



Recurrent early-stage squamous cell carcinoma cervical cancer presenting with isolated ovary metastasis: a rare case report

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Introduction: Ovarian metastatic squamous carcinoma of the cervix is rare, accounting for about 0.4%. This study reports a single case of metastatic recurrent cervical cancer in the ovary.

Case presentation: A 46-year-old patient with a history of cervical cancer T1b2N0M0 underwent a radical hysterectomy, bilateral pelvic lymph node dissection, and ovarian preservation. One year later, the patient was admitted to the hospital because of abdominal pain in the left iliac fossa; the abdominal computed tomography image showed a left ovarian tumour. The patient underwent laparoscopic left oophorectomy. Postoperative histopathology confirmed ovarian squamous cell carcinoma. From this case, we would like to review the literature on epidemiology, diagnosis, treatment, and prognosis.

Clinical discussion: Ovarian preservation during surgery in patients with cervical cancer offers many benefits, but careful patient selection is required. However, it should be selected carefully and closely monitored.

Conclusions: Clinicians should be aware of this situation of ovarian metastasis in patients with early cervical cancer undergoing ovarian-conserving surgery.

Keywords: cervical cancer, ovary metastasis, recurrent

Introduction

Cervical cancer is the second most commonly diagnosed cancer and the third leading cause of cancer death among females in less developed countries^[1]. The death rate of cervical cancer has been declining because of the successful implementation of screening programs. However, the percentage of new cases of early-stage cervical cancer is increasing greatly^[1]. Cervical cancer with stage IB–IIA, according to the Federation of Gynecology and Obstetrics (FIGO), has a recurrent rate of 11–22%, mainly occurs in the central pattern (cervix and vagina), pelvic zones and most distant metastasis were found in lungs, bone, and liver^[2,3].

Ovarian metastases from squamous cell carcinoma (SCC) of cervical cancer are rare, especially in the early stage, and reported 1.4% in previous studies^[4]. Ovarian preservation in early-stage SCC has been well-established since McCall et al in 1958^[5]. We

HIGHLIGHTS

- Early-stage squamous cell cervical cancer with ovarian metastasis is rare. Diagnosis is often difficult to distinguish from primary ovarian cancer.
- Ovarian preservation during surgery in patients with cervical cancer offers many benefits, but careful patient selection is required.
- Clinicians should be mindful of this situation in early-stage cervical cancer patients undergoing ovarian-conserving surgery.

present a rare case of cervical SCC with ovarian metastasis in a 46-year-old female with cervical cancer of stage FIGO IB2 after one year of Wertheim-Meigs surgery. This work has been reported in line with the SCARE 2020 criteria^[6].

Case presentation

A 46-year-old female was diagnosed with FIGO IB2 cervical cancer (the tumour with a diameter of 3 cm—according to the classification of FIGO 2018)^[7]. Consequently, a radical total hysterectomy with bilateral lymph node dissection (pelvic and aortic lymph node) was performed. During this surgery, the patient's ovaries were thoroughly evaluated as entirely normal. Because of the young patient with early stage and her expectation, she underwent ovarian transposition to preserve ovarian function. Postoperative pathology demonstrated a grade III of SCC, extensive to one-third of the thickness of the epithelium, lymphovascular invasion, no bilateral pelvic lymph node metastasis,

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and no parametrial invasion. Applying SEDLIS standards, patients received adjuvant radiation therapy with radiation therapy dose of 50Gy + brachytherapy HRD x 3 sessions. After treatment, the patient was discharged from the hospital in May 2021. After that, the patient was examined every three months for the first year by clinical examination, gynaecological examination, abdominal ultrasound, chest X-ray, and blood SCC marker test. In addition, the patient received additional computed tomography (CT) and MRI scans if a suspicious lesion were detected on ultrasound or X-ray.

