Case Report

Skin metastasis from squamous cell carcinoma of the cervix to the lower extremities: Case report and review of the literature

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Abstract

Squamous cell carcinoma of cervix commonly metastasizes to the lymph nodes of the pelvis and skin metastasis is a rare presentation even in the late stages of cervical cancer. We report here the first case of cervical cancer with skin metastasis in Saudi Arabia in a 69-year-old female that preceded the diagnosis of cervical carcinoma. Microscopic examination of the skin lesion revealed poorly differentiated squamous cell carcinoma. The patient was in stage IVB based on the International Federation of Gynecology and Obstetrics (FIGO) staging system. Due to her late presentation and advanced stage, the decision was to place the patient on palliative therapy. Later, the patient passed away due to the progression of her disease. The case reported in this paper emphasizes the need for a complete clinical assessment to rule out metastatic disease from cases with known cervical cancer and include skin examination in their follow-up.

Keywords: Carcinoma of the cervix, cervical cancer, cutaneous metastasis, skin metastasis

Introduction

According to the latest statistics of the Saudi Cancer Registry, there was 177 cases of cervical cancer with incidence of 1.2 per 100,000 population.[1] The incidence of carcinoma of cervix has dramatically decreased in the developed countries due to the increased awareness and availability of screening using PAP smears test. Yet, the awareness of PAP smear is poor among Saudi women.[2]

Squamous cell carcinoma of cervix commonly metastasizes to the lymph nodes of the pelvis and a distant metastasis is uncommon which frequently detected in liver, lung, and bone.[3,4] Skin metastasis is a rare presentation even in the late stages of the cervical cancer and the incidence rate of cutaneous metastasis in stage I, stage II, stage III, and stage IV are 0.8%, 1.2%, 1.2%, and 4.8%, respectively.[5,6] The most frequent sites of skin metastasis of cervical cancer in descending order are the abdominal wall, vulva, and anterior chest wall.[4] Sadly, the prognosis after cutaneous metastasis is poor and usually a terminal presentation as it is often associated with disease recurrence and the treatment is mostly palliative.[5]

As far as author's knowledge, no similar cases have been reported in Saudi Arabia. We report here the first case of cervical cancer with skin metastasis in Saudi Arabia.

Case Presentation

A 69-year-old postmenopausal Yemeni female was diagnosed with cervical cancer after presenting with vaginal bleeding and abdominal heaviness 6 months ago. On August 2018, the patient was referred to Dermatology clinic at King Abdulaziz University

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Hospital for evaluation of right leg ulceration that was noticed by the patient 4 months back. Ulcers were preceded by appearance of painless and non-pruritic papules that later was increased in size and began to ulcerate. Week later, same papular lesions started to appear on the left leg.

Skin examination showed multiple, erythematous, firm, non-tender skin papules, and plaques of variable sizes, along with shallow ulcers on the medial side of her right leg [Figure 1]. Fewer papules and plaques were located on the anterior right thigh, right sole, and medial side of the left leg. Skin punch biopsy was done, and microscopic examination revealed poorly differentiated squamous cell carcinoma [Figure 2]. On immunohistochemistry examination, tumor cells were positive for CK 5/6m p63 and p16. These results supported the diagnosis of skin metastasis from cervical cancer. A previous abdominopelvic CT scan done on February 2018 revealed uterine cervix enlargement with disfigurement, paraaortic lymphadenopathy, liver enlargement, and mild compression fracture D11 vertebral body. On a recent CT scan of the abdomen and pelvic area, imaging showed, an exophytic mass measuring 5 cm and closely related to, and inseparable from the urinary bladder and the rectum. Abdominal lymph nodes were enlarged and involved; right internal iliac, para aortic, and portacaval. There were hydroureters, hydronephrosis, multiple ill-defined and enhancing liver masses, and tiny peripheral nodules in the lower cut of the lung. Head CT scan was unremarkable. The patient was in stage IVB based on the International Federation of Gynecology and Obstetrics (FIGO) staging system. Due to her late presentation and advanced stage, the decision was to place the patient on palliative therapy. One month later, on September 2018, the patient passed away.

