High Grade Spindle Cell Carcinoma of the Ovary Arising in an Endometrioid Cystadenoma: A Case Report*

Ephraim R. Bacani, MD[1], Gilbert F. Reyes, MD, FPOGS[2], Grace P. Cayabyab, MD, FPSUOG, FPSMFM[2], Rene V. Sotto, MD, FPOGS, FSGOP[2], Lara Mae A. Angeles, MD, FPSP[2]

ABSTRACT

Spindle Cell Carcinoma of the Ovary is a rare form of cancer with controversial histogenesis. It shares the histologic, cytologic, and molecular properties of both epithelial and mesenchymal differentiation of ovarian neoplasms, which makes diagnosis very challenging among pathologists. Endometrioid cystadenoma is a benign ovarian neoplasms classified under epithelial ovarian tumors. Malignant transformation of benign ovarian neoplasms is known as a rare complication, occurring in approximately 0.9% of patients with ovarian endometriosis. Clear cell adenocarcinoma is the most common endometriosis-associated ovarian cancer followed by endometrioid cancer. This is the case of a 56-year old post-menopausal patient initially presenting with increasing abdominal girth. Whole abdominal ultrasound revealed a large pelvo-abdominal mass. Transvaginal and transabdominal ultrasound findings of bilateral ovarian new growth with benign sonologic features. The patient underwent bilateral salpingo-oophorectomy. Histopathologic findings of the specimen submitted revealed high-grade spindle cell carcinoma arising in an endometrioid cystadenoma of the right ovary, and endometrioid cystadenofibroma with focal epithelial proliferation.

Keywords: ovarian spindle cell carcinoma, sarcomatoid carcinoma, malignant transformation

INTRODUCTION

Ovarian cancer is the second most common malignancy of the lower part of the female genital tract. It is the 10th most common cancer in the Philippines, with the Philippines ranking 16th among the top 25 countries with the highest rates of ovarian cancer. It is considered to be the most common cause of death from gynecologic neoplasm in the United States. It can be classified depending on its specific histologic characteristics.

Endometrioid cystadenoma is a benign ovarian epithelial neoplasm. These are tumors that consist of epithelial cells resembling those of the endometrium, that develop in relation to endometrioisis. Endometriosis is a benign condition described with the presence of functioning endometrial glands and stroma outside the uterus, most commonly in the pelvic peritoneum and ovaries. Endometriosis in the ovary, or endometrioma, is known to have an increased risk for developing endometriosis- associated ovarian cancer. Malignant transformation is known as a rare complication occurring in approximately 0.9% of patients with ovarian endometriosis. Clear

Disclosures: *The author has formally acknowledged and signed a disclosure affirming the absence of any financial or other relationships (including personal connections), intellectual biases, political or religious affiliations, and institutional ties that could potentially result in a conflict of interest.*

***West Visayas State University Medical Center**
[1]Resident, Department of Obstetrics and Gynecology, Veterans Memorial Medical Center, Quezon City
[2]Co-Authors, Department of Obstetrics and Gynecology, Veterans Memorial Medical Center, Quezon City

ovarian endometriosis. Clear cell adenocarcinoma is the most common endometriosis-associated ovarian cancer followed by endometrioid cancer. Further investigation is warranted to understand the mechanisms involved in malignant transformations.

Spindle Cell Carcinoma, also known as Sarcomatoid Carcinoma, is a rare form of cancer with controversial histogenesis. It is a spindle cell neoplasm that simulates a sarcoma and demonstrates epithelial differentiation in both immunohistochemistry and electron microscopy. It shares histologic, cytologic, and molecular properties of both epithelial and mesenchymal differentiation of ovarian neoplasms. It is one of the three subtypes of ovarian anaplastic carcinoma, which is an exceedingly rare ovarian neoplasm. Most cases have unfavorable diagnosis. According to literature, it comprises 3% of all cases of Squamous Cell Carcinoma.

