



Case Report

Splenic oligometastasis from cervical adenocarcinoma three years after disease free survival: A case report and a review of literature

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ABSTRACT

Introduction: Cervical cancer is the fourth most common cancer among females. Squamous cell carcinoma is the most common subtype of cervical cancer, followed by adenocarcinoma. The most reported sites of metastasis are the lungs, bones, liver, and brain. One of the rarest sites of metastasis, particularly from the adenocarcinoma subtype, is the spleen, with only four reported cases in the literature.

Case report: A 54-year-old post-menopausal female was diagnosed with adenocarcinoma of the endocervix (FIGO stage IIIB) after she presented to the gynecologist complaining of post-coital vaginal bleeding. The patient received chemoradiotherapy followed by brachytherapy. After completion of treatment, she had a restaging work-up which revealed a complete radiological and pathological response. During her routine follow-up, she was found to have a new splenic lesion by surveillance abdominopelvic MRI three years after completion of treatment. Surgical resection was performed, and pathological analysis confirmed the diagnosis of metastatic cervical adenocarcinoma to spleen.

Conclusion: Cervical cancer metastasis to spleen is very rare, especially in the cervical adenocarcinoma subtype. A high index of suspicion is necessary during follow-up. Once there is a suspicion of splenic metastasis, surgical intervention should be considered for both curative and palliative intents.

1. Introduction

Cervical cancer is the fourth most common cancer in the female population as of 2018, with an incidence of 570,000 women worldwide, and accounting for a total of 311,000 deaths [1]. Squamous cell carcinoma (SCC) is the most common subtype of cervical cancer (70%), followed by adenocarcinoma (AC) (25%–30%) [2,3]. Recent studies showed a rise in the incidence of cervical AC. Yet, the literature concerning its management and prognosis remains scarce [2]. Metastatic cervical cancer is most encountered in the lungs, bones, liver and brain, with a percentage of 59%, 23%, 16% and 2%, respectively [4]. Some studies reported other unusual sites of metastasis from cervical AC such as the abdominal wall, spleen, hand and orbit [5–8]. A limited number of studies report the metastasis of cervical cancer to the spleen, yet most of them were histopathologically found to be SCC [9–14]. Upon extensive literature review, we only found four cases reporting the metastasis of cervical AC to the spleen [6,15–17]. In this study, we report a rare

case of splenic oligometastasis from cervical AC along with a table reviewing the other four reported cases in the literature. This case report has been reported in line with the SCARE Criteria [18].

2. Case report

A 54-year-old post-menopausal female, medically free, presented to the gynecologist complaining of post-coital vaginal bleeding with no history of constitutional symptoms. She was found to have a cervical mass on pelvic examination. The laboratory data was unremarkable except for an increase in CA 125 level (814 U/mL). Cervical biopsy showed moderately differentiated AC of the endocervix. Pelvic magnetic resonance imaging (MRI) revealed an irregular uterine cervix soft tissue mass involving the anterior and right lateral aspect of the cervix. The mass was also extending beyond parametrium borders and protruding anteriorly into the posterior wall of urinary bladder (Fig. 1A).

Computerized tomography (CT) scan of chest, abdomen and pelvis

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for complete staging showed no distant metastasis but multiple left internal iliac and obturator enlarged lymph nodes were noted. The International Federation of Gynecology and Obstetrics (FIGO) staging was IIIB (T3N1M0). The case was discussed in a multidisciplinary tumor board meeting and the decision was made to start the patient on chemoradiotherapy which was followed by brachytherapy. Restaging after treatment showed complete radiological and pathological response.

The patient was kept on regular follow-up in a tertiary hospital until she was discovered to have a new splenic lesion by surveillance abdomen and pelvic MRI three years after treatment completion. The lesion was in the lower medial pole of the spleen measuring 3.5×3.2 cm. It demonstrated a central hyper-intensity and peripheral low signal intensity in T2-weighted images, low signal intensity in T1-weighted images with peripheral post-contrast enhancement. (Fig. 1B–D). Positron emission tomography (PET) scan was done and showed FDG avid ill-defined hypodensity seen in the spleen medially (Fig. 1E). The case was discussed once more in the multidisciplinary tumor board meeting, which was concluded with the decision to proceed for splenectomy. Unfortunately, she developed lower limb deep venous thrombosis before surgery which required anticoagulation treatment and inferior vena cava (IVC) filter insertion to avoid delaying surgery.

