



Case report

A rare case of endometrial cancer metastatic to the uveal choroid

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1. Background

Cancer of the endometrium is the most common gynecologic cancer in the United States with 61,380 new cases and 10,920 endometrial cancer-related deaths predicted in 2017 (American Cancer Society, 2017). Most cases are diagnosed at an early stage and low International Federation of Gynecology and Obstetrics (FIGO) grade, allowing for a good prognosis with surgical resection and adjuvant therapy when indicated (Creasman et al., 1987).

The most common histological type of endometrial cancer is endometrioid adenocarcinoma, also known as type 1 endometrial cancer. Type 1 endometrial cancer is thought to be less aggressive, confined to the uterus at time of diagnosis, and less likely to metastasize quickly (American Cancer Society, 2017). Conversely, uterine serous carcinoma (USC), clear cell and FIGO grade 3 are more aggressive histologies of endometrial cancers and more likely to metastasize (American Cancer Society, 2017).

Endometrial cancer commonly spreads via the lymphatic system, in a stepwise fashion from the pelvic to the scalene nodes. Hematogenous metastases, while less common, can also occur, and these most commonly arise in lung, liver, brain and bones (Hoffman et al., 2016). Choroid metastases from gynecologic cancers, specifically endometrial cancer, are extremely rare. We report a case of a 75 year-old female with choroid metastases from endometrial cancer three years after successful cytoreduction surgery.

2. Clinical scenario

In September of 2013, a 75 year-old Caucasian female underwent an exploratory laparotomy, total abdominal hysterectomy, bilateral

salpingo-oophorectomy, pelvic lymph node dissection, and omental biopsy. No washings were obtained. She had fourteen negative pelvic lymph nodes and a negative omental biopsy. Given her low risk for recurrence with a stage IA FIGO grade 2 endometrioid adenocarcinoma confined to a polyp, she did not receive adjuvant treatment and was monitored with serial exams.

Two years after diagnosis the patient had a biopsy proven left vaginal sidewall recurrence. She was treated with 4500 centigray (cGy) external beam radiation over 25 treatments, followed by high-dose brachytherapy. She remained without evidence of disease for fifteen months until she presented to her local ophthalmologist with a one month report of bilateral blurry vision and decreased visual acuity of the left eye. She also endorsed “flashes” in her right eye that were increasing in frequency.

Metastatic cancer was suspected after initial fundoscopic exam revealed two darkened, raised areas in the choroid of the left eye in December of 2016 (Fig. 1). Visual acuity was 20/25 vision in her right eye and 20/300 in her left eye. Slit lamp exam demonstrated findings of a normal anterior chamber bilaterally with notable mild nuclear cataract changes occurring bilaterally. Dilated fundus exam revealed choroidal lesions elevating the retina in both eyes. Two choroidal lesions were noted along the superior arcade in the macula of the left eye, and the right eye had evidence of two choroidal lesions inferonasally. Masses were confirmed and characterized with ultrasound. Whole body positron emission tomography (PET) showed diffuse metastatic disease throughout the bones, lungs, mediastinal and subclavicular lymph nodes, left globe, and left shoulder subcutaneous nodule. Ultrasound guided fine needle aspiration biopsy of the supraclavicular node resulted as metastatic poorly differentiated carcinoma harboring high

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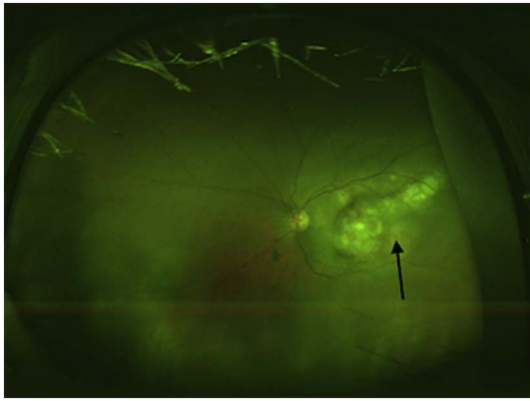


Fig. 1. Choroid lesion (solid arrow) seen on funduscopy exam of patient's left eye.

grade features (Fig. 2). On second opinion pathology review of her hysterectomy specimen demonstrated high grade endometrial adenocarcinoma with endometrioid and serous features with no lymphovascular space nor myometrial invasion (Fig. 3).

