JAMA Dermatology Clinicopathological Challenge

Pigmented Plaque in the Axilla

Lan Zhang, PhD; Xing-Hua Gao, PhD; Jiu-Hong Li, PhD

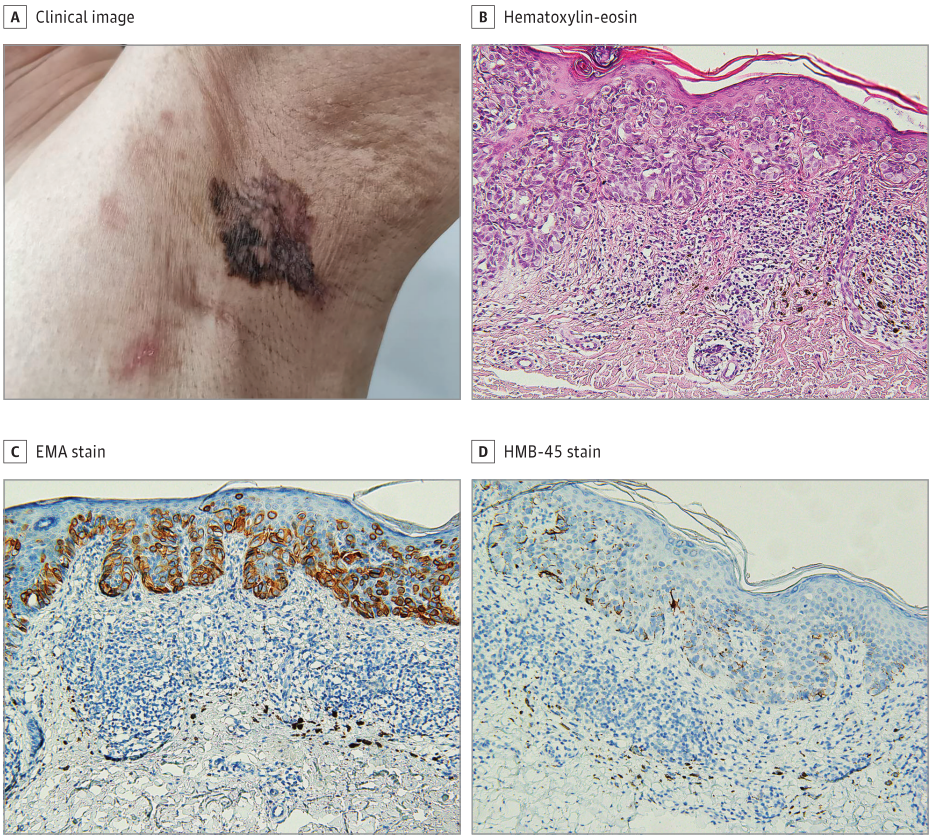

Figure. A, Clinical presentation of pigmented plaque in the axilla with well-demarcated margins. B, Histologic findings revealed an intraepidermal neoplasm consisting of pagetoid cells, characterized by round, pale, vacuolated cytoplasm, and large pleomorphic nuclei (hematoxylin-eosin; original magnification ×200). C, Immunohistochemical findings showed positive staining for EMA (original magnification ×200). D, The lesion was surrounded by numerous reactive dendritic HMB-45–positive melanocytes scattered among the tumor cells (original magnification ×200).

A woman in her 70s presented with an enlarged and variegated plaque on her left axilla, which she had had for 4 years. The lesion started as a small eczematous, pink-to-brown plaque. As the lesion was asymptomatic and slow growing, she did not initially seek treatment. Recently, the color of the lesion had changed to an alarming dark brown color (**Figure**, A). No breast mass or lymphadenopathy was observed. Her medical and family history was unremarkable. A skin biopsy specimen was obtained and submitted for further histopathologic analysis.

WHAT IS YOUR DIAGNOSIS?

- **A.** Pagetoid Bowen disease
- **B.** Inverse lichen planus
- **C.** Pigmented extramammary Paget disease
- **D.** Superficial spreading melanoma

Diagnosis

C. Pigmented extramammary Paget disease

Microscopic Findings and Clinical Course

An incisional biopsy revealed an intraepidermal neoplasm consisting of pagetoid cells, characterized by a round, pale vacuolated

cytoplasm and large pleomorphic nuclei. Immunohistochemical staining revealed that the lesion was positive for CK7, EMA, and surrounded by numerous reactive dendritic HMB-45–positive melanocytes scattered among the tumor cells (Figure, B-D). Based on these clinical and histologic manifestations, a diagnosis of pigmented extramammary Paget disease (EMPD) was formulated.

Discussion

Extramammary Paget disease is an intraepithelial adenocarcinoma that most commonly involves the vulva but can also occur in the perianal skin, scrotum, penis, and axilla. It is sometimes associated with underlying adnexal or visceral cancer. Extramammary Paget disease usually manifests as dermatitis and/or eczematous lesions.[1] Occasionally, the lesion is pigmented. Pigmented EMPD is a very rare clinical-pathologic variant of EMPD. Although its clinical features are often indistinct and difficult to distinguish from other pigmented entities, appropriate histologic and immunohistochemical analysis is essential in securing a definitive diagnosis.