Intraoperatively the lesion was found to be adherent to the tail of pancreas. Therefore, a distal pancreatectomy and splenectomy were performed. Grossly the specimen showed the lesion in lower medial pole of the spleen (Fig. 2). The final histopathology of the spleen showed metastatic AC consistent with the known primary cervical origin (CEA: positive, CK7: positive, P16: positive, CK20: negative). The tail of the pancreas and the associated 13 lymph nodes showed no evidence of malignancy. (Fig. 3A–D). There were no complications or adverse outcomes after the surgery. After full recovery she was started on adjuvant chemotherapy and eventually the IVC filter was removed. The patient is currently on regular follow-up. To the date of this report, the patient remained disease free, which accounts for more than three years since metastasectomy.

3. Discussion

Splenic metastasis, although rare, usually occurs as part of a disseminated disease. Solitary splenic metastasis is extremely rare, with less than 100 cases reported in the literature [6,19]. Sixty percent of the cases were metastases from gynecological carcinomas, with the majority being ovarian and endometrial cancer as the primary tumors [19]. The most recent review published in 2020 found a total of eight cases of solitary splenic metastasis from cervical cancer in the literature where two of them were AC and the rest were SCC [10]. This could be explained by the higher prevalence of SCC compared to AC [2]. To the

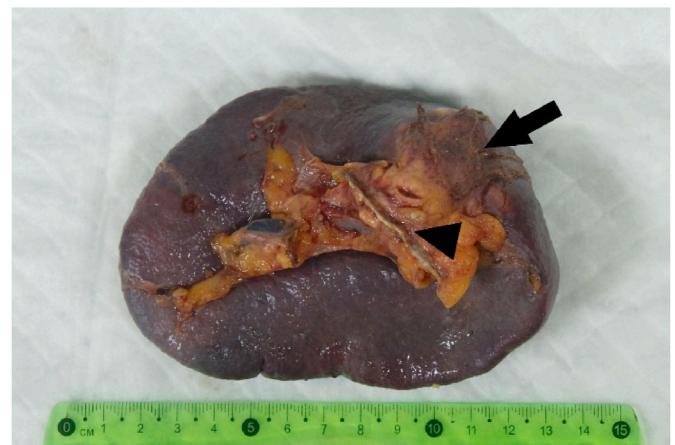


Fig. 2. Gross picture of the spleen showing the metastatic lesion in the lower medial part of the spleen (arrow) and the tail of the pancreas (arrowhead).

best of our knowledge, there have been only four cases of AC of the cervix causing solitary splenic metastasis reported in the literature till date [6,15–17]. The details of these cases are highlighted in Table 1.

The spread of cervical cancer generally starts by local spread to the paracervical tissue then extends further into the pelvis and para-aortic lymph nodes. Hematogenous spread could occur with involvement of the lungs, liver, bones, and supraclavicular lymph nodes [20]. The spleen is considered an uncommon site of metastasis from solid tumors and usually occurs through the splenic artery, splenic vein, or its lymphatics [21,22]. The rarity of its involvement has been attributed to several factors. Anatomical factors include the presence of a splenic capsule, the sharp angle and tortuosity of the splenic artery, in addition to the absence of afferent lymphatics in the splenic parenchyma. Other factors relating to the inherent immunity of the spleen and its ability to prevent metastatic cell growth could also play a role in the low number of cases reported to metastasize to the spleen [23].

The mainstay treatment of cervical cancer consists of concurrent chemoradiotherapy especially in locally advanced disease [9,24]. Some studies suggest that adjuvant surgery may have a role in cases where residual tumor is still present after chemoradiotherapy [24]. In our case the patient had complete radiological and pathological response after treatment with chemotherapy followed by brachytherapy, but she developed splenic oligometastasis afterwards. With regards to cervical cancer splenic metastasis, surgical intervention by splenectomy is the definitive treatment in case of solitary splenic metastasis [9,10,12]. However, many authors recommend adjuvant chemotherapy in isolated

