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Conservative treatment of the Areola in Paget's disease of the breast

Abstract

Introduction: Paget's disease (PD) is an uncommon malignant breast pathology, typically presenting with pruritus and erythema of the areola and nipple. It may be associated with ductal carcinoma in situ (DCIS) or invasive carcinoma; historically, mastectomy was the standard treatment.

Objective: The aim of this study is to demonstrate the feasibility of conservative areolar management in PD, including cases associated with DCIS or invasive carcinoma.

Materials and methods: Patients with histologically confirmed PD treated at Hospital Alemán, Español, Naval, and Clínica Privada de Morón (Buenos Aires) between April 1981–July 2005, and at Hospital Alemán (2005–2024) were included. All patients underwent mammography and breast ultrasound. In the absence of suspicious findings, magnetic resonance imaging (MRI) was requested in accordance with the latest international guidelines. Variables considered included age, the number of patients with PD associated with DCIS or invasive carcinoma, type of surgery, feasibility of areolar preservation, axillary evaluation, adjuvant treatments administered, follow-up, and recurrences

Results: Forty-three patients included (mean age 62 years, range 35–90). Imaging evaluation was performed in all cases (43 mammograms and ultrasounds; 1 MRI due to inconclusive imaging). Surgery was performed in 41 patients (34 conservative; 7 mastectomies)—two were followed clinically despite PD due to comorbidities, with no progression at 2 and 4 years.

Among surgical patients, areola preservation occurred in 31, while 10 underwent nipple–areola complex excision. Axillary staging: 16 axillary dissections, 21 sentinel node biopsies (SNB), and 4 cases without axillary evaluation.

Radiotherapy at median dose 50 Gy (range 45–54 Gy) was administered post-conservative surgery. Adjuvant treatment was administered according to standard protocols for each individual case.

Recurrences occurred in 2 cases (4.65%), both treated with salvage mastectomy. Regarding axillary evaluation, only one case showed nodal involvement. No axillary recurrences were observed. One patient was lost to follow-up, and three died from causes unrelated to breast pathology. As previously mentioned, the two patients who did not undergo surgical treatment showed no clinical progression of the disease at the time of study closure. No local skin recurrences, distant metastases, or axillary relapses were observed.

Conclusion: Conservative areolar treatment for PD limited to the nipple yields excellent disease control, with acceptable cosmetic results. Preserving part of the areola yields favorable cosmetic and emotional outcomes in women. In selected patients with negative imaging or DCIS-only disease, axillary staging (SNB or dissection) may be safely omitted.

Keywords: Paget disease, breast conserving surgery, DCIS, nipple areola complex, radiotherapy, areola preservation

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Abbreviations: PD, Paget's disease; DCIS, ductal carcinoma in situ; MRI, magnetic resonance imaging; SNB, sentinel lymph node biopsy; SLNB, sentinel lymph node biopsy; NAC, nipple–areola complex; EORTC, European organization for research and treatment of cancer

Introduction

PD was first described by Velpeau in 1856[1] and by Sir James Paget in 1874[2] as a chronic eczema-like lesion of the nipple–areola complex preceding breast cancer by at least two years, in no instance was the development of cancer localized to the previously diseased skin.

PD accounts for 1–3% of breast cancers. It affects women aged 26–88 years, with early symptoms including pruritus and erythema, often misdiagnosed as eczema, delaying diagnosis by 6–12 months. Advanced stages may show nipple retraction, ulceration, or serosanguineous discharge. Mammography may reveal nipple–areolar thickening.

The diagnosis requires full-thickness biopsy of the nipple–areola complex, identifying Paget cells, usually accompanied by underlying DCIS or invasive carcinoma, or as an isolated entity. The observed incidence of multifocality and multicentricity in the underlying carcinoma ranged from 32% to 41%. The characteristic histopathological feature of Paget's disease is the presence of adenocarcinoma cells (Paget cells) within the keratinized epithelium of the nipple epidermis. Microscopically, these cells exhibit abundant pale cytoplasm containing mucin-secreting vacuoles and hyperchromatic nuclei. They are often isolated within the superficial layers of the epidermis but tend to cluster in the basal layers.

Additional microscopic features that may complicate diagnosis include epidermal hyperplasia and hyperkeratosis, which can be pronounced enough to mimic pseudoepitheliomatous hyperplasia. The superficial dermal stroma of the nipple is frequently infiltrated by a lymphocytic reaction, sometimes quite intense. In such cases, ulceration may denude the affected epithelium, exposing only the inflamed stroma. For this reason, it is essential that histopathology reports explicitly state the presence or absence of epidermal tissue, as its omission can lead to a misdiagnosis of an inflammatory condition."

