Vulvar Extramammary Paget's Disease Secondary to Urothelial Carcinoma Presenting with a Small Painful Erosion of the Vulva

Yu-Chen Chen, Cheng-Lin Wu[1], J. Yu-Yun Lee

Departments of Dermatology and [1]Pathology, National Cheng Kung University Hospital, Tainan, Taiwan

A 75-year-old female presented to our clinic complaining of a very painful lesion in the vulva area for more than 1 month. Examination revealed a 1-cm, round erythematous erosion on the left vulva [Figure 1]. KOH smear revealed presence of pseudohyphae and budding yeast forms, indicating candidiasis. The symptoms improved after topical antifungal treatment. A skin biopsy specimen of the erosion revealed an extensive intraepidermal infiltration of atypical cells with hyperchromatic pleomorphic nuclei [Figure 2]. The tumor cells were melan-A (–), weakly CK7 (+) [Figure 3], strongly CK20 (+) [Figure 4], GATA3 (+) [Figure 5], and uroplakin (UP)-III(-) [Figure 6]. A diagnosis of Extramammary Paget's Disease (EMPD) was made and secondary EMPD was suspected. Further questioning revealed urinary frequency in recent month. Urine cytology reported presence of suspicious malignant cells. Cystoscopy showed papillary tumors in the bladder neck, extending to the urethra. Pathology of the bladder tumor showed extensive

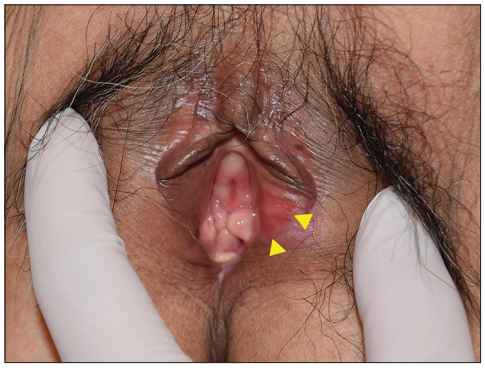

Figure 1: A 1-cm erythematous erosion (arrow heads) on the left vulva without a visible tumor

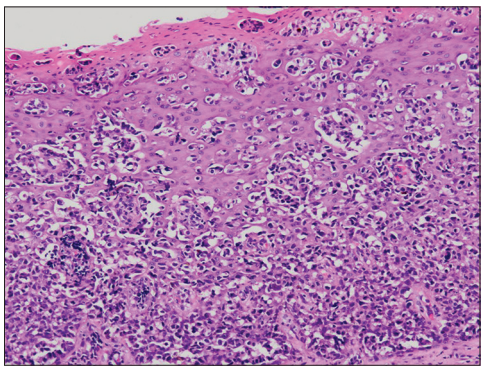

Figure 2: Biopsy of the vulvar lesion reveals an extensive infiltration of atypical cells, singly and in nests, throughout the epidermis. The tumor cells have enlarged hyperchromatic, pleomorphic nuclei and moderately abundant cytoplasm (H and E stain, ×200)

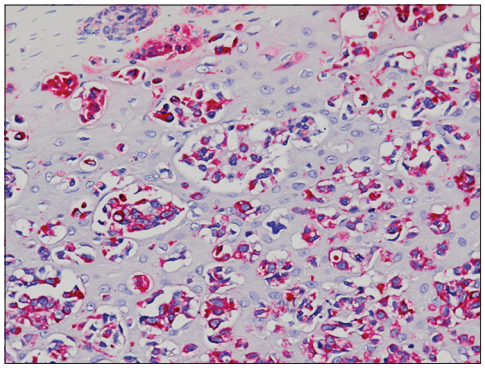

Figure 3: The tumor cells are CK7 (+) (immunohistochemistry, ×400)

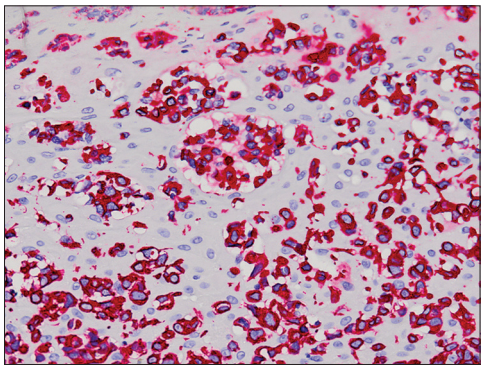

Figure 4: The tumor cells are CK20 (+) (immunohistochemistry, ×400). The expression of CK20 is stronger than that of CK7

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Address for correspondence:
Dr. J. Yu-Yun Lee, Department of Dermatology, National Cheng Kung University Hospital, Tainan, Taiwan.
E-mail: yylee@mail.ncku.edu.tw

