



# Mammary Paget's Disease: a Rare Case of Early Dermal Invasion

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## Abstract

**Introduction:** Mammary Paget's Disease (MPD) is a rare cancer that typically involves an eczematous lesion of the nipple with underlying intra epidermal cancer. Mammary Paget's disease with dermal invasion is an unusual and poorly documented disorder, characterized as Paget disease that invades through the basement membrane into the dermis.

**Presentation:** We present a 64 years old female with a 6 months history of left nipple rash. Her physical exam and subsequent workup was suspicious for Paget's disease of the left nipple with Ductal Carcinoma *In Situ* (DCIS). Punch biopsy confirmed MPD with early dermal invasion, ER/PR negative, and HER2 positive. A left breast MRI guided biopsy revealed a single duct profile suspicious for DCIS. She underwent a left central partial mastectomy and subsequently a sentinel lymph node biopsy.

**Discussion:** Mammary Paget's disease is a rare cancer that represents 1% to 3% of breast cancers. The surgical treatment for Paget's disease is debatable. Most common form of MPD is intraepidermal the rare case of dermal invasion has minimal documented cases. Thus, further clinical investigation and research is required for the surgical treatment for MPD with dermal invasion. The few cases, including our case with documented Paget's disease with dermal invasion have been treated with breast conserving therapy.

**Conclusion:** We conclude that the management of MPD with dermal invasion requires further clinical investigation. Our case and the few others explored here reveal that a diagnosis of MPD with dermal invasion-based on histopathological criteria-can favor conservative operative management with radiation.

## Introduction

Mammary Paget Disease is a rare cancer that typically involves an eczematous lesion of the nipple with underlying intraepidermal cancer. Most cases of Paget's disease are due to DCIS or invasive carcinoma located deeper in the breast [1]. MPD with dermal invasion is an unusual and poorly documented disorder that is characterized as Paget's disease with invasive characteristics that invades through the basement membrane into the dermis. Dermal Paget's cells are unrelated to any underlying DCIS or malignancy. Little data supporting therapeutic indications for MPD with dermal invasion exist. Distinguishing criteria for the difference in surgical management of MPD and MPD with dermal invasion remain unknown.

## Case Presentation

64 years old female, with family history of breast cancer in a paternal aunt diagnosed at age 65, presented with a complaint of a left nipple red, dry and scaly rash for 6 months with no response to topical treatment. A mammogram showed no abnormality, with left nipple retraction seen on the CC view only (Figure 1). A diagnostic ultrasound of the left breast was unremarkable. A breast MRI showed asymmetric retraction and enhancement of the left nipple areolar complex with asymmetric smooth linear enhancement extending 2.5 cm from the left nipple, suspicious for Paget's disease and DCIS (Figure 2). On physical examination, the left breast showed erythematous change of the nipple extending onto the areola laterally, suspicious for Paget's disease (Figure 3). Punch biopsy of the left nipple revealed MPD with early dermal invasion, ER and PR (-), HER2 (+) (Figure 4). An MRI guided biopsy of the subareolar enhancement revealed DCIS. She underwent a left central

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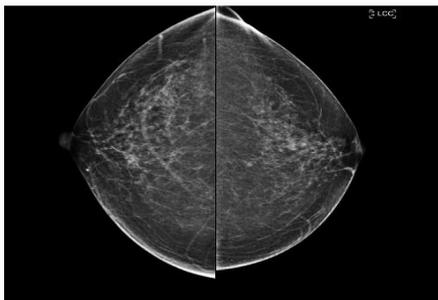
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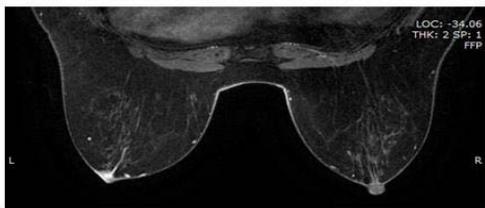
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**Figure 1:** Side by side Cranio-Caudal (CC) mammograms show left nipple retraction (right image marked LCC), compared to normal right nipple position (left image).



**Figure 2:** Non-subtracted T1 contrast-enhanced MRI shows asymmetric Left nipple enhancement and adjacent linear enhancement (breast left side mark L) consistent with Paget disease with subareolar ductal carcinoma *in situ*.



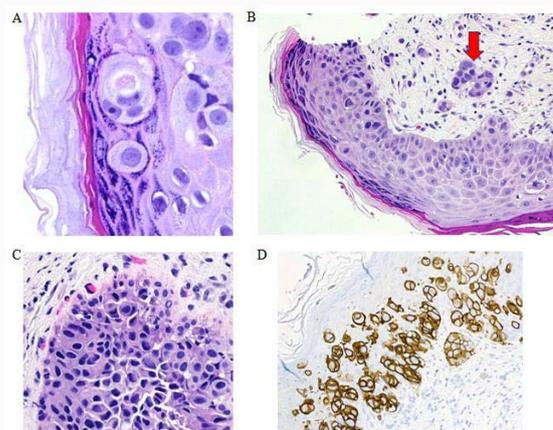
**Figure 3:** Clinical picture of the breast.

partial mastectomy, pathology revealed Paget's disease of the nipple invading 1 mm into the dermis, and high grade DCIS. A sentinel lymph node biopsy was subsequently performed which revealed benign pathology. She is currently being treated with weekly Paclitaxel with Herceptin for 12 weeks; this will be followed by radiation, which will be delivered during the Herceptin administration every 3 weeks, which will extend to 1 year.

