Human Pathology (2016) 47, 70–77

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Human PATHOLOGY

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Original contribution

# Primary invasive extramammary Paget disease on penoscrotum: a clinicopathological analysis of 41 cases☆

Bo Shu MD[a,1], Xu-Xia Shen MD[b,c,1], Peng Chen MD[d], Xin-Zhi Fang MD[e], Yong-Lian Guo MD[a], Yun-Yi Kong MD, PhD[b,c,*]

[a]*Department of Urology, Central Hospital of Wuhan, Wuhan 430014, People's Republic of China*
[b]*Department of Pathology, Fudan University Shanghai Cancer Center, Shanghai 200032, People's Republic of China*
[c]*Department of Oncology, Shanghai Medical College, Fudan University, Shanghai 200032, People's Republic of China*
[d]*Department of Urology, Affiliated Tumor Hospital, Xinjiang Medical University, Ürümqi, Xinjiang 830011, People's Republic of China*
[e]*Department of Pathology, Affiliated Tumor Hospital, Xinjiang Medical University, Ürümqi, Xinjiang 830011, People's Republic of China*

Received 18 June 2015; revised 28 August 2015; accepted 4 September 2015

**Keywords:**
Extramammary Paget disease;
Invasive;
Histology;
Immunohistochemistry;
Prognosis

**Summary** To investigate the clinicopathological and immunohistochemical features and prognostic factors for invasive extramammary Paget disease (EMPD) on penoscrotum, we described the clinical presentations, histopathology, and follow-up courses of 41 cases. The age of the patients ranged from 42 to 84 years. All the patients were treated with wide surgical excision, and 14 were confirmed to have lymph node metastasis. During follow-up, 18 patients (43.9%) developed local or distant recurrence, and 13 patients (31.7%) died of the disease. Histologically, glandular formation with true lumina within the epidermis was found in 29 cases, and signet ring cells were seen in 11 cases. In invasive components, nodular/micronodular growth pattern, glandular formation, and strands/solid sheets existed in 95.1% (39/41), 43.9% (18/41), and 24.4% (10/41) of the cases, respectively. More than half of the cases had at least 2 different types of invasive growth pattern. CK7 was diffusely positive in all cases, whereas CK20 was focally positive in 8 cases. GCDFP-15 was expressed to a variable degree in 24 cases. Presence of strands/solid sheets, lymphovascular invasion, and perineural invasion in invasive EMPD were found to be correlated with higher lymph node metastatic rate. Univariate analysis revealed that patients with one of the following prognostic factors: delay in diagnosis more than 7.5 years, depth of invasion more than 1 mm, invasive pattern of strands/solid sheets, marked inflammation, lymphovascular invasion, and lymph node metastasis at diagnosis, had significantly shorter cancer-specific survival. We concluded that invasive EMPD is a rare malignant skin neoplasm with morphological diversity. Invasive pattern of strands/solid sheets is significantly associated with both lymph node metastasis and worse prognosis. Delay in diagnosis, depth of invasion, marked inflammation, lymphovascular invasion, and regional lymph node status are important prognostic factors.


☆ Funding/Support: This study was supported in part by Shanghai Natural Science Fund (12ZR1406600).
* Corresponding author at: Department of Pathology, Fudan University Shanghai Cancer Center, 270 Dong'an Road, Shanghai 200032, People's Republic of China.
*E-mail address:* kyunyidb@126.com (Y. -Y. Kong).
[1] Bo Shu and Xu-Xia Shen have contributed equally to this article.

http://dx.doi.org/10.1016/j.humpath.2015.09.005
0046-8177/

## 1. Introduction

Extramammary Paget disease (EMPD), first described by Crocker in 1889 [1], is a distinct form of rare malignant skin neoplasm. It is considered to be most likely derived from undifferentiated pluripotent cells of the epidermis and/or its adnexa [2]. EMPD often occurs in older patients between the ages 50 and 80 years on areas rich in apocrine sweat glands such as vulva, scrotum, perineum, perianal area, and axilla. Penoscrotal area is the second most commonly involved site by EMPD after vulva [2,3].

Most patients with EMPD have a good prognosis because EMPD progresses slowly and is usually limited to the epidermis and cutaneous adnexal structures. However, in some cases, tumor can invade the dermis and subcutaneous tissue and may have the potential for metastasis and lethality. Because of its rarity, previous studies on invasive EMPD consisted mainly of case reports or constituted only a small part of the whole study population [3-8]. Large series of studies were quite few [9,10], especially that focusing on detailed histopathologic features of stromal invasion and its relationship with lymph node metastasis and cancer-specific survival. Here, we performed a study of 41 cases on penoscrotum to elucidate the clinicopathological and immunohistochemical features of invasive EMPD and to explore the prognostic factors for this rare entity.