The reason for the presence of melanocytic colonization and reactivation remains unclear, and several hypotheses have been put forward to explain these processes. For example, it has been suggested that chemoattractant factors or cytokines may be involved. These agents have the potential to mediate the transfer of melanin pigment to tumor cells; produce phagocytosis of melanin by surrounding carcinomatous cells; and induce reactive melanophages in the dermal infiltration to generate a lesion with a pigmented appearance.[2] Further studies will be required to clarify the mechanisms of hyperpigmentation in pigmented EMPD at the molecular level.[3]

Treatments for pigmented EMPD are similar to those for EMPD, and include surgery, radiotherapy, photodynamic therapy, and administration of topical immunomodulators. The patient was treated with Mohs surgery under local anesthesia. No recurrence or metastasis was observed at 8 months of follow-up.

Generally, these differential diagnoses contain similar features with regard to pigmented manifestations. Pagetoid Bowen disease (BD) clinically presents with a well-demarcated plaque, which in some cases may be pigmented. Histologically, pagetoid BD is characterized by nests of atypical keratinocytes with round nuclei and abundant pale cytoplasm.[4] These neoplastic cells show immunohistochemical features of squamous cells and are generally negative for CK7 and CEA. In contrast, these markers are positive in EMPD.[5] Inverse lichen planus is an uncommon variant of lichen planus confined to the intertriginous zones, including axilla, inguinal creases, gluteal cleft, limb flexures, and submammary region.[6] Clinically, erythematous lesions with poorly defined borders and lichenification are seen, and pigmentation of the individual lesions is also typical.[7] The histologic feature that serves to differentiate this lesion is vacuolar degeneration of the epidermal basal cell layer, band-like or superficial perivascular lymphocytic infiltration, as well as pigmentary incontinence and melanophages. Superficial spreading melanoma shows a slightly raised light brown-to-black colored plaque or macule with irregular borders, and has a greater proportion of melanoma associated with nevus, as well as total nevus and dysplastic nevus counts, which serve as salient features for its diagnosis.[8] Histopathologic features include asymmetry, poor circumscription, and an absence of cellular maturation. Atypical epithelioid melanocytes with abundant cytoplasm and large nuclei are dispersed throughout the layers of the epidermis as single cells or nests.[9]

This rare case of EMPD presented with a pigmented plaque on the axilla in the absence of any underlying carcinoma. Early biopsy of these lesions is critical to arrive at a correct diagnosis and initiate appropriate treatment. Regular clinical follow-up of patients with EMPD is recommended.

ARTICLE INFORMATION

Author Affiliations: Department of Dermatology and Key Laboratory of Immunodermatology, the First Hospital of China Medical University, Shenyang, China.

Corresponding Author: Jiu-Hong Li, PhD, Department of Dermatology, the First Hospital of China Medical University, Shenyang 110001, China (pfkl2011@126.com).

Published Online: September 16, 2020. doi:10.1001/jamadermatol.2020.3250

Conflict of Interest Disclosures: None reported.

Funding/Support: This research is supported by grants from the National Natural Science Foundation of China (81803148) for data collection and patient management.

Role of the Funder/Sponsor: The National Natural Science Foundation of China had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Additional Contributions: We thank the patient for granting permission to publish this information. We also thank Dr Song Zheng, MD, PhD, The First Hospital of China Medical University, for his assistance in pathology. He was not compensated.

Self-assessment Credit: This article is eligible for journal-based self-assessment (1 credit) for Maintenance of Certification (MOC) from the American Board of Dermatology (ABD). After completion of an activity, please log on to the ABD website at www.abderm.org to register your credits. This may be done after each exercise or after accumulating many credits.

REFERENCES

1. Morris CR, Hurst EA. Extramammary paget disease: a review of the literature-part I: history, epidemiology, pathogenesis, presentation, histopathology, and diagnostic work-up. *Dermatol Surg*. 2020;46(2):151-158. doi:10.1097/DSS.0000000000002064

2. Kiavash K, Kim S, Thompson AD. Pigmented extramammary paget disease'-a potential mimicker of malignant melanoma and a pitfall in diagnosis: a case report and review of the literature. *Am J Dermatopathol*. 2019;41(1):45-49. doi:10.1097/DAD.0000000000001208

3. Petersson F, Ivan D, Kazakov DV, Michal M, Prieto VG. Pigmented Paget disease—a diagnostic pitfall mimicking melanoma. *Am J Dermatopathol*. 2009;31(3):223-226. doi:10.1097/DAD.0b013e3181930dc6

4. Lee J, Kim M, Moon J, Yoon HS, Cho S, Park HS. Pagetoid bowen disease initially misdiagnosed as ectopic extramammary paget's disease. *Ann Dermatol*. 2018;30(2):218-221. doi:10.5021/ad.2018.30.2.218

5. Zhu T, Wang T, Ma DL, Wang YN, Li L. A case of pagetoid bowen's disease. *Chin Med J (Engl)*. 2017;130(24):3023-3024. doi:10.4103/0366-6999.220315

6. Lehman JS, Tollefson MM, Gibson LE. Lichen planus. *Int J Dermatol*. 2009;48(7):682-694. doi:10.1111/j.1365-4632.2009.04062.x

7. Gaertner E, Elstein W. Lichen planus pigmentosus-inversus: case report and review of an unusual entity. *Dermatol Online J*. 2012;18(2):11.

8. Howard MD, Wee E, Wolfe R, McLean CA, Kelly JW, Pan Y. Differences between pure desmoplastic melanoma and superficial spreading melanoma in terms of survival, distribution and other clinicopathologic features. *J Eur Acad Dermatol Venereol*. 2019;33(10):1899-1906. doi:10.1111/jdv.15759

9. Situm M, Buljan M, Kolić M, Vučić M. Melanoma--clinical, dermatoscopical, and histopathological morphological characteristics. *Acta Dermatovenerol Croat*. 2014;22(1):1-12.