



Case Report

Skin metastases originated from cervical cancer: A rare case report

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ABSTRACT

Introduction: Metastases in cervical cancer could be spread through direct local invasion, lymphatic dissemination, or hematogenous dissemination. The most common sites of distant metastases are lungs, bone, and liver. Skin metastases from cervical cancer are categorized as a rare occurrence of metastases. This rarity of the cases has led us to report it.

Case description: A 66-year-old multiparous woman diagnosed with stage IIA cervical cancer seven years ago, then she came into our outpatient clinic complained about a brownish white color mass on the left side of the neck that keeps getting bigger over time came from a skin lesion. The lesion was first treated with topical steroid but there was no improvement. Biopsy was done and the result showed a carcinoma metastasis that led to adenosquamous carcinoma or cervical adenocarcinoma. The patient went through chemoradiation with biosensitizer paclitaxel 120 mg/m² for six cycles, which began in August 2019 until October 2019. The treatment progress showed a promising result. We observed the patient during treatment until two months after finishing the treatment. At the last visit, the patient came to our outpatient clinic, the mass size decreased significantly, and the skin showed an excellent regeneration sign.

Conclusion: The physicians should always consider the patient's history and pay more attention to skin lesions in patients with a history of cervical cancer. The physicians should also perform a thorough physical examination and biopsy to confirm the diagnosis.

1. Introduction

Among all of the diseases related to cancer in women, cervical cancer (CC) is still ranked as the fourth most diagnosed cancer and the fourth leading cause of death following breast, lung, and colorectum cancer. It is estimated for 570,000 cases and 312,000 deaths globally. In Indonesia, CC contributes 17.2% cases and 8.8% deaths of all new cancer cases in women in 2018 [1]. Based on the Indonesian Society of Gynecologic Oncology data, CC staging in Indonesia was dominated by stage IIIB with 43% of all CC cases. In histopathology type, CC was dominated by epidermoid carcinoma (59%), followed by adenosquamous carcinoma and adenocarcinoma [2].

Currently, one of the treatment guidelines used in treating cervical cancer is the European Society of Gynaecological Oncology that aim covering comprehensively staging, management, and follow-up for patients with cervical cancer, including fertility sparing [3]. Metastases in

CC are divided into three main routes. It could be spread through direct local invasion, lymphatic dissemination, or hematogenous dissemination [4]. The most common sites of distant metastases are lungs, bone, and liver [5], while the less frequent sites of spreading were the bowel, adrenal gland, spleen, and brain [4]. Skin metastases from CC are categorized as a rare occurrence of metastases [5]. This rarity of the cases has led us to report it.

2. Case description

A 66-year-old multiparous woman was diagnosed with stage IIA cervical cancer in 2012. She complaint about postmenopausal bleeding and foul-smelling vaginal discharge. She had the symptoms for around one month, and never experienced this symptoms before. She had no previous disease and did not consumed any other medications. There was no history of malignancy in the family. Her daily activities were

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doing household chores so it considered as a moderate activity. Patient had no complaint on her sexual behaviour, and there was no history of multiple sexual partner. She went through total laparotomy hysterectomy with bilateral salphingo-oophorectomy that was done by Gynecologic oncologist at dr. Cipto Mangunkusumo Hospital, a national reference hospital. Lymphadenectomy was also performed on multiple sites. Histopathological findings from cervix showed adenocarcinoma cervix, and from lymph nodes showed cancer cells suggesting metastases, the patient then was treated with chemotherapy with 600 mg of Carboplatin and 300 mg of Paclitaxel as a sensitizer for six cycles. The patient had a complete response after chemotherapy and no evidence of disease for seven years.

