Diagnosis of Paget's Disease of The Breast Associated With High-Grade Ductal Carcinoma In Situ and Microinvasion: A Case Report and Literature Review

Putu Agus Sukarna[1,2]*, Ida Ayu Dewi Dhyani[3]

[1,2,]Fakultas Kedokteran dan Ilmu Kesehatan, Universitas Warmadewa, Denpasar-Bali, Indonesia
[2]Rumah Sakit Umum Warmadewa, Gianyar-Bali, Indonesia
[3]Fakultas Kedokteran Universitas Mahasaraswati, Denpasar, Bali, Indonesia
*Corresponding author:
Email: p.agussukarna680@gmail.com

Abstract.
Background: Paget's disease of the breast is a rare malignancy involving the nipple–areolar complex, frequently associated with underlying ductal carcinoma in situ (DCIS) or invasive carcinoma. Its clinical presentation often resembles benign dermatological conditions, potentially leading to delayed diagnosis. Objective: This case report aims to describe the clinical presentation, diagnostic challenges, histopathological findings, and surgical management of mammary Paget's disease associated with high-grade DCIS and focal microinvasive carcinoma. Methods: A descriptive case report was conducted involving a 59-year-old postmenopausal woman presenting with a persistent ulcerative lesion of the right nipple. Clinical history, physical examination, mammography, ultrasonography, incisional biopsy, surgical intervention, and final histopathological findings were retrospectively reviewed and analyzed descriptively. Results: A 59-year-old female presented with wound on nipple area complex (NAC) right breast since 10 years ago followed by redness and itches. Physical examination revealed and ulcer on right nipple area complex (NAC) and a little amount of serous discharge. There was no palpable breast mass and no axillary lymphadenopathy. Mammography examination found calcification with grouped distribution with skin thickening due to BIRADS 2. Already done operated wide excision without complication and final Histopathological examination result was Paget's disease of breast with underlying high grade ductal carcinoma in situ (DCIS). Discussion. The clinical presentation of Paget's disease is different from the changes seen in inflammatory carcinoma of the breast in which patients have diffuse breast erythema and secondary involvement of the skin and nipple. Histological finding of Paget's disease of the breast is mainly characterized by epidermal Paget cells. Mammograms can detect masses or calcification that represent invasive or DCIS. Conclusion. This report described a Paget's disease with underlying DCIS. Diagnosis of Paget's disease is still challenging, especially to exclude the existence of malignancy.
Key words: *Paget's Disease; breast cancer and ductal carcinoma in situ.*

I. INTRODUCTION

Paget's disease of the breast (PDB) is a relatively rare form of breast malignancy, accounting for approximately 1–4% of all breast cancer cases. It is characterized by the proliferation of malignant glandular epithelial cells known as Paget cells in the epidermis of the nipple-areolar complex (NAC). Although its initial manifestations are often limited to skin changes in the nipple area, the condition has clinical significance because most cases are associated with underlying malignancies, particularly ductal carcinoma in situ (DCIS) and invasive breast carcinoma. Paget's disease is more common in postmenopausal women, particularly in the sixth decade of life. These characteristics make it an important diagnosis to consider in the evaluation of unilateral nipple skin disorders (Kuzmiak & Ferre, 2024; Ortuz Lessa et al., 2025).

Clinically, Paget's disease has a slowly progressive course that progresses over months to years. Initial manifestations typically include pruritus, erythema, desquamation, and eczema-like changes on the nipple, which can then spread to the areola and surrounding skin. In more advanced cases, lesions can develop into erosions, ulcerations, skin thickening, nipple retraction, and nipple discharge. A major problem in clinical practice is the confusion of these manifestations with benign dermatological diseases, such as dermatitis, psoriasis, and eczema. Consequently, diagnosis is often delayed because patients and healthcare providers may mistake the disorder for a common skin disorder. A systematic review by Volfson et al. (2025) demonstrated that initial misdiagnosis is a significant problem in the management of Paget's disease of the breast. The study identified 32 cases that had previously been misdiagnosed, with an average delay of approximately 2.3 years. These findings reinforce clinical vigilance for unilateral nipple lesions that persist or do not improve.

