Patients' Experiences With Extramammary Paget Disease: An Online Pilot Study Querying a Patient Support Group

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OBJECTIVE To illustrate the heterogeneous care delivered to patients with extramammary Paget disease (EMPD), a rare and lethal malignancy with poorly described treatment methodologies, by characterizing the clinical and pathologic characteristics of an international patient support group.

MATERIALS AND METHODS Institutional review board approval was obtained to develop and distribute a nonvalidated survey to patients from an international, online EMPD support group. The survey was developed to capture patient clinical and pathologic details and was distributed between January 2017 and February 2017.

RESULTS Forty-two patients completed the survey. At a mean age of 64 years, patients most commonly developed rash, pruritus, or erythema in the genital and perianal regions. Patients presented to their primary care physician, gynecologist, or dermatologist and were initially treated with topical agents for benign diagnoses. After failing conservative treatments, patients underwent biopsy by a dermatologist or gynecologist and were diagnosed with EMPD on average 21 months after the onset of symptoms. Wide local and Mohs excisions were the most frequently administered treatments with positive margins reported in 43% of patients. Fewer patients underwent noninvasive treatment with imiquimod cream and radiation. In total, 29% of patients developed regional recurrence and distant disease. There was wide variation regarding medical specialties involved, diagnostic evaluation, treatment, and clinical follow-up.

CONCLUSION This study provides a novel view of the varied clinical and pathologic details from patients treated across varying institutions and medical specialties. This study will hopefully educate providers of the overall disease process of EMPD and encourage the development of standardized treatment recommendations. UROLOGY 111: 214–219, 2018. © 2017 Elsevier Inc.

Extramammary Paget disease (EMPD) is a rare and lethal intraepithelial malignancy with poorly described treatment methodologies and outcomes. Incidence has been reported as 0.12 per 100,000 people, with an overall survival of 60% at 120 months post diagnosis.[1,2] EMPD develops most frequently in the genital, perianal, and axillary regions, and commonly presents with symptoms of erythematous or pruritic rash or plaque (Fig. 1). Patients often initially undergo rounds of ineffective treatments for a benign diagnosis before a correct diagnosis of EMPD is obtained. EMPD may present as poorly defined, multifocal, and subclinical lesions making the initial diagnosis challenging. Lesions may also become invasive, precluding definitive treatment. EMPD has also been associated with secondary internal malignancies, such as rectal, bladder, prostate, and endocervical cancers.[3]

Because of the low incidence of the disease, current studies evaluating EMPD are based on single-institution case reports and small cohort series that have not comprehensively assessed the clinical journey from initial disease presentation to diagnosis to treatment and through follow-up. The impetus for our current study is the increased number of patients with EMPD that we have treated over the past 4 years. These patients were referred having received a variety of care by outside providers that prompted us to query patients regarding their own experiences. We developed an online survey to illustrate the heterogeneous care delivered to patients with EMPD by characterizing the clinical and pathologic characteristics of an international, online patient support group treated across different institutions.

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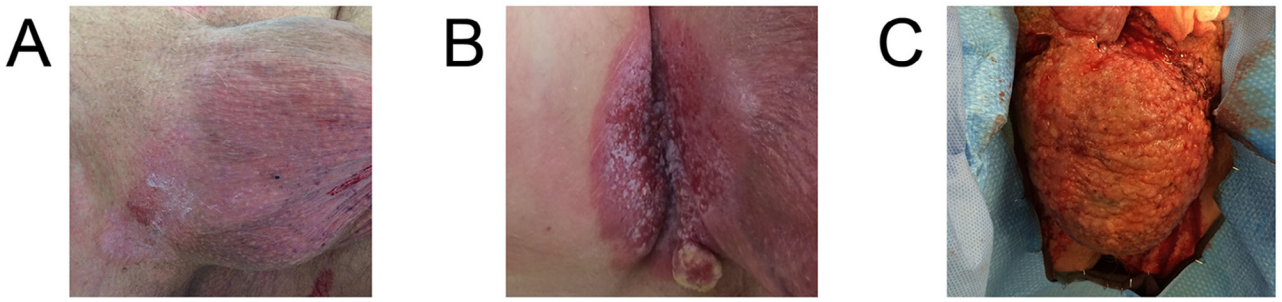

Figure 1. Representative extramammary Paget disease (EMPD) lesions that are confined to the scrotum **(A, B)** and locally advanced **(C)**. (Color version available online.)