## Discussion

Paget's disease was initially described by Sir Paget in 1874 after Paget observed 15 women with chronic nipple lesions that progressed to develop cancer of the involved breast. Thus, Paget's disease of the breast, also known as MPD, was viewed as an erythematous, scaly eczematous lesion of the nipple with underlying breast cancer. Paget's disease is a rare entity occurring in 1% to 3% of breast cancers [1]. Mammary Paget's disease with dermal invasion has been reported in a selection of female patients 4 times and in 2 male patients in the last two decades. A study in 2012 revealed that out of 146 patients with MPD there were 6 who classified as MPD with dermal invasion, a 4% incidence [2]. The low detection of this entity is most likely due to the lack of information regarding its clinical relevance. The rare case presented here will add to the few cases of MPD with dermal invasion that underwent breast-conserving therapy.

Differentiating underlying breast cancer with invasion to the skin



**Figure 4:** (A) Typical Paget's cells located in the granular layer of skin 600x. (B) Mammary Paget's disease with dermal invasion in the superficial dermis observed at 200x located at the tip of the arrow. (C) DCIS cells located in the duct at 400x. (D) (+) HER2 staining in invasive tumor at 200x.

and PMD with dermal invasion is important to prevent the more aggressive treatment that is performed on the former. The diagnosis of dermal invasion in MPD is based on histopathological criteria that were initially based on extra mammary Paget's disease, which more commonly features dermal invasion [3]. Paget cells are characterized as microscopically large clear cells with an abundant cytoplasm and hyperchromatic nuclei that is commonly found in the epidermal layer [1]. The diagnosis for MPD with dermal invasion is pathologically characterized by the isolated or clustered Paget cells that have invaded the dermal-epidermal junction. It is important to differentiate between MPD with dermal invasion and breast cancer invasion to the skin that is more common and carries a poorer prognosis and has been documented to present with increased numbers of lymph node metastases. Invasive MPD (with dermal invasion) is an under recognized entity, however, with careful pathological analysis; we can differentiate between these two entities with a vast difference in prognosis and treatment.

In accordance with the American Joint Committee on Cancer (AJCC) and Union for International Cancer Control (UICC) classification, skin invasion from underlying breast cancer carries a T4b classification. An institutional study in 2012 found 6 patients with MPD and dermal invasion, which underwent breast conserving therapy with no evidence of recurrence after an average of 20 months of follow up [3]. Sanders et al. [4] in 2013 concluded that patients with MPD with dermal invasion who underwent breast conserving therapy either with or without sentinel lymph node biopsy did not need further operative intervention and all sentinel lymph nodes were negative for malignancy. Those patients underwent radiation therapy, none received chemotherapy, and after an average of 20 months follow-up showed no evidence of recurrence [4]. On the other hand, there is one documented case in 2015 of invasive MPD, HER2 negative, involving axillary metastasis that had undergone sentinel lymph node biopsy [2,5]. According to the current NCCN guidelines, adjuvant chemotherapy with weekly Paclitaxel and Trastuzumab can be considered for T1, N0, M0, and HER2-positive cancers; particularly if the primary cancer is ER negative.

Overall, MPD with dermal invasion is treated with breast conserving surgery with or without sentinel lymph node biopsy. Despite one documented case involving axillary metastasis, most

documented cases were treated with breast conserving therapy and radiation post-operatively. Whether a sentinel lymph node biopsy should be performed on all patients with invasive MPD is unknown. Only one institutional study in 2014 compared invasive and non-invasive MPD together. It retrospectively compared survival outcome in invasive MPD and noninvasive MPD and found no significant difference between the two patient populations with regard to underlying breast cancer, immunohistochemical stain for ER or HER2, rate of distant metastasis or recurrence, and treatment modality. The overall survival and disease-free interval were not significantly different [6]. Thus treatment for MPD with dermal invasion should be the same as the treatment for non-invasive Mammary Paget's Disease.

## Conclusion

Our case reports a rare finding of MPD with early dermal invasion that was successfully managed with left central partial mastectomy with sentinel lymph node biopsy. Few cases have been reported of Paget's disease of the breast with dermal invasion and there are no studies outlining the difference in surgical treatment between invasive MPD and non-invasive MPD. The patients in the three studies reported above on this rare form of MPD all underwent breast conserving surgical therapy with no evidence of recurrence on follow up [2-4,6,7]. Distinction between underlying breast cancer invasion of skin and MPD with dermal invasion is critical as the latter exhibits a favorable prognosis. Although prior studies have shown that invasive MPD favor a treatment similar to non-invasive MPD with good response; it remains an under recognized disease. According to the current NCCN guidelines, adjuvant chemotherapy with weekly Paclitaxel and Trastuzumab can be considered for T1, N0, M0, and HER2-positive cancers; particularly if the primary

cancer is ER negative. The clinical significance of invasive Paget's disease of the breast is unknown as all studies have a limited follow up time interval. Further studies are required to dictate its clinical significance and surgical management.

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