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Case Report

A case report of lung metastasis in a cervical cancer presenting as a consolidation ☆,☆☆

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ABSTRACT

Cervical cancer is a preventable cancer in the United States. We discuss a case of a 43-year-old woman who presented with signs and symptoms of Cerebrovascular accident (CVA) as well as shortness of breath and chest tightness. Upon investigation, it was concluded that she had developed multiple brain infarcts, pulmonary embolism, and deep venous thrombosis in both lower extremities. However, after her pulmonary symptoms worsened, further investigations revealed an uncommon occurrence of infiltrative lung metastasis. This finding was particularly surprising as she had recently been diagnosed with squamous cell carcinoma of the cervix. It is important to note that patients who have not undergone regular cervical cancer screening can remain without symptoms until the disease has reached an advanced stage, as is the case with this patient. Various screening methods, such as Pap smear cytology, human papillomavirus (HPV) DNA testing, and visual inspection tests, are available to detect and prevent cervical cancer.

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Introduction

In 2020, cervical carcinoma was responsible for 4272 cancer-related deaths in women, making it a significant cause of mortality according to the CDC [1]. The main risk factors for cervi-

cal neoplasia include specific types of human papillomavirus (HPV), such as types 16, 18, 31, 33, and 45 [2]. However, due to age-appropriate screening measures, the incidence and mortality rates of cervical cancer in the United States have decreased by 70% since the 1950s [3]. Primary prevention through HPV vaccination and effective treatment of preinvasive

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Table 1 – Biochemical tests.

White cell count	Prothrombin time	Arterial blood gas pH
13.3 × 10 ³ /uL	12.4 s	7.47
Hemoglobin	International randomized ratio	Arterial blood gas pCO ₂
8.7 g/dL	1.2	35.6 mm Hg
Platelet	Activated partial prothrombin time	Arterial blood gas pO ₂
285 × 10 ³ /uL	26.5 s	80.0 mm Hg
Sodium	HCO ₃	Lactic acid
139 mmol/L	24 mmol/L	1.1 mmol/L
Potassium	BUN	Calcium
3.3 mmol/L	9 mg/dL	8.8 mg/dL
Chloride	Creatinine	Phosphorus
102 mmol/L	0.8 mg/dL	4.7 mg/dL
Total Bilirubin	AST	Procalcitonin
3.5 mg/dL	27 U/L	0.05 ng/mL
Direct Bilirubin	ALT	TSH
0.5 mg/dl	7 U/L	0.76 uIU/mL
ALP	Albumin	Random cortisol
104 U/L	3.4 g/dL	20.7

lesions have also contributed to this decline [4]. Nevertheless, cervical cancer remains a major health issue in underdeveloped countries.

While early-stage or locally advanced cervical cancer has a better prognosis compared to advanced stages, where the median survival is 8-13 months, distant metastasis can occur. The lungs are the most common site of metastasis in cervical cancer, with an incidence ranging from 4.16% to 7.7% [5]. In this case report, we present the case of a patient with cervical cancer who initially exhibited signs and symptoms resembling a cerebral vascular accident. Further examination revealed lung metastasis characterized by patchy opacities and consolidations in both lung bases. The patient was ultimately diagnosed with squamous cell carcinoma of cervical cancer with lung metastasis.

Case presentation

A 43-year-old woman with no notable medical history, who had not undergone age-appropriate cancer screening, arrived at the Emergency Department complaining of symptoms consistent with a cerebral vascular accident, such as visual loss, dysarthria, and weakness in the right face and arm. Additionally, she experienced a gradual increase in shortness of breath during physical activity, accompanied by chest tightness. The patient was also hypoxic (low oxygen levels) and had an elevated heart rate. She denied experiencing any vaginal bleeding or discharge.