MATERIALS AND METHODS

Institutional review board approval was obtained to develop and distribute a survey to patients from a private, online EMPD support group. The survey and content were developed by the authors of this article using Research Electronic Data Capture electronic data tools hosted at the University of Washington.[4] The survey was not validated but was reviewed with a patient with EMPD from our institution to ensure readability and pertinence of questions. We reviewed the patient's responses to the online questionnaire and noted agreement with his clinical course. This patient was a member of the support group used for this study and posted the survey link to the respective support group members. The survey link included the purpose of the study, estimated time to complete the survey, risks and benefits of participation, electronic storage of protected data details, and plans to present and publish study results. Patients voluntarily completed the survey between January 2017 and February 2017.

RESULTS

Initial Disease Presentation

Forty-two patients from an international, online EMPD support group completed the electronic survey with a 76% response rate (n = 55). Patients underwent EMPD treatment within the United States (24 states), United Kingdom (n = 1), and New Zealand (n = 1). Mean age at presentation of symptoms was 64 years (range 45-84), and 55% (n = 23) of patients were male (Table 1). Initial presenting symptoms included rash (71%, n = 30), pruritus (64%, n = 27), erythema (40%, n = 17), swelling (12%, n = 5), and pain (14%, n = 6). All patients presented with EMPD of the genital or perianal region. No patient developed axillary disease. For men, EMPD involved the scrotum (43%, n = 10), groin (43%, 10), perineum (26%, n = 6), perianal region (9%, n = 2), and penis (4%, n = 1). For women, EMPD involved the labia or vulva (82%, n = 14), perianal region (18%, n = 3), and groin (6%, n = 1).

Table 1. Patient demographics and clinical presentation

	#	%/Range
Patient demographics		
Number of patients	42	—
Mean age at presentation, y	64	45-84
Male	23	55%
Personal history of cancer	18	43%
Family history of cancer	30	71%
Family history of EMPD	2	5%
Presenting symptoms		
Rash	30	71%
Pruritus	27	64%
Erythema	17	40%
Swelling	5	12%
Pain	6	14%
Involved locations		
Men		
Scrotum	10	43%
Groin	10	43%
Perineum	6	26%
Perianal	2	9%
Penis	1	4%
Female		
Labia or vulva	14	82%
Perianal	3	18%
Groin	1	6%

EMPD, extramammary Paget disease.

Initial Treatment and Diagnosis

Patients first sought medical treatment on average 8 months (range 1-43) after the onset of symptoms (Table 2). Patients initially sought treatment from their primary care physician (49%, n = 21), gynecologist (23%, n = 10), or dermatologist (19%, n = 8) but rarely from a urologist (2%, n = 1), medical oncologist (2%, n = 1), or plastic surgeon (2%, n = 1). Patients initially underwent treatment with topical medications (64%, n = 27), lotions or powder not containing medication (12%, n = 5), or medical oral therapy (2%, n = 1). Seven patients underwent immediate biopsy (14%, n = 6) or wide local excision (2%, n = 1). Two patients were referred to a gynecologist and general surgeon for further evaluation by their primary care physician without any initiation of treatment. The most common initial diagnoses patients received were fungal infection (36%, n = 15), EMPD (17%, n = 7), contact dermatitis (7%, n = 3), and yeast infection (7%, n = 3).

