Glassy Cell Carcinoma of the Endometrium Presenting as an Intracavitary Leiomyoma on Ultrasound

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Conflict of interest: None declared

Patient: Female, 58
Final Diagnosis: Endometrial poorly differentiated adenosquamous carcinoma • glassy cell carcinoma tumor
Symptoms: Postmenopausal spotting
Medication: —
Clinical Procedure: Endometrial biopsy then robotic total hysterectomy • bilateral salpingooophrectomy • pelvic lymph node mapping and bilateral pelvic lymphadenectomy
Specialty: Obstetrics and Gynecology

Objective: Rare co-existence of disease or pathology
Background: Glassy cell carcinoma of the endometrium is an extremely rare variant of adenosquamous carcinoma, and it has a poor prognosis. In postmenopausal women it typically presents as unprovoked, painless uterine bleeding. Tissue sampling is necessary to establish the diagnosis.

Case Report: A 58-year-old postmenopausal woman on no hormone replacement therapy experienced 2 months of intermittent uterine bleeding. An office transvaginal ultrasound discovered a 1.7-cm intracavitary leiomyoma, but because the endometrial stripe was not visualized, an endometrial biopsy was performed. She was found to have a Stage 1 A endometrial poorly-differentiated adenosquamous carcinoma, glassy cell carcinoma tumor of 1.5 cm in greatest dimension. She underwent a robotic total hysterectomy, bilateral salpingo-oophorectomy, pelvic lymph node mapping, and bilateral pelvic lymphadenectomy.

Conclusions: Glassy cell carcinoma of the endometrium can present as an intracavitary leiomyoma in postmenopausal women.

MeSH Keywords: Carcinoma, Adenosquamous • Endometrial Neoplasms • Leiomyoma

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Background

Unprovoked postmenopausal uterine bleeding (PMB) is reported to occur in 10% of women [1]. It is caused by a benign condition in over 90% of cases [2], and proper management requires timely evaluation, which includes an examination and pelvic ultrasound. Uterine leiomyomas are the most common benign tumors of the uterus, and are found in around 6% of women with PMB. Typically, diagnosing leiomyomas is straightforward because of the characteristic physical and ultrasound findings. Depending on the leiomyoma size and patient symptoms, most leiomyomas are managed simply by observation and periodic re-evaluation. Glassy cell carcinoma (GCC) of the endometrium is an extremely rare malignancy that is considered to be an uncommon variant of poorly-differentiated adenosquamous carcinoma [3,4]. GCC accounts for 0.5% of all endometrial carcinomas and to date less than 15 cases have been described [4]. It can also present with unprovoked PMB and, in the early stages, an unremarkable clinical examination. Standardized treatment protocols are lacking. The primary therapy is an aggressive surgical approach. We describe a case of GCC of the endometrium that presented with painless, unprovoked PMB and a transvaginal ultrasound (TVUS) image diagnosing the cancer as a small fundal leiomyoma.