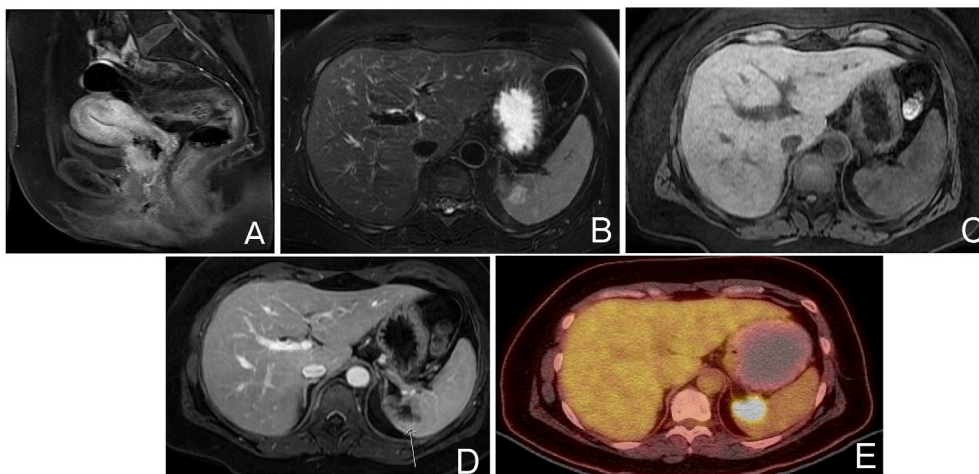


Fig. 1. (A) MRI pelvis (T1) post contrast image showing an irregular uterine cervix soft tissue mass involving the anterior of the cervix, extending beyond parametrium borders and protruding anteriorly into the posterior wall of urinary bladder. Follow-up MRI abdomen & pelvis showing a splenic lesion with (B) a central hyper-intensity and peripheral low signal intensity in T2-weighted images, (C & D) low signal intensity in T1-weighted images with peripheral post-contrast enhancement. (E) PET Scan showing FDG avid lesion in the medial part of the spleen.

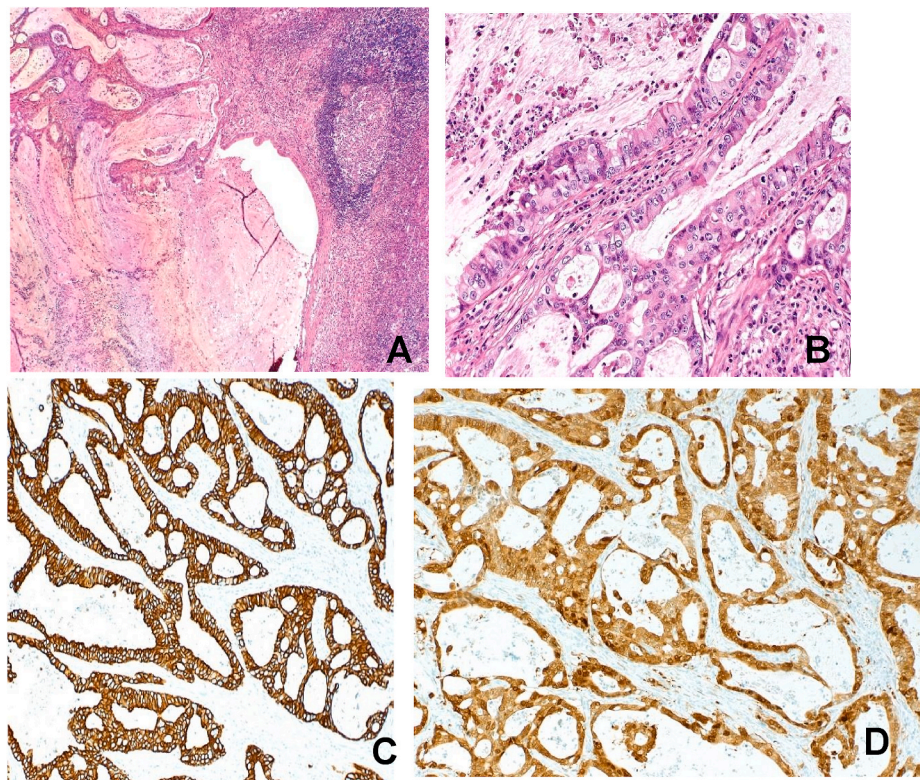


Fig. 3. Histopathological examination & immune staining of the splenic metastasis (A & B) Microscopic examination using H & E staining (X10) showing the spleen parenchyma largely replaced by moderately differentiated AC showing focal glandular cribriform pattern lined by atypical glandular cells. (C) Positive CEA immunohistochemistry staining. (D) Positive P16 immunohistochemistry staining.