EMPD Diagnosis

Patients were eventually diagnosed with EMPD at a mean of 21 months (range 0-101) after the onset of symptoms. The majority of diagnoses were obtained by a dermatologist (60%, n = 24), gynecologist (23%, n = 9), or general

Table 2. Disease diagnosis and treatment

	#	%/Range
Initial diagnosis and treatment		
Time to initial evaluation from presentation, mo	8	1-43
Initial physician		
Primary care physician	21	49%
Gynecologist	10	23%
Dermatologist	8	19%
Medical oncologist	1	2%
Plastic surgeon	1	2%
Urologist	1	2%
Initial diagnosis		
Fungal infection	15	36%
EMPD	7	17%
Rash	5	12%
Contact dermatitis	3	7%
Yeast infection	3	7%
Unknown	3	7%
Lichen sclerosis	2	5%
Herpes	1	2%
Ringworm	1	2%
Squamous cell carcinoma	1	2%
Initial treatment		
Medical topical skin therapy	27	64%
Biopsy	6	14%
Lotions or powder not containing medication	5	12%
Wide local excision	1	2%
Medical oral therapy	1	2%
Other	2	5%
EMPD diagnosis		
Time to EMPD diagnosis from presentation, mo	21	0-101
Diagnosing physician		
Dermatologist	24	60%
Gynecologist	9	23%
General surgeon	3	8%
Primary care physician	1	3%
Medical oncologist	1	3%
Plastic surgeon	1	3%
Urologist	1	3%
Diagnosed by biopsy	40	95%
Positive lymph node disease	3	7%
Positive metastatic disease	0	0%
Secondary cancer malignancy evaluation		
CT or MRI	14	34%
Secondary cancer screening		
PSA, men only	16	70%
Pap smear, female only	10	53%
Cystoscopy	20	48%
Colonoscopy	26	62%
New secondary cancer diagnosis	0	0%

CT, computed tomography; MRI, magnetic resonance imaging; PSA, prostate-specific antigen.

surgeon (8%, n = 3), whereas the minority were obtained by a primary care physician (3%, n = 1), urologist (3%, n = 1), medical oncologist (3%, n = 1), or plastic surgeon (3%, n = 1). Diagnosis was obtained by biopsy (95%, n = 40) or wide local excision (5%, n = 2). At presentation, 7% (n = 3) of patients reported lymph node involvement, whereas no patients reported knowledge of distant metastases. Two of the 3 patients with lymph node involvement were diagnosed promptly at 2 and 3 months after presentation; however, the third patient was diagnosed with lymphadenopathy at 15 months following initial presentation. Imaging (computed tomography [CT] or magnetic resonance imaging [MRI]) was obtained in 34% (n = 14) of patients. Serum carcinoembryonic antigen (CEA) levels were obtained in 15% (n = 4) of patients.

Secondary Cancer History and Screening

Eighteen patients (43%) reported a prior cancer history: basal cell (n = 4), melanoma (n = 3), breast (n = 3), endometrial (n = 1), prostate (n = 3), renal cell (n = 2), colon (n = 1), cervical (n = 1), and bladder (n = 1) cancer. Thirty patients (71%) reported a family history of cancer, whereas 2 patients (5%) reported a family history of EMPD. Additional prostate-specific antigen and Pap smear cancer screening were performed in 70% (n = 16) of men and 53% (n = 10) of women, respectively. Cystoscopy was performed in 48% (n = 20) of patients and colonoscopy in 62% (n = 26) of patients. No patients reported a new cancer diagnosis from these secondary cancer-screening evaluations.

