Scientific Research Publishing

Case Reports in Clinical Medicine, 2023, 12, 93-101
https://www.scirp.org/journal/crcm
ISSN Online: 2325-7083
ISSN Print: 2325-7075

Recurrence of Poorly Differenciated Cervical Cancer by Single Splenic Metastasis: Case Report and Literature Review

Céline Petit[1], Grégory Demolin[1], Athena Stamatiou[2], Samir Saadi[3], Thierry Vandingenen[4]

[1]Department of Obstetrics and Gynecology, CH Epicura, Hornu, Belgium
[2]Department of Surgery, CH Epicura, Hornu, Belgium
[3]Department of Pathological Anatomy, CH Epicura, Hornu, Belgium
[4]Department of Medical Oncology CH Epicura, Hornu, Belgium
Email: gdemolin@yahoo.com

How to cite this paper: Petit, C., Demolin, G., Stamatiou, A., Saadi, S. and Vandingenen, T. (2023) Recurrence of Poorly Differenciated Cervical Cancer by Single Splenic Metastasis: Case Report and Literature Review. *Case Reports in Clinical Medicine*, **12**, 93-101.
https://doi.org/10.4236/crcm.2023.124013

Received: March 8, 2023
Accepted: April 10, 2023
Published: April 13, 2023

Abstract

Background: The incidence of cervical cancer in Belgium is 11.1 per 100,000. With the introduction of cervical cytology screening and more recently anti-HPV vaccination, this rate has been decreasing for almost 20 years. Despite this, some patients are missed by the screening and prevention system and cervical cancer is still diagnosed at an advanced stage. Recurrences by splenic metastases are rare and are most often found at autopsy. Case Study: We describe the case of a 41-year-old caucasian patient with a single splenic recurrence after radiotherapy, chemotherapy, brachytherapy, and surgery for a poorly differentiated adenocarcinoma of the cervix grade 3 at an initial stage IIB according to FIGO. This recurrence happens 3 years after the initial treatment. After monitoring this asymptomatic lesion, the size increase results in laparoscopic splenectomy. Histology demonstrates a splenic metastasis recurrence of adenocarcinoma of endocervical origin. Conclusion: The spleen is a rare metastatic site in cervical cancer. Splenectomy followed by chemotherapy is the therapy most often found in the literature, which is however poor in this regard.

Keywords

Cervical Cancer, Recurrence, Splenic Metastasis, Human Papillomavirus

1. Introduction

Cervical cancer is the tenth most common cancer in the world of all ages and all sexes, according to the World Health Organization in 2018. In Europe, the incidence of cancer of the cervix is 13, 4 per 100,000, with a mortality rate of around

5%. In Belgium [1], there was an incidence of 11.1 per 100,000 (634 cases) in 2015, with 200 deaths, making cervical cancer the 12th most common cancer in women, while remaining a rare cause of death (1.7% of total cancer mortality). Almost entirely attributable to the HPV virus (99%) and its persistence, the incidence has been reduced from 60% to 90% and the mortality rate by 90% since screening with the PAP smear test. Thanks to HPV vaccination in Belgium from 2005 to 2015, the incidence decreased from 12.3% to 11.1%. The impact is still minimal to date but should be more significant in the years to come. In fact, the natural history of precancerous lesions towards invasive cancer is 15 years on average. Nevertheless, efforts are still to be made in the vaccination campaign, especially in the Wallonia-Brussels Federation. Indeed, vaccination coverage is 29% compared to 83% for Flanders [2]. In Belgium, the current coverage of cervical cytology screening, performed every 3 years, is 59%. Despite the almost systematic screening, some patients escape the system and we still see cervical cancer in advanced stages. In the case of invasive cancer [3], dissemination is preferably done by lymphatic route and hematogenous dissemination occurs often later. Typical preferred hematogenous metastatic sites are the lungs, liver and bone system.

Here we report the case of a recurrence by single splenic metastasis. These splenic metastases are rare and are more often found during autopsies. In the literature, 16 articles relate spleen metastases in the context of recurrent cervical cancer.

