

Prolonged Survival (>48 months) in a Squamous Cell Carcinoma of the Cervix After Late Skin Metastasis (>5 year) to Incision Site: A Case Report

Geç cilt metaztazı (>5 yıl) yapmış skuamöz hücreli serviks kanserinde uzamış sürvi (>48 ay): bir vaka sunumu

Batuhan Özmen, Yavuz Emre Şükür, Cem Atabekoğlu, Mete Güngör
University of Ankara, Department of Obstetrics and Gynecology, Ankara, Turkey

Abstract

Metastasis to the incision site of squamous cervical cancer (SCC) is an extremely rare entity which is strictly related with extremely poor prognosis. The vast majority of the reported cases died in a year due to distant recurrences, whereby skin metastases were predominantly observed close to the primary tumor site. A SCC with skin metastasis which was diagnosed 5 years after the radical surgery and postoperative radiotherapy which involved the midline incision site was reported. Large surgical excision of the metastasis with remaining surgical free margins (>2 cm) and combined chemo-radiotherapy with single agent (cisplatin) was performed. The patient did not show any recurrences for 4 years follow-up. Apparently, palliative combined chemo-radiotherapy along with large excision seems favorable for controlling symptoms and progression of skin metastasis of squamous cervical cancer. (J Turkish-German Gynecol Assoc 2009; 10: 175-7)

Key words: Cervical cancer; Skin metastasis; Prolonged Survival; Chemotherapy; Radiotherapy

Received: 9 May, 2009

Accepted: 19 July, 2009

Özet

Servikal skuamöz hücreli kanserde insizyon alanına metaztaz oldukça seyrek görülür ve kötü prognoz ile ilişkilidir. Bildirilen vakaların çoğunda hasta özellikle uzak metaztazlardan sonraki 1 yıl içerisinde yaşamını yitirmiştir. Beş yıl önce cerrahi ve radyoterapi görmüş servikal skuamöz kanserli bir hastada geç dönemde ortaya çıkan insizyon yeri metaztazı bildirildi. Metaztazın geniş lokal ekizyonu ve tek ajan (sisplatin) kemoradyoterapi kombinasyonu ile hasta tedavi edildi. Operasyon sonrası 4 yıl hasta rekürrens göstermedi. Görüldüğü kadarıyla cilde metaztaz yapmış skuamöz hücreli kanserin en uygun tedavisi geniş ekizyona kombine edilmiş kemoradyoterapidir.

(J Turkish-German Gynecol Assoc 2009; 10: 175-7)

Anahtar kelimeler: Serviks kanseri, cilt metaztazı, uzamış sürvi, kemoterapi, radyoterapi

Geliş Tarihi: 09 Mayıs 2009 **Kabul Tarihi:** 19 Temmuz 2009

Background

Carcinoma of the cervix, the second most common gynecological malignancy, metastasizes mainly to the lung, bone, and liver (1,2). Involvement of skin in cervical cancer is a rare entity (0.1 to 2%), especially diagnosed in advanced stages, and is closely related with extremely poor prognosis (3,4). Adenocarcinomas are the most common histological type rather than squamous cell carcinomas (SCC) in cases with skin metastases (3). The vast majority of the SCC with skin metastases are observed in the abdominal wall, vulva, anterior chest wall or lower extremities, respectively (4). Herein, a SCC case of the cervix with skin metastasis to the midline incision site which was treated with a combined chemo-radiotherapy with single chemotherapeutic agent and large excision of lesion was reported.

Case

A 32 year-old woman, was referred to the Ankara University Faculty of Medicine, Department of Gynecological Oncology

for the evaluation of postcoital bleeding and leucorrhoea. The initial gynecological examination revealed a 4cm cervical lesion extending to the upper part of vagina and a 4x4 cm solid mass at the cervical site was confirmed both by transvaginal ultrasonography (with intrauterine hypoechogenity) and by computerized tomography. The cervical biopsy revealed an undifferentiated SCC. Intravenous pyelography showed no abnormality on each kidney. Examination under anesthesia along with cystourethroscopy and sigmoidoscopy verified a FIGO stage II A lesion. After preoperative tests the patient underwent radical hysterectomy type III and pelvic-periaortic lymph node dissection. On histological examination, involvement of the lymphovascular space was diagnosed and three of the sampled pelvic and periaortic lymph nodes (left 3/6, right 0/9, periaortic 0/5) were found to be positive for metastasis. Subsequently, radiotherapy was performed and the patient received 6000 CGy of external beam irradiation in 30 sessions over 6 weeks.

