Case Report

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Primary ovarian leiomyosarcoma in a postmenopausal woman diagnosed using immunohistochemistry

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Abstract:

Primary ovarian leiomyosarcoma is a very rare tumor which is most commonly seen in postmenopausal women. Primary ovarian leiomyosarcoma has a very poor prognosis, with less than 20% of patients being alive at 5 years. The case is a 51-year-old female who presented with a lower abdominal mass secondary to an ovarian new growth. An exploratory laparotomy, peritoneal fluid cytology, unilateral salpingo-oophorectomy with malignant frozen section of affected ovary, which revealed malignant tumor, proceeded with surgical staging total abdominal hysterectomy contralateral salpingo-oophorectomy, then proceeded to complete surgical staging with infracolic omentectomy, Jackson-Pratt drain insertion was performed. Microscopic and immunohistochemical findings established the diagnosis of primary ovarian leiomyosarcoma. Surgery is the cornerstone of treatment, while the role of chemotherapy and radiotherapy is still not clear because substantial data are lacking. The prognosis of primary pure ovarian leiomyosarcomas is extremely poor and there is no established treatment modality for this rare type of tumor.

Keywords:

Immunohistochemistry, ovarian leiomyosarcoma, ovarian new growth

Introduction

Primary ovarian leiomyosarcoma is relatively rare, representing <2%–3% of all malignant ovarian tumors. Due to their rare occurrence, the diagnosis is often difficult, and there is currently no established standard treatment for ovarian leiomyosarcomas.[1] Their origin, etiology, histologic features, clinical behavior, and optimal treatment are still obscure. Malignant behavior is almost always associated with any 2 of coagulative necrosis, cellular atypia, and mitotic index >10. Immunohistochemical and electron microscopic evaluations may improve diagnostic accuracy. Surgery is the cornerstone of treatment. Benefits and modality of adjuvant therapy are controversial. The prognosis of primary pure ovarian leiomyosarcomas is extremely poor depending on tumor stage, tumor size, grade, and mitotic index and it mostly recurs in the abdomen and pelvis.

This case report illustrates a case of a 51-year-old female with an ovarian new growth. An exploratory laparotomy, adhesiolysis, peritoneal fluid cytology, malignant frozen section of the affected ovary, total abdominal hysterectomy, bilateral salpingo-oophorectomy, infracolic omentectomy, and JP drain insertion were performed. Immunohistochemistry was done, revealing consistent findings of ovarian leiomyosarcoma.

Objectives

1. To present a rare case of primary ovarian leiomyosarcoma in a 51-year-old postmenopause
2. To present the incidence, clinical manifestations, and prognosis of primary ovarian leiomyosarcoma

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3. To discuss the dilemma in diagnosing and managing the ovarian leiomyosarcoma
4. To discuss the importance of immunohistochemistry in aiding the diagnosis of this rare sarcoma.

Case Report

This is a case of a 51-year-old female, Gravida 4 Para 3 (3013) postmenopause, Filipino, married, Catholic, who sought consultation due to gradual abdominal enlargement.

Ten months before consult, the patient noted dull nonradiating abdominal pain 5/10 in severity. Neither consult was done nor were medications taken. Eight months before consult, the patient noted enlarging abdominal girth due to a palpable mass at the hypogastric region, approximately 12 cm × 12 cm associated with sudden weight loss. She sought consult with a private physician, where ultrasound revealed a complex right hemi-abdominal mass measuring 10.1 cm × 8.0 cm, hence was advised to seek consult in a tertiary hospital.

Interim, still with enlarging abdomen now associated with abdominal pain 7–8/10 in severity and constipation hence consult withgeneral surgery was done wherein whole abdomen ultrasound revealing a complex right hemi abdominal mass measuring 10.1 cm × 8.0 cm. On further work up, whole abdomen computed tomography (CT) scan with contrast a large enhancing complex abdominopelvic complex cystic mass, measuring 32.7 cm × 26.2 cm × 18.6 cm, exhibiting enhancing septations and some solid components, probably arising from right ovary was seen. An ovarian new growth probably malignant was considered hence was referred to our service wherein patient was requested for tumor revealing an elevated cancer antigen 125 (653) and a normal carcinoembryonic antigen (0.672). The impression was an ovarian new growth probably malignant. Tumor markers were done with an elevated cancer antigen 125 (653) and a normal carcinoembryonic antigen (0.672).

