Parenchymal Splenic Metastasis from Ovarian Cancer: A Report of Two Cases and Literature Review

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ABSTRACT

Aim: We report two cases of splenic metastasis from ovarian cancer.

Background: Parenchymal splenic metastasis from ovarian cancer is rarely encountered.

Case description: Two cases of ovarian serous carcinoma presented by isolated recurrent parenchymal splenic metastasis that was managed by splenectomy as secondary cytoreductive surgery.

Conclusion: Thorough follow-up of ovarian cancer cases including careful clinical examination, computed tomography (CT), and tumor markers assessment, when clinically indicated, can early detect any recurrence events even isolated splenic recurrence.

Clinical significance: Although being rare, parenchymal splenic metastasis from ovarian cancer should be suspected in advanced stage ovarian cancer.

Keywords: Case report, Ovarian cancer, Splenic metastasis.

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BACKGROUND

Worldwide, ovarian cancer accounts for 3.4% of newly diagnosed cancer cases and 4.4% of cancer-related mortality among females.¹ It spreads mainly through peritoneal dissemination, hematogenous, or lymphatic routes, and is optimally managed by cytoreductive surgery.² Splenic metastasis from malignant tumors is extremely rare ranging from 2.3% to 7.1% in autopsy studies, and a reported incidence of 1.3% in splenectomy studies.^{3,4} To the best of our knowledge, approximately 24 cases of isolated parenchymal splenic metastasis from ovarian cancer were reported in English-based literature.

CASE DESCRIPTION

Case 1

A case of 53-year-old woman without relevant medical history was referred to our center. She had history of subtotal hysterectomy and bilateral salpingo-oophorectomy in 2012 with a postoperative pathology report revealing bilateral high-grade papillary serous ovarian carcinoma with infiltration of the fallopian tubes, for which she received eight cycles of taxol/carboplatin regimen till October 2013. Unfortunately, the patient lost follow-up till May 2017 when she developed postcoital bleeding. Pelvic magnetic resonance imaging (MRI) revealed a small uterine stump lesion less than 2 cm, the punch biopsy from it revealed nonkeratinizing squamous cell carcinoma (Fig. 1A). Radiological evaluation of the chest and abdomen by CT revealed a complex cystic lower pole splenic focal lesion of 5 × 7 cm in diameter mostly metastatic with enlarged hilar lymph nodes encasing the splenic artery (Fig. 2). The decision of our multidisciplinary team (MDT) was neoadjuvant chemotherapy where she received further four cycles of the same regimen and then she was referred back for surgery. She was planned for surgery in October 2018 where she underwent splenectomy, omentectomy, and excision of cervical stump. Postoperative pathology report revealed infiltration of the splenic tissue by malignant tumoral proliferation

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of solid sheets of malignant epithelial cells with high-grade atypia, pleomorphism, increased nucleo-cytoplasmic ratio, eosinophilic cytoplasm, vesicular nuclei, and occasional mitotic figures, with an infiltration of 2 out of 10 splenic hilar lymph nodes. Positive cytoplasmic staining for immune histochemical stain (cytokeratin) CK and positive nuclear staining for Wilms tumor 1 (WT-1) confirming the diagnosis of metastatic ovarian serous carcinoma (Fig. 3), while uterine stump showed no residual tumor cells with complete response to previous treatment (Figs 1B and C). Afterward, the patient received further four cycles of taxol/carboplatin regimen as an adjuvant therapy with no remarkable events till writing this article.

Case 2

A 72-year-old woman who had history of subtotal hysterectomy without an available postoperative pathology report outside our

Figs 1A to C: (A) Nonkeratinizing squamous cell carcinoma of cervix formed of sheets of neoplastic squamous cells with abundant cytoplasm, nuclear pleomorphism, frequent atypical mitotic figures, and no detected keratinization (H&E, $\times 400$); (B) Nonkeratinizing stratified squamous epithelium and elastic stroma of ectocervix free from tumor tissue (H&E $\times 200$); (C) Free endocervical glands from tumor tissue (H&E, $\times 200$)

