

Case Series

Brain metastasis in two patients with stage IA papillary serous carcinoma of the uterus

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ABSTRACT

We report two cases of brain metastasis in patients initially diagnosed with extremely early stage UPSC after extensive staging surgery. They did not receive either adjuvant chemotherapy or adjuvant pelvic or vaginal cuff radiation. At the same time that these patients were diagnosed with systemic metastasis, they both had a local “drop” metastasis in the vulva or the vaginal cuff. After the initial response to palliative chemotherapy, they both developed brain metastasis. The pattern of recurrence with the lack of adjuvant treatment underscores the urgent need in further evaluation of the potential benefits of adjuvant treatment, including chemotherapy and possibly in combination with radiation in this highly aggressive disease.

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1. Introduction

Papillary serous carcinoma of the uterus (UPSC) is a rare entity among the endometrial malignancies. In contrast to endometrioid adenocarcinoma of the endometrium, UPSC has a higher chance of abdominal and systemic recurrence, which is independent of myometrial invasion (Fader et al., 2009). In early stage UPSC cases with myometrial invasion, adjuvant chemotherapy and/or radiation are recommended (National Comprehensive Cancer Network, 2015). Here we report two patients with stage IA uterine papillary serous cancer who did not receive any adjuvant radiation or chemotherapy, who then developed vaginal, or vulvar recurrence and brain metastasis.

2. Case 1

An 81 year old female was diagnosed with stage IA G3 uterine papillary serous cancer after comprehensive surgery including total abdominal hysterectomy (TAH), bilateral salpingo-oophorectomy (BSO), pelvic lymph node dissection and omentectomy. The pathology showed superficial myometrial invasion (2 mm out of 11 mm) and lymphovascular space invasion, and none of the 13 lymph nodes from the pelvic and para-aortic area were involved. It was staged T1aN0M0. She was advised to take adjuvant chemotherapy and pelvic radiation

but the patient decided against it. At the same time, the patient was also diagnosed with a noninvasive papillary urothelial cancer of the bladder which was resected by a transurethral approach. Past history was significant for a stable small meningioma and hypothyroidism. Family history was significant for breast cancer in her sister. Twenty four months later, a vulvar lesion was noted at routine follow-up which on biopsy showed metastatic papillary serous cancer. On further workup, several scattered new nodular opacities were found in the lungs which on biopsy also showed metastasis from the serous uterine cancer. Patient received palliative chemotherapy with gemcitabine and carboplatin for 3 months with radiographic regression of the lung nodules. This regimen was chosen due to her lifelong history of allergies to numerous allergens and her extreme concern regarding a possible allergic reaction to paclitaxel, as well as the known efficacy of gemcitabine and carboplatin combination (Gordon et al., 2011). Patient then opted for observation. Eight months after stopping chemotherapy and 3 years after initial surgery, she developed mental status changes and was found to have cerebral metastases (3 × 4cm right temporoparietal lesion, 2 cm left parietal lesion) for which she received palliative whole brain radiation (Fig. 1). After completion of radiation, there was a small decrease in size of the temporoparietal lesion (Fig. 1) but there were two new metastatic lesions (4 mm, left frontal and 6 mm, right occipital) (Fig. 2). Patient died of the disease 4 months after diagnosis of cerebral metastasis.

3. Case 2

A 62 year old woman who presented with post-menopausal bleeding was diagnosed initially with poorly differentiated endometrial

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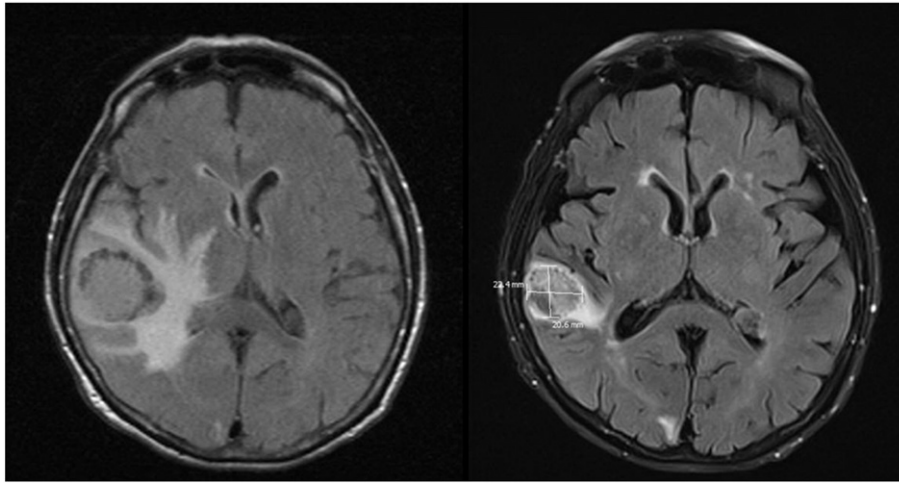