In April 2019, the patient had a complaint about a brownish lesion in the left anterior side of the neck. She then consult to a dermatologist and treated with topical steroid at first, but the lesion did not show any changes. In July 2019, the patient came into our outpatient clinic complained about a mass on the site of the lesion that kept growing significantly from a few months before. From the physical examination,

the mass was multiple with the biggest mass size was 62 mm × 39 mm. The mass had brownish-white color, fixated to the skin and had soft consistency (Fig. 1). After the patient did a CT-Scan examination, the result showed that there was no sign of other metastases sites from the lungs or lymph nodes. From the examination, there were no signs of local metastasis. We suspected the mass could be the evidence of cervical cancer metastases to the skin. The patient underwent a biopsy, and then evaluated by immunohistochemistry. The immunohistochemistry result supported a carcinoma metastasis that led to adenosquamous carcinoma or cervical adenocarcinoma (Fig. 2). This finding showed the same histology with the prior primary tumor.

We did not do a resection of the mass of the first place because of the mass was extensive, and it spread through the upper left chest, thus, we decided to do chemoradiation. The patient went through chemoradiation 25 × 2 Gy with biosensitizer paclitaxel 120 mg/m² for six cycles, beginning in August 2019 until October 2019, and the patient committed to the whole regiment of the treatment. We observed the patient during treatment until two months after chemotherapy to



Fig. 1. Skin Metastasis from Cervical Cancer. The mass shown on the first visit before chemotherapy (A), The skin condition after chemotherapy (B).

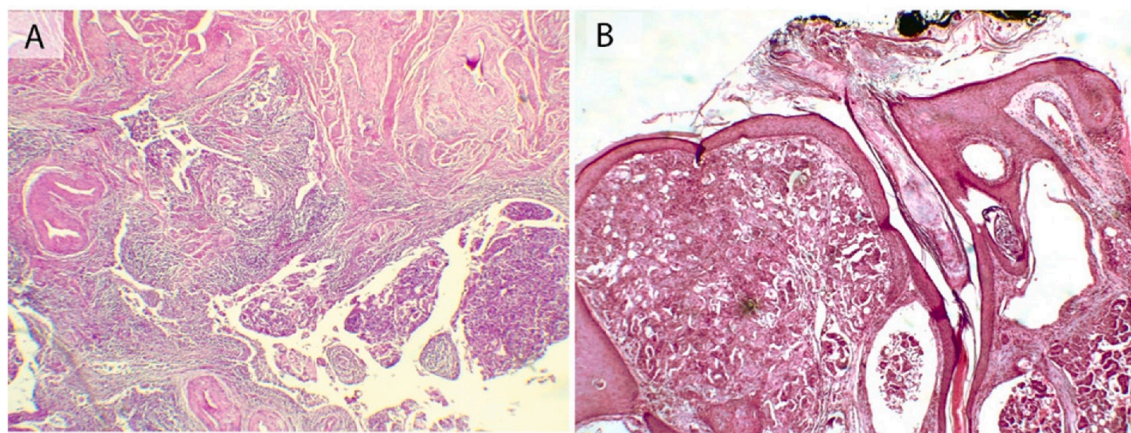


Fig. 2. Histopathology biopsy from Cervix(A) left anterior side of the Neck(B).

evaluate any sign of side effects. The treatment progress showed a promising result and we concluded that additional intervention was not necessary. There was no sign of any toxicity reported in this Case such as anemia, leukopenia, and thrombocytopenia. At the last time the patient visited our outpatient clinic, the mass size decreased significantly. From physical examination, the skin showed an excellent regeneration sign, the imaging and laboratory results also showed no signs of recurrence. The patient was discharged with no additional treatment and declared as a complete remission (Fig. 1).

3. Timeline

Date	Information
2012	Postmenopausal bleeding and foul-smelling vaginal discharge. The patient was diagnosed with cervical cancer stage IIA. She underwent laparotomy total hysterectomy with lymphadenectomy and bilateral salpingo-oophorectomy at another hospital. Pathology anatomy result: adenosquamous carcinoma dd/cervical adenocarcinoma. The patient went through chemotherapy completely.
2013–2019	NED*
April 2019	A brownish lesion on the left anterior side of the neck, consult to a dermatologist and treated with topical steroid.
July 2019	A Mass on left anterior side of the neck with rapid growth, 62 mm × 39 mm for the biggest size, brownish-white color, and soft consistency. Biopsy results showed carcinoma metastasis that led to adenosquamous carcinoma or cervical adenocarcinoma.
August 2019–October 2019	Chemoradiation 25 × 2 Gy with biosensitizer paclitaxel 120 mg/m ² for 6 cycles.