Case Report

A 58-year-old gravida 0 female on no hormonal therapy presented with painless, unprovoked postmenopausal bleeding that had occurred twice over the past 8 weeks. Each current bleeding episode lasted less than 2 days and was characterized as ‘spotting’. She was taking no anticoagulants or herbal remedies, and there was no family history of breast, colon, or endometrial cancer. Her gynecologic history consisted of menarche at age 12 years. She was on and off oral contraceptives for all of her adult life, without notable dysfunction, and denied a history of polycystic ovarian disease or other background gynecologic disturbance that required medical intervention. Her menopause occurred at 50 years old. Physical examination was negative. Her uterus was normal size and shape and was freely movable, and adnexa were normal. Vaginal tissue was consistent with menopause. Her BMI was 24 kg/m². A transvaginal ultrasound evaluation (Figure 1) revealed the uterus to measure 3.4×3.1×3.9 cm, but the endometrial stripe was not measurable, presumably because of a 1.7-cm intracavitary leiomyoma. She underwent an endometrial biopsy, revealing a grade 3 endometrial adenocarcinoma. Computed tomography (CT) scans of the abdomen and pelvis performed afterwards were unremarkable. She underwent a robotic total hysterectomy, bilateral salpingo-oophorectomy, pelvic lymph node mapping, and bilateral pelvic lymphadenectomy. Pathology confirmed stage 1A FIGO (International Federation of Gynecology and Obstetrics) endometrial poorly-differentiated adenosquamous carcinoma, glassy cell carcinoma tumor of 1.5 cm in greatest dimension (Figure 2). The uterus weighed 28 g. Within the anterior aspect of the uterus at the right cornua was a 1.5×1.3×0.6 cm papillary white mass corresponding to the ultrasound ‘intracavitary leiomyoma’. The endometrium was atrophic. Twenty-three lymph nodes were sampled and all were negative. She was referred to Radiation Oncology but elected to follow up with surveillance alone. IHC (immunohistochemistry) staining showed no evidence of p53 (tumor protein) nuclear staining or p16 (multiple tumor suppressor 1) mosaic pattern staining of tumor cells. Vimentin and EMA (epithelial membrane antigen) were seen with strong cytoplasmic staining (Figure 3). ER and PR (estrogen-receptor and progesterone-receptor) showed positive staining. Next-generation sequencing showed PTEN (phosphatase and tensin), KRAS (v-Ki-ras2 Kirsten rat sarcoma viral oncogene), and TP53 (tumor protein) gene mutations. No targetable chemotherapy associated with these genes was recognized. At 18 months after diagnosis, she has no evidence of disease.

Figure 1. Transvaginal ultrasound, longitudinal view. No endometrial stripe is visualized. A 1.7×1.4 cm mixed-density mass interpreted as a leiomyoma was seen.

Figure 2. The tumor cells have abundant eosinophilic ground-glass-appearing cytoplasm, distinct cell walls, large vesicular nuclei, and prominent nucleoli (hematoxylin and eosin stain; original magnification ×400).
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The second important item in this case is that because this tumor is so rare, definitive conclusions regarding treatment options cannot be standardized. Early observations of GCC of the cervix suggested they were aggressive at all stages and relatively resistant to radiation therapy [7]. Endometrial GCC was also listed early on as a highly aggressive malignancy with a poor prognosis. In fact, whether radiation therapy is combined with surgery or not, over 50% of cases with stage I tumors experienced recurrence of or death due to disease within 5 years after diagnosis, suggesting that glassy cell carcinomas arising in the uterus also behave aggressively [4]. This malignant potential emphasizes even more strongly the importance of an early diagnosis. Another important feature of this malignancy is that, other than stage, there are no apparent pathologic or molecular factors that are consistent prognostic variables in predicting treatment response. One isolated case report [8] described a complete response to a synthetic progestin with antiestrogenic properties in a patient with lung metastasis. This is indirect evidence of the presence of progesterone receptors, which could have been helpful in our case, considering the positive hormonal receptors. However, other than the positive hormonal receptor, there were no targeted laboratory findings that would have resulted in novel immunotherapy or altered multimodal recommendations that would have changed her treatment. Consequently, she declined radiation and is disease-free at 18 months.

Conclusions

GCC of the endometrium is an exceedingly rare malignancy with a natural history that is unpredictable. There are too few cases to develop a comprehensive counseling strategy, but early discovery may be a critical component in the prognosis. An aggressive surgical approach offers the highest chance of success. PMB is common and TVUS is a necessary, and sometimes final, diagnostic element in the workup of the bleeding. Office-based endometrial sampling is now safe, fast, and reliable.

Conflicts of interest

None.

Reference:

Figure 3. Tumor cells demonstrate strong and uniform EMA immunoreactivity (epithelial membrane antigen stain; original magnification ×100).
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