Fig. 1. MRI: Before radiotherapy. A. 3×4 cm right temporo-parietal metastatic lesion with surrounding vasogenic edema, mass effect and midline shift, approximately 0.5 cm shift to the left. B. Post radiotherapy image showing interval decrease in size in the right temporo-parietal lesion now measuring 2.2×2.0 cm with marked decrease in the surrounding vasogenic edema, resolution of the mass-effect on the lateral ventricles and the midline shift.

cancer in an endometrial polyp. She underwent TAH, BSO, pelvic lymph node dissection and omentectomy. Final pathology showed necrotic endometrium with no residual cancer in the specimen, and 5 pelvic lymph nodes were sampled and were negative. It was staged as T1aG3N0M0. Immunohistochemistry staining for mismatch repair (MMR) protein was performed on the endometrial biopsy specimen, all four genes produced proteins, indicating MMR proficient status, therefore it was unlikely that the patient had hereditary nonpolyposis colon cancer syndrome (HNPCC). Her past medical history includes aortic and mitral valve replacements (metallic) due to rheumatic heart disease, atrial fibrillation, hypertension, hyperlipidemia and adenocarcinoma in situ in a colonic tubulovillous adenoma. Family history was significant for lung cancer in the father and uterine cancer in her paternal grandmother at the age of 40. The patient was advised to take vaginal brachytherapy due to poorly differentiated cancer histology, however it was not done as her postoperative course was complicated by two episodes of small bowel obstruction related to adhesions. One year later, she developed vaginal bleeding, and was found to have recurrence in her vaginal vault, as well as in the pelvic and para-aortic lymph nodes. A

CT guided biopsy of the pelvic lymph node showed features of serous adenocarcinoma. She was sent for a second opinion at an outside academic institution and all slides were reviewed by a gynecological pathologist there. Serous uterine cancer was found in the initial biopsy specimen as well as in the pelvic lymph node biopsy specimen. In addition, a small focus of serous carcinoma was found in the hysterectomy specimen. Patient received salvage treatment with concurrent weekly cisplatin with pelvic radiation followed by vaginal brachytherapy, which was complicated with thrombocytopenia and spontaneous subdural hematoma. She also developed gastrointestinal bleeding from extensive arterio-venous malformations. Six months after completion of chemotherapy and pelvic radiation she developed weakness in her right hand and was found to have a 2 cm solitary metastatic lesion in the left frontal area. Stereotactic resection of the brain metastasis was performed and the pathology was consistent with papillary serous carcinoma. Her post-operative course was complicated by bleeding into the surgical site resulting in right hemiparesis. She did not receive brain radiation or chemotherapy due to poor performance status. She was enrolled to hospice thereafter and passed away 34 months after initial diagnosis.

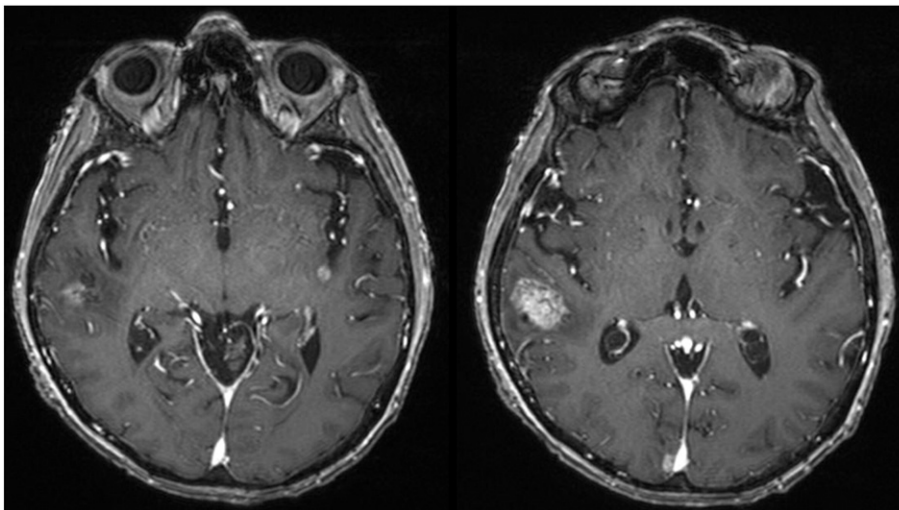


Fig. 2. MRI: Postradiotherapy images with new metastatic lesions. A. 4 mm metastatic lesion in Left frontal lobe abutting the sylvian fissure. B. 6 mm metastatic lesion in the right occipital lobe.

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