Uterine papillary serous carcinoma: A rare type of endometrial carcinoma with worse outcomes

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Abstract
Introduction: Uterine papillary serous carcinoma (UPSC) is a clinically aggressive type of endometrial carcinoma. They represent about 10% of endometrial carcinomas and are responsible for 40% of deaths and recurrences associated with endometrial cancer.

Patient Presentation: JM is a 75 year old woman who presented with eight months’ postmenopausal vaginal bleeding, loss of weight and low abdominal pain. Except for obesity and bilateral pitting edema, she had normal findings on physical examination.

Management and Outcome: Pelvic ultrasound showed an intra-uterine mass of increased echo (4×4 cm) and a pelvic CT scan showed a bulky uterus bulky with prominent endometrium. Visual inspection with acetic acid and Lugol’s iodine was negative for cervical cancer whereas Pipelle biopsy indicated endometrial cancer. She had total hysterectomy with bilateral salpingo-oophorectomy. She is due to start chemotherapy.

Conclusion: Even though endometrial biopsy using a Pipelle is highly sensitive for detection of high-grade endometrial carcinomas, it is less accurate at predicting UPSC. Patients undergoing surgery for endometrial cancer should therefore have a comprehensive surgical staging as the patient may have UPSC. Due to the risk of recurrence, adjuvant chemo-radiation should be administered after surgery.

Keywords: Postmenopausal bleeding, Uterine papillary serous carcinoma, Endometrial serous carcinoma, Endometrial cancer.

Introduction
The patient that this case report discusses was diagnosed with abnormal/postmenopausal uterine bleeding secondary to uterine papillary serous carcinoma (UPSC), which is also known as endometrial serous carcinoma (ESC), after histology. Endometrial carcinoma causes bleeding in approximately 10% of postmenopausal women with abnormal uterine bleeding, which occurs in approximately 4-11% of these women. UPSC accounts for about 10% of all endometrial carcinomas. They are therefore a rare type of endometrial cancer. However, UPSCs are an aggressive histotype and are responsible for 40% of all deaths and recurrences associated with endometrial carcinoma. Usually, these patients also present at comparatively higher stages. For example, up to 37% of UPSC cases that display no invasion in the uterus have stage III or IV disease.

Endometrial biopsy using a Pipelle has high sensitivity for detecting high-grade endometrial carcinomas. However, it is less accurate at predicting UPSC and may not give this histological subtype of endometrial carcinoma. It may therefore be diagnosed after surgery, which is usually curative for women at low risk of disease recurrence. The aim of this case report is to emphasize the need for comprehensive surgical staging for any endometrial carcinoma, and that both radiation therapy and chemotherapy should be added postoperatively to treat women with both early and advanced-stage disease. The patient consented to the writing of this case report for learning purposes. See attached signed form.

Case Presentation
A 75 year old widow presented to the gynecology outpatient clinic (GOPC) with vaginal bleeding for 8 months and low abdominal pains for 1 year.

The patient had been well until one year ago when she started experiencing moderately severe cramping low abdominal pain that radiated to the back. There were no provoking factors. The pain would be relieved by taking painkillers (buscopan) or would just go away on their own. The pain did not follow any diurnal or other specific pattern.

Four months later she started having spontaneous vaginal bleeding that would often be preceded by the abdominal pains, although the vaginal bleeding would occasionally occur independent of the abdominal pain. Most of the time it would just flow freely but occasionally there would be clots as well. It was not predictable and she would notice the bleeding when she went to the toilet. It would go on for up to two weeks then disappear for a week before it returns. She would use between two and three pads in a day.

She also developed bilateral leg swelling and chest pains. There was marked loss of weight as reported by the patient. This was corroborated by her daughter in law. There were no headaches, dizziness, blurring of vision, easy fatigability, palpitations or other signs of anemia. She didn’t have drenching night sweats.