Two pathogenic theories exist: one posits in situ transformation of epidermal keratinocytes; the alternative theory suggests that Paget cells are ductal carcinoma cells that have migrated from the ducts into the epidermis of the nipple.

Traditional treatments have ranged from central excision to total mastectomy, with axillary assessment variable. Mastectomy, with or without axillary dissection, has been standard due to imaging false negatives and frequent multicentric disease. Nonetheless, multiple studies report comparable survival with conservative management and acceptable local recurrence rates (~5% at 5 years). Mastology is evolving toward therapeutic de-escalation, while maintaining favorable oncological outcomes. Furthermore, conservative treatment—which may include preserving part of the areola—can positively impact women both aesthetically and psychologically.

Sentinel node biopsy (SNB) is now standard for axillary staging in early breast cancer, including PD—even in imaging-negative cases—but its exact role remains under discussion.

The aim of this study is to retrospectively analyze the outcomes of conservative breast treatment in patients with Paget's disease (PD) associated with underlying ductal carcinoma in situ or invasive carcinoma, without requiring complete areolar excision.

Materials and methods

This retrospective study included female patients with PD treated surgically (plus or minus radiotherapy) from April 1981 to July 2005 at Hospital Alemán (with additional institutions) and Hospital Alemán until 2024. Exclusions: recurrent breast cancer, metastatic disease, neoadjuvant therapy, other primary tumors, and male patients. Data collected: age, imaging at diagnosis (mammography, ultrasound, MRI if needed), surgical approach, recurrence, and survival.

A total of 43 patients were histopathologically confirmed with PD. The mean age was 62 years (range 35–90). All had both mammogram and ultrasound; MRI was used selectively. Surgical treatment included conservative surgery or mastectomy; in conservative cases, partial areola preservation was considered.

Results

Of the 43 patients, 29 (67.4%) had PD with DCIS, 12 (27.9%) with invasive carcinoma, and 2 (4.65%) had pure PD. In age group analysis, DCIS-associated PD was more frequent in women >51 years, while invasive PD was more common in 35–50-year-olds. Among invasive cases, 66.6% lacked palpable tumors; 33.3% had palpable tumors. No multifocal or multicentric imaging was observed. Mean tumor size: non-palpable 0.91 cm (range 0.5–1.2); palpable 1.3 cm (range 1.2–2.0).

Regarding the surgical treatment performed, as previously mentioned, 41 patients underwent surgery and two were managed with clinical follow-up due to associated comorbidities. A total of 7 mastectomies—4 due to prior irradiation—and 34 conservative surgeries). Breast-conserving surgery primarily included radio-guided biopsies and quadrantectomies, allowing the preservation of part of the breast. At the level of the nipple-areola complex, the nipple was resected while part of the areola was preserved. Areola preservation was performed in 31 conservative cases, with a 0.5 cm areolar margin after nipple resection, all achieving clear margins.

Regarding nodal assessment, until 1999 axillary lymph node dissection was routinely performed. From that year onward, sentinel lymph node biopsy (SLNB) began to replace routine dissection. It included 16 axillary dissections, 21 SNBs, and 4 cases without axillary evaluation. Only one patient with palpable invasive disease had nodal metastasis.

Radiotherapy was administered to all patients undergoing conservative surgery, with a median dose of 50 Gy (range 45–54 Gy); adjuvant treatment followed standard care.

Recurrence: Two cases recurred as invasive carcinoma—one DCIS case at 8 years, and one invasive case at 5 years—both treated with salvage mastectomy; the areola was disease-free histologically.

After an average follow-up of 14.7 years, no distant metastases were observed in any patient. Cosmetic outcomes were satisfactory in all cases.

Discussion

PD of the nipple, as a distinct form of breast cancer, remains a rare clinical entity. The mean age in our study was 62 years, slightly higher than the peak incidence reported in the literature, which typically ranges between 50 and 60 years. Symptoms (pruritus, discharge, eczema) were universal; 40–50% of cases may have palpable masses, and 20–60% may show diseases beyond the nipple–areola complex. In our series, 20% of palpable cases were remote from the nipple complex (one case the tumor was located away from the nipple–areola complex). Six cases (20.68%) of the 29 patients with PD associated with in situ carcinoma, and 6 cases (50%) of the 12 patients with PD associated with invasive carcinoma, showed suspicious microcalcifications on mammography. In 3 cases, both ultrasound and mammography revealed no suspicious findings. In one of these patients, magnetic resonance imaging was requested in accordance with current guidelines. In the remaining two patients, the diagnosis of PD was made prior to the introduction of MRI as an additional evaluation method in breast pathology.