Another important aspect is the relationship between Paget's disease and underlying breast malignancy. The literature indicates that over 90% of Paget's disease cases are associated with DCIS or invasive breast

carcinoma, although not all patients present with a palpable mass. Clinically, the presence of a breast mass may provide protection against invasive factors, while patients without a palpable mass are more likely to have DCIS as an underlying condition. This suggests that the absence of a lump on physical examination cannot be used to exclude malignancy. From a pathogenesis perspective, the epidermotropic theory is the most widely accepted mechanism, involving the migration of malignant cells from the mammary ducts to the nipple epidermis via the lactiferous duct structures. Meanwhile, the transformation theory suggests that epidermal cells can undergo local malignant transformation. Both mechanisms explain the relationship between skin changes in NAC and the presence of breast malignancy (Kuzmiak & Ferre, 2024; Ortuz Lessa et al., 2025).

Establishing a diagnosis of Paget's disease requires the integration of clinical, radiological, and histopathological findings. Mammography is one of the initial examinations to identify masses, microcalcifications, nipple retraction, and skin thickening. Ultrasonography can be used as an additional modality to visualize breast tissue and identify lesions not visible on mammography. However, this second examination has limitations, especially in patients without a palpable mass. Magnetic resonance imaging (MRI) can provide additional information regarding lesion extension, nipple-areolar complex involvement, and the possibility of DCIS or invasive malignancy not detected by conventional examination. Mousa-Doust et al. (2024) reported that the agreement between mammographic and ultrasonographic lesion size and pathological size is still limited. These findings demonstrate that imaging should be interpreted in conjunction with tissue examination results, rather than used as the sole basis for determining the diagnosis or extent of malignancy.

Histopathological examination through tissue biopsy is a key component in confirming the diagnosis. Paget's cells are microscopically characterized by large epithelial cells, abundant and pale cytoplasm, pleomorphic nuclei, and prominent nucleoli. These cells can be found individually or in clusters within the epidermis. Immunohistochemical tests, such as those for cytokeratin 7 (CK7), epithelial membrane antigen (EMA), and HER2, can help confirm the diagnosis and differentiate Paget's disease from other disorders with similar morphological features, including melanoma and certain dermatological conditions. Identification of the underlying malignant component is also important for determining tumor characteristics and subsequent management strategies (Kuzmiak & Ferre, 2024; Ortuz Lessa et al., 2025).

Management of Paget's disease is determined by the presence and characteristics of accompanying malignancies, the extent of the lesion, the status of the lymph nodes, and the patient's clinical condition. Mastectomy is one treatment option, while breast-conserving surgery may be considered in selected patients with disease characteristics that permit complete resection and appropriate adjuvant therapy. Treatment decisions ideally involve a multidisciplinary approach involving surgeons, radiologists, anatomic pathologists, and oncologists. Research by Mousa-Doust et al. (2024) suggests that breast-conserving surgery may be an alternative in patient selection, so the choice of treatment should not be based solely on the diagnosis of Paget's disease, but also on a comprehensive evaluation of the underlying malignancy.

Based on these issues, this case report has clinical relevance because it describes a 59-year-old woman with an ulcerative lesion on the nipple-areolar complex of the right breast that had persisted for approximately 10 years, accompanied by redness and itching, without a palpable mass. Mammography examination showed calcifications in a clustered distribution and skin thickening, while ultrasonography showed no significant abnormalities. Histopathology examination after wide excision confirmed Paget's disease with high-grade ductal carcinoma in situ and one microinvasive focus.

The uniqueness of this case lies in its long-term course, clinical manifestations resembling benign skin disorders, the absence of a mass on physical examination, and the presence of an underlying malignancy despite unremarkable ultrasonography. Therefore, this case report aims to describe the clinical characteristics, diagnostic robustness, radiological and histopathological findings, and management approach of Paget's disease of the breast with high-grade DCIS and microinvasive foci. This report is expected to raise clinical awareness of persistent unilateral nipple lesions and emphasize the importance of histopathological confirmation in ruling out breast malignancy.

II. METHOD

Study Design and Reporting

This study used a descriptive case report design to document the clinical presentation, diagnostic evaluation, histopathologic findings, and surgical management of a patient diagnosed with Paget's disease of the breast associated with high-grade ductal carcinoma in situ (DCIS) and focal areas of microinvasive carcinoma. This case report was prepared in accordance with the CARE (CAse REport) guidelines to ensure systematic and transparent reporting of the patient's clinical course, diagnostic procedures, therapeutic interventions, and clinical outcomes.

A brief literature review is included to contextualize the clinical findings and diagnostic challenges associated with Paget's disease of the breast. This literature review is intended to support the interpretation of the reported cases and is not intended to be a systematic review.