Discussion

Cervical cancer is the third commonest malignancy in women worldwide.[7] Distant metastasis from cervical cancer frequently affects bone, lung, and liver in an increasing order.[3,4] Cutaneous metastasis from carcinoma of the cervix has been rarely reported in literature. We were able to retrieve around 80 cases from 1982 up to 2017.

The incidence of skin metastasis from solid tumors ranges from 0.7 to 9%[8,9] and breast cancer is the highest propensity to metastasize to the skin.

Incidence of skin metastasis from cervical cancer is rare, and it ranges from 0.1 to 2%.[6,10,11] In a large case series, Imachi *et al.* studied 1,190 patients with cervical cancer. He found the incidence of skin metastasis in these patients to be 1.3%.

Most of the cervical cancer patients present with cutaneous metastasis at the third stage (IIIB) of their disease.[12] This is the fifth case in literature in which the patient was initially diagnosed with cervical cancer and presented with skin metastasis at stage IVB. In four of these five cases, patients have never received any type of treatment before their presentation. One of the five cases received radiotherapy 1 month before appearance of skin metastasis.[6,13,14]

Clinical morphology of cutaneous metastasis varies, and the three commonest forms in decreasing order are nodular, plaques, and inflammatory telangiectasia.[12] The first two tend to ulcerate, and the latter might resemble cellulites.[13,15] Other clinical presentations are maculopapular lesions, scar infiltration, and neoplastic alopecia.[16-19] Multiple lesions are less commonly seen than a solitary lesion. Lesions in most cases are asymptomatic, but pruritic or painful rash might precede the appearance of skin metastasis.[12] In our case, the lesion started as erythematous papules and later formed ulcerated plaques.

Cutaneous metastasis tends to occur more frequently at proximity to the site of primary malignancy. The commonest sites of skin metastasis are the abdominal wall, followed by anterior chest wall and vulva.[6] Back, extremities, face, and scalp were less commonly reported in the literature. Out of the 80 cases we reviewed, lower extremities were the location of metastasis in

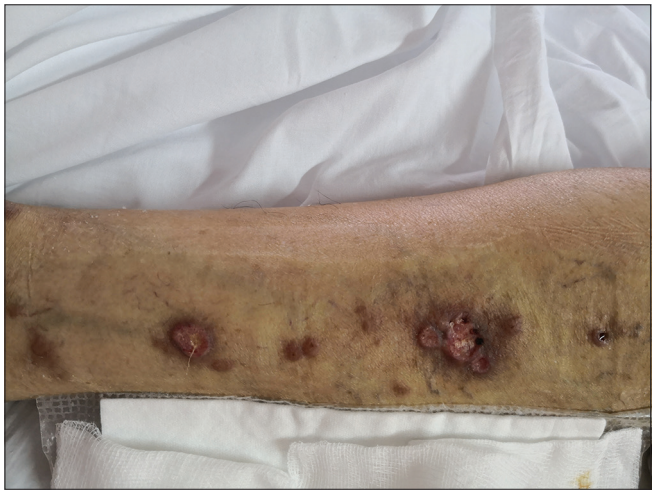

Figure 1: Cervical squamous cell carcinoma metastasis to the skin of the right leg

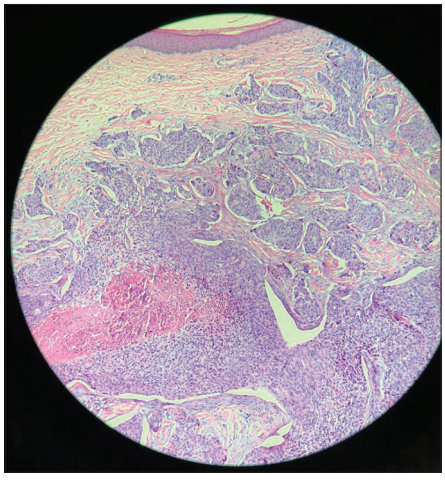

Figure 2: Skin Biopsy at 10 × magnification showing poorly differentiated squamous cell carcinoma