OBJECTIVES

Main Objective

To report on the presentation and diagnosis of a rare case of spindle carcinoma of the ovary arising in an endometrioid cystadenoma

Specific Objectives:

1. To report the clinical presentation of a patient with increasing abdominal girth
2. To present the operative diagnosis of malignancy of an ovarian mass with benign sonologic features
3. To describe the histologic diagnosis of malignancy arising in a benign ovarian pathology
4. To describe the role of immunohistochemical staining in obtaining a definitive tissue diagnosis
5. To present the progressively deteriorating course of spindle cell carcinoma

CASE REPORT

This is the case of a 56 y/o post-menopausal patient with a chief complaint of increasing abdominal girth.

History started three months prior to admission when she noted a hypogastric mass, described to be firm and non-tender, accompanied by early satiety. There were no accompanying symptoms of nausea, vomiting, stool changes, or weight loss. No initial consultation was done. Interval history revealed progressive enlargement of the hypogastric mass, persistence of early satiety, and increasing abdominal girth.

Two months prior to admission, the persistence of symptoms prompted consultation with an internist. Whole abdominal ultrasound revealed a huge unilocular pelvoabdominal mass, well-circumscribed, unilocular, measuring 22.62 x 22.67 x 14.52 cm, probably gynecologic in origin. The patient was subsequently advised gynecologic consult prompting consultation at our service. On pelvic examination, the cervix was firm, smooth, closed. The uterus and adnexa was difficult to assess due to abdominal distention. Rectal examination revealed no palpable pole of mass. Transvaginal ultrasound revealed myoma uteri and bilateral ovarian new growth, the right mass measured 21.75 x 21.47 x 14.67 cm, described as unilocular, with medium level echoes, no color on Doppler flow (color score of 1), benign by IOTA simple rules, (Figure 1), and ovarian new growth, left, measuring 6.72 x 6.24 x 5.21 cm, unilocular, with low level echoes, with solid component measuring 3.05 x 2.86 x 3.14 cm, with color score of 2, 96.7% benign by IOTA ADNEX model (Figure 2). CA-125 was elevated at 118 U/mL.

The patient has no known medical comorbidities. There is no family history of malignancy. She is a non-smoker and not an alcoholic beverage drinker. She is regularly menstruating, with complaints of dysmenorrhea on days 1-2 of menses. She is a nulligravid.

The patient was then advised total abdominal hysterectomy with bilateral salpingo-oophorectomy. Intraoperatively, approximately 2 liters of ascitic fluid was drained. The right ovary was cystically enlarged to 20 x 20 cm, highly vascularized, with a point of rupture revealing greenish serous fluid (Figure 3). The left ovary was enlarged to 7 x 5 cm with smooth external surface (Figure 4). The uterus was not enlarged. The appendix was densely adherent to the right ovary. There were dense bowel adhesions posteriorly. Adhesiolysis was attempted by General Surgery but there was no plane of dissection from the adherent bowels were appreciated. Hence, the surgical team did not proceed with performing hysterectomy and the procedure was limited to peritoneal fluid cytology, enterolysis, appendectomy, bilateral salpingo-oophorectomy. The patient tolerated the procedure well and no post-operative complications were noted.

Histopathologic study of the specimens submitted revealed *Endometrioid Cystadenofibroma with Focal Proliferation, Left Ovary* and *Poorly Differentiated Carcinoma, Right Ovary.* Microsections of the right ovarian tumor showed glandular cells of epithelial origin, resembling the endometrium, with cystic structures seen. There are fragments of ovarian tissue infiltrated by cohesive group of spindle-shaped neoplastic cells seen mostly in sheets on a background of extensive necrosis and hemorrhage. The individual neoplastic cells resemble a spindle pattern, containing enlarged, pleomorphic, vesicular to hyperchromic nuclei, with prominent nucleoli exhibiting irregular contour with several mitotic figures (Figure 5). Additional immunostaining revealed diffusely positive in the neoplastic cells of interest with Vimentin and Pancytokeratin, positive in some atypical cells of interest with Calretinin, and negative expression in the cells of interest with Inhibin, suggesting a combination of mesenchymal and epithelial tumor. The right ovary was then signed out as *High-Grade Spindle Cell Carcinoma arising in an Endoemtrioid Cystadenoma.*