A year later, she complained of abdominal pain in the left iliac region. Clinical examination revealed that the left iliac fossa had a well-demarcated soft-density mass. The vagina appeared normal with no recurrent lesions. Abdominal ultrasound revealed a cystic structure measuring 48 × 62 mm with an internal wall, no abnormal lymph nodes, and no abdominal ascites. Abdominal CT showed a heterogeneous density mass with fluid, enhancing walls and tissues, 56 × 70 × 78 mm, and well-defined and sharp margins in the left hypogastric area. There were no remarkable lesions in the brain MRI, chest computer tomography, and bone scan. The serum level of tumour markers was examined, including CA 12.5 (33,01 U/ml), HEA (41,12 pmol/l), and SCC (0,706 ng/ml), which all showed normal. Initially, we suspected ovarian cancer with the history of treated cervical cancer and the differential diagnosis of ovarian metastases from cervical cancer. Our patient underwent a laparoscopy. The abdominal cavity was

clear, with no recurrent lesion in the pelvis. The left-transposition ovary had a round, smooth-surface mass with a size of 5 × 6 cm; the right ovary was normal. We decided to remove the left ovary, the surgical procedure did not rupture the tumour, and the result of the frozen section was carcinoma. At that time, pathology could not differentiate primary ovarian cancer and metastatic ovary. Therefore, we removed the right ovary and greater omentum as well (Fig. 1).

Postoperative pathologic findings

Macroscopically, the left ovary tumour consists of a 5 × 6 cm cystic wall specimen cut through the tough pink, a thin wall with a smooth lumen, with part of a solid structure measuring 1.5 cm in size, cut through solid yellow. With the HE staining method, microscopically, epithelial cells have rounded, irregular, highly alkaline nuclei, coarse chromatin, clear nuclei, wide cytoplasm, and many divided nuclei; Tumour cells arranged in disorder, lost polarity and infiltrated stroma. The stroma contains several structurally normal mucinous glands with chronic inflammatory infiltrates. All point to metastatic nonkeratinizing SCC of the ovary. The great omentum and the left ovary were benign.

The patient was diagnosed with ovarian metastasis from cervical cancer. She was treated with chemotherapy of paclitaxel–cisplatin–bevacizumab after surgery. After six cycles, the patient was stable with no recurrent lesions, and the level of SCC (0.5 ng/ml) was normal range. The patient was discharged from the hospital and