Study Location and Patient Information

This case involves a 59-year-old female patient who presented with a persistent ulcerative lesion involving the right nipple-areola complex. The patient was evaluated and managed at Sanglah General Hospital, Bali, Indonesia, as reported in the original clinical manuscript.

The patient's clinical history, physical examination findings, radiologic investigations, histopathology reports, and surgical treatment were reviewed to establish the clinical characteristics and diagnostic progression of the disease. Relevant medical history included no family history of breast cancer, menopausal status for approximately 14 years, no history of hormonal contraception, and no reported alcohol consumption. The patient initially presented with a small lesion on the right nipple that progressively enlarged and caused erythema and pruritus over approximately 10 years.

Clinical Assessment and Physical Examination

The clinical assessment includes a detailed history of the presenting complaint, duration of symptoms, development of nipple lesions, associated symptoms, and relevant breast cancer risk factors. The physical examination focuses on inspection and palpation of both breasts, particularly the nipple-areola complex, surrounding skin, and regional lymph node areas.

The examination documented:

a) Location, appearance, and extent of nipple lesions.
b) The presence of erythema, ulceration, peeling, and fluid discharge.
c) Whether or not there is a palpable breast lump.
d) The presence or absence of axillary lymphadenopathy.
e) Other clinically relevant breast abnormalities.

The initial physical examination identified an ulcerative lesion measuring approximately 5 × 5 cm on the right nipple, accompanied by a small amount of serous fluid. There was no palpable breast mass or axillary lymphadenopathy.

Diagnostic Investigations

Diagnostic assessment consists of radiologic and histopathologic examinations to evaluate the primary nipple lesion and investigate the possibility of underlying breast malignancy.

a. Mammography

A mammogram was performed to assess the breast parenchyma, identify suspicious calcifications, evaluate skin thickening, and detect possible underlying malignancies. The examination revealed clustered, round calcifications and skin thickening approximately 0.45 cm in size in the right breast. These findings were initially interpreted as benign (BI-RADS 2) in the initial clinical report. These findings were then considered in conjunction with the histopathology results.

b. Breast ultrasound

A breast ultrasound was performed as an additional imaging modality to evaluate breast tissue and identify any underlying masses or structural abnormalities. The examination revealed no significant abnormalities in the breast parenchyma.

c. Histopathological examination

An incisional biopsy of the right nipple skin lesion was performed to establish a definitive diagnosis. The tissue specimen was examined microscopically to identify cellular abnormalities and assess for the presence of malignant intraepidermal cells.

a) Histopathological assessment focuses on:
b) Morphology and distribution of cells in the epidermis.
c) Characteristics of the cytoplasm.
d) Nuclear pleomorphism and nucleolar prominence.
e) Mitotic activity.
f) Evidence of associated ductal carcinoma or invasive component.

Following the initial biopsy, the patient underwent wide excision of the affected breast lesion. The excised surgical specimen was then examined to determine a final histopathologic diagnosis and identify any underlying malignancy. Final histopathology confirmed Paget's disease of the breast associated with high-grade DCIS and a single focal area of microinvasive carcinoma.

Therapeutic Intervention

Surgical management was performed after clinical and histopathological evaluation. Wide excision of the right breast lesion was performed to remove the affected nipple-areola tissue and obtain a definitive histopathological assessment. The surgical intervention was documented according to the operative procedure, the extent of tissue removed, and the intraoperative findings available in the medical record. Postoperative assessment included evaluation of surgical complications and the patient's immediate clinical condition. The original clinical report documented that the surgical procedure was completed without any reported complications.

Data Collection and Analysis

Data were obtained retrospectively from available patient medical records and clinical documentation. Information reviewed included:

a) Patient demographic characteristics and relevant medical history.
b) Initial clinical picture and duration of symptoms.
c) Physical examination findings.
d) Mammography and ultrasound findings.
e) Initial incisional biopsy results.
f) Operative findings and surgical interventions.
g) Final histopathological findings.
h) Documented postoperative outcomes.

The collected information was organized descriptively according to the patient's clinical progression and diagnostic pathway. No statistical analysis was performed because this report involved only one patient. Findings were interpreted through a descriptive clinical approach and compared with relevant published literature on Paget's disease of the breast, associated breast malignancies, diagnostic imaging, histopathologic characteristics, and surgical management.

