

Received: 2019.02.20
Accepted: 2019.04.12
Published: 2019.07.05

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





Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

ABEF 1 **Courtney Fox**
BCE 2 **Veronica Schimp**
BCD 3 **Li Ge**
DE 4 **Yehuda Galili**
ABDEF 1,5 **Steve J. Carlan**

1 Department of Obstetrics and Gynecology, Orlando Regional Healthcare, Orlando, FL, U.S.A.
2 Division of Gynecologic Oncology, Orlando Regional Healthcare, Orlando, FL, U.S.A.
3 Department of Pathology, Orlando Regional Healthcare, Orlando, FL, U.S.A.
4 Department of Internal Medicine, Orlando Regional Healthcare, Orlando, FL, U.S.A.
5 Division of Academic Affairs and Research, Orlando Regional Healthcare, Orlando, FL, U.S.A.

Corresponding Author: Steve J. Carlan, e-mail: stevecarlan@gmail.com
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 salpingo-oophorectomy • 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
Full-text PDF: <https://www.amjcaserep.com/abstract/index/idArt/915809>

 1118  —  3  8



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

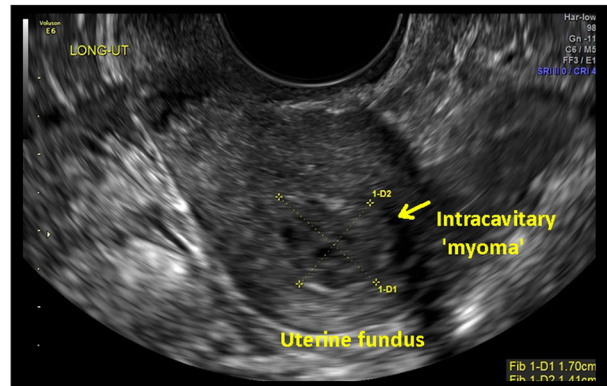


Figure 1. Transvaginal ultrasound, longitudinal view. No endometrial stripe is visualized. A 1.7×1.4 cm mixed-density mass interpreted as a leiomyoma was seen.

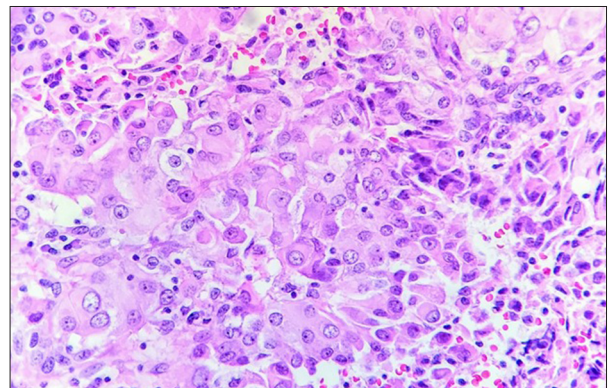


Figure 2. The tumor cells have abundant eosinophilic ground-glass-appearing cytoplasm, distinct cell walls, large vesicular nuclei, and prominent nucleoli (hematoxylin and eosin stain; original magnification ×400).

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.

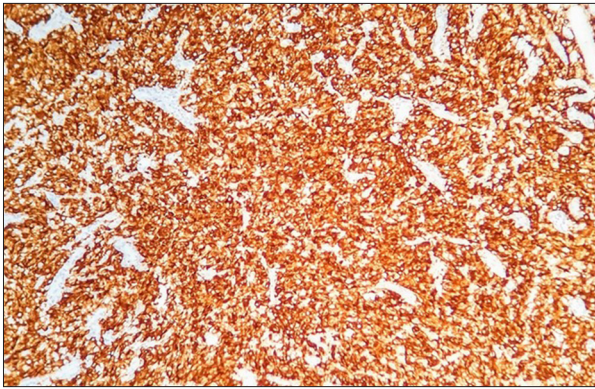


Figure 3. Tumor cells demonstrate strong and uniform EMA immunoreactivity (epithelial membrane antigen stain; original magnification $\times 100$).

Discussion

This case is important for 2 reasons. First, it demonstrates the importance of not presuming a tissue diagnosis based on history, examination, and imaging alone. This malignancy presented clinically as painless vaginal bleeding, which is a common complaint in postmenopausal women. There was no delay in the patient's examination, and an office TVUS discovered what appeared to be a straight-forward intracavitary leiomyoma, which was a plausible explanation for her symptoms. In general, histologic confirmation is not required to proceed with management under these circumstances, except in cases in which another lesion is suspected. Consequently, for the presumed leiomyoma, further diagnostic testing with sonohysteroscopy, hysteroscopy, magnetic resonance imaging (MRI), or biopsy was elective, and simple observation was a reasonable treatment option [5]. However, because the endometrial stripe was not visualized on TVUS, tissue diagnosis was offered and performed. Ironically, based on the final pathology report, the endometrium was not visualized because it was atrophic, not because of an anaplastic process. Most data now suggest a biopsy or hysteroscopy is indicated in PMB if the endometrial stripe is >4 mm by TVUS or if it is not measureable, as in our case [6]. Offering hysteroscopy or biopsy for all women with PMB and a sonographically-detected intracavitary myoma, regardless of the stripe, may not be cost effective [5], but the speed, safety, and reliability of in-office diagnostic uterine sampling techniques currently offered is compelling and notable.

References:

1. Astrup K, Olivarius Nde F: Frequency of spontaneously occurring postmenopausal bleeding in the general population. *Acta Obstet Gynecol Scand*, 2004; 83: 203–7
2. Van den Bosch T, Amey L, Van Schoubroeck D et al: Intra-cavitary uterine pathology in women with abnormal uterine bleeding: A prospective study of 1220 women. *Facts Views Vis Obgyn*, 2015; 7: 17–24
3. Cherry C, Glucksmann A: Incidence, histology, and response to radiation of mixed carcinomas (adenoacanthomas) of the uterine cervix. *Cancer*, 1956; 9: 971–79
4. Ferrandina G, Zannoni GF, Petrillo M et al: Glassy cell carcinoma of the endometrium: A case report and review of the literature. *Pathol Res Pract*, 2007; 203(4): 217–20

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.

5. Dueholm M, Lundorf E, Hansen ES et al: Accuracy of magnetic resonance imaging and transvaginal ultrasonography in the diagnosis, mapping, and measurement of uterine myomas. *Am J Obstet Gynecol*, 2002; 186: 409–15
6. Sladkevicius P, Opolskiene G, Valentin L: Prospective temporal validation of mathematical models to calculate risk of endometrial malignancy in patients with postmenopausal bleeding. *Ultrasound Obstet Gynecol*, 2017; 49: 649–56
7. Tamimi HK, Hesla J, Cain JM et al: Glassy cell carcinoma of the cervix redefined. *Obstet Gynecol*, 1988; 71: 837–41
8. Dawson EC, Belinson JL, Lee K: Glassy cell carcinoma of the endometrium responsive to megestrol acetate. *Gynecol Oncol*, 1989; 33: 121–24