*NED: No Evidence of Disease; There were neither sign and symptoms nor any complaints from the patient. The examination result after the procedure certified that the patient was cancer free.

4. Discussion

Cervical cancer is the fourth most common malignancy in women worldwide accounted for an estimated 570,000 new cancer cases and 312,000 deaths. In Indonesia, the estimated number of new CC cases is 17.2% of all cancer cases in 2018 [1]. The risk factors of cervical cancer development are varied from the HPV as the main etiology of the disease, sexual behaviors, previous and current condition of the patient, family history, drug consumption, to the socio-economical status of the patient [4]. The staging system for CC is the FIGO (The International Federation of Gynecology and Obstetrics) staging system, which is based mainly on clinical examination [6]. For the histopathology type distribution: squamous cell carcinoma (69%), adenocarcinoma-including adenosquamous cancer (25%), and other histological types (6%) [4].

There is various etiology of skin metastases from a solid tumor in

women, including breast (60%–90%), gastrointestinal tract (9%), lung, and ovary. Skin metastases from CC are unusual, ranging from 0.1 to 2% of all reported events [5]. From all reported skin metastases from CC, the most common sites are the lower abdominal wall and lower extremities. The morphology of metastatic skin could be nodules, plaques, or inflammatory telangiectatic lesions [7,8]. The metastases was thought to be caused by retrograde dissemination of the tumor secondary to lymphatic obstruction [9]. A retrospective study conducted by Imachi et al., 1993 showed from 1190 patients, the mean incidence of skin metastases were 1.3%, wherein stage 1 is 0.8%, in both stage 2 and 3 is 1.2%, and stage 4 is 4.8% [7,10]. Summary of reported skin metastases from CC can be seen in Table 1.

Skin metastases could be a pre-terminal sign. It is usually associated with local recurrence and other distant metastases, and the prognosis is poor in such cases. No effective treatment was identified until now, there was no clear guideline regarding the skin metastases treatment, and the treatment usually remains palliative rather than curative [5,11].

In our Case, we reported a rare case of skin metastases from CC [14]. From the last treatment, until the first appearance of the skin lesion on the left anterior colli was 84 months, which rarely happens. Because of this vast gap in the cancer-free period, the clinical manifestation could be misdiagnosed as other primary skin tumors. Because the patient was first treated with topical steroid and did not show any improvement, it is important to analyze the skin lesion through biopsy to evaluate the lesion whether came from a primary skin malignancies or it could be a skin metastasis from other site of cancer. CC metastases could be spread through direct local invasion, lymphatic dissemination, or hematogenous dissemination [4]. Because of the history of surgical treatment, at the time of the examination, this tumor was not suspected as a skin metastasis. Later we found the lesion was a skin metastasis based on the clinical features, laboratory workup, radiological findings, histopathology, and prior knowledge of the patient's history of CC. The metastases of CC through hematogenic pathway are a rare event that could be found in only 5% of all CC cases. It is more common in poorly differentiated and aggressive tumor cells [4]. Although the patient had undergone surgery in 2012, the skin biopsy came out similar to the previous cervical cancer. In our case, the patient's treatment was chemoradiation with biosensitizer paclitaxel, and the result showed a good outcome [3]. According to our case, there is a possibility of occurring distant metastases in unusual site from cervical cancer. This rare case could provide an insight on how to approach skin malignancy with previous history of cervical cancer.

5. Conclusion

We are reporting an unusual Case of skin metastases from stage IIA cervical cancer with 84 months. The physicians should always consider

Table 1
Reported cases of skin metastasis in cervical cancer.