She completed five of six planned cycles of intravenous carboplatin and dose-dense paclitaxel in May of 2017; the final cycle was held secondary to neuropathy. A complete response was seen on PET scan one month post-treatment; however, two months later, follow-up ophthalmologic examination revealed decreased visual acuity in the left eye, diminished to the point of only being able to count fingers placed three feet from the patient. Fundoscopic exam and ultrasound testing demonstrated enlargement of macular choroidal lesions in the left eye. After presenting to her medical oncologist with persistent nausea and vomiting three months following completion of chemotherapy, a brain magnetic resonance imaging (MRI) showed multiple brain metastases, including within the left choroid (Fig. 4). The patient began whole brain radiation and completed 1000 cGy of the prescribed 3000 cGy. Due to declining health, the patient elected for hospice and died in September of 2017.

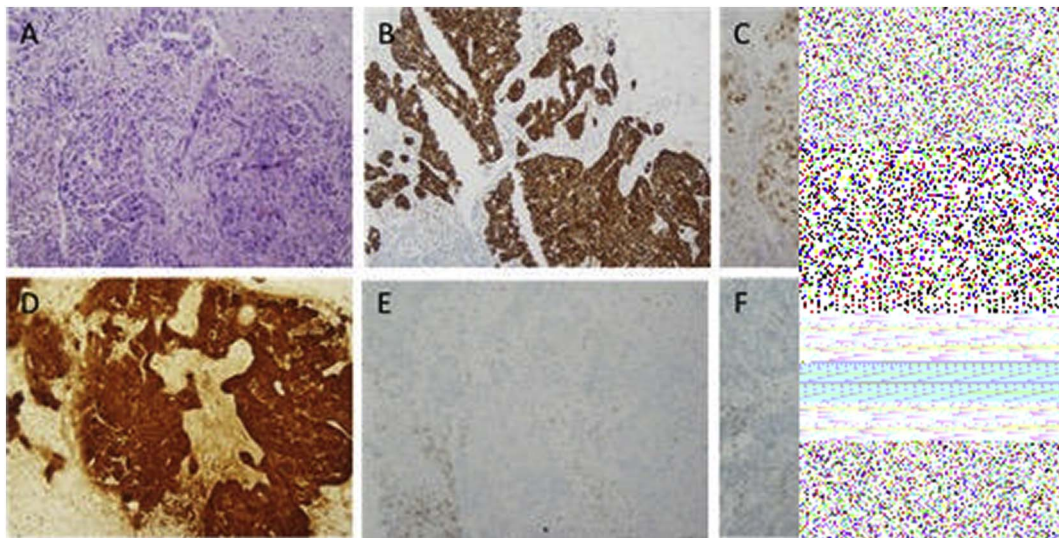


Fig. 2. Hematoxylin and eosin stain of supraclavicular lymph node with metastatic poorly differentiated carcinoma harboring high grade features (A). The tumor cells demonstrate diffuse positivity for cytokeratin (B), PAX-8 (C) and p16 (D) with no expression of p53 (E) and ER (F) (Original magnification $\times 200$ [A–F]).