Literature Review Approach

A brief narrative literature review was conducted to support the clinical interpretation of the case. Relevant publications were identified through PubMed/MEDLINE and other accessible scientific literature databases. The search term included the following keyword combinations: "Paget's disease of the breast," "Paget's disease of the breast," "Nipple-areola complex," "Ductal carcinoma in situ," "Microinvasive breast carcinoma," "Diagnostic imaging," "Histopathologic findings," and "Surgical management."

Priority was given to peer-reviewed publications, clinical reviews, observational studies, and relevant case reports published between 2021 and 2026. Selected previous publications were retained if they provided essential baseline information. The literature was narratively synthesized to compare patient clinical presentations, diagnostic findings, and treatment approaches with previously reported evidence.

Ethical Considerations

Patient confidentiality was maintained throughout the preparation of this case report. Personally identifiable information has been removed from the manuscript. Written informed consent was obtained from the patient, allowing the sharing of her medical history for educational and publication purposes.

III. ANALYSIS RESULTS

A 59-year-old woman with no family history of cancer presented with a lesion on her right breast that had been present for 10 years. Initially, the lesion was a small spot, but then it widened to cover the entire right nipple. The lesion was followed by redness and swelling.itchyThe patient reported no swelling, pain, or discharge from her right breast. Her weight was stable. She went through menopause 14 years ago and had no history of hormonal contraception. She reported no history of alcohol consumption.

Physical examination revealed a 5 x 5 cm ulcer on the right nipple (Figure 1) containing a small amount of serous fluid. There was no palpable breast mass and no axillary lymphadenopathy. Mammography revealed round calcifications in a clustered distribution accompanied by skin thickening (±0.45 cm) and enlarged lymph nodes, consistent with benign findings in the right breast (Figure 2). Breast ultrasound was performed without abnormal findings.



Fig 1. Clinical picture of the patient

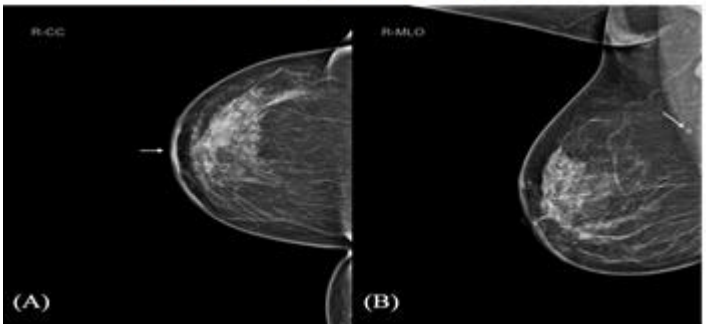


Fig 2. Mammography shows round calcifications with a clustered distribution (A) (arrow) skin thickening (±0.45 cm); (B) (arrow) enlarged lymph nodes

An incisional skin biopsy of the right breast revealed scattered single and clustered intraepidermal atypical cells with pale, wide cytoplasm, round, oval, pleomorphic nuclei, irregular nuclear membranes, and prominent nucleoli. Mitoses were readily observed from the basal to the superficial layers. A wide excision of the right breast was then decided. The histopathological findings of the excised tissue were consistent with those of the incisional biopsy sample. Furthermore, there was a focal high-grade ductal carcinoma in situ and one focus of microinvasive carcinoma.

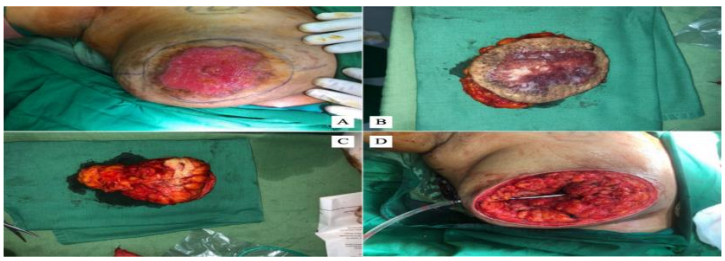


Fig. 3. (A) Surgical design and resection margins; (B) Anterior view of the removed lesion; (C) Posterior view of the removed lesion; (D) Placement of the drain in the middle areola pocket.