Surgical Treatment History

Patients underwent a variety of treatments: wide local excision (57%, n = 24), Mohs excision (26%, n = 11), imiquimod cream (26%, n = 11), radiation (21%, n = 9), laser treatment (7%, n = 3), cryotherapy (2%, n = 1), chemotherapy (2%, n = 1), photodynamic therapy (2%, n = 1), and other not described (10%, n = 4) (Table 3). Patients underwent a mean of 2 surgeries (range 0-28). Most patients underwent primary wound closure (56%, n = 23), whereas the remaining underwent closure by secondary intention (24%, n = 10), skin or muscle flap (17%, n = 7), or split thickness skin graft (15%, n = 6). Of the 43% (n = 16) of patients with positive margins, 44% (n = 7) underwent immediate surgery to remove the positive margins, 25% (n = 4) underwent initial monitoring followed by surgical excision, whereas 31% (n = 5) underwent monitoring alone. In regard to the cohort who underwent monitoring alone, only 1 of the 5 patients answered the follow-up question regarding eventual recurrences.

Follow up

Average follow-up since time of EMPD diagnosis for patients was 36 months (range 2.5-310). During this time, 71% (n = 22) of patients reported being disease free, 23% (n = 7) reported developing a recurrence in the same genital and rectal region, and 6% (n = 2) reported developed a recurrence outside of the initial genital and rectal region. Statistical analysis of recurrence rates was not possible because of the variable response rates regarding technical questions pertaining to follow-up dates and dates of recurrence. Patients followed up with a dermatologist (50%, n = 21), general surgeon (29%, n = 12), medical oncologist (24%, n = 10), plastic surgeon (21%, n = 9), urologist (17%, n = 7), or gynecologist (14%, n = 6). Follow-up evaluation included a physical examination (81%, n = 34), biopsy (33%, n = 14), blood work (17%, n = 7),

Table 3. EMPD treatment and follow-up

	#	%/Range
Treatment		
Wide local excision	24	57%
Mohs excision	11	26%
Imiquimod	11	26%
Radiation	9	21%
Laser treatment	3	7%
Photodynamic therapy	1	2%
Cryotherapy	1	2%
Chemotherapy	1	2%
Other	4	10%
Surgical treatment history		
Median number of procedures	2	0-28
Wound closure		
Primary closure	23	56%
Secondary intention	10	24%
Skin or muscle flap	7	17%
Split thickness skin graft	6	15%
Positive margins present	16	43%
Management of positive margins		
Immediately surgically removed	7	44%
Initially monitored, eventually removed	4	25%
Currently monitored, have not been removed	5	31%
Follow-up		
Time since diagnosis, mo	36	2.5-310
Disease status		
Remains disease free	7	44%
Developed a regional recurrence	5	31%
Developed a distant recurrence	4	25%
Physician		
Dermatologist	21	50%
General surgeon	12	29%
Medical oncologist	10	24%
Plastic surgeon	9	21%
Urologist	7	17%
Gynecologist	6	14%
Primary care physician	4	10%
Diagnostic tests		
Physical examination	34	81%
Biopsy	14	33%
Blood work	7	17%
CT or MR imaging	5	12%
Confocal laser scanning microscope	2	5%
Genomic studies	2	5%
Other	3	7%

CT or MRI (12%, n = 5), confocal laser scanning microscope (5%, n = 2), genomic studies (5%, n = 2), and other not described (7%, n = 3). Patients obtained information about EMPD from medical websites (81%, n = 34), physician visits (55%, n = 23), patient support groups or message boards (45%, n = 19), medical journals (31%, n = 13), and pamphlets (21%, n = 9). Overall, 79% (n = 27) of patients were satisfied with their treatment, and 82% (n = 31) would agree to undergo the same treatment regimen.

COMMENT

As a result of limited data and knowledge regarding the demographics of EMPD, we developed an online survey to characterize the clinical and pathologic characteristics of patients belonging to an international EMPD patient support group. We acknowledge that utilization of an online patient support group has limitations, including recall bias; however, we believe that the rarity of EMPD warrants use of the online support group to provide additional granularity regarding how EMPD is diagnosed and treated. A notable finding of our study was the wide variation among medical specialties who diagnose EMPD. We hypothesize that this has led to varied diagnostic and therapeutic approaches, which was also a notable finding of our descriptive analysis. We postulate that this varied management across specialties has also hindered the lack of clinical guidelines and consensus statements for EMPD. Our end goal with this study is to educate providers, encourage discussion among different medical specialties, and foster the development of treatment recommendations for the goals of improving patient care and outcomes.

