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A rare breast cancer in a patient with pierced nipples

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Abstract

Paget disease of the breast is a rare form of breast cancer that affects the nipple and areolar complex. Clinicians should have a high suspicion for this condition in patients who fail conservative treatment for benign-appearing dermatologic findings regardless of age or sex. This article describes a patient with whose presumed nipple infection was initially thought to be related to her nipple piercing.

Keywords

Paget disease; breast; nipple; piercing; cancer; calcification

CASE

A 24-year-old woman self-referred to Memorial Sloan Kettering Cancer Center presented for further management of a nipple infection that began 8 months ago.

History

The patient has no significant medical history and denied a family history of cancer. She had both nipples pierced years earlier. Eight months ago, she noticed crusting over her left nipple. She visited her primary care provider, who recommended that she remove her nipple piercing and begin treatment for a local infection. After the symptoms failed to improve with treatment, the patient pursued consultations by multiple specialists who continued to treat for a local skin infection. Treatments included topical lanolin, mucopiricin, silver sulfadiazene, Vaseline, Neosporin, and oral antibiotics. During this interval, she noted brief improvement in her symptoms; however, she continued to experience yellow crusting and scabbing around her nipple.

Physical examination

The patient’s left nipple was excoriated and erythematous. No scaling was noted. Breasts with normal asymmetry. No skin dimpling or masses were appreciated. No abnormalities were seen on the right breast, and no axillary lymphadenopathy was felt.

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Diagnostic testing

A skin biopsy was performed and revealed a human epidermal growth factor receptor 2 (HER2) and cytokeratin 7 (CK7) intraepidermal carcinoma. A bilateral mammogram with tomosynthesis was obtained. Segmental calcifications were found in the left retroareolar area extending into the subareolar region and the nipple. Bilateral breast ultrasound and MRI corresponded with the mammographic calcifications. No additional suspicious findings were identified. A vacuum-assisted ultrasound guided biopsy of the calcifications yielded benign parenchyma tissue which was discordant with the imaging studies. Surgical excision was recommended for definitive diagnosis. A comprehensive breast cancer genetic panel was obtained and found to be negative for any genetic mutations.

Treatment

The patient underwent a left breast seed localized lumpectomy with the removal of the left areolar complex. A left axillary sentinel lymph node biopsy (SLNBX) was also performed to avoid the possibility of a second surgery if pathology was found to be invasive. Given her age, mastectomy with reconstruction was presented as an option; however, she elected to undergo breast conservative surgery. Final surgical pathology confirmed the diagnosis of Paget disease with ductal carcinoma in situ (DCIS). DCIS also was present in the underlying calcifications. Clear margins were obtained. There was no lymph node involvement. A purse-string suture technique was used at closure to recreate a natural areolar projection.

The patient underwent local radiation treatment and was monitored closely with follow-up diagnostic testing. She obtained excellent cosmetic results and later had nipple tattooing to create the appearance of an areola.

DISCUSSION

Paget disease of the breast is a rare form of cancer involving the nipple and areolar complex of the breast, and accounts for 1% to 4% of all cases of breast cancer.[1] Most patients are women, with the average age of diagnosis being 57 years, but men and young adults also can be affected.[2,3] An underlying *ductal carcinoma in situ (DCIS)* or an invasive breast carcinoma such as invasive ductal carcinoma (IDC) can be found in 90% to 100% of patients.[4]

Signs and symptoms

Paget disease of the breast typically begins unilaterally at the nipple with further involvement of the surrounding areola. Patients may notice scaling, vesicular or ulcerated lesions, which can lead to pain such as burning or pruritus.[2,3] Crusting, serous, or bloody nipple discharge and nipple retraction also may occur.

Pathogenesis

Given the rarity of Paget disease of the breast, establishing its pathogenesis has been challenging. The epidermotropic theory suggests that Paget cells originate from cancer cells in the duct that migrate to the nipple.[4] A motility factor produced by normal skin cells called heregulin-alpha, when fueled by HER2, has been shown to induce breast cancer cell

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migration to the nipple and throughout the areolar epidermis.[5] Although this is the most accepted theory, it does not explain occurrences of Paget disease of the breast in patients without an underlying breast carcinoma.

The transformation theory proposes that Paget disease of the breast is an epidermal carcinoma and independent of an underlying cancer.[6] In a study of the site of origin and pattern of tumor spread in patients with Paget disease of the breast, 19 pathology slides were analyzed and 5 cases were identified that supported the origin in the nipple, specifically the superficial portion of the lactiferous duct.[6] Given the rarity of Paget disease of the nipple without an underlying carcinoma, this finding will not account for most cases.[6] However, it does continue the discussion of the possibility of multiple origin sites.

