A Rare Case of Synchronous Uterine Leiomyosarcoma and Endometrial Endometrioid Adenocarcinoma

Samir Neupane,1 Sampurna Tuladhar,1 Srijana Koirala,1 Jitendra Pariyar2

1Department of Pathology, Civil Service Hospital, Minbhawan, Kathmandu, Nepal
2Department of Obstetrics and Gynecology, Civil Service Hospital, Minbhawan, Kathmandu, Nepal

Abstract

Synchronous primary neoplasms are defined when two or more neoplasms take place concurrently in the same patient. Concomitant endometrial adenocarcinoma and uterine leiomyosarcoma are extremely rare. Here we present an extremely rare case of uterine leiomyosarcoma coexisting with endometrial endometrioid adenocarcinoma of the uterus. A 52-year-old woman was reported to a gynecology outpatient clinic with chief complaints lower abdominal pain, severe dysmenorrhea, and irregular vaginal bleeding for 7 months. Ultrasound of pelvis and abdomen showed a solitary intramural fibroid measuring 10x10 cm. Surgery was planned and a simple total abdominal hysterectomy with bilateral salpingo-oophorectomy was performed and specimen was sent to the laboratory for examination. Histopathological examination from intramural mass showed high-grade leiomyosarcoma, spindle cell type with less than 50% of myometrial invasion. Sections from thickened endometrium showed endometrial endometrioid adenocarcinoma, FIGO grade I with an invasion of superficial fascicles of myometrium (<50%). Morphological diagnosis was supported by immunohistochemistry. Here we report an exceptionally rare case of synchronous uterine leiomyosarcoma and endometrial endometrioid adenocarcinoma. Our study may contribute to understand the prognosis of such multiple malignancies, common associations, and etiology of the disease so that a proper plan for further management of the patient can be implemented.

Keywords: Adenocarcinoma, endometrium, leiomyosarcoma, synchronous, uterus

Introduction

Synchronous primary neoplasms are defined when two or more neoplasms take place concurrently in the same patient. These neoplasms should be histologically discrete and separated from each other through healthy tissues, such as basal lamina or stroma.1 Such cases account for approximately up to 6% of female genital tract malignancies. The occurrence of neoplasms involving different organs or tissues, either concurrently or in succession, is a phenomenon that has long been observed but continues to be little understood.2 The most commonly described are synchronous ovarian and endometrial cancers.3 Concomitant endometrial adenocarcinoma and uterine leiomyosarcoma (LMS) are extremely rare.4 LMSs are rare malignancies of the uterus that account for only 1–2% of all uterine malignancies.5 Most women with LMS lack symptoms or present with a rapidly enlarging pelvic mass. LMS is usually diagnosed following the surgery, although in rare conditions, a frozen section is used during the surgery.6 In most cases, the diagnosis of LMS is made by pathological examination of hysterectomy or myomectomy specimen.5 Here we present an extremely rare case of uterine LMS coexisting with endometrial endometrioid adenocarcinoma of the uterus.

Case Presentation

A 52-year-old woman was reported to gynecology outpatient clinic with chief complaints lower abdominal pain, severe dysmenorrhea and irregular vaginal bleedings for 7 months. She was a known case of type II diabetes for 6 years and primary hypothyroidism for 4 years. She was found to be non-smoker and non-

© The Author(s) 2023. This work is licensed under a Creative Commons Attribution-NonCommercial 4.0 International (CC BY-NC)
alcoholic. She didn’t have any family history of medical illness. On her general examination, she had no pallor and peripheral lymphadenopathy. Respiratory and cardiovascular systems were normal. Her abdominal examination revealed a midline palpable mass extending up to the lower border of umbilicus. The mass was mobile and non-tender. During speculum examination cervix and vagina were found to be healthy with no discharge and any growths. Bimanual examination revealed an enlarged uterus of 18 cm in size and was mobile. Bilateral fornices were free. On laboratory investigations, her hemoglobin was 9.7gm% and HbA1C was 4.6%. Fasting blood glucose and postprandial blood sugar was within the normal range. Renal function tests, liver function tests and thyroid function tests were within normal range as well. Ultrasound of pelvis and abdomen showed enlarged uterus measuring 18x12 cm, a solitary intramural fibroid measuring 10x10 cm and normal endometrial echo complex of 5 mm in thickness. Bilateral adnexa were reported as normal. Because of an underlying disease process, she was planned for surgery and a simple total abdominal hysterectomy with bilateral salpingo-oophorectomy was performed and the specimen was sent to the laboratory for examination.