Similar to prior reports, patients in our study developed symptoms of EMPD at a mean age of 64 years.[5,6] Patients frequently presented to their primary care physician, gynecologist, or dermatologist with rash, pruritus, and erythema in the genital and perianal regions. Patient neglect may have been a contributing factor to the delay in diagnosis since they sought medical attention on average 8 months after developing symptoms. Medical specialists frequently initiated topical treatments for benign diagnoses including fungal infection, lichen sclerosis, and contact dermatitis. Only 17% of patients were diagnosed with EMPD at first presentation.

Patients in our study experienced a delay to diagnosis of EMPD (mean 21 months after the onset of symptoms) similarly described in published studies.[5,6] The diagnosis was most frequently obtained by biopsy performed by a dermatologist or gynecologist. To avoid delayed diagnosis, providers should biopsy persistent lesions unresponsive to several weeks of conservative therapy. Furthermore, providers uncertain of physical examination findings or management should refer patients to a specialist (dermatologist, gynecologist, general surgeon, or urologist) to decrease the risk of delay in diagnosis.

An association between EMPD and secondary intra-abdominal malignancies (colorectal, genitourinary, and endocervical) has been suggested in up to 10%-20% of patients.[3,7] Literature recommends screening for these secondary malignancies, but there are no conclusive recommendations as to which tests and studies should be obtained. Patients in our study underwent the following screening or diagnostic studies: prostate-specific antigen testing (70%), colonoscopy (62%), Pap smear (53%), cystoscopy (48%), and CT or MRI (34%). Fortunately, no patients were identified with a new secondary malignancy. Serum CEA level is a tumor marker for EMPD, rectal, colon, and cervical carcinomas. Elevated CEA levels have been linked to cases of metastatic but not early stages of EMPD.[8] Only 15% of patients in our study reported knowledge of undergoing CEA testing. Further evaluation is needed to verify whether secondary malignancy screening is justified and if so, which tests should be performed.

There are no studies comparing invasive (wide local excision, Mohs excision) and noninvasive (imiquimod cream, laser therapy, topical chemotherapy, photodynamic therapy, radiation) treatments for EMPD. In fact, only 1 clinical trial currently exists with a primary aim to evaluate the clinical efficacy, safety, and immunological response of imiquimod cream for vulvar disease (NCT02385188). Patients in our current study most frequently underwent or received wide local excision (57%), Mohs excision (26%), imiquimod cream (26%), or radiation (21%). Our survey addressed the types of treatment received, not specifically the order of treatment, why a specific modality was selected, or the stage of disease at the time of treatment.

