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Verrucous Carcinoma of the Vulva: A Case Report and Literature Review

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Patient: Female, 50
Final Diagnosis: Verrucous carcinoma of the vulva
Symptoms: Itch • tumor
Medication: —
Clinical Procedure: Surgery
Specialty: Surgery

Objective: Rare disease

Background: Verrucous carcinoma (VC) of the vulva is a variation of squamous carcinoma (SCC). Etiology and treatment of VC are still unclear.

Case Report: A 50-year-old female visited our clinic with a giant vulvar tumor (8 cm of diameter maximum). Biopsy revealed a suspicious well differentiation squamous cancer. PET/CT (positron emission tomography/computed tomography) scan found suspicious lymph node in bilateral iliac vessel region and bilateral inguinal region. She underwent radical vulvectomy and bilateral inguinal lymph node dissection, and bilateral pelvic lymph node dissection. Pathology turns out to be VC and no lymph nodes involvement. Due to the large defection, vulvar reconstruction was performed 5 weeks later using skin grafts and pudendal thigh flap. This patient was disease free after 12 months follow-up.

Conclusions: In patients with VC, a satisfactory biopsy is important and systemic inguinal lymphadenectomy might be omitted. For patients with large defection, flap-based reconstruction is recommended.

MeSH Keywords: Carcinoma, Squamous Cell • Carcinoma, Verrucous • Lymph Node Excision • Vulvar Neoplasms

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Background

Verrucous carcinoma (VC) is a very rare variant of squamous cell carcinoma (SCC) that accounts for less than 1% of VC [1]. VC were first described in 1948 by Ackerman [2], and other locations, such as cervical, vagina, and bladder, have also been described [3].

As VC is a rare disease, all cases of vulvar VC were reported in case or case series. Pathogenesis and treatment remain unclear. The precursors of VC and the relationship between human papillomavirus (HPV) infection and VC is controversial. Vulvar acanthosis with altered differentiation has been considered a precursor of VC, and although HPV testing is negative in most cases, the role for HPV is doubtful [4]. In addition, surgical treatment and follow-up therapy needs to be further discussed. VC usually presents with giant tumor size and palpated inguinal lymph nodes, however, metastasis of those palpated lymph nodes are rare.

We report a case of VC treated in Fudan University Shanghai Cancer Center (FUSCC) and reviewed the cases reported during January 1, 1998 and March 31, 2018 in PubMed. The aim of this study was to clarify the clinicopathologic characteristics of VC and optimal treatment of the disease. The study was approved by the ethics committee in FUSCC, Shanghai, China, and informed consent was obtained.

Case Report

She suffered vulvar pain and itch for almost 20 years. She visited a gynecologist and was diagnosed as having a white lesion of the vulva without pathology confirmation. Five months ago, the patient found a vulvar mass of 1.0 cm and biopsy confirmed papilloma of squamous epithelium. She was diagnosed as vulvar condyloma acuminate and underwent laser treatment. However, the patient developed a giant tumor in the next 5 months (8 cm of diameter maximum). Then, she consulted in Department of Gynecological Oncology, FUSCC. On clinical examination, an exophytic tumor of 8 cm in maximum was involving mons pubis and without urethra and vagina involvement. Enlarged lymph nodes were palpated in bilateral inguinal region. Tumor biomarker squamous cell carcinoma antigen (SCCA) was 7.8 ng/mL. PET/CT Positron emission tomography/computed tomography PET/CT scan found suspicious lymph node in bilateral iliac vessel region and bilateral inguinal region. Biopsy of the vulvar lesion revealed a suspicious well differentiation squamous cancer. The patient underwent radical vulvectomy and bilateral inguinal lymph node dissection, and bilateral pelvic lymph node dissection was performed trans laparoscopy. Pathological examination of the specimen confirmed a 7.5×5×4.5 cm VC with negative margin and a <1 mm stroma invasion but no vessel invasion. There was no sign of metastasis of the removed lymph nodes (0/58). According to FIGO 2009 staging criteria, the tumor was classified as IB (size >2.0 cm). Due to the large defection, vulvar reconstruction was performed 5 weeks later using skin grafts and pudendal thigh flap. All flaps survived without infection or necrosis (Figure 1). This patient was disease free after 12 months follow-up.