Under systemic review, she had no headache, blurring of vision, double vision, weakness or difficulty in speech. There were occasional para-ternal chest pains. These were not associated with the presenting symptoms. The patient neither had cough or fever. She had no difficulties in breathing. There was no nausea or vomiting. However, she occasionally got heart burns. There was no diarrhea or...
constipation. There were no urinary symptoms. Apart from the bleeding, she had not noticed vaginal discharge. She reported that she was not sexually active so we couldn’t ascertain history of dyspareunia or post-coital bleeding. She was obese before the onset of this condition but has lost a lot of weight (subjectively reported by the patient). No weakness was reported.

JM was a para 8+0 with five living children. She had menarche at 13 years and menopause at 50 years of age. She has not been on hormone replacement therapy. She only used oral contraceptive pills for two years after her last delivery in 1981. She finally had a bilateral tubal ligation (BTL) in 1983. She had two still births while the other child died at 37 years.

She was a widow whose husband died in 2001 from diabetes. The patient has been a farmer all her life. She has one sister who is alive and well and has never had any similar condition. She had four brothers but two died from human immunodeficiency virus (HIV) whereas the other died from severe anemia due to leukemia. Her parents were both deceased. The father died in 1940s while the mother died at 96 years after fracturing the neck of her femur. She had five sons and several grandchildren. The first son was an electrician, the second a pastor, the third a teacher, the fourth a teacher who committed suicide at 37 years, the fifth a driver while the sixth died of a similar condition. She had four brothers but two died from diabetes. The patient has been a farmer all her life. She has not been on hormone replacement therapy. She only used oral contraceptive pills for two years after her last delivery in 1981.

The precordium was not resonant on percussion and with vesicular breath sounds central, chest was moving symmetrically with respiration, her abdomen was soft and Kernig’s negative. Her neck was soft and Kernig’s negative. Trachea was central, chest was moving symmetrically with respiration, resonant on percussion and with vesicular breath sounds bilaterally on auscultation. The precordium was not hyperactive while all the pulses were of normal volume and regular. The abdomen was slightly distended but moving with respiration. There were normal bowel sounds, and no ascites, organomegaly or tenderness. Speculum exam showed a normal vulva, vagina and cervix. Full hemogram was normal with hemoglobin of 11.2g/dl.

Cervical cancer screening (visual inspection with acetic acid-VIA): HIV status was negative; vulva, vaginal walls and cervix were normal. The VIA was negative for cervical cancer. Endometrial biopsy using pipelle showed endometrial carcinoma.

A pelvic ultrasound showed that the urinary bladder was full and had regular walls; the uterus was bulky at 99mls and the endometrium was not well visualized; there was a mass of increased echogenicity with irregular walls ~4×4 cm with a clear cervical region; bilateral adnexal region appeared clear; Pouch of Douglas appeared clear. It concluded that these were sonographic features suggestive of an intra-uterine mass of increased echo (4×4 cm).

Serial IV contrast enhanced CT scans of the pelvis were obtained from the mid-abdomen to the pubic symphysis; this showed that the uterus was bulky for age (9.9×5×5.2cm); the endometrium was prominent; the cervix appeared normal in size and CT attenuation; wall calcifications of aorta and iliac arteries were evident; thoracolumbar spine shows moderate degenerative changes; no mesenteric, pelvic or para-aortic enlarged lymph nodes seen. It concluded that the patient had a bulky uterus with prominent endometrium. An impression of abnormal/post-menopausal uterine bleeding due to malignancy was made with differentials of endometrial hyperplasia, uterine polyp or myometrial carcinoma.

The patient thought that she had cancer. She was upbeat that it could be treated. During this meeting, she wanted surgery done and the uterus taken away so that she could be relieved of her symptoms.

**Assessment**

JM was a 75 year old woman who presented with an eight month history of vaginal bleeding associated with low abdominal pain for the last one year. She had been obese but reports marked loss of weight. She is a known hypertensive patient who is controlled on HCTZ, nifedipine and enalapril. She also used tranexamic acid intermittently for the bleeding. She has not been on HRT, Tamoxifen or anticoagulants. The condition had not stopped her from farming. Her pelvic exam was essentially normal. She wanted definitive management for her condition.