2. Case Report

A 41-year-old patient presents to the emergency room for smelly bleeding. The vaginal examination performed under narcosis objectifies a 5 cm cervical mass. The histological analysis of the mass pleads for a florid dedifferentiated epithelial neoplastic process, with a primitive glandular not excluded. The clinical stage according to FIGO is IB. The PET-scan shows a neoplasia of the cervix involving the cervix, the corpus uteri, the left parameter and associated with a bulky left external iliac adenopathy and right common iliac. Pelvic magnetic resonance imaging (MRI) confirms a large tumor lesion of the cervical region of 5cm with infiltration of the parameters and bilateral iliac adenopathies. The rest of the examination is strictly normal. The FIGO stage after imaging is IIB.

Initially, the patient receives 50.4 Gy radiation therapy combined with cisplatin-based chemotherapy on a weekly basis. A new vaginal examination under narcosis shows the persistence of a large friable tumor occupying the cervix and hanging in the vagina of 4 cm. The right parameter is dubious on the internal third. Following this, two brachytherapy sessions with a dose of 7 Gy per session are performed. After a new examination under narcosis, the tumor had shrunk in size and was 3 cm in diameter with a soft parameter. The initial treatment ended with an enlarged hysterectomy with bilateral iliac lymph node dissection for tumor residue. The anatomopathological result confirms a poorly differen-

tiated adenocarcinoma of the cervix of grade 3 of 2 × 1.1 cm with invasion of the right parameter. The surgical margins are clean. 3 out of 19 lymph nodes are invaded. The FIGO stage is IIB, TNM stage ypT2b ypN1. In multidisciplinary oncological consultation, simple monitoring is recommended.

Three years later, the patient presents a recurrence at the splenic level and at the pre-sacral level treated with chemotherapy (paclitaxel and carboplatin 8 cures). 8 months later, the metabolic response to treatment is complete in locoregional and almost complete in splenic location. Three months later, the patient presents a completely asymptomatic and isolated metabolic reactivation at the splenic level measuring 42 mm at MRI with expectant attitude. MRI 6 months later shows an increase in the lesion to 54 × 38 mm (**Figure 1**). 5 months later, a significant increase in size to 69 × 46 mm (**Figure 2**) will indicate the performing of a splenectomy.

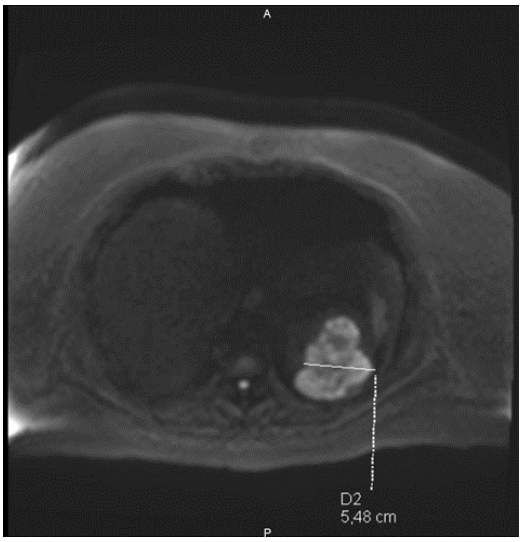

Figure 1. T2 weighted hyperintense lesion.

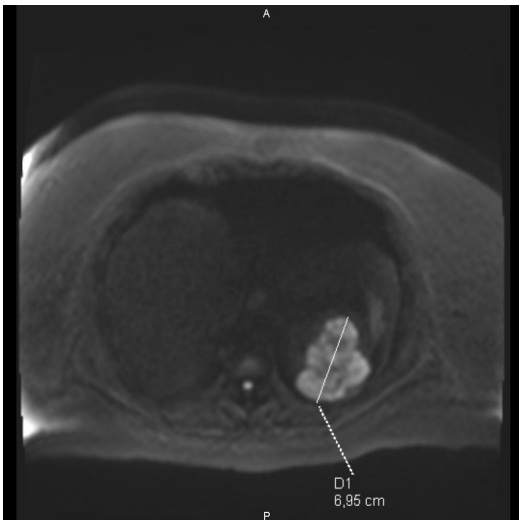

Figure 2. Size increase after 6 months.

The procedure is performed 18 months after the discovery of this unique lesion in the spleen (Figure 3).

On pathology analysis, it is indeed a recurrence of primary cervical neoplasia with a necrotized tumor metastasis of 5 cm corresponding to an adenocarcinoma of endocervical origin (Figure 4 and Figure 5).