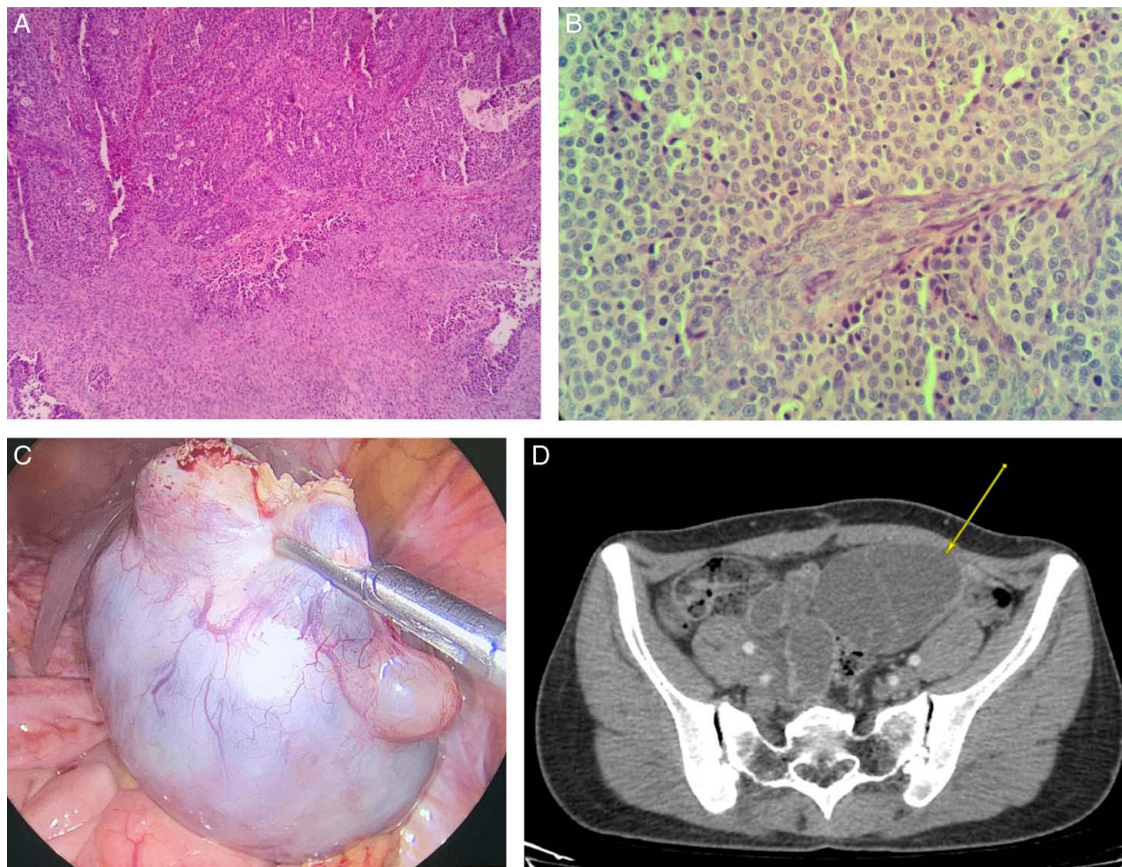


Figure 1. (A) Histopathology of left ovarian tumour × 10. (B) Histopathology of left ovarian tumour × 40. (C) Image of left ovary on laparoscopy. (D) Computerized image of left ovarian tumour (yellow arrow).

periodically examined every 3 months. Currently, after a year of follow-up, the patient did not detect recurrence of the disease.

Discussion

Secondary ovarian lesions account for 13.6% of malignancies in the ovary, in which metastasis from cancer of the gastrointestinal tract is the most common, accounting for more than 70%^[8]. Cervical SCC metastasizes to ovaries are rare, with a rate of 0.4%, while nonsquamous cervical cancer is more likely to metastasize with 8.2%^[9]. Especially early-stage cervical cancer, recurrent with ovarian metastasis alone, is special and rarely reported in the medical literature.

Overall, most reported metastases to the ovary are usually detected post-operatively, unilateral, and confined to ovarian parenchyma^[2,3]. Several potential risk factors for ovarian metastasis include age older than 40 years, pelvic lymph node involvement, parametrial invasion, lymphovascular invasion, bulky tumour, and corpus uteri invasion^[4].

Ovarian conservation surgery in a patient with SCC cervical cancer was proven to benefit many aspects of health for the patient. Furthermore, previous studies reported that ovarian preservation had no adverse effect on the recurrent rate and overall survival of a patient with early-stage cervical cancer. Moreover, this improves young women's quality of life by preventing them from severe menopausal symptoms, including immediate hot flashes, osteoporosis, and emotional problems. Therefore, maintaining normal ovarian endocrine function is crucial for young patients with early-stage cervical cancer^[10]. Oophorectomy should be considered in patients with a high risk of ovarian cancer, such as BRCA1,2 mutation^[11].

Primary ovarian SCC is rare and occurs over a long period of time, and is correlated to preceded by a dermoid cyst, Brenner tumour, and endometriosis^[12]. The incidence of primary ovarian SCC is extremely rare when not associated with these pre-existing ovarian lesions. In our case, at the time of surgery, we carefully examined bilateral ovaries by physical exam and CT scan that showed no remarkable-existing lesion. However, after one year, discovering the right ovarian tumour of 6 cm in size is appropriate with metastatic lesions rather than primary ones because the process from a benign tumour to cancer commonly occurs in several years. Although we used neither immunohistochemistry marker nor determining HPV DNA in ovarian tissue, pathology findings combined with clinical signs still demonstrated the SCC metastasis.