On physical examination, the abdomen was globularly distended with pelvoabdominal mass measuring 43 cm × 31 cm, cystic, fixed, (-) fluid wave, with an abdominal girth of 114 cm, nontender. On internal examination, vagina smooth, the cervix was atrophic and smooth, deviated to the right and anteriorly, measuring 1.0 cm × 1.0 cm with the posterior pole of the mass palpable at the posterior cul-de-sac measuring 9.0 cm on the widest diameter, cystic, and nontender. Rectovaginal examination revealed the right parametrium occupied by a cystic extraluminal mass 8 cm in the widest dimension, left parametria free, fecal is impacted at the rectal vault.

On further workup, a pelvic ultrasound revealed a normal-sized, anteverted uterus. The endometrium was thin, measuring 0.3 cm, hyperechoic, not defined endometrial midline, regular endomyometrial junction, and no color flow (score 1). Posterior to the uterus was a huge pelvoabdominal solid, thick-walled mass measuring 42.0 × 38.6 × 34.0 cm (Volume 2862 mL), which on color flow mapping showed minimal intratumoral flow (score of 2). On IOTA Adnex Model, the risk for malignancy is 99.4% (risk for borderline is 0.6^, risk for stage I ovarian cancer is 7.2%, risk stage II-IV ovarian cancer is 82.15%, and risk metastatic cancer to adnexa is 9.5%) and the chance for the benign tumor is 0.6% [Figure 3a]. The contralateral ovary was not visualized. There was moderate ascites noted.

The operative plan was exploratory laparotomy, peritoneal fluid cytology, total abdominal hysterectomy with bilateral salpingo-oophorectomy, frozen section of the affected ovary, complete surgical staging if malignant (bilateral lymph node dissection, random peritoneal sampling, and infracolic omentectomy).

Deep vein thrombosis was considered due to a Well's score of 3 hence DVT screening was done which revealed evidence of a nonrespirophasic waveform pattern of the venous suggestive of a venous outlet obstruction and interstitial edema. Patient was started on antiembolic measures, including Enoxaparin 0.4 cc subcutaneously once a day. On further investigation, hepatobiliarytree ultrasound revealed fatty infiltration in the liver with bile sludge.

Whole abdomen CT with triple contrast was done for further studies, which revealed a large heterogeneously enhancing pelvoabdominal mass [Figure 3b]. Primary consideration is a neoplastic process, likely ovarian in origin. Consideration includes: (1) dermoid cyst with aggressive features, (2) cystadenocarcinoma, ill to fairly defined hypodense hepatic lesions at segment 8, worrisome for metastasis, diffuse hepatic steatosis, left, mild hydronephrosis, left, nephrolithiasis, right; thoracolumbar spondylosis noted. Compression and posterior displacement of the right liver lobe, spleen, pancreas, bilateral kidneys, and abdominal vascular structures are noted. The pelvoabdominal mass abuts the right liver lobe, pancreas, right kidney, and abdominal aorta. Compression and contacting of the small and large bowels are noted. The mass appears to encircle the rectosigmoid area. A multidisciplinary team was formed, composed of colorectal surgeon, thoraco cardiovascular surgeon, urologist, gynecologic oncologist, and gynecologist and all on standby for the planned procedure.