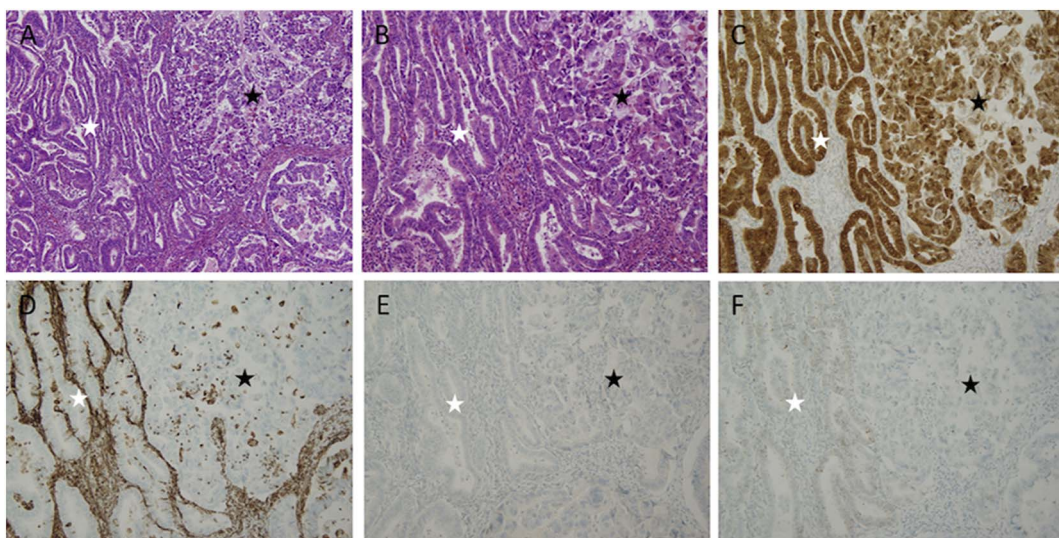


Fig. 3. High-grade endometrial adenocarcinoma with endometrioid and serous features (A & B). Ancillary studies demonstrate diffuse positivity for p16 (C), and minimal expression of vimentin (D) with lack of p53 immunoreactivity (E), and estrogen receptor expression (F). (Original magnification $\times 100$ [A]; original magnification $\times 200$ [B–F]; hematoxylin and eosin (A&B)). Area shown by white asterisk represents carcinoma with endometrioid features and the area shown by black asterisk represents carcinoma with serous features.



Fig. 4. Top: Sagittal T1 weighted flair MRI showing multiple lesions, including left globe lesion (arrow). Bottom: Axial T2 weighted Propeller MRI of left globe lesion (arrow).

3. Discussion

Generally, stage IA endometrioid adenocarcinoma has a good prognosis with an overall five-year survival of 88% (National Cancer Institute, 2017). Surgical management is the definitive treatment of choice. Recurrence most commonly occurs in the vagina and salvage rates with radiation are high (Nag et al., 2002). In contrast, stage I USC has a five-year survival of 79.9% (Binder and Mutch, 2014), and the recurrence rates are much higher at 50–90%, with the majority being extrapelvic (El-Sahwi et al., 2012).

To our knowledge, only 3 cases of choroid metastases from endometrial cancer have been described in the literature (Cormio et al., 2006; Lawrence et al., 2010; Saxena et al., 2012). Lawrence, et al. described a 70 year-old patient with stage IVB USC who presented four years after surgery and adjuvant chemoradiation with sudden onset of severe pain and vision loss in her right eye, requiring enucleation. Six months prior to presentation, the patient had received additional palliative chemotherapy for pulmonary metastases (Lawrence et al., 2010). Saxena et al. reported a 56 year-old patient with stage IV endometrioid adenocarcinoma who presented one year after surgery and adjuvant radiation with a one month history of gradual and painless decrease in

vision of her right eye, and died within one month of presentation (Saxena et al., 2012). Cormio et al. reported a case in which a 31 year-old patient with suspected early stage endometrial cancer received fertility-sparing megestrol acetate for 6 months with serial clinical exams thereafter. Two years after initial treatment she recurred and underwent a total abdominal hysterectomy, bilateral salpingo-oophorectomy and lymph node sampling, revealing stage IA grade 1 endometrioid adenocarcinoma, requiring no adjuvant therapy. This patient was disease-free for three years, until she had multi-focal recurrence noted in her lungs, pelvis and left eye. She was treated with intravenous carboplatin and paclitaxel every three weeks, with minimal response in the choroid lesion, although response was seen in her lung metastases. After completing six cycles of chemotherapy, MRI confirmed left choroid and multiple metastatic brain lesions. The patient declined further treatment and died within one month (Cormio et al., 2006).

While extremely rare, metastatic disease to the eye should not be overlooked in a patient with a history of endometrial cancer and new onset vision changes. Posterior ciliary arteries, a large component of the high flow choroidal vasculature, are thought to aid in the hematogenous dissemination of tumor emboli from distant primary tumors (Cormio et al., 2006; Shields et al., 1997). As seen in our patient, the most common symptoms at time of presentation are blurry vision, decreased visual acuity, flashers and floaters, and pain; however, some patients may have no symptoms. Vision complaints in patients with a history of any gynecologic cancer warrant timely evaluation, including funduscopic examination to rule out metastatic lesions. Currently the American Academy of Ophthalmology recommends all adults receive a comprehensive eye evaluation at age 40 (American Academy of Ophthalmology, 2015). Given the average age at time of diagnosis of endometrial cancer is 60 (American Cancer Society, 2017), patients should have a routine baseline eye exam established upon diagnosis. Furthermore, it is important to ensure endometrial cancer patients with new vision symptoms have a comprehensive eye exam to assess for possible metastatic disease. Upon the diagnosis of uveal metastatic disease, patients should undergo contrast-enhanced MRI which is more sensitive than computed tomography or FDG-PET scan to detect brain metastases (Fink and Fink, 2013). Treatment is dependent upon the primary tumor with external beam radiation or primary site-specific systemic chemotherapy being the two most common treatment modalities.

Ethical statement

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal upon request.

Conflicts of interest

The authors of this paper have no conflicts of interest.

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