Historically, mastectomy was routine due to imaging limitations and multicentric lesions identified in 20–80% of cases surgically. Le Pennec et al. reported an 80% rate of multicentricity in mastectomy specimens, while Gunhan-Bilgan and Oktay found multicentricity in 21% of 51 mastectomy cases. In our study, none of the patients with in situ carcinoma presented with multifocal or multicentric lesions, and among those with invasive carcinoma, multifocality was observed in 11% of cases.

Early conservative efforts by Lagios et al. (1984) showed 20% recurrence. In 1984, Lagios et al. were among the first to implement conservative treatment. A total of 5 patients with PD and no suspicious imaging findings underwent conservative management with partial or complete resection of the nipple–areola complex (NAC). One recurrence was observed within 12 months. In our case series, two recurrences were observed, representing 4.65% of the patients.

In other studies, Dixon et al.[3] (40%) and Polgar et al. (33%) also noted higher recurrence without radiotherapy. Both studies concluded

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that conservative treatment was insufficient for patients with Paget's disease.

The recurrence of invasive carcinoma is associated with a poor prognosis in patients treated with conservative management. In recent years, the principles of breast-conserving treatment and sentinel lymph node biopsy (SLNB) for axillary staging have emerged as the standard of care for patients with early-stage breast cancer. Based on this conservative approach, several studies have proposed this treatment modality for patients with Paget's disease, even in the absence of a palpable tumor or suspicious mammographic findings.

Large studies support conservative surgery with radiotherapy in early PD: Fourquet et al. reported on 20 patients with nipple Paget's disease, without clinical or radiological signs of associated intraductal or invasive carcinoma, who were treated with radiotherapy alone or limited surgery of the areolar complex followed by radiotherapy. An 81% disease-free survival rate at 7 years was observed. Pierces et al. reported 100% distant disease-free survival; Marshall et al. found local control of 91%, 83%, and 76% at 5, 10, and 15 years, respectively.

The European Organization for Research and Treatment of Cancer (EORTC) conducted a prospective study involving 61 patients with PD who were treated with conservative surgery (resection of the nipple–areola complex and underlying breast tissue) followed by whole-breast radiotherapy. This was one of the largest patient cohorts in the literature. At diagnosis, 97% of patients had no palpable tumor, and 84% showed no suspicious findings on mammography. With a follow-up of 6.4 years, only 4 patients (7%) experienced local recurrence, supporting the feasibility of conservative treatment in patients with PD associated with underlying ductal carcinoma in situ. The results suggest that the prognosis differs between patients with and without palpable tumors. Those with palpable tumors had a higher incidence of associated invasive carcinoma and greater rates of axillary involvement (75–100% vs. 20–30%, and 45–65% vs. 10–20%, respectively).

Laronga et al.[4] evaluated axillary assessment in PD in 2006. They retrospectively analyzed 54 patients with PD, of whom 36 underwent sentinel lymph node biopsy, revealing an 11% rate of axillary involvement.

In our cohort, one palpable disease correlated with nodal metastasis, while non-palpable cases had no nodal involvement. Two recurrences occurred, both managed effectively, without distant metastasis.[5–24]

Conclusion

Paget's disease is frequently accompanied by DCIS or invasive carcinoma, but local recurrence rates are low. Conservative treatment should be the first option, especially in patients without palpable tumors and with disease limited to the nipple. When lesion extent is circumscribed, partial areola preservation is feasible. Preserving part of the areola yields favorable cosmetic and emotional outcomes in women.

Despite limitations—small cohort, retrospective design, heterogeneous cases—our data support conservative surgery with radiotherapy as an acceptable alternative to mastectomy in early PD. Selected cases with disease limited to the nipple can safely preserve the areola, maintaining excellent oncologic control and cosmetic outcome.

Appendix: clinical photographic record

The following clinical photographs correspond to different patients diagnosed with mammary Paget's disease, treated with a conservative surgical approach aimed at preserving the areola and reconstructing the nipple. All images were obtained and used with the patient's informed consent for academic and scientific purposes (Figure 1) (Figure 2).

Figure 1 Pre and postoperative images following conservative surgery with areola preservation.

Figure 2 Erythematous and scaly lesion centered on the nipple, with preoperative surgical marking outlining the area to be excised while preserving the areola. Conservative surgical approach aimed at maintaining breast aesthetics.

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Conflicts of interest

The authors declares that there is no conflict of interest.

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