Intraoperatively, there was minimal ascitic fluid noted. The right ovary was cystically enlarged to

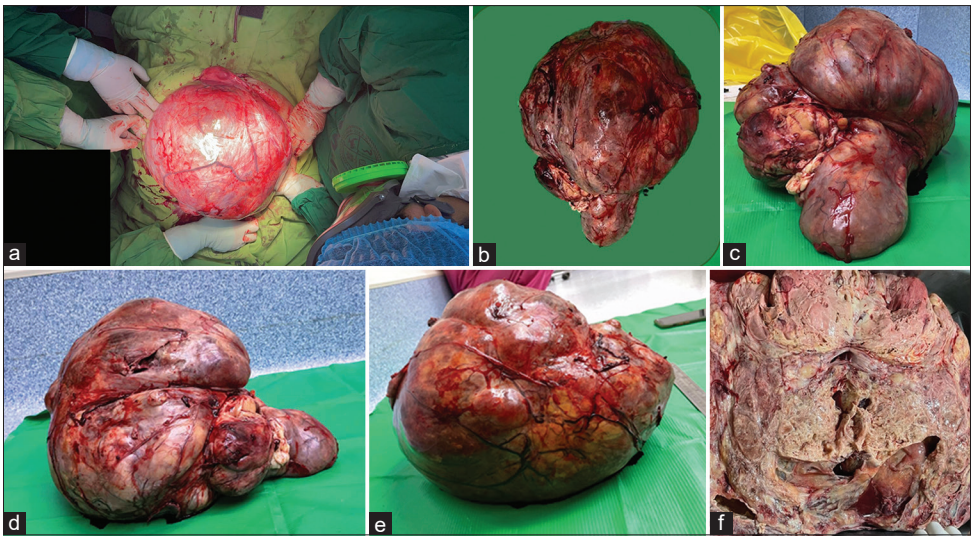

Figure 1: (a) Upon full abdominal exposure of the ovarian new growth, the right ovary was cystically enlarged to 30 x 30 x 10 cm with irregular, smooth, multiple lobulated surface, the smallest of which measuring 4.0 x 2.5 x 1.5 cm and largest measuring 19 x 17 x 6.0 cm. (b) Gross picture of the ovarian new growth upon resection, posterior view with tumor size of 33.0 cm in widest dimension. (c) Gross picture of the ovarian new growth, inferior view showing multiloculation, the smallest of which measuring 4.0 x 2.5 x 1.5 cm and largest measuring 19 x 17 x 6.0 cm. (d) Gross picture of the ovarian new growth, right side. (e) Gross picture of the ovarian new growth, superior view. (f) On cut section of the right ovary, it was predominantly solid with areas of necrosis and yellowish sebum, with interspersed locules containing serosanguinous fluid. The capsule was thin walled with no areas of hemorrhage. The right fallopian tube is stretched out measuring 19 x 1.5 x 0.8 cm and is grossly unremarkable. Frozen section of the right ovary was malignant

30 cm × 30 cm × 10 cm with irregular, smooth, multiple-lobulated surfaces, the smallest of which measuring 4.0 cm × 2.5 cm × 1.5 cm and the largest measuring 19 cm × 17 cm × 6.0 cm as seen in [Figure 1a-e]. On the cut section of the right ovary, it was predominantly solid with areas of necrosis and yellowish sebum, with interspersed locules containing serosanguinous fluid [Figure 1f]. The capsule was thin-walled with no areas of hemorrhage. The right fallopian tube is stretched out, measuring 19 cm × 1.5 cm × 0.8 cm and is grossly unremarkable. Frozen section of the right ovary was malignant. Uterus measured 8.0 cm × 7.5 cm × 2.5 cm with a smooth and intact serosal surface. Noted multiple myoma nodules, smallest of which measures 2 cm × 1.5 cm × 0.5 cm and largest measuring 2.5 cm × 2.5 cm × 0.5 cm on the anterior lower uterine segment which on cut section shows white whorled pattern. On the cut section of the uterus, the endometrial canal measures 5.5 cm with a 0.1 cm endometrial stripe. The cervix is smooth, measuring 2.5 cm × 2.0 cm × 0.5 cm. On cut section, the endocervical canal measures 2.5 cm. The left ovary was grossly normal. The estimated blood loss was 2500 cc.

On histopathologic examination of the specimen, high grade undifferentiated sarcoma with the following differentiations: rhabdomyosarcoma, leiomyosarcoma, and liposarcoma. Tumor size of 33.0 cm in the widest dimension without lymphovascular space invasion was not demonstrated as well as tumor invasion to other pelvic structures and adjacent organs. Other findings on the specimen are as follows chronic cervicitis with nabothian cysts, endometrial polyp, and atrophic endometrium. The immunohistochemistry of the specimen was strongly positive for desmin, caldesmon, SMA, and MSA and negative for MyoD1, Myogenin, and MDM2; which were all consistent findings with ovarian leiomyosarcoma as seen on [Figure 2a-c].