The physical examination shows bilateral crackles, tachycardia, and breathlessness at rest. The blood work showed a slightly elevated white blood cell count (13.3 × 10³/uL), along with hypoxemia and low hemoglobin (8.7 g/dL). Moreover, the ABG was as the following: PH = 7.47, pCO₂ = 35.6 mm Hg, HCO₃ = 24 mmol/L, and pO₂ = 80.0 mm Hg (Table 1). A brain CT scan revealed the presence of multiple acute and subacute

infarcts, indicating an embolic phenomenon. A chest computed tomography angiography (CTA) showed an extensive sub-massive pulmonary embolism on the right side, affecting the main, lobar, segmental, and subsegmental arteries (Fig. 1). A duplex venous ultrasound (US) examination identified deep venous thrombosis in both lower extremities, and an echocardiogram indicated right ventricular dilation with wall hypokinesia, consistent with right ventricular strain. Additionally, a patent foramen ovale was detected. The patient was initiated on therapeutic anticoagulation and broad-spectrum antibiotics. Following the administration of anticoagulant medication, the patient began experiencing vaginal bleeding. To further investigate this complication, a CT scan of the abdomen and pelvis was performed. The scan revealed an enlarged uterus accompanied by bilateral pelvic lymphadenopathy. A transvaginal ultrasound showed the presence of a 6.4 cm cervical mass, with a potential invasion of the bladder wall measuring approximately 2.2 cm. A subsequent biopsy confirmed the diagnosis of cervical squamous cell carcinoma. Due to the patient's significant burden of venous thrombosis and limited pulmonary circulation reserve, an inferior vena cava filter was inserted. After nearly 2 weeks of hospitalization, the patient was discharged and prescribed Apixaban along with home oxygen therapy of 2L via a nasal cannula. The patient was advised to follow up with imaging studies in 1 month.

After a 2-week period following discharge, the patient was readmitted to the hospital due to a deterioration in her shortness of breath and an increased need for oxygen support. Initially, she required a high-flow nasal cannula to maintain her oxygen saturation above 94%. A chest CTA was performed, which revealed a worsening of bilateral multifocal infiltrates in her lungs. Moreover, new findings of nodules measuring up to 4 mm were observed in the right upper lobe, indicating a resolution of her prior pulmonary embolism (Fig. 2).

The patient was transferred to our center's intensive care unit and immediately started on broad-spectrum antibiotics to address potential infections caused by various types of bacteria. Tests for COVID-19, RSV, and influenza A/B were per-

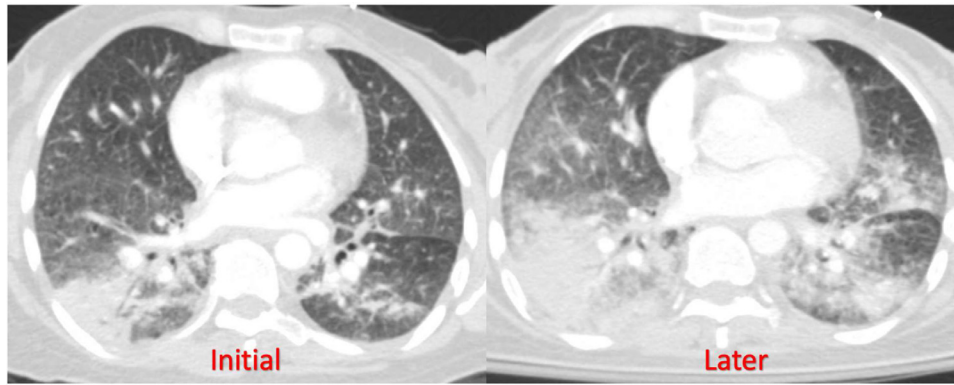
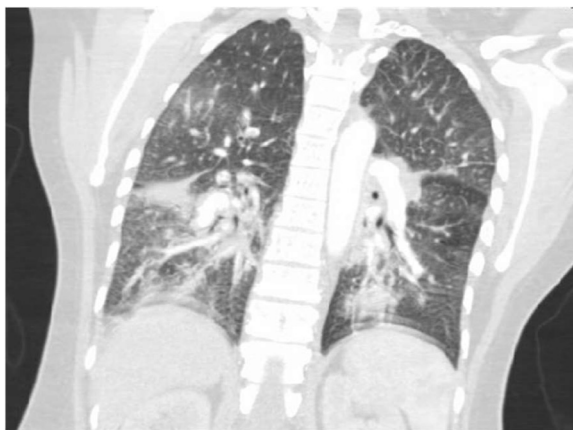
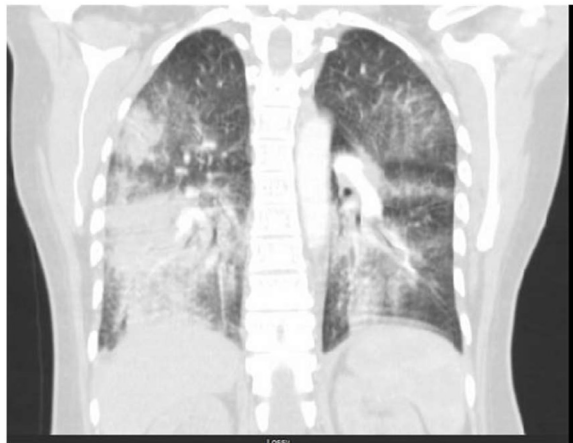