Because the exact underlying cause of Paget disease of the breast is unknown, risk factors are difficult to characterize. Genetic predisposition and environmental factors are known to propagate cancer progression; this also applies to Paget disease of the breast. Cancer cells can emerge via inflammation-induced epigenetic reprograming, in which inflammation results in changes in the transcriptional programming of skin parenchymal cells, causing the development of cancer cells.[7] Once skin is sensitized to inflammation, it reacts faster when faced with a secondary assault.[8] Genetic alterations that mobilize stem cells more rapidly often are associated with accelerated wound repair and increased susceptibility to cancer. Connections exist between wounds and tumors at the molecular level.[9] The markers that drive wound repair are a similar driving force in cancer cells.[10] Similarities of the cytokines associated with tissue injury have been shown to promote the growth of breast cancer.[11]

Complications associated with nipple piercings include delayed wound healing for 6 to 12 months, increased risk of infection, and the development of abscesses.[12,13] Because documented data about complications of nipple piercings are not available, correlation cannot be made about whether the chronic inflammatory state contributes to patients' risk of developing cancer. No conclusive evidence supports the possibility that nipple piercing leads to Paget disease of the breast, and the rarity of the disease compared with the number of patients who have nipple piercings makes the connection unlikely. In the case patient, the two conditions appeared coincidental.

Diagnosis and management

Benign dermatologic diseases commonly affect the nipple-areolar complex (Table 1). Consider Paget disease of the breast if the patient has persistent abnormalities after treatment is initiated. Delayed diagnosis can lead to delayed treatment and potential adverse outcomes for the patient.

All patients with suspected Paget disease of the breast should undergo a skin biopsy for diagnosis. After a diagnosis is confirmed, further testing, including mammography, ultrasound, and possible MRI is required to investigate the extent of the disease.[14,18] Further work-up for surgical planning include core biopsies of suspicious breast lesions and fine-needle aspiration of axillary lymph nodes if palpable on physical examination.

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Paget disease of the breast requires removal of the entire nipple-areolar complex. The presence of an underlying breast cancer will determine further treatment strategies which should follow standard breast cancer treatment guidelines. The location of the breast cancer will determine whether the patient will need a total mastectomy or is a candidate for breast-conserving surgery with whole-breast radiation.[3,15,18] No evidence supports mastectomy as superior in overall survival outcomes to breast-conserving surgery with whole-breast radiation.[15] Multicentric disease, diffuse calcifications, or a tumor far from the nipple-areolar complex may warrant a mastectomy.[15] Another factor in surgical choice is whether negative margins can be obtained and acceptable cosmetic results can be achieved.

A palpable mass is associated with a higher chance of invasive carcinoma.[15–17] These patients should undergo **SLNBX** at the time of excision. A full **axillary lymph node dissection (ALND)** is recommended if disease is present in the lymph nodes.[18]

Patients without a palpable mass most likely have DCIS.[15–17] These patients do not require SLNBX at the time of excision unless lymph nodes are palpable, or the surgical pathology is upgraded to invasive carcinoma on final review.[18]

Evidence does not support the role of endocrine therapy for treating Paget disease of the breast alone; however, it may play a role in the treatment of the underlying carcinoma. Follow breast cancer treatment guidelines for the use of this therapy.[2,3,18]

Several factors dictate the treatment course for an individual patient. As discussed, current recommendations include excision of the NAC for the Paget disease of the breast and treatment for underlying cancer as per standards breast cancer guidelines. The treatment plan exhibited in this case study is a reflection of the shared decision model approach. The patient's concerns and requests were considered alongside best practice when formulating her treatment plan.

Prognosis

The survival rate of patients with Paget disease of the breast depends on the underlying breast carcinoma, if present.[14] Recent data suggests that when associated with Paget disease of the breast, an underlying DCIS or IDC can have a higher risk of an aggressive tumor profile, leading to worsened survival outcomes (Chen,2019). However, those with favorable histology have similar survival outcomes to other patients with breast cancer when standard treatment recommendations for breast cancer are followed.[15,17 15,17]Significantly worse outcomes are associated with the presence of a palpable mass, advanced tumor stage, axillary lymph node metastases, and invasive cancer on histology.[16]

CONCLUSION

Consider Paget disease of the breast in patients who present with suspicious skin changes of the nipple that do not respond to conservative local treatment. Delay in diagnosis can lead to poor outcomes. Breast cancer is extremely rare in younger adults. Follow standard breast cancer screening recommendations to reduce unnecessary interventions that may create complications.[13]