Postoperatively, the patient developed acute limb ischemia on the right upper extremity and succumbed to death 4 days' postoperatively due to pulmonary embolism despite antiembolic precautions.

Discussion

Primary leiomyosarcoma of the ovary is rare tumors usually originating from mesenchymal tissue occurring <1% of all adult malignancies. This cancer usually arises from the embryonic mesoderm with some contribution from the neuroectoderm. According to Roberts *et al*., they would either originate from smooth muscle cells or from precursor mesenchymal stem cells having a predilection for soft tissues and abdominopelvic organs compared to extremities.[2] Mangla and Yadav (2022) observed leiomyosarcoma to start after the third decade of life, and peaks in the perimenopausal age group during the fifth decade of life.[3] These findings are furthermore supported by studies done by Seracchioli *et al*. in 2003, wherein, "among 72 cases, 69% of patients were >50 years old," hence, it can be concluded that primary ovarian leiomyosarcoma is associated with the postmenopausal age group as well.[4] He *et al*. noted that the prognosis of primary ovarian leiomyosarcoma

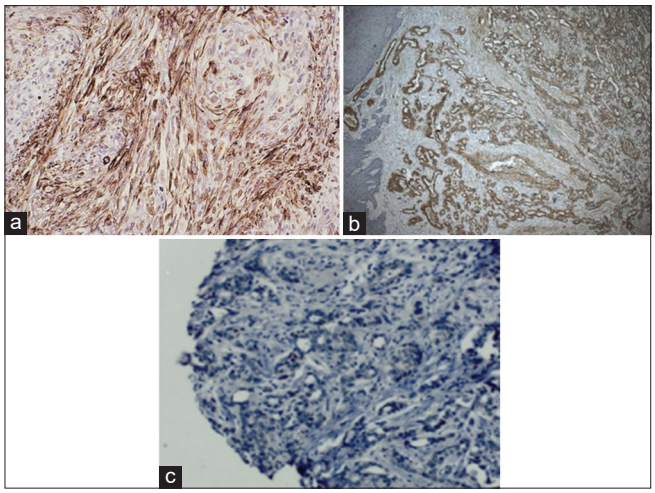

Figure 2: (a) IHC, SMA positive. (b) IHC, Desmin Positive. (c) IHC, MDM2 negative

