

CASE REPORT

The Rare Occurrence of Splenic Metastasis of Cervical Cancer: A Case Report

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Abstract: Splenic metastasis of solid tumors has a low occurrence rate and an incidence of only 2.9%–9%. Given its rarity, only a few cases of splenic metastasis of cervical cancer have been reported. This report presents a case of 76-year-old woman with stage IB1, moderately differentiated adenocarcinoma of cervix, coupled with invasion of cervical stroma and cervical canal. The patient had a cancer antigen 125 (CA-125) level of 150 U/ml and was treated with hysterectomy and pelvic lymphadenectomy. She received 45 Gy pelvic radiotherapy and then 24 Gy brachytherapy. She developed abdominal pain two years later. Computed tomography (CT) examination found two solid lesions of the spleen and no lesions in the rest of the abdominal cavity and chest. Her CA-125 level increased to 2,733 U/ml. Histopathological findings showed splenic metastasis of well differentiated adenocarcinoma in cervix. Immunohistochemical tests revealed that the tumor was positive for carcinoembryonic antigen and negative for estrogen and progesterone receptors. Eight weeks after operation, CA-125 level of the patient was 16 U/ml. She received adjuvant therapy consisting of paclitaxel and cisplatin for 6 cycles. After being followed up for 12 months, the patient was still alive and had no evidence of tumor activity. The spleen is a rare metastatic site. Splenectomy is considered an appropriate treatment to prevent complications, such as splenic rupture and splenic vein thrombosis, and reduce the pain caused by splenomegaly.

Keywords: Cervical cancer, Splenic metastasis, Splenectomy

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1. Background

Cervical cancer is the most common gynecological malignant tumor in the world. It ranks third in industrialized countries, and second only to endometrial cancer and ovarian cancer. It ranks first in morbidity and mortality in developing countries^[1].

In 2008, about 603,800 women worldwide were diagnosed with cancer, of which 529,000 suffered from cervical malignancies, accounting for 8.8% of the total number of tumors, and 274,000 died of cancer, accounting for 8.2% of the total number of cancer deaths^[1]. As of 2013, it has been estimated that there were

about 12,340 new cases of cervical cancer and 4,030 deaths associated with the disease in the United States, making it the third leading cause of care for gynecological cancer and the third leading cause of death for reproductive malignancies^[2].

In Mexico, in 2006, according to the epidemiological profile of malignant tumors, cervical cancer ranked second among female tumors, second only to breast cancer. In the same year, 7,840 new cases of cervical cancer were diagnosed, accounting for 7.38% of the total number of malignant tumors in women. In terms of mortality, 4,036 people died of cervical cancer in 2008, accounting for 11.2%; the number of deaths per 100,000 hectares is 3.8^[3].

Splenic metastasis of solid tumor is a rare event, and the incidence in large autopsy is only 2.9% to 9%^[4-6]. Lam and Tang^[7] reviewed that the most common types of primary tumors where splenic metastasis occurs, based on 92 cases, were lung cancer with 19 cases (21%), gastric cancer with 15 cases (16%), and pancreatic cancer with 11 cases (12%). Metastasis of gynecological cancer is less common. Ovarian cancer accounts for 4%, which is usually caused by the direct expansion of the disease, and cervical cancer accounts for only 1%.

2. Case presentation

This report presents a case of a 76-year-old female patient with cervical endometrial adenocarcinoma who had a medication history of captopril in the treatment of hypertension and dyslipidemia. She is often treated with bezafibrato and pravastatin.

The patient came to our unit for treatment due to abnormal genital bleeding. After further examination using pelvic ultrasound, endometrial legrado biopsy, as well as cervical and cervical canal biopsy, we found that well differentiated cervical endometrial adenocarcinoma invaded the matrix and cervical canal. The tumor diameter was 3 cm, stage IB1. The level of tumor marker cancer antigen 125 (CA-125) was 150 U/ml before treatment.

Surgical treatment was recommended as the initial treatment, so she underwent Piver III hysterectomy and bilateral pelvic lymphadenectomy. The operation proceeded smoothly and the patient was discharged the next day.