**Management and Outcome**

Patient was admitted to female ward for total extrafascial hysterectomy and bilateral salpingo-oophorectomy with pelvic and para-aortic lymph node dissection. Intra-operative, the uterus seemed larger for age but had no adhesions to pelvic organs; pelvic and para-aortic lymph nodes were not enlarged; abdominal organs looked normal with no signs of metastases; total hysterectomy was performed and when the uterus was dissected open, it was found to have a fungating uterine mass from the anterior uterine wall measuring 6×5×5cm. This mass filled the whole of the uterine cavity and was friable on touch. It was sent for histology.

Her recovery from surgery was uneventful and was allowed home to come for follow up at the GOPC. The incisional site was well healed and her blood pressure was
well controlled during her first clinic visit. She still had some low abdominal pain.

**Histology Report Read:** Grossly it was a polypoid tumor. Microscopy sections showed a tumor composed of well-formed papillae with ‘lobster claw’ appearance. The individual cell showed prominent nucleoli. Myometrial invasion was absent; endometrial atrophy was noted; and desmoplastic reaction was present. It concluded that this was papillary serous carcinoma, high grade and non-estrogen related.

The bad news was broken to the patient and she took it well. The need for adjuvant chemotherapy, with or without radiotherapy, was explained. The patient and her relatives were willing to go ahead with a referral to consult with a gyneco-oncologist. They were therefore referred to Alexandria Cancer Center in Eldoret.

**Discussion**

Postmenopausal uterine bleeding is defined as uterine bleeding after permanent cessation of menstruation occasioned by loss of ovarian follicular activity. Even though the most common cause of spontaneous postmenopausal bleeding is a benign source, the possibility that an underlying malignancy exists must be entertained. Therefore, the primary aim when investigating a woman with postmenopausal bleeding is to exclude endometrial carcinoma and any significant additional abnormalities. In addition, the clinician has to as certain that the woman is not on hormonal replacement therapy or anticoagulants.

The most common cause of bleeding in these women is atrophy of the vaginal mucosa and/or the endometrium. Others are endometrial hyperplasia, polyps, submucosal fibroids, pyometra, hydrometra or hematometra. Gynecological and non-gynecological sources of vaginal bleeding must be ruled out during the physical examination. These are the cervix, vagina, vulva, fallopian tubes or ovarian pathology (gynecological) and the urethra, bladder and lower gastrointestinal tract (non-gynecological).

The first step in the workup should be transvaginal ultrasonography (TVUS) to examine the thickness of the endometrial lining. A blind biopsy is recommended when the uterine thickening is global whereas hysteroscopic-guided biopsy is preferred for focal thickening. Saline infusion sono-hysteroscopy enhances clarity of structures.

Obesity is a risk factor for the development of all endometrial carcinomas including UPSC. However, UPSC demonstrate no hormonal risk factors. UPSC are also more common in women of African descent. Endometrial biopsy using a Pipelle is less accurate at predicting UPSC. Therefore, persistent bleeding should necessitate a dilation and curettage procedure to obtain further histologic diagnosis, especially if Pipelle’s results are negative for malignancy.

Patients with UPSC present at higher stages because alterations in cell adhesion molecules confer upon the malignant cells the ability to disseminate even in the absence of morphologically apparent invasive growth.

**Conclusion**

It is therefore very important to do a comprehensive surgical staging during laparotomy entailing pelvic washings, pelvic and para-aortic lymphadenectomy with/without omentectomy. Between 37-63% of women whose tumors lack myometrial invasion, like the index patient, have high rates of coincident extra-uterine disease and a significant risk for recurrence (up to 21% overall). This often results in poor outcomes if patient management involves surgery alone. Disease recurrences occur quite frequently. Therefore, a low threshold for initiation of platinum/taxane-based adjuvant chemotherapy, with or without radiotherapy, should be considered in the treatment of both early-stage and advanced-stage patients. In addition, careful long-term surveillance is indicated for early identification of recurrence.

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**Declaration**

This paper has not been published elsewhere and/or is not under consideration for publication elsewhere.

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**References**


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