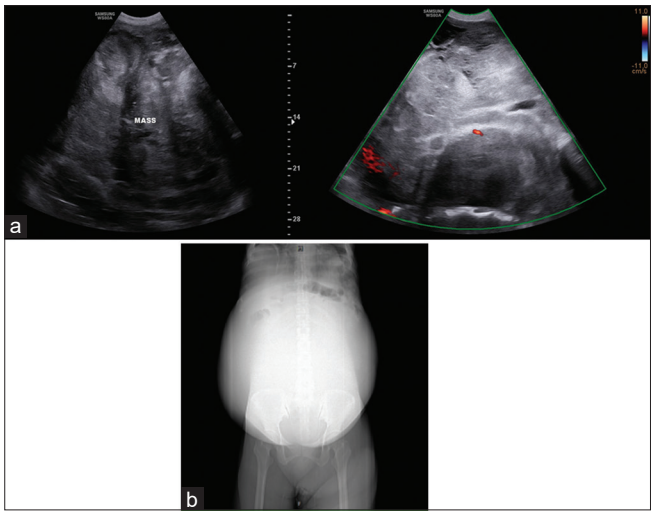

Figure 3: (a) Transvaginal ultrasound + Transabdominal ultrasound with doppler studies. Pelvic ultrasound revealed was a huge pelvoabdominal solid, thick walled mass measuring 42.0 x 38.6 x 34.0 cm (Volume 2862 mL) which on color flow mapping showed minimal intratumoral flow (score of 2). On IOTA Adnex Model, the risk for malignancy is 99.4% (risk for borderline is 0.6^, risk for stage I ovarian cancer is 7.2%, risk stage II-IV ovarian cancer is 82.15 and risk metastatic cancer to adnexa is 9.5%) and the chance for benign tumor is 0.6%. (b) WAB CT Scan with triple contrast. Primary consideration is a neoplastic process, likely ovarian in origin: 1) dermoid cyst with aggressive features 2) cystadenocarcinoma, III to fairly defined hypodense hepatic lesions at segment 8, mild hydronephrosis, left, nephrolithiasis, right; Compression and contacting of the small and large bowels is noted. The mass appears to encircle the rectosigmoid area

is unfavorable and 50% of patients have a mean time of 24 months for survival.[5] Hence, it can be inferred that most cases of primary ovarian leiomyosarcoma are relatively associated with low hormone levels of estrogen and progesterone.

Based on studies done by George *et al*., patients with genetic syndromes such as hereditary retinoblastoma (*RB1* gene deletion) and Li-Fraumeni syndrome (mutation in the *TP53* gene) can develop leiomyosarcoma.[6] Moreover, McClain *et al*. correlated the development of leiomyosarcoma with previous Epstein–Barr virus infection.[7] On the contrary, Serrano and George, supported claims that there is no direct evidence that support the theory that leiomyomas can convert into leiomyosarcoma.[8]

The clinical behavior of leiomyosarcoma and treatment outcome depends on the organ of origin. According to George *et al*., prior history of radiotherapy (RT), which is one of the most significant risk factors for developing soft-tissue sarcoma, can also lead to the development of leiomyosarcoma.[6]

Ovarian leiomyosarcoma has no significant symptoms; however, most of the patients with this disease usually present with abdominal pain or fullness associated with constipation, bowel habit changes, loss of appetite, and difficulty in micturition (Vijaya Kumar *et al*., 2015).[9]

According to Sun *et al*., ultrasonography specifically impedance values garnered during examination is not an accurate tool for the diagnosis of ovarian leiomyosarcoma.[10] Theoretically, a high impedance value (RI > 0.6) indicates a benign mass as compared to low impedance (RI < 0.4), indicating a malignant characteristic. Another assessment tool mentioned in their study was the use of mitotic count. Lerwill *et al*., "*A mitotic index of ≥5 mitotic figures per 10 high powered field in the presence of significant atypia* despite the absence of necrosis *has been proposed as a guiding principle for a diagnosis of leiomyosarcoma*.[11]"

The histogenesis of this tumor is still uncertain as the organ of origin does not contain smooth muscles. According to Kozłowski *et al*., " there are many possible locations from which the neoplasm may develop which include the totipotent ovarian mesenchyme, smooth muscle fiber of ovarian ligaments, the vascular wall, Wolffian duct remnants, smooth muscle metaplasia of ovarian stromal or theca cells or smooth muscle cells that migrate from within the uterus.[12]" Serrano and George, histologically described leiomyosarcoma as "intersecting, sharply marginated fascicles of spindle cells with elongated, hyperchromatic nuclei and abundant eosinophilic cytoplasm and varying degree of pleomorphism can occur resulting to undifferentiated soft-tissue sarcoma.[13]"

According to a clinicopathological study done by Vahini and Journals, soft-tissue tumors are a diverse and heterogeneous group of tumors that is important to be subclassified as to guide clinicians on the treatment and prognosis of the disease.[14] Immunohistochemical stains are used for confirmation, especially of highly undifferentiated tumors, with the use of the following markers to confirm smooth muscle origin: desmin,

smooth muscle actin, and H-caldesmon.[13] As for the case of our patient, specimen was strongly positive for desmin, caldesmon, SMA, and MSA and negative for MyoD1, myogenin, and MDM2, which were all consistent findings with leiomyosarcoma. When considering liposarcoma, S100 is usually the marker with strong positivity as compared to rhabdomyosarcoma, which is strongly positive for desmin and myogenin; meanwhile, leiomyosarcoma exhibits positivity for SMA and desmin, which is accurately seen in our case. Hence, it can be concluded that cell morphology, mitosis criteria, and immunohistochemical staining are the gold standard for the diagnosis of ovarian leiomyosarcoma. Starega-Roslan *et al*. concluded that "tumors of vascular origin showed positivity for h-caldesmon and focally positivity or negativity for desmin while those of nonvascular origin were negative for h-caldesmon with variable levels of desmin expression." Immunohistochemistry in malignant soft-tissue tumors can aid in the diagnosis.[15]