Table 1: Reported cases of lower extremities skin metastasis of cervical cancer

Author	Age, years	FIGO stage	Histology	Site	Morphology	Multiple or Solitary	Interval, months	Treatment of skin mets	Outcome (months)
Reingold[25]	43	-	ASC	A/LE	N	M	-	-	D/UK
Freeman *et al.*[17]	69	-	SCC	thigh (LE)	MPR	-	0	RT/CT	AL (7)
Tharakaram *et al.*[19]	55	IIIb	SCC	thigh (LE)	P	S	48	RT	AL (14)
Fanciolini *et al.*[22]	79	IIIb	SCC	thigh (LE)	N	S	19	SX	D (5)
Bachaud *et al.*[23]	32	IIb	SCC	LE, V, A, and perineum	P	M	30	CT	D (3)
Imachi *et al.*[6]	26	IIb	SCC	C, A, LE/UE	N	M	11	SX/CT	D (16)
Yamamoto *et al.*[26]	40	III	SCC	LE	P	M	4	-	-
Kagen *et al.*[27]	43	Ib	SCC	LE	P	S	12	CT	D (3)
Palaia *et al.*[28]	47	IIb	SCC	A/LE/gluteus	Diffuse rash	-	56	CT	AL (UK)
Chen *et al.*[29]	72	IIb	SCC	Extremities, trunk, scalp	P + N	M	12	RT/CT	D (6)
Khurana *et al.*[30]	77	IIIb	SCC	thigh (LE)	N	S	165	RT/CT	AL (5)
McCarthy *et al.*[31]	55	-	SCC	A, V, LE	P	M	20	-	UK

SCC: squamous cell carcinoma; AC: adenocarcinoma; PDC: poorly differentiated carcinoma; ASC: adenosquamous carcinoma; LE: lower extremity; UE: upper extremity; A: abdominal wall; S: scalp; V: vulva; C: chest wall; morphology; N: nodule; P: plaque; MPR: maculopapular rash; M/S: multiple/solitary; interval: interval between initial diagnosis and appearance of skin metastasis; RT: radiation therapy; CT: chemotherapy; SX: surgery; mets: metastasis; D: dead; AL: alive; UK: unknown

12 patients [Table 1]. Our case is the 13th and first case in which the sole was involved. Unlike of what previously was reported, skin metastasis is more frequent with cervical squamous cell carcinoma than cervical adenocarcinoma.[12] Out of the 80 cases, only 14 were adenocarcinoma, and the majority were squamous cell carcinoma.

Spread of tumor is usually through lymphatics, especially when the lesion is at proximity with the primary neoplasm.[17,19] Hematogenous spread is less frequent, and usually the route for distant metastasis.[20]

The interval between initial diagnosis of cervical cancer and skin metastasis range from 0 to 19 years.[13,21] Treatment includes one or combination of radiotherapy, chemotherapy, and wide local excision.[6,17,19,22-24] However, up to this date, there is no clear guideline regarding treatment of skin metastasis from cervical cancer, and the treatment remains palliative rather than curative.

Skin metastasis is a pre-terminal sign. Its occurrence is usually associated with local recurrence and other metastasis to distant organs, and skin biopsy should be always considered in any skin lesion in these patients.[32]

Since skin diseases is the most common reason for the clinic visit, a family physician may encounter patients with skin metastasis, who frequently present with a lesion mimics ulcer, it is crucial to recognize this condition early and make timely referral to dermatology. This will help in making a proper diagnosis and better prognosis. Therefore, primary physicians need to have a high index of suspicion for skin metastasis in patients with cervical cancer to early detection and proper referral.

Conclusion

Skin metastasis from squamous cell carcinoma of the cervix are rare as it is usually a terminal presentation and have a poor prognosis. The case reported in this paper emphasizes the need for a complete clinical assessment to rule out metastatic disease from cases with known cervical cancer and include skin examination in their follow-up.

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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Conflicts of interest

There are no conflicts of interest.

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