Discussion

A search performed on PubMed database from January 1, 1998 to March 31, 2018 resulted in a total of 12 publications about VC, including case series and case reports [1–12] (Table 1). VC is a rare type of vulvar cancer with a characteristic of slow-growing, giant size, and less metastasis [1]. In our case, after laser treatment, this tumor grows more rapid than usual. This disease usually occurs in postmenopausal women, and some cases of young patients were also reported [12]. Most patients suffered from a long time of precursory symptoms, including bleeding, pruritus and pain (Table 2). In this review, the longest time of precursory symptom to diagnosis was 96 months [2,10]. An exophytic growth tumor with giant size was often presented, and the tumor often diffusely spread on the vulvar with both minor or major labia and mons or clitoris. Diagnosis of VC depends on pathology through biopsy. Since VC sometimes co-exist with SCC, biopsy might lead to misdiagnosis due to the superficial sampling [10]. A satisfying biopsy requires sufficient depth. In our case, the previous diagnosis is SCC and this indicated that a satisfying biopsy is very important for preoperative diagnosis.

According to the terminology of the International Society for the Study of Vulvovaginal Disease (ISSVD), 2 different types of squamous VIN were introduced in the 1986 ISSVD terminology and confirmed in 2004, “usual VIN” (HPV associated) and “differentiated VIN” (not HPV associated). Usual VIN and different VIN differ in clinical presentation, etiology, pathogenesis and histological/immunohistochemistry features [13]. The introduction of the Lower Anogenital Squamous Terminology (LAST) in 2016 changed the final version which was accepted by ISSVD as follows: 1)l low-grade SIL of the vulva or vulvar LSIL; 2) high-grade SIL of the vulvar or HSIL; 3) vulvar intraepithelial neoplasia, differentiated type [14]. The vulvar HSIL and the differentiated VIN are the precursors of the VSSC, leading to 2 separate pathways for developing VSCC. They have different risk factors, affect different populations and have different prognosis.

HPV infection only accounts for part of the VSCC. According to literatures, HPV status was evaluated in many VSCC cases and most of them were negative. HPV test were performed

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Figure 1. (**A**) Giant tumor on vulvar before primary surgery. (**B**) Large defection after tumor remove. (**C**) Defection before second surgery – vulvar reconstruction. (**D**) Appearance of vulvar after reconstruction. (**E, F**) Appearance of vulvar and pudendal thigh flap site at the last follow up.

in 20 patients, no patient with low-risk group infection and 1 patient suffered a multiple type of high-risk group infection [1–4,9]. The low detection rate might indicate that HPV infection and VC was not closely related.

Although surgery is the major treatment of VC, surgical procedures were different in different center due to the limited experience (Table 1). Simple or radical vulvectomy was commonly applied in those reviewed articles. Partial vulvectomy, extensive excision of the damage, and total deep vulvectomy were also performed. Although variety types of surgical procedures were performed, all authors recommend a tumor-free margin. Recent years, due to its favorable prognosis, surgical excision of primary tumor tends to be more conservative. For small tumor,

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Table 1. Clinical information summary of 50 cases.

Author	Published year	Case(s)	Invasion (mm)	HPV infection		Primary surgical treatment	Lymph node metastasis	Follow up time (months)	Status
				Low-risk	High-risk				
Tjalma WA [3]	2017	1	Deep into the dermis	(–)	(–)	Remove the tumor with a margin of 1 cm	Sentinel node(–), not done	29	No signs of recurrence
Campaner AB [5]	2017	1	10	NA		Radical vulvectomy with a V-Y advancement flap technique	Only the palpable lymph node in the left inguinal region was excised, no sign of metastasis	4	No signs of recurrence
Liu G [1]	2016	6		Performed in 2/6, both were (–)		Surgical treatment with tumor-free margins	2/6, no LN involved	Mean 17	No signs of recurrence
Bouquet de Joliniere J [6]	2016	1	1.9	NA		A partial vulvectomy in our department with a vulvoplasty and a replantation of the clitoris	Not done	>6	No signs of recurrence
Lorente AI [7]	2013	1	NA	NA		A complete vulvectomy and clitoridectomy	Sentinel node(–), not done	NA	No signs of recurrence
Boutas I [8]	2013	1	NA	NA		Extensive excision of the damage	Not done	>6	No signs of recurrence
Iavazzo C [9]	2012	1	7	Negative	Type 31–33	Radical wide excision of the tumor with free surgical margins	Not done	36	No signs of recurrence
Haidopoulos D [10]	2005	17	1	NA		5/17 radical vulvectomy +LND (3/5 biopsy CSC,2/5 palpable); 12/17 simple vulvectomy,2 with CSC+LND	7/17,no LN involved	51 months (range: 13–119)	None died of the disease. 3/17 local relapse, and managed by wide local excision of the tumour
Iwamoto I [11]	2004	1	Vascular invasion by the tumor was absent	(–)		Total deep vulvectomy with en-block inguinal femoral LND	no LN involved	1	No signs of recurrence
Nascimento AF [4]	2004	9	NA	5/9(–)		NA	NA	NA	NA

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Table 1 continued. Clinical information summary of 50 cases.