The patient will remain without recurrence to the Pet-scanner performed at 4 and 8 months. But at 13 months, she will present an aggressive recurrence in the form of lung, peritoneal and left adrenal metastases. This recurrence will lead to the patient's death 14 months after the splenectomy was performed.

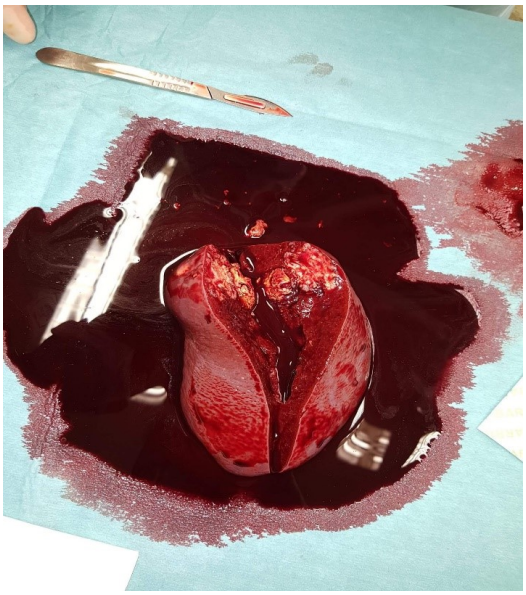

Figure 3. Metastasis in splenectomy specimen.

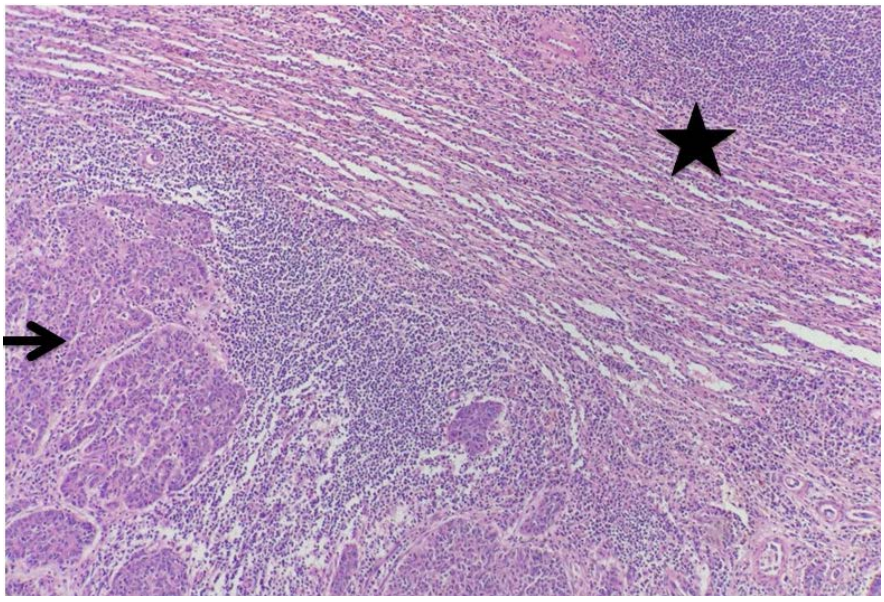

Figure 4. Splenic parenchyma infiltrated by the tumor. Arrow: tumor; Star: Splenic parenchyma. (HE; obj 10x).