Table 1

A Review of the Literature of the reported Cases of Isolated Splenic Metastasis from Cervical Adenocarcinoma.

Author	Year	Age	FIGO stage	Treatment of primary tumor	DFI	Symptoms	Method of splenic metastasis detection	Treatment of splenic metastasis	Overall survival
AlQattan et al.	2021	54	IIIB	Chemoradiotherapy followed by brachytherapy	36 Months	Asymptomatic	MRI scan	Splenectomy and AC (paclitaxel + carboplatin)	Alive, 36 months
Villalón-López et al. [16].	2014	76	IB1	Hysterectomy and pelvic lymphadenectomy, pelvic radiotherapy then brachytherapy	24 Months	Abdominal pain	CT scan + elevated CA-125	Splenectomy and AC (paclitaxel + cisplatin)	Alive, 12 months
Kim et al. [15].	2008	46	IIB	Radiotherapy (External beam irradiation and brachytherapy), chemotherapy (cisplatin)	11 Months	Asymptomatic	MRI scan	Splenectomy and AC (paclitaxel + cisplatin)	Alive, 16 months
Valls et al. [6].	1992	55	N/A	TAHBSO and external beam radiotherapy	14 Months	N/A	CT scan	Splenectomy	N/A
Campagnut et al. [17]	1992	47	IIB	Radical hysterectomy then reoperated due to pelvic recurrence and received radiotherapy	60 Months	Left sided abdominal pain	CT scan + hepatosplenic scintigraphy	Splenectomy	Alive, 7 months

FIGO: International Federation of Gynecology and Obstetrics. **DFI:** Disease Free Interval. **AC:** Adjuvant Chemotherapy. **TAHBSO:** Total Abdominal Hysterectomy Bilateral Salpingo-Oophorectomy. **N/A:** Not Available.

splenic metastasis as it is considered a form of distant metastases [9,11]. Disseminated metastatic disease is treated with palliative chemotherapy. Palliative surgery might be considered in case of symptomatic splenomegaly to improve the quality of life and to avoid complications such as splenic rupture, splenic vein thrombosis and painful splenomegaly [9,10,12,20].

Histologically, the architecture and cytology of disseminated splenic metastasis and the primary tumor are generally similar. Interestingly, Marcu et al. found that four out of the seven reported cases of solitary splenic metastasis from SCC demonstrated a worse morphology of the metastatic lesions compared to the primary tumor [9].

Reported recurrence after treatment of the primary tumor with either surgery or radiotherapy can reach up to 20% (stage IB-IIA).

However, once there is lymph node involvement, the recurrence rate reaches 70% [12]. Follow-up protocol should include clinical examination, vaginal cytology, tumor markers and imaging [9,15]. Increase in the levels of tumor markers, such as SCC antigen can predict the presence and recurrence of metastasis in 46–92% of cases six months before it can be detected clinically (range 2–7.8 months) [9,10,13,15]. Radiological evaluation using CT, PET and MRI is necessary in follow-ups to restage the patient and confirm recurrence [6,10,14]. Although FIGO staging predicts the risk of metastasis, site of recurrence and type of relapse, it is not related to the appearance nor the prognosis of solitary splenic metastasis [9,11,20]. In the literature, the median survival time from diagnosis of splenic metastases varied from 5 to 30 months in solitary metastasis patients while in widespread cases, the median

survival time decreased to 3 to 12 months [9,10,12]. To date, the patient is asymptomatic with a normal biochemical profile and has no disease recurrence neither locally nor systematically according to the most recent imaging.

Conflicts of interest

All authors declare the absence of any financial or personal relationships that can be construed as a potential conflict of interest.

Sources of funding

This study did not receive any funding from governmental or private organizations.

Ethical approval

No human or animal studies are present in the study.

Consent

Written informed consent was obtained from the patient for publication of this case and accompanying images.

Author contribution

All authors have contributed equally in the process of writing the manuscript.

Registration of research studies

The study did not involve human participants.

Guarantor

Abdullah Saleh AlQattan, Jumana Husain Masoudi.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.amsu.2021.103144>.

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