The patient was subsequently discharged on the 7th hospital day. She was advised to undergo chemotherapy three to four weeks after discharge. However, during the interim, patient developed poor appetite, hematochezia, and generalized weakness. This prompted readmission at our institution. Routine RT-PCR revealed COVID-19 infection. Patient was managed medically by the service of Gastroenterology. However, persistence of gastrointestinal bleeding lead to severe anemia and hypovolemic shock. The patient's condition progressively deteriorated and she ultimately expired at the 40th post-operative day due to hypovolemic shock secondary to the gastrointestinal bleeding.

CASE DISCUSSION

Spindle cell carcinomas, also known as sarcomatoid carcinomas, are rare malignancies that have been reported in many organs such as the breast, urinary bladder, kidneys, and lungs.[1] It comprises of up to 3% of all cases of squamous cell carcinoma.[2]

In the ovaries, it is one of the subtypes of ovarian anaplastic carcinomas.[3] Histologically, it simulates a sarcoma and presents epithelial differentiation in both immunohistochemistry and electron microscopy.[2] It is characterized by a morphologically biphasic tumor showing a carcinoma with surface epithelial change ranging from dysplasia to invasive carcinoma, and

underlying sarcomatoid proliferation. This makes its diagnosis challenging for pathologists. However, immunohistochemical staining aids in its diagnosis. The co-expression of cytokeratin and vimentin suggests epithelial origin. Metaplasia of squamous cells or multidirectional differentiation of carcinoma cells are indicative of spindle cell transformation.

Endometrioid cystadenoma is a benign ovarian epithelial neoplasm. These are tumors that consist of epithelial cells resembling those of the endometrium.

Endometriosis is a benign condition described with the presence of functioning endometrial glands and stroma outside the uterus, most commonly in the pelvic peritoneum and ovaries. It has been proven to be estrogen-dependent in the reproductive age women. In the ovaries, it is known to have an increased risk for developing endometriosis-associated ovarian cancer. Malignant transformation is known as a rare complication occurring in approximately 0.9% of patients with ovarian endometriosis.[5] This malignant transformation begins with the development of atypical endometriosis and its subsequent progression to endometriosis-associated ovarian cancer.[3] According to one study, the risk factors for malignant transformation include older age (>45 years) and large tumor size (>7 cm).[5]

Endometrioisis-associated Ovarian Cancer (EOAC) is thought to develop from ovarian endometrial cysts.[6] Clear cell adenocarcinoma is the most common endometriosis-associated ovarian cancer followed by endometrioid cancer.[7] The clinical presentation may not be indicative of a malignancy. Hence, the diagnosis of an Endometriosis-Associated Ovarian Cancer is often done post-operatively with histopathologic findings. However, it is difficult to ascertain the probability of ovarian cancer being diagnosed in surgical specimens of endometrial cysts. A retrospective single-center study in Taiwan included 7629 surgeries performed following preoperative diagnosis of endometrial cyst and 0.14% (11 cases) were diagnosed with ovarian cancer postoperatively.[8] Another study in the Taiwan National Health Insurance Research Database showed that among patients diagnosed with endometriosis who underwent surgery from 2000 to 2010, ovarian cancer occurred in 39/5945 cases.[9] The World Endometriosis Society however stated that the relative and absolute risk of ovarian cancer in women with endometriosis is very low and routine screening for ovarian cancer was not recommended.[10]

Clinically, patients may present with abdominal pain, abdominal enlargement, ascites, palpable abdominal mass, or constitutional symptoms of anorexia and weight loss.[1,11,12] Likewise, some patients may be asymptomatic.[2] At present, there are no validated clinical or radiological criteria that can be utilized to distinguish benign from malignant tumors.[13] As such, in malignant cases, the patients are usually diagnosed at an advanced stage.