IV. DISCUSSION

Sir James Paget described a disease in 1874 characterized by itching, excoriation, erythema, and nipple discharge, and associated with breast cancer. Paget's disease can present with eczematous or scaly changes beginning in the nipple, then extending to the areola, and in more advanced cases to the surrounding skin, as eczematous, erythematous, thickened, moist, or crusted lesions with irregular borders, with or without fine flaking, induration, infiltration, secretion, bleeding, ulceration, and nipple invagination. Early changes, including flaking and redness, can be mistaken for benign conditions such as eczema or other inflammatory conditions, leading to delays in diagnosis (Filho et al., 2015; Yasir et al., 2022; Merril et al., 2017; Gaurav et

al., 2018). As in our case, the diagnosis was made 10 years after the appearance of the initial, pinpoint lesion. As the disease progresses, diagnosis may be delayed due to the mistaken belief that the lesion is a benign condition.

Paget's disease of the breast is rare compared to other types of breast cancer, occurring in approximately 1-4.3%. This condition usually occurs in women, but in rare cases, Paget's disease can also occur in men with similar symptoms. It occurs most often in postmenopausal women in their sixth decade, but it has also been observed in adolescents and elderly patients (Yasir et al, 2022; Karakas, 2011).

There are no clear clinical or epidemiological factors that predispose patients to Paget's disease, except for several risk factors common to other breast cancers. These risk factors include advanced age (over 50 years), a history of breast abnormalities such as lobular carcinoma in situ or atypical hyperplasia, a family history of breast or ovarian cancer, dense breast tissue on mammogram, radiation exposure to the chest, BRCA1 and BRCA2 gene mutations, postmenopausal estrogen therapy, and heavy alcohol consumption (Yasir et al., 2022; Karakas, 2011). In our case, the only risk factor consistent with this theory was advanced age. However, there was no history of breast abnormalities, a family history of cancer, estrogen therapy, and alcohol consumption. Other risk factors were not studied.

The clinical presentation of Paget's disease differs from the changes seen in inflammatory breast carcinoma, where patients present with diffuse breast erythema and secondary skin and nipple involvement. Lesions are mostly unilateral, as we found in our case, and are rarely bilateral. Paget's disease of the breast is most likely associated with an underlying breast cancer, usually a central, multifocal tumor, particularly located near the areola. Approximately half of these patients present with a palpable breast mass. Patients with a palpable mass are more likely to have invasive carcinoma. Meanwhile, patients without a breast mass are more likely to have ductal carcinoma in situ (DCIS) (Filho et al., 2015; Gaurav et al., 2018; Karakas, 2011). In our case, the patient did not present with a palpable mass. Histological findings will be discussed in the following paragraphs.

In the diagnosis of Paget's disease, investigation of breast glandular neoplasms is crucial. Careful clinical and imaging examinations are necessary to establish the diagnosis. Mammograms can detect masses or calcifications, representing invasive or DCIS, respectively (Filho et al., 2015; Gaurav et al., 2018). In our case, we found round, clustered calcifications accompanied by skin thickening in the right breast, which raised suspicion of DCIS. Although we found abnormalities on mammograms, this procedure is not always reliable in detecting Paget's disease of the breast. Several studies report a mammographic miss-detection rate of 15-65%, particularly for DCIS (Filho et al., 2015).

In cases with negative mammogram results, breast ultrasound may be useful. However, its findings are nonspecific, showing parenchymal heterogeneity, hypoechogenic areas, discrete masses, skin thickening, and ductal dilatation (Filho et al, 2015). In our case, no abnormalities were found during breast ultrasound. Magnetic resonance imaging (MRI) is highly sensitive and recommended for the diagnosis of breast neoplasms, especially if mammography and ultrasound are normal. MRI can demonstrate thickening of the papillary-areolar complex, increased nipple size, detection of DCIS or invasive tumor, or a combination of both, even in cases without clinical manifestations (Filho et al, 2015; Gaurav et al, 2018).

The histologic findings of Paget's disease of the breast are primarily characterized by epidermal Paget cells, malignant glandular epiphytic cells with abundant, clear cytoplasm, usually containing mucin, and pleomorphic and hyperchromatic nuclei. These cells appear arranged in clusters, with a nest-like or glandular structure, and are preferentially located in the basal layer of the epidermis. The number of cells varies from few to numerous, and they can even completely replace epidermal cells (Filho et al., 2015). In our incisional biopsies, we found single and scattered intraepidermal atypical cells with pale, wide cytoplasm, round, oval, pleomorphic nuclei, irregular nuclear membranes, and prominent nucleoli consistent with the appearance of Paget cells.