The main routes of metastasis from the cervix to the ovary: hematogenous, lymphatic, or tubal implantation^[4]. The ovaries have an abundant lymphatic system linked to each other through the pelvic lymph nodes, so lymphatic metastasis is the most common. When a pelvic lymph node is metastasized, retrograde or collateral circulation occurs that can allow cancer cells to reach the ovary. In our patient, although the results of the dissection of the pelvic and abdominal aortic nodes were chronic inflammation, the histopathology sample showed that the tumour had invaded the lymphatic vessels, so this metastatic pathway could not be ruled out. The study of the author Matsuo and colleagues on 5000 patients with cervical cancer stage IB–IIB showed that tumour invasion of lymphatic vessels is one of five independent factors that increase the rate of ovarian metastasis. If only this one prognostic factor is present, as in our patient, the reported ovarian metastasis

rate is 0.16%^[13]. The average time from initial treatment to discovering ovarian metastasis was commonly reported about 3 years and even 8 years in some reported cases^[14].

The management of recurrent cervical cancer remains challenging. Despite the progress in a therapeutic approach to recurrent cervical cancer, the 5-year overall survival rate of this group was only 22.3% with extensive therapy^[15]. Surgical therapy plays an important role in treating recurrent cervical cancer, especially for operable cases like our patients. In our clinical case, surgical therapy helps us confirm the diagnosis and relieve the patient's symptoms. In the study of Chao *et al.*^[16], surgical therapy alone led to an overall survival that was non-inferior to those with other therapies in patients with recurrence only within the pelvic cavity and with a radiotherapy history. Besides, the study showed that operable case has longer overall survival than those who are medically inoperable. Radiotherapy is an adjuvant therapy following surgery or in a recurrent patient that have no prior radiotherapy history.

The GOG 240 trial showed that adding bevacizumab to combination chemotherapy in patients with recurrent, persistent or metastatic cervical cancer improved the median overall survival and progression-free survival^[17]. This therapy also is a preferred recommendation in a guideline of NCCN (National Comprehensive Cancer Network) 2022. We decided to choose paclitaxel–cisplatin–bevacizumab. In a recent study, Keynote-826 showed that pembrolizumab potentially improves overall survival and progression-free survival in a patient with recurrent cervical cancer of CPS ≥ 1 ^[18]. However, that regimen was not achievable because of her financial status.

The standard treatment approach for ovarian cancer metastatic from cervical squamous carcinoma is controversial. In the clinical case report of Hidaka, the disease showed only partial response after surgical treatment, chemotherapy regimen paclitaxel–carboplatin combined with pelvic radiation therapy and progression after surgery 14 months^[19]. The study of Shimada showed that the 5-year survival rate of patients with stage IB cervical cancer with ovarian metastases was 46.6%^[20]. In our case, after surgery to remove the ovaries on both sides and the great omentum, the patient continued chemotherapy with paclitaxel–cisplatin–bevacizumab regimen. Currently, the disease has not recurred after 1 year of treatment. We will continue to monitor the patient.

Conclusions

Early-stage SCC of the ovary with metastases of the ovary is rare. However, it should be considered in the patient's history of cervical cancer. Our clinical case is even more special because the patient presented with isolated ovarian metastasis after 1 year of treatment. When deciding to preserve ovaries in cervical cancer patients, clinicians must carefully evaluate and closely monitor the patient after surgery.

Ethical approval

The manuscript approved by ethical committee of Viet Nam National cancer hospital.

Consent

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

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Author contribution

C.T.L.: primary doctor who treated the patient, revised manuscript. A.Q.N., H.T.D.P., L.T.T., H.V.T.: doctors who treated the patient, wrote manuscript. D.B.N., H.V.T., D.D.N.: follow up the patient, revised manuscript.

Conflicts of interest disclosure

None.

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