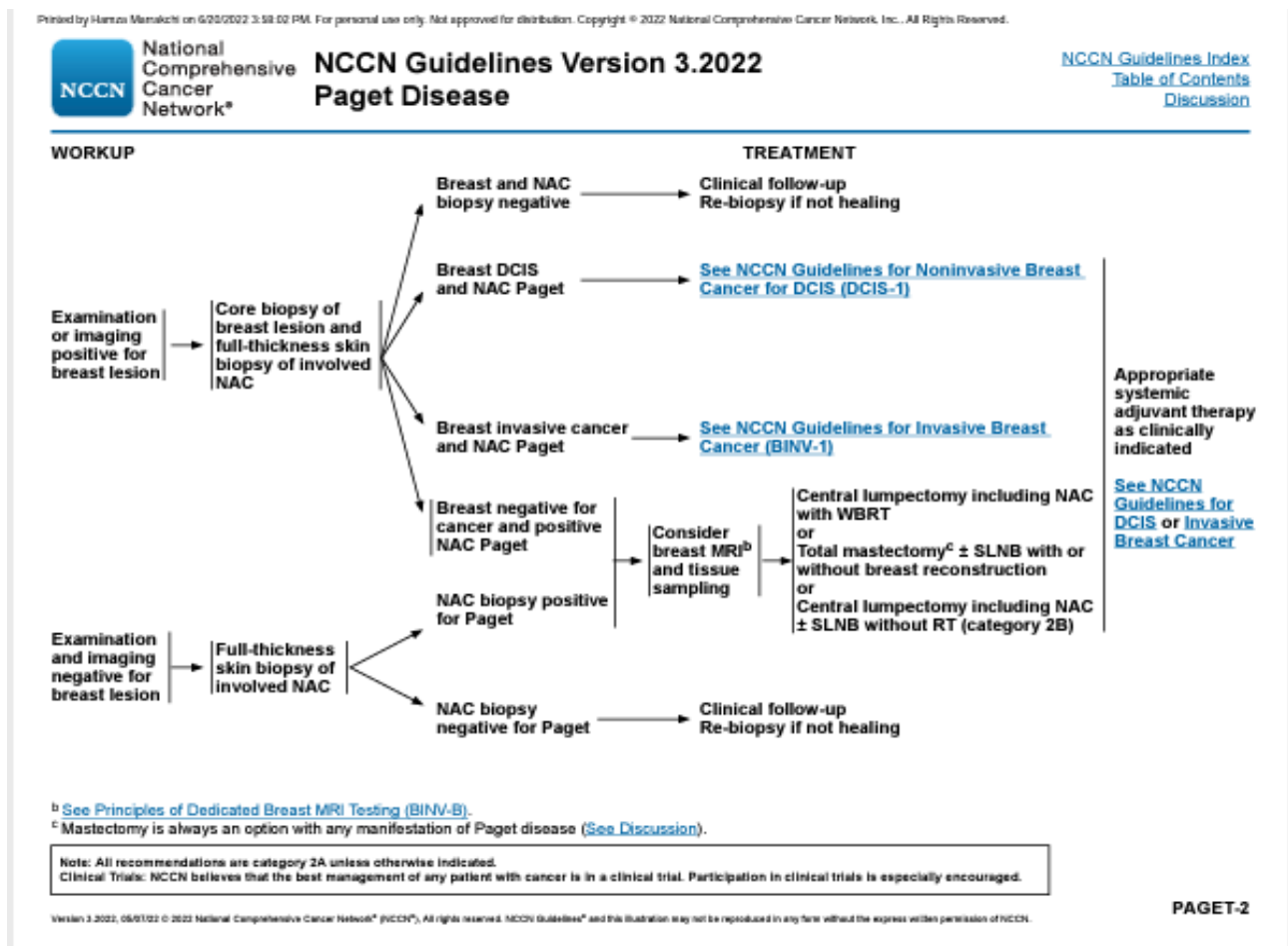


Figure 10: NCCN breast guidelines version 3.2022 (Paget disease)

CONCLUSION

Tumors of the areola and nipple are rare. Any persistent unilateral lesion should attract attention and have a cytological scratching of the nipple performed in search of Paget's disease. Paget's disease of the nipple is a rare variant of DCIS. It is associated with underlying mammary adenocarcinoma in more than 80% of cases. Its research must be systematic in imaging. It is recommended to perform a breast MRI before considering conservative surgery, to detect occult carcinoma as well as multi-focus or multi-centricity.

REFERENCES

- Wells, G.L. (n.d). Paget's disease of the nipple (Paget's disease of the nipple; Paget's disease of the breast). By Staff Dermatologist, Ada West Dermatology, St. Luke's Boise Medical Center, and St. Alphonsus Regional Medical Center <https://www.cancer.ca/fr-ca/cancer-information/cancer-type/breast/breast-cancer/cancerous-tumours/paget-disease-of-the-breast/?region=on#ixzz5XbWTDot>
- <https://sante-medecine.journaldesfemmes.fr/faq/15314-maladie-de-paget-du-mamelon-symptomes-et-traitement>
- Geffroy, D., Doutriaux-Dumoulin, I., Labbe-Devilliers, C., Meingan, P., Sagan, C., Jaffre, I., Ricaud-Coupré, M. (n.d). Paget's disease of the nipple and its main differential diagnoses.
- Harris, J.R., Lippman, M.E., Morrow, M., Osborne, C.K. (n.d). Diseases of the breast Lippincott Williams & Wilkins; *Third Edition Chap 62*, 1007-13.
- Sawyer, H.R., Asbury, D.L. (1994). Mammographic appearances in Paget's disease of the breast. *Clin Radiol.*, 49, 185-8.
- Burke, E.T. (1998). Paget's disease of the breast: A pictorial essay. *Radiographics*, 18, 1459-64.
- Ikeda, D.M. (1993). Paget's disease of the nipple: radiologic-pathologic correlation. *Radiology*, 189, 89-94.
- Bijker, N. (2001). Breast conserving therapy for Paget's disease of the nipple. A prospective European organization for research and treatment of cancer study of 61 patients. *Cancer*, 91, 472.
- NCCN breast guidelines version 3.2022 Paget Disease.