Depending on its origin, this type of sarcoma has three types: teratoid, mesenchymal, and Müllerian. Lesions of mesenchymal origin are more common in postmenopausal women and are more likely to metastasize, whereas those of teratoid origin occur in younger women and are usually unilateral.[15]

The prompt diagnosis together with cytoreductive surgery is two essential principles to improve patient's survival. The management includes control of symptoms, tumor debulking through surgery and prolonged survival. Localized tumors are usually managed by surgical resection whereas metastatic disease has a poor prognosis. In highly staged diseases, RT can play a role by local control secondary to the reduction of local recurrence and preservation of function.[6] According to Cojocaru *et al*., in 2021, surgery should be followed by close surveillance for 10 years.[16] Palliative chemotherapy used for other soft-tissue sarcomas has shown some benefit in metastatic leiomyosarcoma; most commonly used regimens containing doxorubicin ± ifosfamide, gemcitabine-docetaxel, trabectedin, and platinum salts.

The usual cause of death in these cases is pulmonary embolism, as studies revealed that 1.2% had PE and 0.4% had a fatal PE.[17] It can be explained that sarcomas have an increased tendency to develop emboli; hence tumor emboli account for a minority of PE in sarcomas but are associated with a high mortality rate. According to Latchana *et al*. in 2017, tumor embolus secondary to sarcoma is usually located in the lower extremity; however, some literature points origin from the retroperitoneum.[17] It is, therefore, prudent to start aggressive prophylaxis to cases with a high index of suspicion with respiratory-related symptoms, particularly dyspnea. As in the case of our patient, during the 3rd postoperative day, the patient started to experience dyspnea accompanied by coarse crackles. It was also noted that the right radial and ulnar pulses of the patient were undetected associated with cyanosis of the right arm and the presence of hematomas over the right upper extremity. Due to increased D dimer, patient was diagnosed with acute limb ischemia of the right upper extremity secondary to tumor emboli. Embolectomy of the right upper extremity was initially planned however patient was a poor surgical candidate and further deterioration was noted until she became hemodynamically unstable which lead to the patient's further demise. Sun *et al*. noted that 80% of patients with stage II IV succumb to death within 1 year from diagnosis. It was noted that "patients often die of disseminated metastases but also because of extensive local disease and its pressure effect over abdominal organs."[10]

Conclusion

Primary ovarian leiomyosarcoma is a rare disease making diagnosis and management as there has been no established standard for this disease. Usually, patients present with a pelvoabdominal mass with compressive symptoms; hence, surgery is the primary treatment, while immunohistochemistry confirms the diagnosis. A multidisciplinary team was made to handle this case which included gynecologists, gynecology-oncologists, colorectal surgeons, thoracic cardiovascular surgeons, urologists, and internists.

Soft-tissue tumor continues to be a challenge due to their biological behavior and histogenesis, and this is one of the key areas in surgical pathology where immunohistochemistry plays an important role in both precise diagnosis and subcategorization. The prognosis of primary ovarian leiomyosarcoma is extremely poor, and surgery is the established treatment modality for this rare type of tumor; however, the role of chemotherapy and RT is still not clear. Using histological parameters (tumor differentiation, necrosis, and mitotic activity) together with immunohistochemistry, the accuracy of diagnosis can be strengthened. With the rarity, variability, and diversity of soft-tissue tumors, it is vital to document such cases as these can be widely applied in future researches.

It is recommended to investigate the response rate, metastatic rate, and treatment outcomes of primary ovarian leiomyosarcoma as compared to other metastatic leiomyosarcoma or another leiomyosarcoma of other soft tissue in origin. Future collaborative efforts with other specialists in sarcoma are required to improve the outcome of patients.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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