



Time for detailed clinical management of Paget's disease of the breast

Chaofan Li, MD^a, Yusheng Wang, MD^b, Mengjie Liu, MD^a, Jingkun Qu, PhD^{a,*}, Shuqun Zhang, MD^{a,*}

Dear Editor,

Paget's disease (PD) of the breast is a rare form of mammary carcinoma, with an estimated incidence of 1–3% among all breast cancer patients^[1]. It is clinically distinguished by an eczematoid lesion on the nipple, which could extend to the areola, accompanied by other skin signs, such as pruritus, erythema, nipple erosion or ulceration, bloody nipple discharge, and nipple retraction^[1]. The infiltration of large epidermal adenocarcinoma cells, called Paget's cells, within the nipple epidermis is the main histopathological characteristic of mammary PD^[2]. Since mammary PD was first described and connected with an underlying cancer by Sir James Paget in 1874, the prognosis and management of the disease have been the subject of debate^[3].

PD of the breast can be divided into three categories according to the underlying malignancy, which is associated with its prognosis. Approximately 50–60% of mammary PD patients have concurrent invasive ductal carcinoma (PD-IDC), 30–40% of patients also have ductal carcinoma in situ (PD-DCIS), and only 10% of patients involve skin changes alone (PD)^[4]. PD with IDC or DCIS are both related to worse survival outcomes and more aggressive tumor characteristics than the corresponding disease without PD. Even so, the 15-year overall survival (OS) and breast cancer-specific survival (BCSS) rate of PD-DCIS who were treated with breast-conserving surgery (BCS) and radiotherapy can reach 90% and 97%, respectively^[5]. However, the prognosis of PD-IDC is much worse; over 50% of PD-IDC patients were positive for lymph node metastasis compared with about 30% of IDC-alone patients^[4], and the 5-year OS of PD-IDC patients with positive lymph nodes was only 20–25%^[6].

Some studies showed that BCS followed by radiotherapy might be a feasible treatment alternative^[7,8] for PD-IDC patients,

compared with mastectomy. Another recent meta-analysis indicated that except for mammary PD alone, BCS alone is not recommended for treating PD-IDC and PD-DCIS^[9], which emphasized the necessity of radiotherapy after BCS. However, BCS alone presents a nonsignificant difference in local recurrence rate when compared with mastectomy and BCS with radiotherapy in the MPD-alone subgroup. Further, we have to consider whether the choice of radiotherapy needs to be precisely grouped, for example, T3, T4, or N1. Apart from this, there are no studies discussing the role of chemotherapy and the choice of chemotherapeutic agents. The role of endocrine therapy in patients with PD-IDC needs to be further elucidated. As stated in this article, we need to study PD in subgroups and manage it with precision.

Moreover, this study revealed that tumor characteristics with palpable mass, positive lymph node status, or the histology type of underlying invasive breast cancer are more associated with poorer prognosis. One possible explanation is that patients with PD with IDC are more likely to exhibit masses and axillary lymph node metastases, which in turn leads us to think about the important role of axillary lymph node biopsy as an indication for the treatment of patients with PD. It is necessary to carefully investigate the presence of IDC in patients with positive axillary lymph node biopsy in order to intensify treatment and prevent recurrence.

In addition, PD is a rare disease, and it is hard to conduct randomized controlled trials to compare the effect of different treatments; thus, conducting multicenter clinical studies will therefore be the direction of future work.

Ethical approval

The data from the SEER database is publicly available. Thus, the present study was exempted from the approval of local ethics committees.

Consent

Because the data are publicly available and do not include personally identifiable patient information, this retrospective cohort study was approved by the Institutional Review Board of the Second Affiliated Hospital of Xi'an Jiaotong University, which decided to waive informed consent.

Sources of funding

This work was funded in part by the following: National Science Foundation of China (82174164, to S.Q. Zhang, 82103569, to J.K. Qu); Key Science and Technology Program of Shaanxi Province (2021KW-60, to J.K. Qu). Construction project of Shaanxi Provincial Key Laboratory of Integrative Traditional

^aDepartment of Oncology and ^bDepartment of Otolaryngology, The Second Affiliated Hospital of Xi'an Jiaotong University, Xi'an, Shaanxi, People's Republic of China

Chaofan Li and Yusheng Wang have contributed equally to this work and share the first authorship.

Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

*Corresponding author. Address: Department of Oncology, The Second Affiliated Hospital of Xi'an Jiaotong University, 157 West Fifth Street, Xi'an, Shaanxi, People's Republic of China. Tel.: +86 180 668 89811. E-mail: qujingkun@xjtu.edu.cn (J. Qu), and Tel.: +86 138 918 41249. E-mail: shuqun_zhang1971@163.com (S. Zhang).

Copyright © 2023 The Author(s). Published by Wolters Kluwer Health, Inc. This is an open access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 (CCBY-NC-ND), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal.

International Journal of Surgery (2024) 110:1266–1267

Received 29 September 2023; Accepted 9 October 2023

Published online 26 October 2023

<http://dx.doi.org/10.1097/JS9.0000000000000855>

Chinese Medicine and Western Medicine for Cancer Prevention and Control (2022-ZXY-SYS-002 to S.Q. Zhang).

Author contribution

C.L., J.Q., and S.Z.: conceptualization; C.L. and Y.W.: writing – original draft preparation; Y.W. and M.L.: writing – review and editing; J.Q. and S.Z.: supervision. All authors have read and agreed to the published version of the manuscript.

Conflicts of interest disclosure

The authors declare no conflict of interest.

Guarantor

Jingkun Qu and Shuqun Zhang.

Data availability statement

This is a commentary; no original data is reported.

References

- [1] Chen CY, Sun LM, Anderson BO. Paget disease of the breast: changing patterns of incidence, clinical presentation, and treatment in the U.S. *Cancer* 2006;107:1448–58.
- [2] Choridah L, Sari WK, Dwianingsih EK, *et al.* Advanced lesions of synchronous bilateral mammary Paget's disease: a case report. *J Med Case Rep* 2020;14:119.
- [3] Markarian S, Holmes DR. Mammary Paget's disease: an update. *Cancers (Basel)* 2022;14:2422.
- [4] Wong SM, Freedman RA, Sagara Y, *et al.* The effect of Paget disease on axillary lymph node metastases and survival in invasive ductal carcinoma. *Cancer* 2015;121:4333–40.
- [5] Marshall JK, Griffith KA, Haffty BG, *et al.* Conservative management of Paget disease of the breast with radiotherapy: 10- and 15-year results. *Cancer* 2003;97:2142–9.
- [6] Karakas C. Paget's disease of the breast. *J Carcinog* 2011;10:31.
- [7] Yao Y, Sun L, Meng Y, *et al.* Breast-conserving surgery in patients with mammary Paget's disease. *J Surg Res* 2019;241:178–87.
- [8] Wu Q, Ding X, Li J, *et al.* Surgical treatment in Paget's disease with invasive ductal carcinoma: an observational study based on SEER. *Sci Rep* 2017;7:45510.
- [9] Lin CW, Chiang MH, Tam KW. Treatment of mammary Paget disease: a systematic review and meta-analysis of real-world data. *Int J Surg* 2022;107:106964.