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REFERENCES

1. National Cancer Institute. Paget disease of the breast. www.cancer.gov/types/breast/paget-breast-fact-sheet. Accessed October 22, 2021.
2. Arora N, Simmons RM. Paget disease of the breast. In: Kuerer HM (ed). Kuerer's Breast Surgical Oncology. New York, NY: McGraw-Hill Professional, 2010.
3. Michael SS, Donald LW. Paget disease of the breast. In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. Accessed on 7/23/2019. www.uptodate.com
4. Dubar S, Boukrid M, Bouquet de Joliniere J, et al. Paget's breast disease: a case report and review of the literature. Front Surg. 2017;4(51):1–5. [PubMed: 28194399]
5. Schelfhout VJ, Coene ED, Delaey B, et al. Pathogenesis of Paget's disease: epidermal heregulin, motility factor, and the HER receptor family. JNCI Cancer Spectre. 2000;92(8):622–628.
6. Mai KT, Yazdi HM, Perkins PG. Mammary Paget's disease: evidence of diverse origin of the disease with a subgroup of Paget's disease developing from the superficial portion of lactiferous duct and a discontinuous pattern of tumor spread. Pathol Int. 1999;49(11):956–961. [PubMed: 10594841]
7. Todoric J, Karin M. The fire within: cell-autonomous mechanisms in inflammation-driven cancer. Cancer Cell. 2019;35(5):714–720. [PubMed: 31085174]
8. Naik S, Larsen SB, Gomez NC, et al. Inflammatory memory sensitizes skin epithelial stem cells to tissue damage. Nature. 2017;550:475–480. [PubMed: 29045388]
9. Foster DS, Jones RE, Ransom RC, et al. The evolving relationship of wound healing and tumor stroma. JCI Insight. 2018;3(18):e99911.
10. Yejing G, Gomez NC, Adam RC, et al. Stem cell lineage infidelity drives wound repair and cancer. Cell. 2017;169:636–650. [PubMed: 28434617]
11. Arnold KM, Opdenaker LM, Flynn D, et al. Wound healing and cancer stem cells: inflammation as a driver of treatment resistance in breast cancer. Cancer Growth Metastasis. 2015;(8):1–13.
12. Kapsimalakou S, Grande-Nagel I, Simon M, et al. Breast abscess following nipple piercing: a case report and review of the literature. Arch Gynecol Obstet. 2010;282(6):623–626. [PubMed: 20582428]
13. Jayasinghe Y.Preventive care and evaluation of the adolescent with a breast mass. Semin Plast Surg. 2013;27(1):13–18. [PubMed: 24872733]
14. Sandoval-Leon AC, Drews-Elger K, Gomez-Fernandez CR, et al. Paget's disease of the nipple. Breast Cancer Res Treat. 2013;141(1):1–12. [PubMed: 23929251]
15. Yao Y, Sun L, Meng Y, et al. Breast-conserving surgery in patients with mammary Paget's disease. J Surg Res. 2019;241:178–187. [PubMed: 31026796]
16. Zakaria S, Pantvaidya G, Ghosh K, Degnim AC. Paget's disease of the breast: accuracy of preoperative assessment. Breast Cancer Res Treat. 2007;102:137–142. [PubMed: 17028984]
17. Yim JH, Wick MR, Philpott GW, et al. Underlying pathology in mammary Paget's disease. Ann Surg Oncol. 1997;4(4):287–292. [PubMed: 9181226]
18. National Comprehensive Cancer Network. Bone cancer. www.nccn.org/professionals/physician_gls/pdf/breast.pdf. Accessed November 18, 2021.
19. Nicholson BT, Harvey JA, Cohen MA. Nipple-areolar complex: normal anatomy and benign and malignant processes. Radiographics. 2009;29(2):509–523. [PubMed: 19325062]
20. Whitaker-Worth DL, Carlone V, Susser WS, et al. Dermatologic diseases of the breast and nipple. J Am Acad Dermatol. 2000;43(5):733–754. [PubMed: 11050577]

Chen S, Chen H, Yi Y, et al. Comparative study of breast cancer with or without concomitant Paget disease: An analysis of the SEER database. Cancer Med. 2019;8(8):4043–4054. doi:10.1002/cam4.2242 [PubMed: 31134761]

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Table 1.

Common benign diseases of the nipple[19, 20]

Disease	Signs/symptoms, Pertinent history	Treatment
Eczema	• Erythema, scaling, weeping, crusting, excoriations, lichenification, intense pruritus • Known history	• Avoid triggers • Topical corticosteroids • Emollients • Oral H_1 antihistamines (for pruritus)
Psoriasis	• Well-demarcated pink plaque, minimal or no scaling,mild pruritus • Known history	• Topical corticosteroids • Topical vitamin D • Emollients • Oral H_1 antihistamines
Bacterial infection secondary to trauma (*Staphylococcus aureus*)	• Evolving erythema, weeping, pustules, crusting • Known source of infection (chronic dermatitis, piercing, wound, friction burn)	• Topical antibiotics • Oral antibiotics
Fungal infection (*Candida albicans*)	• Beefy erythema, satellite papules, pustules • Breastfeeding	• Topical antifungals • Oral antifungals
Viral infection (herpes simplex)	• Punched-out erosions, hemorrhagic crusts, vesicles, pruritus • Previous history, new exposure	• Oral antiviral therapy