Figs 2A and B: Postcontrast computed tomography (CT) abdomen axial images: (A) Large splenic lower pole complex soft tissue mass measures 5×6 cm, no extracapsular extension; (B) Splenic hilar nodal deposit encasing the splenic artery

center in 2011 sought medical advice at our clinic in 2014 because of a radiologically malignant looking bilateral adnexal masses that measured $8 \times 10.5 \times 15$ cm and $6 \times 6.5 \times 7$ cm. Metastatic workup revealed a suspicious omental cake of 5×6 cm and revealed an elevated cancer antigen (CA) 125 = 231 (reference up to 35). The decision of our MDT was surgical exploration aiming at optimal cytoreduction. The patient underwent bilateral salpingo-oophorectomy, infracolic omentectomy, excision of uterine stump, iliac and paraortic lymphadenectomy, and peritoneal biopsy. Postoperative pathology revealed moderately differentiated papillary serous cystadenocarcinoma with infiltrated omentum (International Federation of Gynecology and Obstetrics (FIGO) stage IIIc). The patient then received six cycles of taxol/carboplatin regimen then she was subjected to follow-up. In July 2017, a routine follow-up of CT revealed a splenic complex cystic lesion of 3×4 cm with a gastrosplenic peritoneal deposit of 2.5×4 cm (Fig. 4). CA 125 was reevaluated, and it was within normal range, so ultrasound-guided fine needle aspiration cytology (FNAC) was requested and cytological report revealed malignant smear of papillary adenocarcinoma. Multidisciplinary discussion recommended reexploration aiming for a secondary cytoreduction. Exploration was performed on October 2017 and no evidence of tumor recurrence was found other than splenic lesions, so splenectomy was done. Pathology report revealed infiltration of splenic tissue by papillary structures with fibrovascular core lined by malignant

cells with hyperchromatism, increased nucleocytoplasmic ration, pleomorphism, vesicular nuclei, prominent nucleoli and psammoma bodies, and immune histochemical staining was positive for WT-1 and P53, and negative to P-16 confirming the diagnosis of metastatic papillary serous ovarian carcinoma (Fig. 5). The patient then received two cycles of Gemzar/cisplatin and is now on follow-up with no evidence of recurrence till last follow-up visit in March 2019.

DISCUSSION

Ovarian cancer is a common gynecological malignancy that presents in an advanced stage in more than 80% of the patients.⁵ Cytoreductive surgery is considered the cornerstone in management of ovarian cancer aiming at prolongation of overall survival rates and obtaining sound quality of life.⁶

Splenic metastasis is rare, and it had been reported more commonly with breast, lung, colorectal carcinomas, and melanoma.⁷ Parenchymal splenic metastasis from ovarian cancer is rare accounting for 2–3% of cases.⁸ Splenic capsular involvement secondary to peritoneal seedling is much more encountered.⁹

Isolated splenic metastasis from ovarian cancer is a rare presentation. To the best of our knowledge, 24 cases of isolated splenic metastasis were reported in English-based literature (Table 1). It is frequently found as a part of widespread disease metastasis rather than solitary splenic involvement.¹⁰ In contrast,

Figs 3A to E: (A) Splenic tissue showing infiltration by solid sheets of high-grade serous ovarian carcinoma (H&E, $\times 40$); (B) Sheets of atypical epithelial cells exhibiting marked nuclear atypia, pleomorphism, atypical mitotic figure, and prominent nucleoli (H&E, $\times 400$); (C) Splenic hilar lymph node showing malignant deposits of high-grade serous ovarian carcinoma (H&E, $\times 100$); (D) The tumor cells show strong diffuse cytoplasmic staining for cytokeratin (DAB, $\times 200$); (E) The tumor cells show diffuse nuclear staining for Wilms tumor 1 of metastatic high-grade ovarian serous carcinoma in the spleen (DAB, $\times 200$)

Figs 4A and B: Postcontrast CT abdomen axial images: (A) Parenchymal splenic soft tissue mass measures 3×4 cm, and it is seen abutting the splenic vessels without invasion; (B) Gastrosplenic peritoneal deposit infiltrating the spleen, and it measures 2.5×4 cm

ovarian cancer cases with capsular splenic deposits represented 19–52% of epithelial ovarian cancer cases at autopsy.¹¹

This rare presentation could be explained by several mechanisms including the rhythmic contractions of the splenic capsule, paucity of afferent lymphatics to the spleen, sharp splenic artery angle when originating from the celiac artery, and the antitumor effect of the splenic microenvironment against tumor cells due to the presence of large number of immune cells.¹² In our first case, there was no evidence of widespread

metastasis, and splenic metastasis was the only pattern of recurrence which supports the possibility of hematogenous route of spread.

