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Skin metastases of vulvar squamous cell carcinoma. Presentation of a rare case

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Summary

Skin metastases secondary to vulvar carcinoma is an infrequent clinical entity. The authors describe a case of squamous vulvar carcinoma, which presented with cutaneous involvement as a part of distant spread. After a radical vulvectomy, bilateral inguino-femoral lymphadenectomy, and adjuvant radiotherapy, the patient developed multiple cutaneous metastases in lower extremities. This case was unique in presentation, with skin metastases secondary from vulvar carcinoma, and indicated advance disease and poor prognosis.

Key Words: Vulvar cancer; Skin metastases; Surgery; Radiotherapy.

Introduction

Vulvar cancer is an uncommon tumor type accounting for 2% to 5% of all gynecological cancers [1]. It appears mostly in postmenopausal women. Ninety percent of all cases represent squamous carcinomas, while melanomas, adenocarcinomas, basal cell carcinomas, verrucous carcinomas, and sarcomas can also occur.

Cutaneous metastases arising from vulvar carcinoma are extremely rare. There are only seven cases reported in the current literature (Table 1) [2]. All these cases were located on the skin of the thigh and lower abdomen except for one reported on the forearm. The cutaneous metastases can develop in five to 62 months after the carcinoma diagnosis. They can present as a solid dermal nodule or multiple inflammatory teleangiectactic lesions and their appearance represents a sign of extended disease and poor prognosis [3].

In this study the authors present a case with vulvar cancer and highlight the importance of a multidisciplinary approach to cancer treatment. Radiotherapy in association with hyperthermia and ultimately local immunomodulators represent an alternative treatment therapy with promising outcomes [4].

Case Report

A 71-year-old, gravida 2, para 2 woman with a medical history of hypertension and hyperlipidemia consulted in the present department of Obstetrics and Gynecology Unit. She presented with complaints of local pain, vaginal bleeding, burning, and odour over the previous two months. Initial physical examination revealed an ulcerative bleeding vulvar mass measuring 2.5 cm located on the left labia minoris near to os externum of the urethra with no associated palpable bilateral inguinal lymphadenopathy. A colposcopy and biopsy of the primary pedunculated mass was performed and the results were consistent with primary squamous vulvar carcinoma grade III. Pap smear of cervix and vagina was normal. Laboratory examinations were performed but did not lead to any remarkable finding. Magnetic resonance imaging (MRI) revealed the presence of a vulvar mass with no nodal involvement The patient underwent wide local excision and bilateral inguino-femoral lymphadenectomy. The histological examination revealed a poorly differentiated epidermoid vulvar carcinoma measured 2.5×12 cm in size, infiltration depth of 4.5mm, extended to midline without infiltration of the urethra, with clear margins, and lymphovascular invasion (Figures 1A, B). The inguino-femoral lymph nodes were negative for malignancy (FIGO Stage II). The patient underwent postoperative adjuvant groin and pelvic irradiation for lymphovascular invasion (LVSI). External beam radiation therapy (EBRT) was used bilaterally to the inguinal and femoral dissection beds and pelvic nodes. The delivered total radiation dose was 50.4 Gy in 1.8 Gy fractions to control occult microscopic disease.

One year after the completion of the treatment, she presented with diffuse and painful, round to oval-shaped purple to violet-colored skin lesions, that were fixed beneath the skin of lower extremities. The lesions were three to four cm in size and occasionally formed plaques by merging. Fine needle aspiration cytology of the skin lesions was performed. A cytological diagnosis favoring squamous carcinoma was rendered. She received palliative radiotherapy of lower extremities skin with electrons (30 Gy in ten fractions) in conjuction with microwave hyperthermia with an clinical improvement in the pain intensity (Figures 2A, B). Patient died seven months later.

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Table 1. — *Cutaneous metastases from vulvar cancer: literature survey.*

Author	Ghaemmaghami *et al.*	Tjalma *et al.*	Dudley *et al.*	Kulkarni *et al.*	Tobias *et al.*	Santala *et al.*	Cianfran *et al.*
Year	2003	2003	1998	1995	1995	1989	1956
Age at initial diagnosis	38	73	79	59	57	54	72
Medical history	Diabetes mellitus	-	BrCa	-	-	-	BrCa
Treatment RVBGN+RT	RVBGN RVBGN+RT	RVBGN	RVBGN	RVBGN	RVBGN		
Stage	III	IB	?	?	II	?	?
Nodes	Negative	Negative	Negative	Positive	Negative	Positive	Positive
Histology	SCC	SCC	SCC	SCC	SCC	SCC	SCC
Grade	II	III	I	I	II	?	I
First recurrence (months)	7	9	60	5	8	?	6
Location	Vulva, lower abdomen, buttocks, groin	Vulva	Vulva	Abdomen, limbs	Thigh	Abdomen, vulva, thighs	Abdomen
Treatment	CT	RT	S	-	?	S	CT
Second recurrence		8 months later	6 months later				
Location		Vulva	Vulva + pelvis				
Treatment		S	S+RT				
Third recurrence		3 months later	3 months later				
Location		Thigh, calve	Thigh				
Leg edema	Yes	No	Yes	Yes	No	?	?
Treatment	CT	CT	None		?		
DOD	7 months later, septic shock	4 months later	3 months later, lung metastases	Half month later	?	10	Few months later

DOD: dead of disease, RT: radiotherapy, RVBGN: radical vulvectomy and bilateral groin nodes dissection, SCC: squamous cell carcinoma.