Author	Published year	Case(s)	Invasion (mm)	HPV infection		Primary surgical treatment	Lymph node metastasis	Follow up time (months)	Status
				Low-risk	High-risk				
Gualco M* [2]	2003	10	NA	Negative in all cases		Simple vulvectomy-radical vulvectomy (two radical vulvectomy with bilateral groin LND)	2/10 in primary surgery, another underwent LN after recurrence, no LN involved	NA	None died of the disease, no signs of recurrence
Massad LS [12]	1999	1	NA	NA		Anterior exenteration was performed, with ileal conduit construction, omental transposition, and neovaginal construction with pudendal flaps	16 removed nodes showed only reactive changes	16	No signs of recurrence

NA – not available; CSC – co-exist with SCC; LND – lymph node dissection; LN – lymph node; * article written by pathologists.

Table 2. Clinical pathological characters of verrucous carcinoma of vulva.

Clinical pathological characters of VC of vulva	
Age (range), years	32 to 93
Mean (range disease course, month)	5 to 96
Symptoms (31 cases available)	
Bleeding, pruritus, pain	67.74% (21/31)
Location (41 cases available)	
Clitoris	4.88% (2/41)
One side of minor or major labia or mons	41.46% (17/41)
Diffusely spread on the vulvar	51.22% (21/41)
Urethra or bladder involvement	2.44% (1/41)
Tumor size (cm)	1 to 15.5

Clinical pathological characters of VC of vulva	
Stage (FIGO 2015) (19 case available)	
IA	21.05% (4/19)
IB	47.38% (9/19)
II	26.32% (5/19)
III	0
IVA	5.26% (1/19)
IVB	0
Adjuvant radiotherapy	2.44% (1/41)
Coexistent SC (CSC)	16% (8/50)

wide local vulvectomy was performed, and for large size tumor, radical vulvectomy was often performed. As VC often with giant size, and resection of tumor often leave large skin defection. Skin or skin flap based vulvar reconstruction is an option for defect repair which might help wound healing and improve patient's quality of life. Lymph node dissection in VC is still controversial. In our study, preoperative imaging evaluation and physical examination suggested suspicious lymph node metastasis even with PET/CT scan. Therefore, we performed a bilateral inguinal lymph node dissection, and bilateral pelvic lymph node dissection. However, consistent with the previous literatures, all lymph nodes were free of disease on histology. We reviewed 50 VC patients, among them lymph nodes status of 17 patients was assessed during surgery or by pathology.

All excised lymph nodes were free of disease. Previous study also illustrated the same phenomenon [1]. Liu et al. [1] reviewed 24 cases underwent unilateral or bilateral groin dissection or

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sampling and also found no lymph node involvement was detected. Although vascular invasion depth ranged from 1 mm to 10 mm in 5 patients, lymph node metastasis rarely occurs on VC. We speculated that simple or radical vulvectomy is sufficient for VC, systemic lymph node dissection might not be recommended as routine procedure for surgical therapy even in patients with large tumors. VC sometimes might coexist with SCC, and diagnosis might be affected by biopsy, if coexist with SCC is confirmed, further lymphadenectomy is needed after tumor dissection [10].

Only 1 patient underwent radiotherapy after surgery [8], and the other patients were follow-up regularly. Three patients suffered local relapse and received wide local excision [10], and there were no signs of recurrence of the other patients. No patient died of this disease. Therefore, we speculated that sufficient surgery is enough for VC and adjuvant therapy might not need.

Conclusions

VC is a rare type of vulvar cancer with slow growing and giant size, but usually non-metastasis. Etiology of VC is still unknown. Surgery is the major treatment of VC, and enough margin is very import because inadequate might lead to local recurrence. Systemic lymph node dissection might not be recommended as routine procedure for surgical therapy. Outcome of VC promising based on correct diagnosis and appropriate treatment.

Conflict of interest

None.

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