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A Unique History of the First Cases with Simultaneous Bone and Skin Metastasis in Vulvar Squamous Cell Carcinoma

Setare Nasiri,[1,*] Azamosadat Mousavi,[1] Shahrzad Sheikh Hasani,[1] Mohammad Rahim Vakili,[2] Mitra Modarres Gilani,[1] Setare Akhavan,[3] and Monire Mirzaei[1]

[1]Department Gynecology Oncology, Tehran University of Medical Sciences, Tehran, Iran
[2]Department Thorax surgery, Tehran University of Medical Sciences, Tehran, Iran
[3]Department Gynecology Oncology, Iran University of Medical Sciences, Tehran, Iran

[*]*Corresponding author*: Setare Nasiri, Department Gynecology Oncology, Tehran University of Medical Sciences, Tehran, Iran. Tel: 982161192363, Fax:982161192363, E-mail: setare_n99@yahoo.com

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Abstract

Introduction: The incidence of vulvar cancer is nearly 5% of all gynecologic malignancies and almost 95% of vulvar cancers are squamous cell carcinoma (SCC). Recurrence is possible in 4 ways: local, regional, pelvic, and distant. In a cohort of 391 patients with vulvar SCC, distant metastasis was reported 5% .The common sites of distant metastasis are pelvic nodes, lung, and liver. Both skin and bone metastasis are rare in vulvar SCC.
Case Presentation: The current report presented a 58-year-old female with the diagnosis of vulvar SCC. She was the 11th cutaneous metastasis, 13th bone metastasis, and the 1st case with simultaneous bone and skin metastasis reported in the last 60 years.
Conclusions: It is necessary to consider any lesion on the vulve, especially in menopause females, and it should be the low threshold for biopsy to avoid delay in detection. After completion of selective treatment, the exact follow-up should be considered to discover metastases.

Keywords: Squamous Cell Carcinoma, Vulvar Cancer, Cutaneous Metastasis

1. Introduction

The incidence of vulvar cancer is nearly 5% of all gynecologic malignancies and almost 95% of vulvar cancers are histologically squamous cell carcinoma (SCC). Two types of SCC are defined including keratinizing form, which arises in postmenopausal females with poorer prognosis than non-keratinizing form, which is more common in younger patients and is known to be associated with human papillomavirus (HPV) (1).

Tumor size, its grade, and node status are the risk factors for recurrence and the latter is the most important one (2). The current report presented a 58-year-old female with the diagnosis of vulvar SCC who underwent radical vulvectomy and bilateral inguinofemoral lymphadenectomy at Department of Gynecology Oncology, Imam Hossein Hospital affiliated to Tehran University of Medical Sciences, Iran. It is the report of first case with simultaneous bone and skin metastasis in the last 60 years.

2. Case Presentation

The current report presented a 58-year-old female with the diagnosis of vulvar SCC who underwent radical vulvectomy and bilateral inguinofemoral lymphadenectomy at Vali-e-Asr Department of Gynecology Oncology, Imam Hossein Hospital affiliated to Tehran University of Medical Sciences, Iran. Bilateral involvement of lymph nodes with squamous cell carcinoma, FIGO stage III, was reported; surgical margin was free with 1.8 cm distance and the diameter of the tumor was 2.2 cm. The tumor was poorly differentiated. According to preoperational assessment, including lung, abdomen, and pelvic, metastases were not found in physical examination or imaging studies. She had diabetes since 5 years ago. Due to the lymph nodes involvement and stage III cancer, the postoperative adjuvant chemoradiation was given to her. She received 6000 cGy radiation in 28 fractions to groin and pelvic; concomitant chemotherapy with weekly carboplatin and taxol were prescribed. One month after the completion of chemoradiation therapy, multiple painful lesions appeared on the skin of top of right thigh and perineum (Figure 1). In

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physical examination, there were disseminated, tender, and erythematous plaques on groin and perineum. Due to her diabetes history and previous chemoradiation with doubts of immune compromise condition, the infectious lesions appeared and topical as well as oral antibiotics (mupirocin and cloxacillin) were prescribed for 10 days. But, she was not healed and biopsy was performed. Simultaneously, she developed back pain, which did not allow her to rest. Therefore, bone magnetic resonance imaging (MRI) was done. Microscopic examination of the firm plaques revealed infiltrative neoplastic and small nests in sclerotic dermis with poorly differentiated squamous cell carcinoma and confirmed cutaneous metastases (Figure 2). In MRI of spine with and without contrast, multiple signal changes were observed in cervical, thoracic, and lumbar spines. To confirm bone metastasis and determine the extent of it, the whole body bone scanning was performed after intravenous injection of TC 99-MDP, which revealed some focal zones of abnormal increased radiotracer uptake throughout the skeleton including the sternum, spines, and some anterior ribs. According to the patient's medical history, the findings were in favor of multifocal osteomyelitis.