## 2. Materials and methods

Forty-one cases with primary penoscrotal invasive EMPD not associated with any underlying neoplasm were obtained from the surgical pathology archives of Affiliated Tumor Hospital, Xinjiang Medical University and Central Hospital of Wuhan between 2004 and 2013. Available data including clinical presentations, therapeutic regimens, and follow-up information were collected. Informed consent was obtained from each patient, and the study was approved by our institutional ethics committee.

Resection specimens of 41 cases were fixed in 10% formalin and embedded in paraffin, and histologic sections were obtained and stained with hematoxylin and eosin by routine methods. Pathologic slides of all cases were reviewed by 2 experienced dermatopathologists. Histopathologic parameters of the primary skin lesions including epidermal change, growth pattern of Paget cells in the epidermis, adnexal involvement, depth of invasion, histologic pattern of invasive components, chronic inflammation, lymphovascular invasion, perineural invasion, and mitotic activity per 10 high-power fields (HPF) were evaluated. Depth of invasion was measured vertically from the overlying epidermal-dermal junction to the deepest site of stromal invasion in millimeters on hematoxylin and eosin sections under the microscope. Immunohistochemical studies by the EnVision detection system (K5007; Dako, Glostrup, Denmark) were performed with primary antibodies against Cytokeratin 7 (CK7) (OV-TL; Dako), Cytokeratin 20 (CK20) (Ks20.8; Dako), Gross Cystic Disease Fluid Protein-15 (GCDFP-15) (23A3; Dako), Carcinoembryonic Antigen (CEA) (II-7; Dako), and CDX2 (DAK-CDX2, Dako).

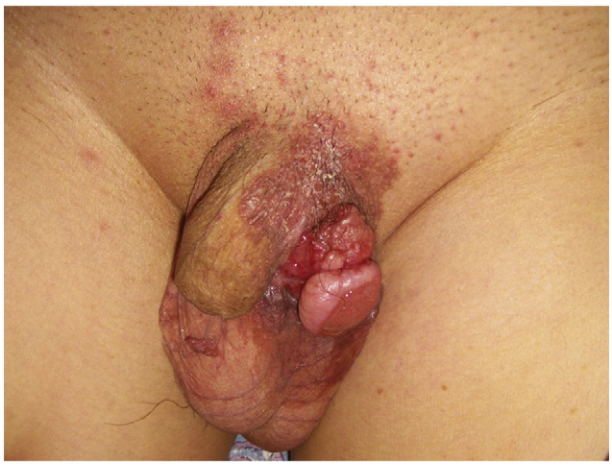

**Fig. 1** Invasive EMPD presented as erythematous scaly skin lesions on penis and scrotum, with a reddish multinodular mass.

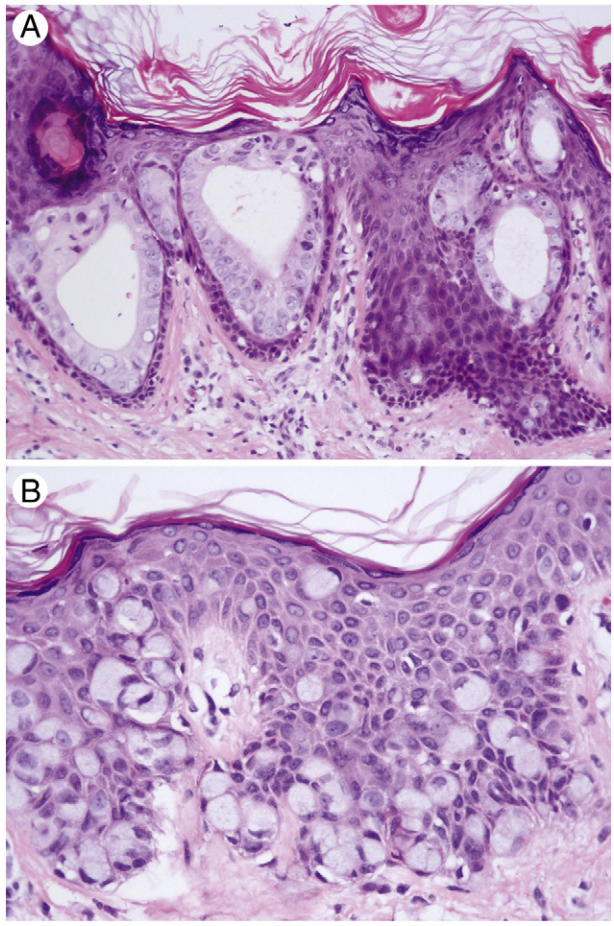


**Fig. 2** A, Glands formation by Paget cells within epidermis. B, Paget cells exhibiting signet ring cell appearance (hematoxylin and eosin, original magnification ×200).