Thanks to the ovarian cancer surveillance program and the routine use of medical imaging and tumor markers evaluation, the diagnosis of splenic metastasis had increased.¹² Splenectomy as a part of or the sole entity of optimal cytoreductive surgery is an ideal option for management of splenic metastasis from ovarian cancer either in primary of recurrent setting.¹³

Figs 5A to D: (A) Splenic tissue infiltrated by metastatic papillary serous ovarian carcinoma formed of complex papillary structures with thin fibrovascular cores and covered by atypical cells showing nuclear stratification (H&E, $\times 40$); (B) Thin fibrovascular cores lined by atypical epithelial cells exhibiting nuclear pleomorphism, hyperchromasia, and prominent nucleoli (H&E, $\times 200$); (C) Strong diffuse nuclear positivity for Wilms tumor 1 of metastatic papillary serous ovarian carcinoma in the spleen (DAB, $\times 200$); (D) Diffuse positive nuclear staining of the tumor cells for P53 (DAB, $\times 200$)

Table 1: Brief literature review of previously reported parenchymal splenic metastasis from ovarian cancer

Author/year	Age	Type/stage	Presentation	Follow-up	Technique
Farias-Eisner 1993 (four cases) ⁸	49–57–59–79	Serous/III (one with stage IV)	Recurrent	Three were alive and free for 3 years, one with recurrence	Open
Klinger 1998 ¹⁴	56	Not available	Not available	Not available	Hand-assisted lap.
Gemignani 1999 (six cases) ¹⁵	58–59–60	Epithelial/III	Recurrent	Free for a median of 25 months	5 open, 1 lap. assisted
Ushijima 1999 ¹⁶	Not available	Not available	Recurrent	Liver mets	Open
Yano 2002 ¹⁷	38	Serous/IIIc	Recurrence	Not available	Hand-assisted lap
Koh 2004 ¹⁸	29	Mucinous (Hx. of borderline tumor)	Recurrence	Recurrence after 3 years	Open
Tserkezoglou 2005 ¹⁹	53	Serous/IIIb	Recurrence	Disease free for 20 months	Open
Furukawa 2006 ²⁰	59	Serous/Ic	Recurrence	Disease free for 60 months	Open
Otrock 2006 ⁹	59	Serous/IIa	Recurrence	Disease free for 8 months after chemotherapy	Laparoscopic
Alloni 2008 (two cases) ²¹	51, 53	Serous/IIIc	Recurrence	Free 7 months after operation	Laparoscopic-assisted open
Yoshioka 2008 ²²	61	Not available	Recurrence	Disease free for 10 years	Open pancreateosplenectomy
Ghani 2010 ⁷	85	Mucinous/IV	Primary	Not available	Open
Olsen 2011 ²³	72	Carcinosarcoma	Recurrence	Not available	Open + partial gastrectomy
Lv 2014 ¹³	53	Clear cell/IV	Primary	Not available	Open
Yasuda 2018 ²⁴	62	Endometrioid/IIIc	Recurrent	Not available	Laparoscopic

CONCLUSION

Splenic metastasis from ovarian cancer is relatively rare. Thorough follow-up of ovarian cancer cases including careful clinical examination, CT, and tumor markers assessment when clinically indicated can early detect any recurrence events even isolated splenic recurrence. Splenectomy as a secondary cytoreductive surgery is a safe procedure that leads to achieving improved both survival and quality of life.

CLINICAL SIGNIFICANCE

Although being rare, parenchymal splenic metastasis should be suspected in advanced stage ovarian cancer. Splenectomy aiming at secondary cytoreduction is the cornerstone of management in resectable disease.

AUTHOR CONTRIBUTION

Mohammad Zuhdy wrote the manuscript and assisted in operative procedure. Khaled Gaballa revised the manuscript. Omar Hamdy revised and formatted the manuscript. Reham Alghandour did the first case presentation writing and patients oncological follow-up. Mohamed G Elmadawy did the second case presentation writing and assistant in operative procedure. Yasmin N Laimon did the pathological diagnosis and interpretation. Gehad A Saleh did the radiological diagnosis and interpretation. Mahmoud M Saleh did the patient follow-up and manuscript reformatting. Dr Amr Hosam is the main operator who was also responsible for manuscript revision and final approval.

INFORMED CONSENT

An informed consent was taken from both cases.

ETHICAL APPROVAL

The type of manuscript is a case report which does not need an Ethical Committee approval.

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