Fig. 1 – CT Chest axial view showing bilateral lung infiltrate progression over 1 month.



Initial



Later

Fig. 2 – CT Chest coronal view showing bilateral lung infiltrate progression over 1 month.

formed, all of which returned negative results. Blood cultures consistently showed no growth of microorganisms. However, her respiratory distress worsened, necessitating intubation 1 day after her transfer. To further investigate the cause, a bronchoalveolar lavage was conducted, which confirmed the pres-

ence of malignancy consistent with squamous cell carcinoma. The lavage tested positive for markers CK4 and CK5/6, which establishes the diagnosis. Despite all interventions, the patient's blood pressure continued to decrease, requiring the administration of 3 vasopressors to maintain a mean arterial pressure above 65 mm Hg. The hypotension was likely due to right ventricular failure, considering her known patent foramen ovale. Given the worsening condition and in accordance with the decision made by her healthcare proxy, the patient's care was shifted to comfort measures only, and she was voluntarily removed from mechanical ventilation (extubated). [Fig. 3](#)

Discussion

Cervical cancer is the growth of abnormal cells in the lining of the cervix. It typically spreads either locally to nearby tissues such as the vagina, uterus, and pelvic cavity, or distant areas like the lungs, para-aortic lymph nodes, and bones [6–8]. Lung metastasis is considered less common in squamous cell carcinoma of the cervix, accounting for less than 5% of cases. Also, the incidence of lung metastasis varies depending on the stage of the cancer, with higher rates observed in advanced stages. For instance, it occurs in approximately 3.2% of stage I cases, 5.0% of stage II cases, 9.4% of stage III cases, and 20.9% of stage IV cases [9].

Lung metastasis can present in different ways, including solitary or multiple nodules dispersed across both lungs, lymphangitic carcinomatosis, tumor emboli, endobronchial metastasis, and pleural effusion [10]. In this case, we observed rapidly progressing bilateral lung infiltrates, presenting as a consolidative pattern resembling pneumonia. Despite antibiotic therapy, further investigation using bronchoalveolar lavage (BAL) has confirmed the presence of squamous cell carcinoma (stage 4 cervical cancer with metastases in both lungs). However, it is important to differentiate between metastatic cervical squamous cell carcinoma and primary pulmonary squamous cell carcinoma. The use of the p16 marker can aid in this distinction, as p16 overexpression is typically seen in HPV-related cervical cancer [11]. Unfortunately, this specific test was not conducted for our patient. Moreover, one of the pathological patterns of cell prolifera-