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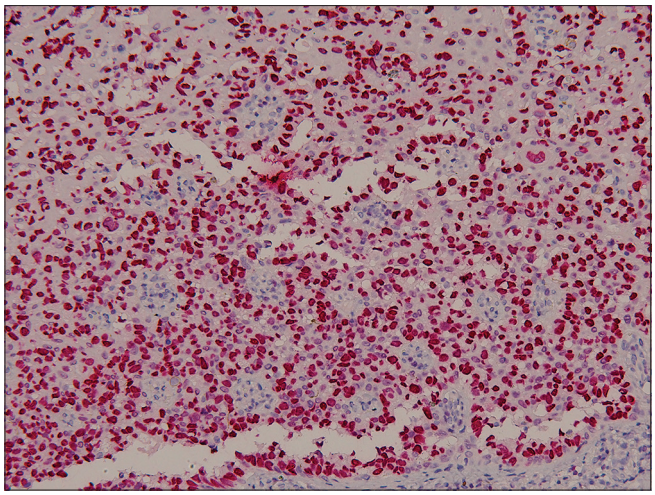

Figure 5: The tumor cells are GATA3 (+) (immunohistochemistry, ×200)

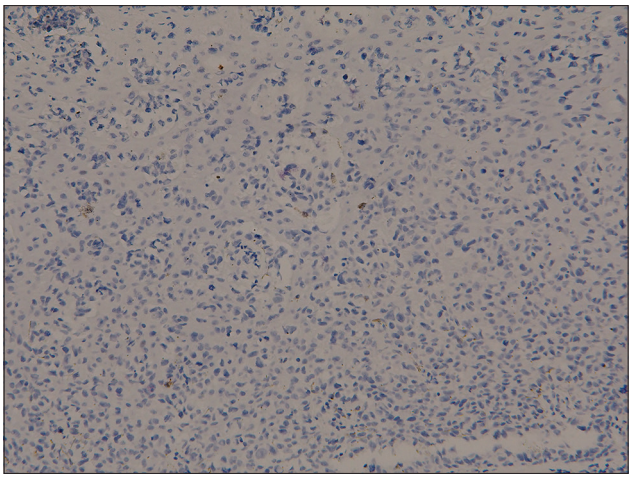

Figure 6: The tumor cells are Uroplakin (UP)-III (-) (immunohistochemistry, ×200)

infiltration of pleomorphic transitional cells, findings consistent with infiltrative urothelial carcinoma. Computer tomography revealed lymph node metastasis and right obturator muscle involvement. The patient was enrolled in a clinical trial 2 months after first presentation.

EMPD is a rare intraepithelial adenocarcinoma most commonly affecting the external genitalia, followed by perianal and axillary areas.[1] Distinction between primary versus secondary EMPD is essential for treatment planning. Vulva pain is more commonly observed in primary EMPD that has dermal invasion or an underlying adenocarcinoma, than in secondary EMPD.[2] Immunophenotyping of pagetoid cells helps to determine the origin of the tumor. In the study by Perrotto *et al.,* primary EMPD was shown to be CK7 (100%+)/CK20 (22%+)/BRST-2 (48%+).[3] In comparison, secondary EMPD were CK7 (100%+)/CK20 (50%+)/BRST-2 (25%+). In all of the CK20+ cases, the expression of CK20 was weaker than that of CK7. Other markers that have been applied in EMPD include DX2, which is positive in 80% of the EMPD of anorectal origin, and GATA3, which is positive in primary and secondary vulvar Paget's disease (VPD)[3] and urothelial carcinoma (67%).[4] In the present case, the expression pattern of CK7/CK20 was unusual for EMPD in that the tumor showed a stronger expression of CK20, and negative expression of UP-III. Although UP-III is more specific for urothelial carcinoma, the sensitivity is low in high-grade tumors,[5] as illustrated in the present case.

VPD secondary to urothelial carcinoma (urothelial VPD) is extremely rare. Seven cases have been reported previously, five had urothelial carcinoma preceding the lesion of vulvar EMPD and two had vulvar EMPD diagnosed 14 years and 6 years, respectively, before diagnosis of urothelial carcinoma. The urethral orifice showed tumor involvement in six cases, but no visible tumor in one. Our patient is unique in that she presented with a recent-onset of painful small vulvar erosion without obvious involvement of the urethral orifice and that there was no history of a prior diagnosis of malignancy. The diagnoses of VPD and urothelial carcinoma were made at the same time. Of all eight cases of urothelial VPD, CK7 was positive in six of six cases, CK20 positive in four of five cases, and UP-III positive in three of four cases. Our case illustrates the importance of including urothelial carcinoma in the differential diagnosis of VPD, even when there is no obvious tumor of urethral orifice or a prior diagnosis of urothelial carcinoma. In such cases, the underlying urothelial carcinoma can be treated appropriately and a vulvectomy can potentially be averted.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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