EMPD begins as an in situ carcinoma in the epidermis and may progress to invade the dermis, at which point the risk for developing lymph node and distant metastases increases.[8] Depth of invasion has also been shown to serve as a predictor of prognosis.[9,10] Therefore, assessing dermal involvement with biopsy or excision is critical in disease management. Complete excision remains the most recommended treatment strategy for EMPD; however, debate exists whether Mohs surgery or wide local excision may result in better cancer control.[11,12] Despite the technique performed, positive margins may occur as frequently as 40%-74%.[5,13,14] Margin status cannot be discerned intraoperatively with the naked eye because of the microscopic and multicentric nature of lesions that can accompany the dominant lesions. Techniques such as fresh sections, frozen sections, preoperative mapping biopsies, and wide margins may help to improve this issue.[5] One study reported the benefit of intraoperative frozen sections in reducing the incidence of positive margins from 74% to 8% of patients.[13] Because positive margins are prevalent and associated with disease recurrence, we recommend providers to not perform complex graft and flap wound closures until final pathology margins are confirmed.[15,16] When necessary, providers should establish relationships with surgeons who are able to help with wound coverage, as 32% of patients required a skin or muscle flap or split thickness skin graft in our report. Wide variation exists in diagnosis and treatment among patients with EMPD, a novel finding that has not been previously described in the medical literature. Perhaps this variation across multiple medical specialties has been a crucial reason for nonuniform methods of treatment and management. Patients in this report most frequently followed up with a dermatologist (50%), general surgeon (29%), medical oncologist (24%), plastic surgeon (21%), urologist (17%), or gynecologist (14%). Follow-up biopsy was performed in 33% of patients. EMPD may recur in 34%-44% of patients even 10-84 months after initial treatment and also be present in otherwise normal-appearing epidermis. Further evaluation is required to better understand the timing of disease recurrence and whether clinical or histologic evaluation is best to evaluate recurrence and treatment response.

Over the past 3 years, we have treated 10 patients with EMPD. Our initial evaluation for EMPD patients has developed to involve a full physical examination and a comprehensive laboratory workup, including a serum CEA level to assess for systemic disease. Elevated CEA levels help to confirm clinical findings of systemic spread for patients with clinical metastasis at initial presentation to our center. CT or MRI is obtained if there is clinical suspicion (elevated serum CEA levels or lymphadenopathy) for systemic disease. Secondary malignancy screening for prostate, bladder, and kidney cancer is performed if a patient meets prostate cancer screening guidelines and hematuria criteria. A referral for colonoscopy and Pap smear is obtained if the patient lapsed recommended screening intervals.

The preferred management at our center is wide local excision. Our current approach has evolved to excising a 2-cm margin of normal-appearing skin around the EMPD-suspicious lesion. Before excision, the tissue is oriented and demarcated into predefined segments. These markings are then photographed and conducted in the presence of a pathologist to aid the pathology report. Additional punch biopsies are taken based on clinical examination when necessary. A xenograft or wet-to-dry dressings are applied depending on the size and location of the wound. Patients are admitted to the hospital while the specimen is expeditiously reviewed over the following 24-48 hours. If positive margins are present, further excision of the corresponding skin segment is performed with similar photographic documentation in case additional excision is necessary. Once negative margins are achieved, delayed primary wound closure or skin grafting is performed during the same hospital admission.

Our systematic approach of obtaining wide margins and documenting excised skin has aided our ability to achieve negative margins for this challenging malignancy. We have not encountered subsequent EMPD recurrence among the 5 patients who presented with clinically localized disease. Patients are followed every 3 months in the first year, followed by semiannually the following year, then yearly thereafter. Physical examination, serum CEA level, and CT or MRI (based on disease burden) are performed at each visit. We have chosen to not administer adjuvant topical treatments such as imiquimod cream, until further clinical data supporting its benefit are available.

We believe patients with EMPD should be referred to centers of excellence in an attempt to improve care and decrease variation in treatment and follow-up. Improving physician awareness of EMPD through descriptive studies published across several disciplines is 1 step in educating physicians and encouraging patient referrals to centers of excellence. Multidisciplinary discussion of EMPD may serve to increase research collaboration, establish treatment recommendations, and define which institutions are indeed centers of excellence. Furthermore, we propose that close collaboration with patient groups help to formulate the patient-centered research and a potential funding.

Limitations of this study include the use of a nonvalidated patient questionnaire and the potential for recall bias. Detailed pathologic, treatment and surgical information were not queried because of the perceived challenge that patients would not be able to consistently recall such details.