Clinical Presentation Timeline

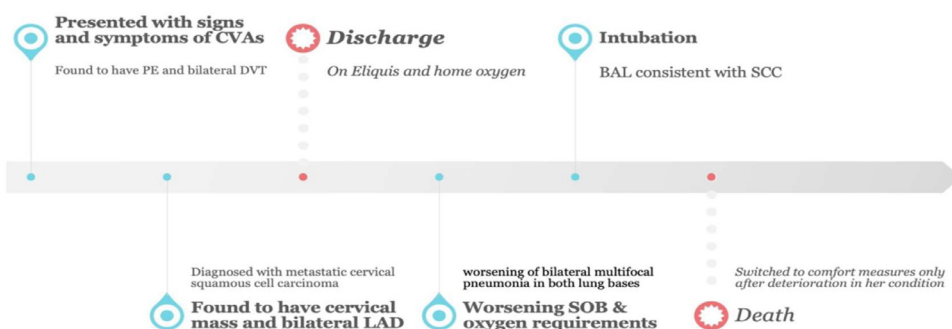


Fig. 3 – Timeline of the clinical presentation.

tion that resemble infectious pneumonia on imaging is the lepidic growth pattern. It refers to the development of tumor cells along intact alveolar walls [12]. Although we did not have pathological confirmation of lepidic growth in the lung, the rapid progression of the metastases over a month in a pneumonia-like manner and the presence of cancer cells in the lavage fluid strongly indicate lepidic growth. It is worth noting that lepidic growth has not been previously described in cervical cancer.

Many cervical cancer patients lack sufficient screening, with over half not having had a Pap smear in the last 5 years [13]. Detection methods include colposcopy, fluorescence spectroscopy, HPV DNA testing, and nuclear aneuploidy detection [14]. Advanced cases may require pelvic MRI and PET-CT [14]. The 2018 International Federation of Gynecology and Obstetrics staging system emphasizes precise tumor size and lymph node details for accurate clinical staging [15]. Enhancing screening rates is crucial, achieved through proactive patient invitations and utilizing urgent care visits for screening, particularly for those less likely to adhere to recommended guidelines. This proactive approach increases the likelihood of early-stage cervical cancer detection [16,17].

Regarding treatments, patients diagnosed with locally advanced cervical cancer could be suitable candidates for primary chemoradiation, which commonly includes cisplatin. However, for those with stage IIA1 disease, surgical therapy with lymphadenectomy may be a possible option instead of primary chemoradiation. Surgery alone is unlikely to result in a cure for people with stage IIB through IVA disease [18]. In stage IVB disease of cervical cancer, the cancer extends via the lymphatic system to the pelvic and para-aortic lymph nodes, or it travels through the bloodstream to distant organs such as the lungs, liver, bones, and other remote sites [19]. In cases where experiencing oligometastatic illness that may be adequately treated locally, definitive radiation or surgical excision of metastases, in conjunction with systemic therapy, could be considered [20]. In circumstances when patients have recurrent or chronic illness localized to the pelvic region after earlier radiation treatments, a surgery known as pelvic exenteration may still be used for treatment.

Currently, there is ongoing research into a new treatment approach that involves the addition of pembrolizumab to

a first-line platinum-based regimen, with or without bevacizumab [21]. While immunotherapy is typically well tolerated, it can cause toxicities in a variety of organ systems, potentially resulting in treatment breaks or termination [22]. Furthermore, the US Food and Drug Administration (FDA) authorized Tisotumab for release in September 2021. The FDA approval was based on the findings of a single-arm experiment with 101 participants. Tisotumab studies are still ongoing, with the goal of gathering more information and knowledge of its efficacy and safety [23]. However, in our case, the cancer has been diagnosed in an advanced stage, and the patient's chances of survival are quite low even with current available treatments.

Conclusion

In summary, our case report underscores the diagnostic challenges in identifying advanced cervical cancer with lung metastasis, initially mistaken for pneumonia. The rarity of this metastatic pattern highlights the need for a comprehensive diagnostic approach. Limited therapeutic options for advanced cervical cancer emphasize the importance of palliative care, prompting ongoing research for improved outcomes. This case underscores the critical importance of effective screening strategies for early detection in such cases.

Patient consent

Informed consent was obtained from the patient's family.

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