Author	Age (years)	FIGO Stage	Histology	Site	Morphology	Interval, (Months)	Treatment	Outcome, (months)
Katiyar et al. [8]	60	IIA	ASC	Lower Abdomen/thighs breast	patchy rash	24	CCT	Dead
Burbano et al. [9]	41	IIIB	ASC	vulva lower extremities	plaques	46	SCT	Dead
Raj S et al. [7]	45	IVA	SCC	breast	nodule	2	RT/CCT	Dead
Qing Cai et al. [12]	45	IVB	SCC	facial	telangiectasia	24	SCT	Lost to follow-up
Alrefaie et al. [11]	69	IVB	SCC	lower extremities	papules, plaques	6	–	Dead
Cherian et al. [13]	52	N/a	SCC	lower extremities	nodules	21	RT/CCT	Dead
Benoulaid et al. [5]	63	IIIB	SCC	abdominal thoracic	nodules	6	SCT	Dead
Benoulaid et al. [5]	48	IIIB	SCC	upper extremities lower extremities	nodules	N/a	RT/SCT	Dead

ASC: Adenosquamous carcinoma; SCC: Squamous Cell Carcinoma; RT: Radiotherapy; SCT: Single-Agent Chemotherapy; CCT: Combination Chemotherapy, N/a: no information acquired.

the patient's history and pay more attention to skin lesions in patients with a history of cervical cancer. The physicians should also perform a thorough physical examination and biopsy to confirm the diagnosis.

6. Patient's perspective

The first time I noticed that there was a growing lump of skin around my neck, I never thought that it was a cancer, moreover that it was originated from cervical cancer that I had seven years ago. Before I was told that it was a cancer, I thought it was a skin rash or some kind of infection. I went to a dermatologist a couple of times for treatment but there was no changes. After a few months, the lump grew bigger and spread to my upper left chest and behind my left ear. I went back to the dermatologist and she took a sample of the mass and the biopsy result showed that it was a cancer spreading from my previous cervical cancer. The dermatologist then referred me to a gynecologic oncologist for further evaluation and treatment. The gynecologic oncologist diagnosed the mass on my neck as a skin cancer metastasized from my previous cervical cancer. I was then went through further evaluation to confirm whether there is another metastases. After the evaluation, the doctor did not find any metastases other than the one on my skin. After the evaluation I was scheduled for chemotherapy and radiation to eradicate the mass on my skin. At first I was concerned about the treatment, whether will it be effective, and the side effects. The doctors then convinced me that it was the best choice of treatment and the side effects will be minimal. I went through the treatment for three-months, along the way the mass was eradicated gradually and there was no severe side effects. After I finished with the treatment, the mass was completely eradicated, no residual mass, and I was asked to come back in two months for evaluation. After two months evaluation, it was decided the treatment was a success, and no further evidence of disease was found.

Ethical approval

This study was reviewed and approved by the Institutional Review Board and Ethical Committee Dr. Cipto Mangunkusumo, a national reference and teaching hospital.

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Author contributions

Sigit Purbadi: conceptualization, methodology, resources, supervision. Sigit Purbadi and Laurensia Scovani: writing-original draft preparation, visualization, writing-review and editing. Sigit Purbadi, Primariadewi Rustamadji, Gatot Purwoto, Fitriyadi Kusuma, Andi

Darma Putra, Laurensia Scovani: investigation, data curation, supervision, Ernest TB Sianturi: writing-review and editing.

Research registration number

The manuscript is a case report that does not involve experiments to human participants.

Guarantor

Sigit Purbadi.

Patient consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written informed consent is available for review by the Editor-in-Chief of this journal on request.

Provenance and peer review

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Declaration of competing interest

The authors declare that we have no financial or personal relationship that may have inappropriately influenced us in writing this article.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at <https://doi.org/10.1016/j.amsu.2021.102363>.

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