Treatment depends on the clinical, radiological, and histopathological features of the associated breast cancer, as well as metastatic lymph node involvement. Mastectomy with or without axillary lymph node dissection, even in the absence of other signs of malignancy, is considered the best therapy for Paget's disease of the breast due to concerns about underlying malignancy and multicentric disease. Alternatively, patients

with Paget's disease can safely undergo breast conservation through a central lumpectomy that removes the nipple-areola complex. However, central breast cancer is a contraindication to breast-conserving surgery. Therefore, in this case, we opted for conventional treatment and performed a wide excision of the right breast (Filho et al, 2015; Merril et al, 2017). Adjuvant therapy, consisting of chemotherapy and/or hormonal therapy, may also be recommended depending on the stage, positive lymph nodes, estrogen and progesterone receptors in the tissue, and HER2 protein expression in the tumor cells (Gupta et al, 2021).

Prognosis of Paget's disease of the breastThe diagnosis depends on the presence of a mass in the breast during clinical and imaging examinations, as well as the stage of cancer in cases of invasive breast carcinoma (Gupta et al, 2021).

V. CONCLUSION

This report describes Paget's disease with underlying ductal carcinoma in situ (DCIS). The diagnosis of Paget's disease remains challenging, particularly in ruling out malignancy. A comprehensive workup is necessary to confirm the diagnosis.

Thank-you note

The authors would like to thank the patient for permission to share her medical history for educational and publication purposes.

Conflict of Interest

The authors declare that there is no conflict of interest.whatever.

REFERENCES

[1] Dalton, J. C., & Plichta, J. K. (2024). Paget's disease of the breast: Insights from imaging to guide surgical management. ***The American Journal of Surgery***, 231, 16–17.https://doi.org/10.1016/j.amjsurg.2024.03.013

[2] Filho, LLL, Lopes, LRS, Michalany, AO, Lopes, IMRS, Enokihara, M., & Matsunaga, N. (2015). Mammary and extramammary Paget's disease. Anais Brasileiros de Dermalogia, 90(2), 225–231.

[3] Gagnier, J. J., Kienle, G., Altman, D. G., Moher, D., Sox, H., & Riley, D. (2013). The CARE guidelines: Consensus-based clinical case reporting guideline development. BMJ Case Reports, 2013, bcr2013201554.https://doi.org/10.1136/bcr-2013-201554

[4] Gaurav, A., Gupta, V., Koul, R., Dabas, S., Sareen, R., & Geeta, K. (2018). Practical consensus recommendations for Paget's disease in breast cancer. ***South Asian Journal of Cancer***, 7, 83–86.

[5] Gupta, A., Pujani, M., & Goyal, S. (2021). Paget's breast disease—A diagnostic dilemma: A case report with review. ***Biomedical Journal of Scientific & Technical Research***, 35(3), 27765–27768.

[6] Karakas, C. (2011). Paget's disease of the breast. ***Journal of Carcinogenesis,*** 10, Article 31.

[7] Kuzmiak, C. M., & Ferre, R. (2024). Paget's disease of the breast: An often-overlooked malignancy. Breast Disease, 43(1), 293–301.https://doi.org/10.1177/15581551241289263

[8] Merrill, A.Y., White, A., & McNatt, M. H. (2017). Paget's disease of the breast: An institutional review and surgical management. The American Surgeon, 83(3), E96–E98.

[9] Mousa-Doust, D., Warburton, R., Pao, J.-S., Dingee, C., Bazzarelli, A., Newman-Bremang, J., & McKevitt, E. (2024). Paget's disease of the breast: Presentation, treatment, and outcomes in a modern cohort. ***The American Journal of Surgery***, 231, 18–23.https://doi.org/10.1016/j.amjsurg.2024.01.026

[10] Ortuz Lessa, C., Fernández Varela Gómez, F., Garzón Ortega, V.H., Sandoval García, A., López Soto, K., & Brito Brito, N.R. (2025). Insights into mammary and extramammary Paget's disease: Diagnosis, management, and recent advances. Cureus, 17(3), e80531.https://doi.org/10.7759/cureus.80531

[11] Volfson, E., Moshkovich, M., Yakubov, R., Dalson, J., & Kirshen, C. (2026). Dermatologic mimickers of Paget's disease of the breast: A systematic review. ***Journal of Cutaneous Medicine and Surgery***, 30(2), 125–131.https://doi.org/10.1177/12034754251364870

[12] Yasir, M., Khan, M., & Lotfollahzadeh, S. (2022). Mammary Paget's disease. In StatPearls. StatPearls Publishing.https://www.ncbi.nlm.nih.gov/books/NBK563228/.