The management and prognosis of spindle cell carcinoma is not yet well established. Prognosis is seemingly highly dependent on tumor location, depth of invasion, and timing of surgical intervention, but is independent of occurrence of spindle cell transformation.[12] In many organs such as the kidney, the breast, and urinary bladder, the prognosis is poor. There is an ongoing debate on the best management practices for this disease entity. Several case reports on its occurrence in the ovary present good prognosis upon surgical management while some reports also presented unfavorable prognosis despite complete surgery and chemotherapy.[1,2,11] The role of radiotherapy remains unclear.[2] The benefits of early diagnosis

and intervention cannot be more emphasized for a better prognosis.[2]

SUMMARY

Spindle cell carcinoma is a rare type of soft tissue carcinoma. In the ovaries, its incidence is even more rare with less than 10 cases reported in the English medical literature. Hence, diagnosis and management of such cases pose a challenge among pathologists and clinicians. Its pathophysiology is not well understood. One possible mechanism of its development is malignant transformation of a benign ovarian neoplasm. Recognizing the imaging characteristics of such transformations can aid in the diagnosis of rare neoplasms and it is important to recognize radiological mimics of malignant transformation. Unfortunately, current imaging criteria for distinguishing these malignant transformations from their benign counterparts remain largely ill-defined and poorly validated. Likewise, sonologic description may differ from gross findings intraoperatively, and morphologic findings histologically. With the lack of validated guidelines in the management of such cases, prognosis may vary significantly and depend highly on tumor size, location, and involvement of other organs.

CONCLUSION

Endometrioisis-associated Ovarian Cancer (EOAC) is thought to develop from ovarian endometrial cysts. The possibility of malignant transformation should always be considered in cases of benign ovarian neoplasms regardless of patient demographics and sonologic description of the tumor. The relative and absolute risk of ovarian cancer in women with endometriosis is very low and routine screening for ovarian cancer is currently not recommended. The importance of timely surgical intervention cannot be overemphasized. However, obtaining a complete histologic diagnosis may be delayed in cases of rare ovarian neoplasms such as in our patient. In cases of rare ovarian neoplasms, utilization of immunohistochemical staining may aid in obtaining a definitive diagnosis.

Spindle cell carcinoma of the ovary is a rare type of carcinoma. Due to its rare occurrence, there are no standard guidelines or recommendations yet on the management of such cases. A review of available literature suggests beneficial role of surgical intervention. However, prognosis is variable and highly dependent on several factors including tumor location, invasion, and metastasis.