Postoperatively, the control visits of the patient were uneventful for five years. However, a 3x2 cm deep subcutaneous mass with a 1,5x1 cm fixed-nodular skin lesion located on

the lower abdominal wall, just adjacent to the midline incision, was noticed after five years of disease free follow up. The fine needle biopsy revealed a metastasis of undifferentiated SCC. Computed tomography of the abdomen and pelvis showed a 4x4 cm mass on the anterior abdominal wall adjacent to the surgical incision site, without any extensions to the abdominal cavity or other recurrences at the primary surgical sites or lung and liver (including vaginal cuff and pelvic organs). Examination of the chest was normal. Surgical excision of the mass by leaving a >2 cm surgically free zone at all surgical borders was performed and confirmed by the frozen sections intraoperatively. The macroscopic and microscopic pathological findings confirmed the skin metastasis of undifferentiated SCC (Figures 1 and 2). Chemotherapy along with radiotherapy was subsequently planned and six courses of chemotherapy with Cisplatinium (50 mg/m²) every 3 weeks after 3000-CGy external beam irradiation in 10 sessions (cobalt) over 2 weeks were given to the patient, sequentially. The patient was then followed by control visits with 6 monthly intervals comprising transabdominal and transvaginal ultrasonography, biochemical tumor markers (CEA, Ca 19-9, CA 15-3, CA 125), direct anterior-posterior chest X ray, and ALP, as well as annually performed computerized tomography, bone scintigraphy and mammography. On the last visit after 4 years of disease free follow up, she had respiratory complaints and on the chest X ray pulmonary

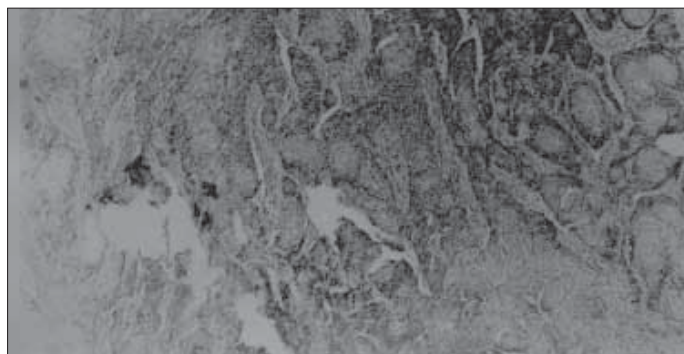


Figure 1. Microscopic view showing squamous cell islets of metastatic squamous cell carcinoma adjacent to vascular and lymphatic structures in incisional scar (x40, hematoxyline-eosin stain)

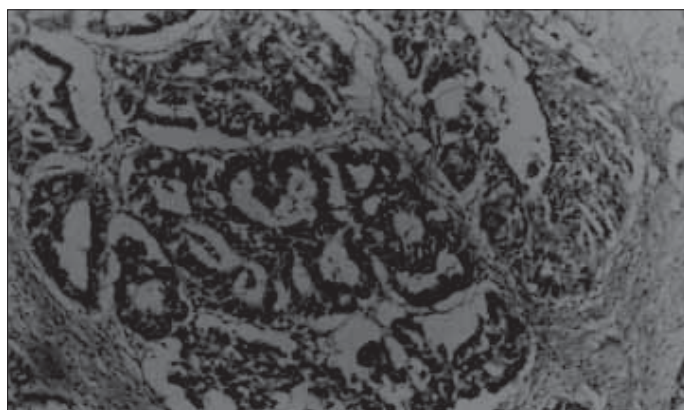


Figure 2. High microscopic view showing clumps of metastatic squamous cell carcinoma in incisional scar (x100, hematoxyline-eosin stain)

edema and on computerized tomography a suspicious nodule in the left pulmonary apex was diagnosed which was thought to be a recurrence. She had no recurrences at the primary or secondary operation sites. Nevertheless, she died in a few months due to cardiopulmonary arrest.