Figure 1. Skin Metastases at the Top of the Thigh

CT scan was conducted to evaluate lung, liver, and pelvis, and all of them were reported normal. She developed lymph edema in the left lower extremity after surgery and underwent supporting treatments.

Palliative radiation for painful bone metastasis and cutaneous lesions was undertaken and concomitant chemotherapy with cisplatin and 5-fluorouracil was prescribed too.

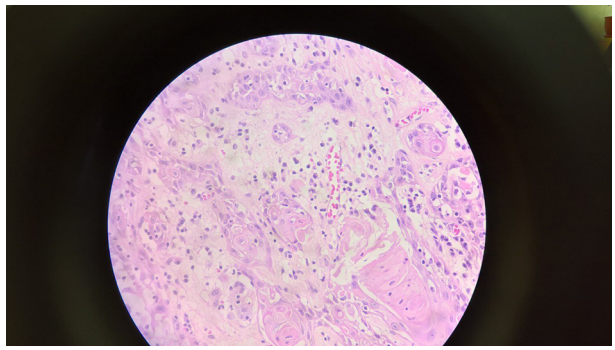


Figure 2. Biopsy of Skin Metastasis

3. Discussion

The incidence of vulvar cancer is nearly 5% of all gynecologic malignancies and almost 95% of vulvar cancers are histologically SCC. Two types of SCC are defined: keratinizing form, which arises in postmenopausal females with poorer prognosis than non-keratinizing form, which is more common in younger patients and is associated with HPV (1).

Tumor size, grade of it, and node status are the risk factors for recurrence and the latter is the most important one (2). After surgical staging, if lymph node involvement is identified, a 5-year overall survival is reported in 57% of the cases, compared with 91% when there is no positive node (3). Recurrence is possible in 4 ways: local, regional, pelvic, and distant. In a cohort of 391 patients with vulvar SCC, distant metastasis was reported 5% (4). The common sites of distant metastasis are pelvic nodes, lung, and liver; although brain, kidney, and heart metastases are reported in 1, 1, and 3 cases, respectively till now (5-7). Spread of malignant cells to distant sites can be caused via lymphatic or hematologic ways. Cutaneous metastasis in vulvar SCC is very rare even in advanced disease and 10 cases were reported so far. In Table 1, all of previous patients as well as the present case are shown. All of the 10 cases had isolated skin metastasis except 1 case, which had skin and groin lymph nodes metastases simultaneously (8). Traditionally isolated skin metastasis is described as the implantation of malignant cells due to destruction of lymphatic canals caused by cancer, surgery, and radiation (9). Lymph edema formation can prevent lymphatic return too (10). According to the Table, in 6 patients lower extremity edema was identified.

The purpose of the current presentation was that she was the 11th cutaneous metastasis, 13th bone metastasis, and the first case with simultaneous bone and skin metastasis reported in the last 60 years. Both skin and bone

Table 1. The Completed Tables Reported by Tjalma and Ghaemmaghami (9, 10) and Wang (8)