On gross examination, the uterus appeared globular and showed intramural mass measuring 10x10 cm (Figure 1A). The cut surface of the mass showed hemorrhage and necrosis. The endometrial cavity was compressed by the mass and the endometrium measured 4 mm in maximum thickness. Cervix, bilateral ovaries, and fallopian tubes were normal. Histopathological examination from intramural mass showed fascicles of atypical cells featuring moderate to marked pleomorphism with increased mitosis (40 mitosis/10 HPF) with atypical figures and coagulative necrosis (Figure 1B,C). Lymphovascular space invasions were also noted (Figure 1D). Tumor however invaded less than 50% of the myometrium and margins were uninvolved. Sections from the thickened portion of endometrium showed back to back arranged glands, tubules, cribriform and papillary-villus pattern. Glands and tubules were lined by moderately pleomorphic pseud stratified columnar epithelium having oval nuclei and abundant pale eosinophilic cytoplasm. Mitotic activity was sparse to absent (Figure 2A,B). The tumor also invaded superficial fascicles of the myometrium (<50%) with no lymphovascular invasions. However, mucosal spread to the endocervical glands was found mimicking it to be endocervical origin (Figure 2C). Immunohistochemistry was performed in separate blocks of intramural mass and endometrial lesion. Selected immunomarkers were applied in both tumors. In endometrial lesion, Er was weakly positive, Pr was strongly positive and p16 was negative (Figure 3A,B,C). SMA and h-Caldesmon were strongly positive and Ki-67 index was 60-70% in the intramural mass (Figure 3D,E,F). A final diagnosis of synchronous endometrial endometrioid adenocarcinoma, FIGO grade I and high-grade LMS, spindle cell type was made.

Discussion

Synchronous gynecological cancers are rarely described. These cases account for approximately up to 6% of female genital tract malignancies. The etiology of synchronous primary neoplasms of the female genital system remains poorly defined. It has been assumed that in genetically predisposed individuals, the Mullerian tissues with similar embryological origin may respond as a single structural entity when simultaneously exposed to carcinogenic, hormonal, therapeutic, or other triggering factors. The presence of synchronous uterine LMS and endometrial endometrioid adenocarcinoma is rare. To our knowledge, only 5 cases of synchronous LMS and endometrial endometrioid adenocarcinoma are reported. Our case will be the sixth case. In 2000, Sheyn et al had reported concomitant well-differentiated endometrial endometrioid carcinoma and LMS of uterus in a 66 year old woman. A similar case study was done by Dudzik et al and have reported synchronous uterine adenocarcinoma and LMS in a 60 year old woman. In 2019, Abbas et al have also reported synchronous well-differentiated endometrioid adenocarcinoma and LMS with pulmonary metastasis in a 50 year old woman. In 2016, another similar case of synchronous uterine adenocarcinoma and LMS was reported in a 60 year old lady. In addition, triple simultaneous primary gynecological malignancies including endometroid endometrial carcinoma, ovarian mucinous cystadenocarcinoma, and LMS of the uterus has also been reported by Isxın Doğan Ekici et al. Uterine LMS was also found to be coexisting with clear cell carcinoma of the ovary as a rare presentation in a case study done by Rettenmaier et al. But, in our case, no abnormalities were seen in bilateral ovaries both grossly and microscopically. In most of the different studies, patients have presented with vaginal bleeding which is similar to our case. It is important to note that the patient also had primary hypothyroidism and such association was not revealed in other cases except a study done by Cserni et al where the patient had secondary parathyroidism along with Ig A-nephropathy and hypertension. In our study also we had type II diabetes and hypertension. However, the patient also had primary hypothyroidism and such association was not revealed in other cases except a study done by Cserni et al where the patient had secondary parathyroidism along with Ig A-nephropathy and hypertension. Most of the time, it is often difficult to predict the uterine lesions preclinically. Transabdominal ultrasonography often reveals a complex mass with solid areas as shown in a study done by Senol et al. Association of diabetes and hypertension was also seen in studies done by Abbas et al and Sheyn et al. The patient in our study also had type II diabetes and hypertension. However, the patient also had primary hypothyroidism and such association was not revealed in other cases except a study done by Cserni et al where the patient had secondary parathyroidism along with Ig A-nephropathy and hypertension. Most of the time, it is often difficult to predict the uterine lesions preclinically. Transabdominal ultrasonography often reveals a complex mass with solid areas as shown in a study done by Senol et al.
Figure 1

A: Gross picture of uterus showing intramural mass with compressed endometrial cavity.