Discussion

The usual route of metastatic spread to the skin in cervical cancer is via the lymphatic system (5). The cutaneous metastases were reported to be caused by retrograde spread of the tumor secondary to lymphatic obstruction. The tumor cells can be demonstrated in dilated lymphatics of the skin lesions.^{5,6} However, the frequency of unusual metastatic sites such as surgical scars in reported cases again raised reasonable concerns about possible direct implantation of tumor cells, or hematogenous metastasis (7-10)

It has been suggested that the incidence of skin metastasis tends to be increased by the advancement of clinical stage and was determined in 1,2 % of stages II-III whereby an incidence of 20 % was defined in undifferential carcinomas (6). The vast majority of the reported cases were SCC especially those that metastasize to surgical scars (9). However, there are also some reports of metastasis to surgical sites such as episiotomy scars with adenocarcinomas.¹¹

The mean interval between the diagnosis of cervical cancer and skin metastasis was reported in a range of 1 to 70 months.⁵⁻⁸ However, there are a few reports about late recurrence or onset of skin metastasis (5-8). Nevertheless, interval to diagnosis seemed to have no negative influence on the prognosis regardless of the clinical stage and/or histological type whereby extremely poor prognosis has been reported in almost all of the cases (6-8)

The mean survival of these patients with skin metastasis was indicated as 3 to 12 months (6-8, 12). However a prolonged survival, more than a year, was reported in just two cases (8, 12) In the current case disease free survival for 48 months was obtained. Possible synchronous primary cervical cancer and primary skin cancer cannot be excluded and molecular genetic techniques for identifying human papillomavirus genes may have a beneficial role.

Cisplatinium is still accepted as the single and most active agent for palliative treatment of recurrent cervical cancer, however palliative radiation is also regarded as helpful in controlling the symptoms of recurrence (13) A combined treatment with single agent chemotherapy and radiotherapy was reported to be favorable in prolongation of survival in another SCC case (FIGO stage IIIB, >1 year) previously reported by Khalil et al (14). In our case, we used combined radiotherapy and chemotherapy sequentially and this application for skin metastases of cervical cancer seems to be successful.

In conclusion, predominance of surgical scars in skin metastasis of cervical cancer raises questions concerning the reported lymphatic metastasis route. Besides this, according to the literature, the histological type of SCC has predominance in contrast to current beliefs. Particularly, a combined regimen based on sequenial chemotherapy and radiotherapy and large excision of the lesion might prolong the expected survival in such cases.

References

1. Berek JS, Hacker NF. Practical Gynecologic Oncology. Lippincott Williams & Wilkins, Philadelphia, 2000; Chap 9: pp 360-80.
2. Disaia PH, Creasman WT. Clinical Gynecology-Oncology, 5th ed. St. Louis, Mosby, 1997; 85-90.
3. Franciolini G, Mamoli G, Minelli L, et al. Cutaneous metastases from carcinoma of the cervix. *Tumori* 1990; 76: 410-2.
4. Brady LW, O'Neil EA, Farber SH. Unusual sites of metastases. *Semin Oncol* 1977; 4: 59-64.
5. Malfetano JH. Skin metastasis from cervical cancer: A fatal event. *Gynecol Oncol* 1986; 24: 177-82.
6. Imachi M, Tsukamoto N, Kinoshita S, et al. Skin metastasis from carcinoma of the uterine cervix. *Gynecol Oncol* 1992; 48: 349-54.
7. Chia-Hui Chen, Kuan-Chong Chao, Peng-Hui Wang. Advanced Cervical Squamous Cell Carcinoma With Skin Metastasis Taiwan *J Obstet Gynecol* 2007; 46: 264-6.
8. Srivastava K, Singh S, Srivastava M, et al. Incisional Skin Metastasis Of A Squamous Cell Cervical Carcinoma 3.5 Years After Radical Treatment: A Case Report. *Int J Gynecol Cancer* 2005; 15: 1183-6.
9. Brownstein MH, Helwig EB. Patterns of cutaneous metastases. *Arch Dermatol* 1972; 105: 862-8.
10. Peterzborn S, Buekers TE, Sood AK. Hematogenous skin metastases from cervical cancer at primary presentation. *Gynecol Oncol* 2000; 76: 416-47.
11. Copeland LJ, Saul PB, Sneige N. Cervical adenocarcinoma: tumor implantation in the episiotomy sites of two patients. *Gynecol Oncol* 1987; 28: 230-5.
12. Hayes AG, Berry AD. Cutaneous metastasis from squamous cell carcinoma of the cervix. *J Am Acad Dermatol* 1992; 26: 849-50.
13. Spanos WJ Jr, Pajak TJ, Emami B, et al. Radiation palliation of cervical cancer. *J Natl Cancer Inst* 1996; 21: 127-30.
14. Khalil AM, Khatib RB, Muffarij RA et al. Squamous cell carcinoma of the cervix implanting in the episiotomy site. *Gynecol Oncol* 1993; 51: 408-10.