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APPENDICES

Figure 1: Sonographic images of the right ovarian new growth

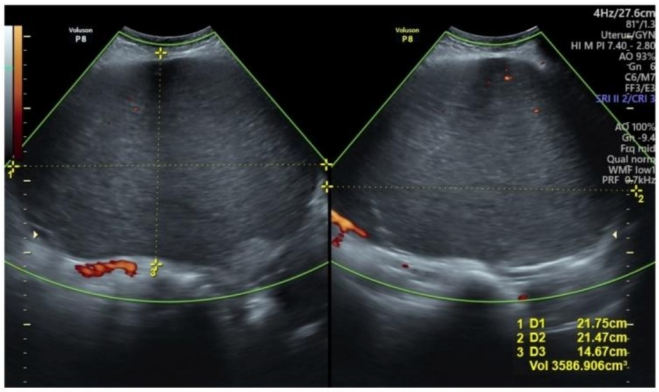

Figure 2: Sonographic images of the left ovarian new growth

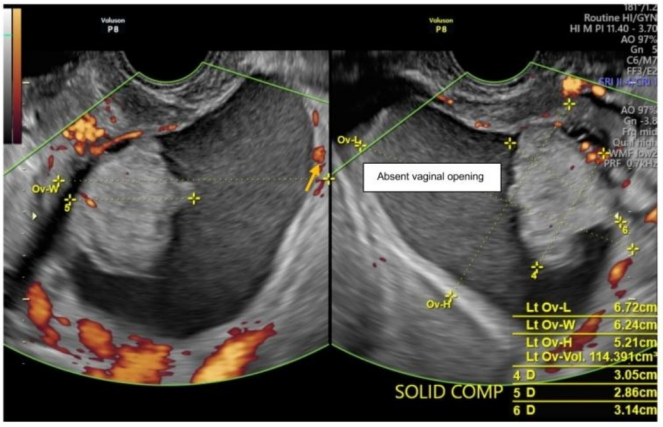

Figure 3: Right Ovary

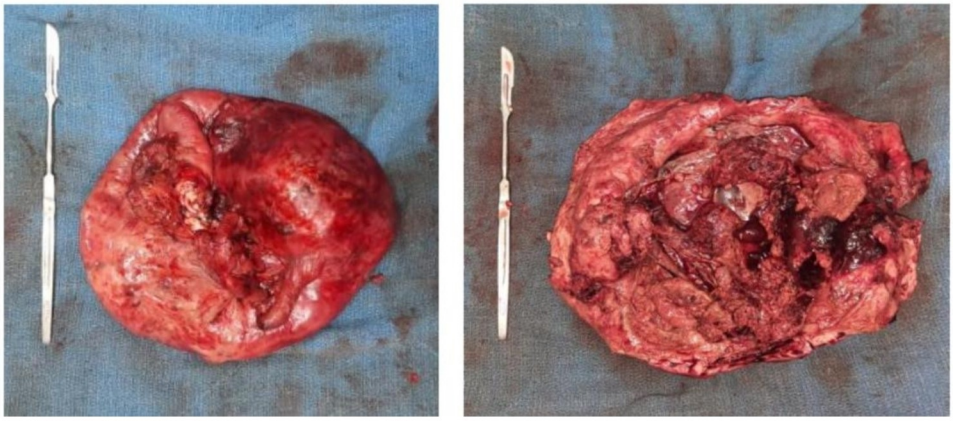

Figure 4: Left Ovary

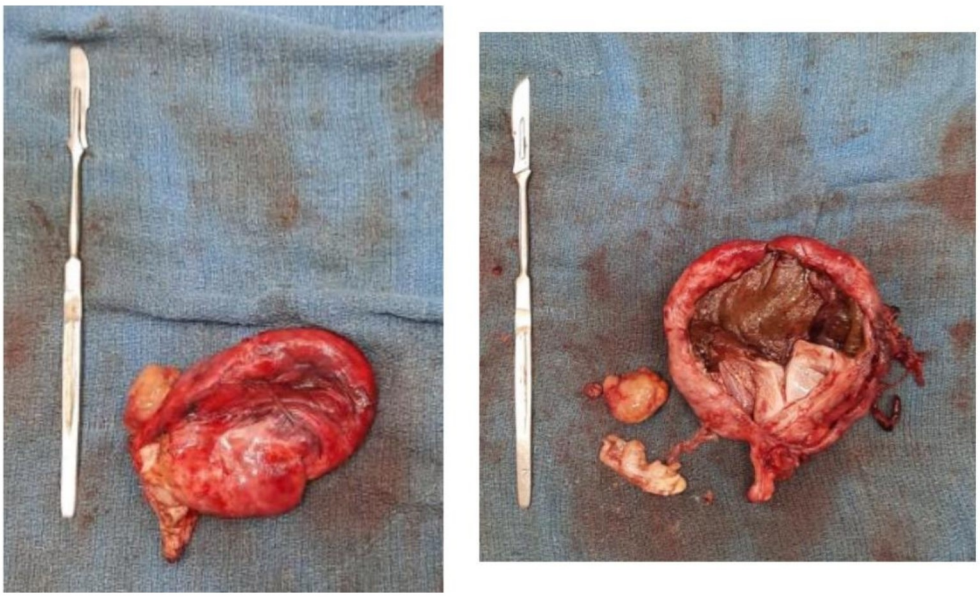

Figure 5: Microsections – Right Ovary