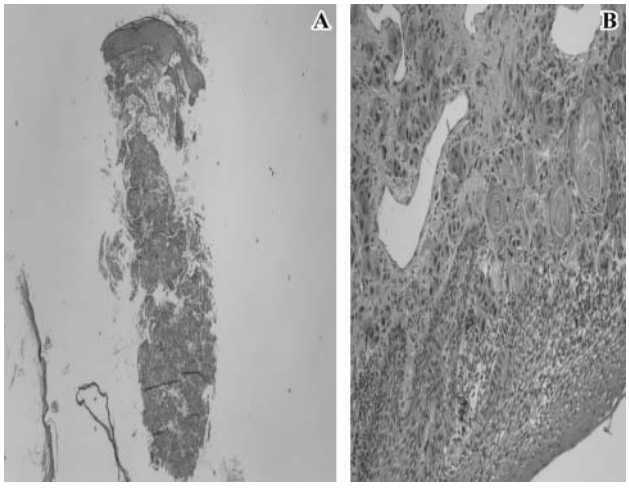

Figure 1. — (A) Poorly differentiated vulvar carcinoma (H&E ×100). (B) Skin replaced by infiltrating vulvar squamous cell carcinoma (H&E ×10).

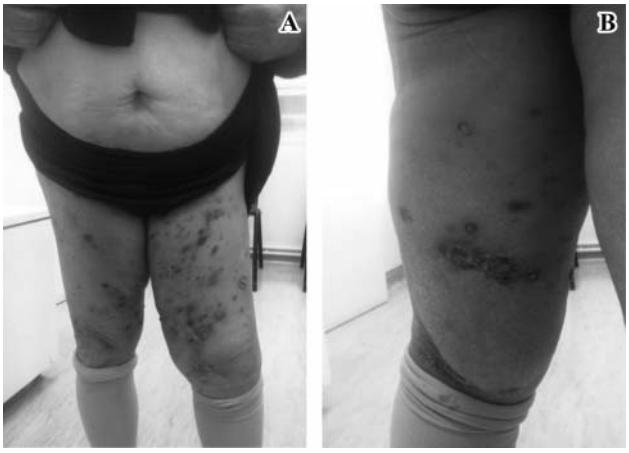

Figure 2. — (A) Skin lesions two months after the end of radiotherapy. (B) Skin lesions two months after the end of radiotherapy.

Discussion

Vulvar squamous cell carcinoma represents a postmenopausal disease affecting women with a median age of 65 years. According to current literature vulvar squamous cell carcinoma incidence is dramatically increased, positioning it to an importance place among genital tract malignancies [5]. The cause of vulvar carcinoma has still to be identified. Some risk factors like congenital or acquired compromised immune status, human papillomavirus (HPV), smoking, vulvar dystrophies (lichen sclerosus, squamous cell hyperplasia), and vulvar intraepithelial neoplasia (VIN) 3 lesions (severe dysplasia or carcinoma in situ) have been reported as predisposing factors [6]. The tumor is usually located on the labia major, but also on the labia minora, clitoris, and perineum. It

is a slow progressive tumor and its main route of dissemination is through lymphatics and transcoelomic spread.

Hematogenous metastases include lung, liver, and bone involvement [7]. The risk of nodal metastases is related to infiltration depth. In presence of a small primary tumor (≤ four cm) in whom clinical and/or imaging assessment reveals no obvious spread to nodes, sentinel node biopsy with subsequent groin observation has emerged as an alternative to groin node dissection [8]. Lymphatic infiltration represents the most determined prognostic in vulvar cell carcinoma. Other prognostic factors are tumor size and tumor location [9].

Radical local excision of the primary represents the preferred therapy for invasive disease. The optimal treatment consists of radical vulvectomy and en bloc lymph node dissection. Lymphedema and wound disorders represent the most frequent postoperative complications [10]. When the location of the primary tumor suggests that surgery will not be able to accomplish secure negative margins without functional compromise, initial chemoradiation may precede conservative local excision or palliative chemoradiation may be used [11]. Radiotherapy is recommended in cases of an invasive stage carcinoma with infiltrated inguinofemoral lymph nodes. During the last decade, mostly in early stage cancer and reproductive age women, management tendency consists of tumor excision and uni- or bilateral inguino-femoral lymph node dissection. Sentinel lymph node excision can certify the lymphatic spread and restrict the management approach in a more conservative way [12].

Cutaneous metastases of vulvar carcinoma are related to distant spread of the lesion and indicates poor prognosis. Histopathological analysis combined with immunochemistry can increase the accuracy rate in even existing lymphatic micrometastases [13]. They can present not only as painful flat or nodule skin lesions, but also as inflammatory telangiectatic abnormalities. All these metastatic lesions are mostly located on thigh skin or lower extremities. Ceydeli *et al.* reported a case of a 77-year-old female patient diagnosed with vulvar cancer and development of a metastatic vulvar lesion located on the anterior aspect of the right forearm [14].

Optimal treatment of multiple metastatic skin lesions consists of radiotherapy. In many cases radiotherapy is combined with superficial and intracavitary hyperthermia, concerning the treatment of solid tumors. The great advantage of this method represents the tolerance of the patients without severe toxicity. Many studies compared the combination of hyperthermia and radiation versus radiation alone, in order to certify the advantage in survival and local control of patients. Generally, the combination of hyperthermia and radiation increase the survival rate and quality life of the patients [15].

In conclusion, cutaneous metastases of vulvar cancer are extremely rare with few cases reported in current literature. Their appearance indicates distant spread of the disease and generally poor prognosis. The optimal treatment consists of tumor excision and uni- or bilateral inguino-femoral lymph node dissection combined with radiotherapy. The multidisciplinary participation reflects the appropriate management of the lesion.

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