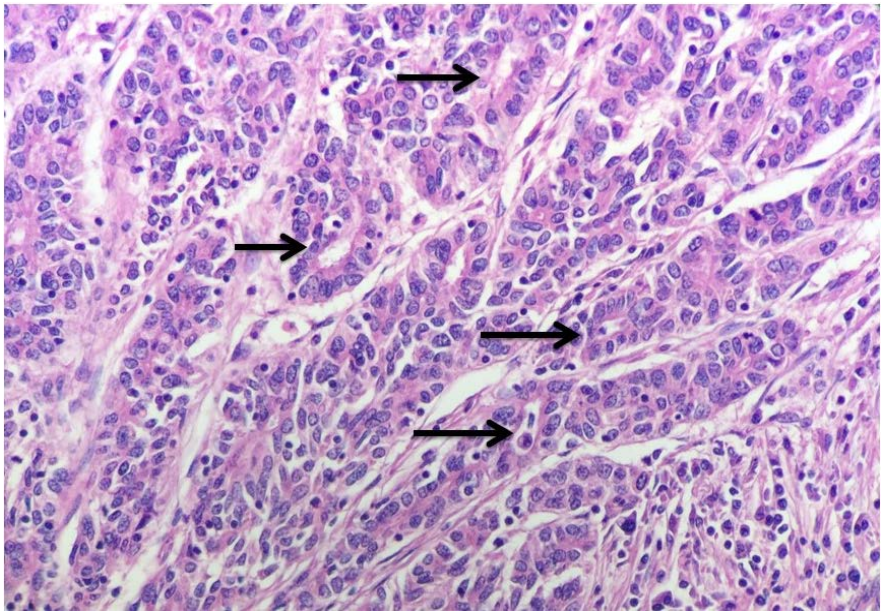

Figure 5. Histological image of adenocarcinoma. Arrows: formation of glandular lumen. (HE coloring; 40x lens).

3. Discussion

The follow-up of cervical cancer recommended by the European Society for medical oncology (ESMO) [4] includes, at least a clinical examination (vaginal examination and rectal examination) and an anamnesis with a cervico-vaginal smear (+HPV typing) 1x/3 - 6 months for 2 years then 1x/6 - 12 months for 3 years. After the 5-year period without recurrence, follow-up is done once a year. When two cervico-vaginal smears have a negative HPV typing, normal monitoring is resumed (smear 1x/3 years). If a recurrence is suspected following a clinical sign, a CT scan or PET-CT is performed.

Some authors [5] suggest the use of SCC antigen (squamous cell carcinoma antigen) [5] for epidermoid cancers, and CEA as a tool for monitoring the disease after primary treatment. Indeed, SCC antigen is a glycoprotein whose rate is influenced by tumor transformation. This biomarker is high in 28% - 88% of patients with epidermoid cancer. In the early stages, a high level of SCC-Ag is associated with a risk for recurrence (lymph node metastasis, stromal invasion, invasion of vascular spaces and big tumor size). We did not use SCC antigen but it probably have had little interest in the follow-up of adenocarcinoma.

In the case of splenic metastasis, the most common complaints are weight loss, pain in the left hypochondrium and nausea, which should therefore lead to an X-ray examination. However, in most cases, splenic metastasis is discovered during a follow-up examination in an asymptomatic patient (as in the case of our patient) or during imaging performed for a completely different reason. The risk of splenic metastasis is painful splenomegaly, thrombosis of the splenic vein and splenic rupture [6].

Splenic metastases are rare entities and are most often associated with lung,

breast or melanoma cancers. Their incidence varies between 2.9% and 9% for solid tumors [7]. They are found in more or less 1% of autopsies [8]. Fewer than 100 cases of single spleen metastases have been reported, 50% of which originate from the female genital tract [9].

To date, in the literature, 16 articles (Table 1 and Table 2) report cases of recurrence in the spleen after primary treatment for cervical cancer, 12 of which describe recurrence of cervical cancer by single splenic metastasis (Table 1). Most cases are published in the form of a case report with review of the literature. In the majority of the situations described, a splenectomy is performed, with anatomo-pathological examination of the nature of the lesion in order to confirm the recurrence [10]. The most frequent histological type is epidermoid cancer. The recurrence delay is between 8 months and 5 years.

Table 1. Single splenic metastasis (RT = Radiotherapy, BT = Brachytherapy, CT = Chimiotherapy).

Year	Author	Histological type	Initial treatment	Time to recurrence	Diagnostic/treatment	Age
1977	Brufman [11]	Epidermoid				
1987	Klein [12]	Epidermoid	RT + BT	4 years	Splenectomy	28
1992	Campagnutta [13]	Adenocarcinoma	Surgery + RT	5 years	Splenectomy	47
1997	Carvalho [14]	Epidermoid	RT	4 years	Splenectomy + CT	47
2004	Goktolga [15]	Epidermoid	Surgery + RT	3 years	Biopsy + Debulcking	45
2004	Pang [16]	Epidermoid	Surgery + RT	5 years	Splenectomye + CT	45
2008	Kim [17]	Epidermoid and Mucinous adenocarcinoma	RT, BT, CT RT, BT, CT	8 months 9 months	Splenectomy + CT for both of them	46 and 54
2010	Di Donato [18]	Epidermoid	Surgery	30 months	Splenectomy	/
2014	Taga [19]	Undifferentiated carcinoma	RT, CT	10 months	Splenectomy	49
2014	Shama [20]	Epidermoid		3 years	Biopsy	
2017	Bacalbasa [21]	Epidermoid		18 months	Splenectomy	31
2017	Applebaum [22]	Epidermoid	Surgery, BT			62

Table 2. Splenic metastasis and other concomitant lesion.