Based on the histopathological findings, the tumor is a well differentiated intracervical adenocarcinoma with lymphatic vascular infiltration and invasion of cervical matrix. The vaginal surgical boundary was 2 cm long and free parameters. 22 pelvic lymphadenectomy nodes free of neoplasm. Because the histological type of adenocarcinoma and the invasion of lymphatic vascular space are the adverse prognostic factors of local and regional recurrence of the disease, radiotherapy doctors were required to evaluate the case. The patient received

adjuvant treatment of extrapelvic radiotherapy. Four field technology was adopted; 45 Gy was divided into 25 times, and the radiotherapy was given 5 times/week for a course of 5 weeks. Then, 3 times of high dose-rate brachytherapy were performed, and 8 Gy brachytherapy was received at Manchester point A until 24 Gy was reached at the end of brachytherapy.

Two years later, the patient approached for consultation with a complaint of persistent abdominal pain of the left hypochondriac region. The pain worsened with increased force applied at the region and forced inhalation, and subsided while resting. There were no other related symptoms. Abdominal and pelvic computed tomography (CT) showed an increase in spleen volume, but there were two substantive lesions, one with 53×55 mm and another greater than 21×22 mm, which were enhanced after injection of contrast agent, while there was no evidence of disease in the other abdominal cavity and chest (**Figures 1 and 2**). Laboratory studies showed that the concentration of serum CA-125 increased, reaching 2,733 U/ml, and other laboratory parameters were normal. The possibility of splenic metastasis of cervical adenocarcinoma was summarized, and uncomplicated splenectomy was proposed and implemented. The patient was discharged the day after the operation.

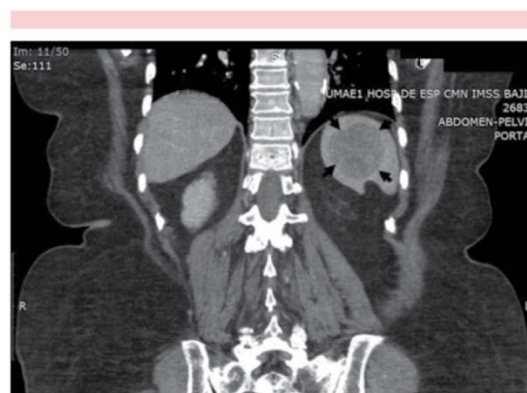


Figure 1. Coronal scan of abdominal axial CT showed enhanced lesions of the upper pole of the spleen after contrast medium (arrow).

The histopathological report of the section showed that the spleen weighed 380 g and was $14 \times 8 \times 6$ cm in dimension. There were no relevant histological changes in the splenic hilum and no tumors in the splenic arteries and veins. Purple-gray serosa in the splenic parenchyma was spotted and central lesions (5 cm in diameter) of the upper pole with amorphous surrounding and central necrosis were also observed. In addition, another metastatic lesion with a diameter of 3 cm was located in the lower pole of the spleen, and the central part was

gelatinous (**Figure 3**).



Figure 2. Two splenic lesions are visible even without contrast medium on axial section of single-phase abdominal CT (arrow).

Under the microscope, well differentiated adenocarcinoma cells could be observed. Besides, the villous structure was covered by high columnar epithelium, the nucleus was pseudostratified, the egg-shaped nucleus without nuclear reticular chromatin was present, and the mitotic index was low. The cytoplasm was clear and vacuolar, with extensive cilia at the cell edge. With less than 5 mitoses in 10 strong dry fields.



Figure 3. Large splenic lesions with central necrotic areas and viable tumors.

Immunohistochemical tests revealed that the tumor was positive for carcinoembryonic antigen and negative for estrogen and progesterone receptors. Eight weeks after the operation, the level of CA-125 was 16 U/ml. The patient received adjuvant therapy consisting of paclitaxel and cisplatin for 6 cycles. The progress of the patient's condition was satisfactory. Twelve months after splenectomy, there was no evidence of disease activity.

3. Discussion

Splenic metastases originated from solid tumors, especially cervical cancer, are extremely rare^[8-10]. The spleen is an organ with low incidence of solid tumor metastatic disease, and various mechanisms have been proposed to explain its rarity. The existence of anti-tumor humoral factors in the spleen destroy the tumor cells reaching the spleen and leads to the dysplasia of lymphatic vessels entering the spleen. It was also mentioned that the rhythmic contraction in the spleen transports blood from the splenic venous sinus to the splenic vein, where the tumor cells maintain constant movement, so as to prevent the implantation of tumor embolus. Similarly, the constant blood flow in the spleen also prevents the implantation of tumor cells. Finally, the special anatomical angle of the splenic artery of celiac trunk prevents the tumor embolus from entering the spleen^[11-16]. Thus, this explains why splenic metastasis of solid tumor is a rare event, with an incidence of only 2.9% to 9% at large autopsy^[4-7,15].