Year	Cianfran 1959 (11)	Santala 1989 (12)	Tobias 1995 (13)	Kulkami 1995 (14)	Dudley 1998 (15)	Ceydeli 2003 (16)	Tjaima 2003 (9)	Ghaemmaghami 2004 (10)	Wang 2008 (8)	Bahner 2016 (17)	Setare Nasiri (Present)
Age	72	54	57	59	79	77	73	38	77	76	58
PMH	BRCA	-	-	-	BRCA	-	-	DM	-	HSV	DM
Surgery	RVBGN	RVBGN	RVBGN	RVBGN	RVBGN	RVBGN	RVBGN	RVBGN	RVBGN	Radiation	RVBGN
Stage	?	?	3	?	?	3	1 B	3	1 or 2	4	3
Node	Positive	Positive	Negative	Positive	Negative	Negative	Negative	Negative	Negative	Positive	Positive
Histology	SCC	?	SCC	SCC	SCC	SCC	SCC	SCC	SCC	SCC	SCC
Grade	1	?	2	1	1	?	3	2	?	3	3
First recurrence, mo	6	?	8	5	60	6	9	7	60	4	1
Location	Skin of abdomen	Skin of abdomen and thigh	Thigh	Abdomen and limb skin	Vulva	Forearm skin	Vulva	Lower abdomen and buttocks	Thigh and inguinal node	Vulva	Thigh and bone
Treatment	Chemo therapy	Surgery	?		Surgery	Surgery	Radiation	Chemotherapy	CIS + Radiation	Chemotherapy	Chemo radiation
Second recurrence	-	-	-		6 months pelvis	4 months Lungs	8 months vulva	-	-	-	-
Third recurrence	-	-	-		3 months	-	3 months thighs	-	-	-	-
Treatment	-	-	-		Radiation	-	Surgery	-	-	-	-
Lymph edema	?	Yes	No	Yes	Yes	?	No	Yes	Yes	?	Yes
Death (month) after skin metastases	Few months later	10 months later	?	2 weeks later	3 months later: lung metastases	12 months after skin metastasis	4 months later	7 months later due to septic shock	Few months later	Few months later	Last 2 month and still alive

Abbreviations: DM, Diabetes Mellitus; PMH, Past Medical History; RVBGN, Radical Vulvectomy with Bilateral Groin Node Dissection; SCC, Squamous Cell Carcinoma.

metastases are rare in vulvar SCC, and the primary tumors, which metastases to the skin, includes breast, colorectal, lung, and ovary. In addition, bone often accepts metastasis from prostate, breast, and lung (15). Skin metastasis pretends to be different forms including nodule, exophytic tumor, erythematous patch, firm plaque, and recently the herpetiform vesicles was reported (17). Osteoblastic metastases often appear in the form of lytic lesions. The patient in the current report had multiple lytic lesions in ribs and spines. She had diabetes with itchy nodules on the labium major of the vulve since a year ago. Unfortunately, due to her diabetes she was merely treated with antifungal and other unspecific agents without any biopsy; therefore, diagnosis was delayed and she was referred to the hospital in an advanced stage of III, and chemoradiation was performed after vulvectomy and bilateral lymphadenectomy.

Risk factors for distant metastasis in her vulvar SCC included stage III, bilateral positive lymph nodes, and poorly differentiated histopathology; additionally, the immunosuppressant condition caused by diabetes could be considered as predisposing factors. Another odd point was that despite the involvement of skin and bone, lung and liver were not involved; whereas the metastases to them are more likely with vulvar SCC, compared with skin or bone.

Given the low number of reported skin and bone metastases of vulvar SCC, there is not a proven treatment and it has a palliative aspect.

Mean survival of the first metastasis in vulvar SCC is reported 5 to 6 months (4). And prognosis of skin metastasis is very poor in Table 1; only 1 patient survived 12 months after the detection of metastasis.

It is 2 months that the patient in the current report is being treated with palliative options.

4. Recommendation

It is necessary to consider any lesion on the vulve, especially in menopause females, and it should be low threshold for biopsy to avoid delay in detection. After completion of selective treatment, the exact fallow-up should be considered to discover metastases. Bone pains can be due to malnutrition and vitamin D and calcium deficiency in the course of treatment or can be due to self-radiation, but these reasons are not the only causes of pain, and bone metastasis may also be listed as the cause of pain.

Any skin lesions within follow-up period should be biopsied even if the rash is simple and it should not merely be related to the radiotherapy skin reactions. Authors used topical 5-fluorouracil and local radiation to relieve lesions and pain .It seems to be a useful palliation, but further studies are necessary to establish better treatments.