B: H&E stain of Leiomyosarcoma showing markedly pleomorphic spindle cells (40X)

C: H&E stain of Leiomyosarcoma showing atypical mitosis (400X)

D: H&E stain of Leiomyosarcoma showing lymphovascular invasions by island of atypical spindle cells (100X)

Figure 2

A: H&E stain of endometrial adenocarcinoma showing back to back arranged glands (100X)

B: H&E stain of endometrial adenocarcinoma showing glands lined by mild pleomorphic pseudostratified columnar epithelial cells (400X)

C: H&E stain of endometrial adenocarcinoma showing endocervical glandular colonization by atypical glands mimicking endocervical origin (100X)

Figure 3

A: Endometrial adenocarcinoma showing weak ER positive tumor cells (200X)

B: Endometrial adenocarcinoma showing PR positive tumor cells (200X)

C: Endometrial adenocarcinoma showing p16 negativity in tumor cells (200X)

D: Leiomyosarcoma showing strong and diffuse SMA positive tumor cells (200X)

E: Leiomyosarcoma showing strong and diffuse h-Caldesmon positive tumor cells (200X)

F: Leiomyosarcoma showing Ki67 expression (60-70%) in tumor cells (200X)
We also had done ultrasonography which revealed an enlarged uterus with a solitary intramural fibroid. Computed tomography scan findings were suggestive of a large, multiloculated, multisepatate growth in the study by Vellanki et al.\textsuperscript{11} However, computerized tomography imaging was not performed in our case.

Uterine LMSs are diagnosed on histology.\textsuperscript{12} Typically uterine LMS shows characteristic hypercellular spindle cells, diffuse moderate to severe cell atypia, a high mitotic index > 15/10 HPF, atypical mitosis and tumor cell necrosis.\textsuperscript{13} All these features were present in our case. The literature offers reports about a positive correlation between Ki-67 expression and tumor aggressiveness, as well as clinical advancement of the disease.\textsuperscript{14} Lusby et al reported Ki-67 overexpression, with an accompanying loss of ER and PR expression in the case of LMS.\textsuperscript{15} We have also done specific markers to LMS to clinch our morphological diagnosis including SMA, h-Caldesmon, and Ki-67, in which the Ki-67 index was 60-70% suggesting an overexpression. In a case reported by Abbas et al, malignant spindle cell neoplasm was positive for anti-smooth muscle actin (SMA) and CD10, focally positive for desmin, cytokeratin AE1/AE3, and cytokeratin Cam 5.2.\textsuperscript{4} In a similar case done by Crean et al, immunohistochemistry was positive for smooth muscle actin and desmin supporting the diagnosis of LMS.\textsuperscript{7} In most of the studies, endometrium showed FIGO grade I endometrioid adenocarcinoma with less than 50% or superficial myometrial invasion when it presented synchronically with uterine LMS.\textsuperscript{1-4} Such findings are similar to our case in which an endometrial lesion revealed FIGO grade I with invasion to superficial myometrium only. On the contrary, a study by Crean et al has shown grade II endometrioid adenocarcinoma that invaded 92% of the myometrium in association with uterine LMS.\textsuperscript{7} We have also noted that the adenocarcinoma in our case had colonized to endocervical glands mimicking it to be originated from the endocervix. Hence, we have applied immunomarkers like Er, Pr, and p16 in the endometrial lesion in which Er and Pr came to be positive and p16 was negative, this confirmed that carcinoma has originated from the endometrium. In most of the studies, the tumor was confirmed morphologically and confined to the endometrium. In one study by Sheyn et al, cytokeratin antibodies to AE1 and AE3/CAM5 revealed strong immunoreactivity of the endometrial endometrioid adenocarcinoma, and no reaction was seen in high-grade LMS.\textsuperscript{2}

**Conclusion**

Synchronous endometrial endometrioid adenocarcinoma and uterine LMS are exceptionally rare. We report the 6\textsuperscript{th} case of such a rare occurrence. Our study may contribute to understand the prognosis of such multiple malignancies, common associations, and etiology so that a proper plan for further management of the patient can be implemented. This study has also emphasized the equal role of ancillary testing like immunohistochemistry which may help to confirm the origin of the tumor and aiding in prognostic factors.

**Acknowledgments**

We would like to thank Dr. Dipesh Shakafor his help in preparing the manuscript.

**References**


How to Cite