According to several authors^[4-6,15], at autopsy, the most common primary tumor site of splenic metastasis is breast cancer, followed by lung and ovarian cancer as well as colon and gastric cancer.

The clinical manifestations associated with splenic metastasis are nonspecific. Left subcostal pain and splenomegaly are usually the most common symptoms associated with splenic metastasis. Although 50% of the cases are usually asymptomatic^[8-11] cases of splenomegaly are rarely the only findings.

The suspicion of tumor history and clinical symptoms should guide the diagnosis of metastatic diseases. Abdominal ultrasound and CT are still the preliminary imaging tools to aid in the diagnosis of splenic metastatic diseases.

The ultrasonic manifestations of solid tumor metastasis to the spleen are single or multiple hypoechoic lesions, which may have diffuse infiltration^[7].

In the comparative study, the CT findings of splenic metastatic diseases were evaluated by evaluating the low-density lesions with the best performance in the portal vein phase^[17]. Magnetic resonance imaging (MRI) showed T1 longitudinal relaxation low-intensity lesions after contrast medium administration^[17].

The application of positron emission tomography in the diagnosis of splenic metastasis of endometrial carcinoma has been reported^[8,11]. In addition, this study helps to document lymph node metastasis or other organ metastasis^[8].

Tumor markers are proteins or enzymes produced by tumor cells or hosts, which are used for screening and monitoring cancer patients. Elevated CA-125 can be detected in 20% to 75% of patients with cervical adenocarcinoma and is associated with adverse prognostic factors, such as advanced stage, large volume tumor, high histological grade, deep invasion of cervical

stroma and lymph node metastasis^[18].

In an important retrospective study involving 77 patients, Duk *et al.*^[19] found that 52% of the study population had increased CA-125 levels before treatment. The normalization of CA-125 is related to the therapeutic effect, but the increase of its level is related to the treatment failure caused by tumor residue or disease recurrence. Thus, the level of CA-125 is an excellent tool for monitoring patients with cervical adenocarcinoma during follow-up. It is believed that CA-125 has potential clinical value in patients with cervical adenocarcinoma^[20], but further evaluation is recommended to improve the level of evidence. The treatment of splenic metastasis, even if it is an isolated disease, is still based on a multimodal approach.

Splenectomy is the first choice for the treatment of solid tumor splenic metastasis^[8-11]. It helps to reduce the risk of complications, such as spontaneous splenic rupture, prevent splenic vein thrombosis, reduce splenomegaly and pain, help to locally control the disease, improve the survival rate, and reduce the risk of distant metastasis^[8].

Splenic radiotherapy, chemotherapy or oral progesterone therapy have been used as adjuvant therapy for splenectomy; good results were obtained. These treatment methods lengthen the survival to more than 46 months^[8]. In the patient presented in the current report, splenic metastasis occurred two years after the initial diagnosis of cervical adenocarcinoma. The initial clinical manifestation of the patient was left subcostal pain. Splenic metastases were located in the upper pole of the spleen without splenomegaly. It should be noted that the serum CA-125 level increased to 2733 U/ml, and returned to the normal level (16 U/ml) after splenectomy. Because the metastatic lesions are considered low-grade (well differentiated cervical adenocarcinoma) and the immunohistochemical tests revealed that the tumor was positive for carcinoembryonic antigen and negative for estrogen and progesterone receptor, we decided to use paclitaxel and cisplatin in a combination chemotherapy as the adjuvant treatment, which was administered in a total of 6 courses, so as to realize the clinical, biochemical and imaging control of the disease. Twelve months after the end of chemotherapy, no tumor activity was reported.

4. Conclusion

Splenic metastasis of solid tumors is rare, and only a few cases have been reported. Some mechanisms have been proposed to explain the low incidence of the metastasis to this organ. Splenic metastasis, although recognized as a single metastasis, can be tackled with a variety of treatment methods. Surgery can help avoid complications. Adjuvant treatment coupled with chemotherapy, radiotherapy and hormone therapy can improve the

survival rate of the patients. In the present report, the imaging-based diagnostic methods, serum tumor markers and treatment of patient undergoing splenectomy and chemotherapy are consistent with those described in the literature.

Conflict of interest

The authors declare no conflict of interest.

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