Year	Author	Histological type	Initial treatment	Time to recurrence	Diagnostic/ treatment	Location	Age
2006	Gupta [6]	Carcinoma	CT, RT	12 months	/	Spleen + Liver	41
2014	Villalon [7]	Adenocarcinoma	Surgery, RT, BT	2 years	Splenectomy + CT	2 splenic lesions	76
2014	Aitelhaj [23]	Epidermoid	Surgery, BT	8 months	Biopsy + CT	Spleen + Bresat	55
2016	Dixit [24]	Epidermoid	Surgery, RT, CT	17 months	Splenectomy +CT	Spleen + Mesentery	46

The spread of cervical cancer occurs more often either by local extension or by lymphatic route. The hematogenous pathway is rare. Therefore, the preferred hematogenous metastatic sites are the lungs, the bones, the mediastinum, the supraclavicular nodes and the liver. Furthermore, the pathophysiology of the mode of dissemination of cervical cancer within the spleen has not been clearly studied, but it seems that it is hematogenous [11]. The spleen is an unfavorable environment for the development of metastases. Several reasons have been put forward to explain this rarity of splenic metastases [22]:

1) Rare hematogenous pathway in cervical cancer; 2) the extension is most of the time local; 3) role of the splenic capsule; 4) poor afferent lymphatic vessels in the spleen; 5) tortuosity of the spleen vessels; 6) constant splenic blood flow with contractions in the spleen which force the blood from the sinusoids to go into the splenic veins; 7) anti-tumor antibodies present in the spleen; 8) concentration of phagocytes in the spleen.

Regarding therapeutic management, no consensus was found. Given that splenic recurrence is associated with a poor prognosis, excision of it by splenectomy seems to several authors to be an acceptable therapeutic option, more or less followed by chemotherapy according to certain publications, in order to improve survival [16]. Our patient had a 9 months disease-free survival, but an aggressive recurrence at 13 months.

4. Conclusion

In cervical cancers, splenic metastases are rare entities. The data in the literature is poor. No consensus is therefore determined for the monitoring and therapeutic management of these lesions. Splenectomy nevertheless seems to be the appropriate treatment to provide pathological confirmation of the recurrence and to avoid complications such as splenic rupture or thrombosis of the splenic vein. Monitoring by biomarkers like SCC antigen may be an approach for epidermoid types but this still requires studies. However, the key to this kind of neoplastic pathology is found upstream of the development of the disease through prevention; on the one hand, primary prevention with HPV vaccination and, on the other hand, secondary prevention with screening for precancerous lesions.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] http://www.kankerregister.org

[2] http://www.mpsservices.be/index.php/2017/10/23/la-couverture-vaccinale-anti-hpv-en-federation-wallonie-bruxelles-totalement-insuffisante

[3] https://www.uptodate.com/contents/invasive-cervical-cancer-epidemiology-risk-factors-clinical-manifestations-and-diagnosis?search+cervical%20cancer&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1

[4] Marth, C., *et al.* (2017) Cervical Cancer: ESMO Clinical Practice Guidelines for Diagnosis, Treatment and Follow-Up. *Annals of Oncology*, **28**, iv72-iv83. https://doi.org/10.1093/annonc/mdx220

[5] Kim, B.G., *et al.* (2013) Squamous Cell Carcinoma Antigen in Cervical Cancer and Beyond. *Journal of Gynecologic Oncology*, **24**, 291-292. https://doi.org/10.3802/jgo.2013.24.4.291

[6] Gupta, T., *et al.* (2006) Splenic Metastases from Cervical Carcinoma: A Case Report. *International Journal of Gynecological Cancer*, **16**, 911-914. https://doi.org/10.1111/j.1525-1438.2006.00220.x

[7] Villalon-Lopez, J.S., *et al.* (2014) Isolated Splenic Metastases from Cervical Cancer: A Rare Entity. *Cirugía y Cirujanos*, **82**, 556-562.