Furthermore, the potential for selection bias also exists as patients who joined the support group and responded to the questionnaire may not represent all patients with EMPD. Participating in the support group and questionnaire required the ability to navigate social media, which not all potential patients may have possessed. Patients who sought out the support group may have also had worse performance status, unfavorable medical experiences, or desired new treatment alternatives. We were unable to perform risk analyses for disease recurrence because of the power of this study and the varied response rates to individual questions. As all patients were required to be living for the study, no survival data were obtained. Despite these limitations, this study provides a unique perspective of the clinical and pathologic details of patients with EMPD who have been treated at several institutions, different from prior single-institution studies.

CONCLUSION

This study provides a novel view of the varied clinical and pathologic details from patients who have been treated across varying institutions. Querying patients via electronic means is a viable and alternative method to study diseases with low incidences and helps to improve the overall understanding of this disease process. We hope that this study will help to raise awareness of the need for treatment recommendations and provide education for physicians who may evaluate and treat patients with EMPD.

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References

1. Herrel LA, Weiss AD, Goodman M, et al. Extramammary Paget's disease in males: survival outcomes in 495 patients. *Ann Surg Oncol.* 2015;22:1625-1630.
2. Cheng PS, Lu CL, Cheng CL, Lai FJ. Significant male predisposition in extramammary Paget disease: a nationwide population-based study in Taiwan. *Br J Dermatol.* 2014;171:191-193.
3. Hegarty PK, Suh J, Fisher MB, et al. Penoscrotal extramammary Paget's disease: the University of Texas M. D. Anderson cancer center contemporary experience. *J Urol.* 2011;186:97-102.
4. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)—a metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform.* 2009;42:377-381.
5. Jung JH, Kwak C, Kim HH, Ku JH. Extramammary Paget disease of external genitalia: surgical excision and follow-up experiences with 19 patients. *Korean J Urol.* 2013;54:834-839.
6. Kang Z, Xu F, Zhu Y, et al. Genetic analysis of mismatch repair genes alterations in extramammary Paget disease. *Am J Surg Pathol.* 2016;40:1517-1525.
7. Chanda JJ. Extramammary Paget's disease: prognosis and relationship to internal malignancy. *J Am Acad Dermatol.* 1985;13:1009-1014.
8. Hatta N, Yamada M, Hirano T, Fujimoto A, Morita R. Extramammary Paget's disease: treatment, prognostic factors and outcome in 76 patients. *Br J Dermatol.* 2008;158:313-318.
9. Crawford D, Nimmo M, Clement PB, et al. Prognostic factors in Paget's disease of the vulva: a study of 21 cases. *Int J Gynecol Pathol.* 1999;18:351-359.
10. Shu B, Shen XX, Chen P, Fang XZ, Guo YL, Kong YY. Primary invasive extramammary Paget disease on penoscrotum: a clinicopathological analysis of 41 cases. *Hum Pathol.* 2016;47:70-77.
11. O'Connor WJ, Lim KK, Zalla MJ, et al. Comparison of mohs micrographic surgery and wide excision for extramammary Paget's disease. *Dermatol Surg.* 2003;29:723-727.
12. Lee SJ, Choe YS, Jung HD, et al. A multicenter study on extramammary Paget's disease in Korea. *Int J Dermatol.* 2011;50:508-515.
13. Yang WJ, Kim DS, Im YJ, et al. Extramammary Paget's disease of penis and scrotum. *Urology.* 2005;65:972-975.
14. Zhu Y, Ye DW, Chen ZW, Zhang SL, Qin XJ. Frozen section-guided wide local excision in the treatment of penoscrotal extramammary Paget's disease. *BJU Int.* 2007;100:1282-1287.
15. Fanning J, Lambert HC, Hale TM, Morris PC, Schuerch C. Paget's disease of the vulva: prevalence of associated vulvar adenocarcinoma, invasive Paget's disease, and recurrence after surgical excision. *Am J Obstet Gynecol.* 1999;180:24-27.
16. Zollo JD, Zeitouni NC. The Roswell Park Cancer Institute experience with extramammary Paget's disease. *Br J Dermatol.* 2000;142:59-65.