References

1. Trimble CL, Hildesheim A, Brinton LA, Shah KV, Kurman RJ. Heterogeneous etiology of squamous carcinoma of the vulva. *Obstet Gynecol.* 1996;**87**(1):59–64. doi: 10.1016/0029-7844(95)00351-7. [PubMed: 8532267].
2. Paladini D, Cross P, Lopes A, Monaghan JM. Prognostic significance of lymph node variables in squamous cell carcinoma of the vulva. *Cancer.* 1994;**74**(9):2491–6. [PubMed: 7923005].
3. Homesley HD, Bundy BN, Sedlis A, Yordan E, Berek JS, Jahshan A, et al. Assessment of current International Federation of Gynecology and Obstetrics staging of vulvar carcinoma relative to prognostic factors for survival (a Gynecologic Oncology Group study). *Am J Obstet Gynecol.* 1991;**164**(4):997–1003. doi: 10.1016/0002-9378(91)90573-A. [PubMed: 2014852] discussion 1003-4.
4. Prieske K, Haeringer N, Grimm D, Trillsch F, Eulenburg C, Burandt E, et al. Patterns of distant metastases in vulvar cancer. *Gynecol Oncol.* 2016;**142**(3):427–34. doi: 10.1016/j.ygyno.2016.07.009. [PubMed: 27401841].
5. Seward SM, Richardson DL, Leon ME, Zhao W, Cohn DE, Hitchcock CL. Metastatic squamous cell carcinoma of the vulva to the lung confirmed with allelotyping. *Int J Gynecol Pathol.* 2009;**28**(5):497–501. doi: 10.1097/PGP.0b013e3181a23c6c.
6. Agrawal A, Wood KA, Giede CK, Chibbar R. A case of kidney metastasis in vulvar squamous cell carcinoma: A case report and review of literature. *Case Rep Clin Med.* 2013;**02**(05):306–9. doi: 10.4236/crcm.2013.25082.
7. Jafri SIM, Ali N, Farhat S, Malik F, Shahin M. The tell-tale heart: A case of recurrent vulvar carcinoma with cardiac metastasis and review of literature. *Gynecol Oncol Rep.* 2017;**21**:20–3. doi: 10.1016/j.gore.2017.06.004. [PubMed: 28664179].
8. Wang AR, O'Brien M, Ross R, Long T, Robinson-Bostom L. Epidermotropic metastasis from vulvar squamous cell carcinoma: a rare cutaneous manifestation. *J Am Acad Dermatol.* 2010;**63**(6):1088–91. doi: 10.1016/j.jaad.2009.07.036. [PubMed: 20226566].
9. Tjalma WA, Watty K. Skin metastases from vulvar cancer: a fatal event. *Gynecol Oncol.* 2003;**89**(1):185–8. [PubMed: 12694676].
10. Ghaemmaghami F, Modares M, Behtash N, Moosavi AZ. Multiple, disseminated cutaneous metastases of vulvar squamous cell carcinoma. *Int J Gynecol Cancer.* 2004;**14**(2):384–7. doi: 10.1111/j.1048-891x.2004.014227.x. [PubMed: 15086744].
11. Cianfrani T, Smith JJ. Inflammatory diffuse cutaneous metastatic carcinoma from epidermal carcinoma of the vulva; report of a case. *Obstet Gynecol.* 1956;**8**(4):500–3. [PubMed: 13370021].
12. Santala M, Syrjanen K, Saarikoski S. Squamous cell carcinoma of the vulva with cutaneous metastases. *Acta Obstet Gynecol Scand.* 1989;**68**(3):271–3. [PubMed: 2618612].
13. Tobias DH, Smith HO, Jones JG, Anderson P, Runowicz CD, Goldberg GL. Cutaneous metastases from squamous cell carcinoma of the vulva. A case report and review of the literature. *Eur J Gynaecol Oncol.* 1995;**16**(5):382–6. [PubMed: 8549604].
14. Kulkarni R, Bradford WP. Squamous cell carcinoma of the vulva metastasizing to the skin. *Acta Obstet Gynecol Scand.* 1995;**74**(7):571–2. doi: 10.3109/00016349509024393. [PubMed: 7618460].
15. Dudley C, Kircik LH, Bullen R, Snow S, Landeck A, Buchler D. Vulvar squamous cell carcinoma metastatic to the skin. *Dermatol Surg.* 1998;**24**(8):889–92. doi: 10.1111/j.1524-4725.1998.tb04268.x. [PubMed: 9723055].
16. Ceydeli A, Rucinski J, Klipfel A. Vulvar squamous cell carcinoma metastatic to skin of the forearm. *Dermatol Surg.* 2003;**29**(6):662–3. doi: 10.1046/j.1524-4725.2003.29162.x. [PubMed: 12786715].
17. Bahner JD, Scott JF, Shoureshi P, Honda K, Gerstenblith MR. Metastatic vulvar squamous cell carcinoma mimicking genital herpes. *JAAD Case Rep.* 2016;**2**(5):387–9. doi: 10.1016/j.jdcr.2016.08.004. [PubMed: 27752532].