[8] Sotto, L.S.J., *et al.* (1960) Postmortem Findings in Cancer of the Cervix. *The American Journal of Obstetrics and Gynecology*, **4**, 791-794. https://doi.org/10.1016/0002-9378(60)90591-3

[9] Piura, E., *et al.* (2010) Splenic Metastases from Female Genital Tract Malignancies. *Harefuah*, **149**, 315-320, 335, 334.

[10] Monclova, L., *et al.* (2013) Laparoscopic Approach for Isolated Splenic Metastasis: Comprehensive Literature Review and Report of 6 Cases. *Surgical Laparoscopy Endoscopy & Percutaneous Techniques*, **23**, 21-24. https://doi.org/10.1097/SLE.0b013e318277b009

[11] Brufman, G., *et al.* (1977) Solitary Metastatic Involvement of the Spleen in Squamous Cell Carcinoma of the Cervix. *Harefuah*, **92**, 349-350.

[12] Klein, B., *et al.* (1987) Splenomegaly and Solitary Spleen Metastasis in Solid Tumors. *Cancer*, **60**, 100-102. https://doi.org/10.1002/1097-0142(19870701)60:1<100::AID-CNCR2820600118>3.0.CO;2-9

[13] Campagnutta, E., *et al.* (1992) Isolated Splenic Metastasis in a Case of Adenocarcinoma of the Uterine Cervix. A Clinical Case. *Minerva Ginecologica*, **44**, 667-670.

[14] Carvalho, L., *et al.* (1997) Squamous Cell Carcinoma of the Cervix Metastatic to the Spleen-Case Report. *Gynecologic Oncology*, **67**, 107-110. https://doi.org/10.1006/gyno.1997.4814

[15] Goktolga, U., *et al.* (2004) Solitary Splenic Metastasis of Squamous Cell Carcinoma of the Uerine Cervic: A Case Report and Review of the Literature. *European Journal of Gynaecological Oncology*, **25**, 742-744.

[16] Pang, L.C., *et al.* (2004) Solitary Recurrent Metastasis of Squamous Cell Carcinoma of the Uterine Cervix in the Spleen: Case Report. *Southern Medical Journal*, **97**, 301-304. https://doi.org/10.1097/01.SMJ.0000078684.66137.89

[17] Kim, J.H., *et al.* (2008) Solitary Splenic Metastases from Uterine Cervical Cancer: Case Reports and Review of the Literature. *The Korean Journal of Pathology*, **42**, 317-322.

[18] Di Donato, V., *et al.* (2010) Splenic Metastasis from Cervical Cancer: Case Report and Review of the Literature. *Journal of Obstetrics and Gynaecology Research*, **36**, 887-890. https://doi.org/10.1111/j.1447-0756.2010.01210.x

[19] Taga, S., *et al.* (2014) Splenic Metastasis of Squamous Cell Carcinoma of the Uterine Cervix: A Case Report and Review of the Literature. *Case Reports in Obstetrics and Gynecology*, **2014**, Article ID: 798948. https://doi.org/10.1155/2014/798948

[20] Sharma, P., *et al.* (2014) Recurrent Carcinoma Cervix Presenting as Metastatic Splenomegaly: (18)F-FDG PET/CT Findings in a Rare Scenario. *Indian Journal of*

Nuclear Medicine, **29**, 200-201. https://doi.org/10.4103/0972-3919.136608

[21] Bacalbasa, N., *et al.* (2017) Solitary Splenic Metastasis after Surgically-Treated Cervical Cancer—A Case Report and Literature Review. *Anticancer Research*, **37**, 2615-2618. https://doi.org/10.21873/anticanres.11607

[22] Applebaum, M., *et al.* (2017) Isolated Splenic Metastasis in a Patient with Squamous Cell Carcinoma of the Cervix. *Applied Radiology*, **46**, 24-25. https://doi.org/10.37549/AR2384

[23] Aitelhaj, M. and Schulz, B. (2014) Breast and Splenic Metastases of Squamous Cell Carcinoma of the Uterine Cervix: A Case Report. *Journal of Medical Case Reports*, **8**, 359. https://doi.org/10.1186/1752-1947-8-359

[24] Dixit, J., *et al.* (2016) Splenic Metastasis from Cancer of Uterine Cervic—A Rare Case. *Indian Journal of Surgical Oncology*, **7**, 479-483. https://doi.org/10.1007/s13193-016-0564-7