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Case Series

Brain metastasis from uterine serous carcinoma: A case report and review of literature

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Introduction

While endometrial cancer is the most common gynecological cancer with a generally favorable prognosis, the histological subtype of serous carcinoma is more aggressive and fortunately uncommon. Uterine serous carcinoma (USC) accounts for about 10% of cases of endometrial cancer and yet 39% of its deaths (Boruta et al., 2009). Brain metastasis from endometrial cancer is also rare, with a rate of 0.6% from a review of over 10,000 patients (Piura and Piura, 2012). This recent review of 35 studies by Piura et al. identified 115 cases of endometrial cancer that metastasized to the brain, of which 4 were USC (Piura and Piura, 2012). A further review of the literature uncovered an additional 4 cases. Here we present a new case from our institution, review the existing literature, and discuss current treatment options.

Case report

The patient is a 55 year-old woman G1P1001 with no significant medical history who was diagnosed with stage IIIC2 USC in Cartagena, Spain. She initially presented with postmenopausal bleeding and pelvic fullness. A CT scan was consistent with an endometrial and left adnexal solid mass, retroperitoneal lymphadenopathy, mild ascites, grades I–II ureterohydronephrosis, and nonspecific pulmonary micronodules. Laboratory studies revealed an elevated CA-125 level of 121 units/mL. Subsequent MRI suggested that the mass invaded greater than 50% of the thickness of the myometrium. In July 2012, she underwent a total abdominal hysterectomy, bilateral salpingo-oophorectomy, pelvic and para-aortic lymph node dissection, omentectomy, and appendectomy, followed by six cycles of carboplatin/paclitaxel, pelvic radiation, and vaginal brachytherapy. She was monitored with serial CT images of the chest/abdomen/pelvis and CA-125 levels. Imaging in April 2013 was negative and CA-125 level was 26 units/mL in May 2013. She then immigrated to the US.

On June 2013, the patient presented to the emergency room with headache and dizziness of 3 days duration. She also reported an episode of urinary incontinence and near-syncope but denied any other focal neurological deficits. Her neurological exam was normal. A head CT scan revealed significant bifrontal edema with suggestion of an underlying lesion. An MRI demonstrated a well-circumscribed heterogeneously enhancing mass involving the anterior body of the corpus callosum and extending superiorly to the falx cerebri, measuring 3.6 × 4.1 cm (Fig. 1). Her CA-125 level was 107 units/mL. A CT of the chest, abdomen and pelvis was negative for metastatic disease.

Later that month, she underwent a bifrontal craniotomy and tumor resection via right sided para-falcine approach. Histology revealed cerebral metastasis from serous carcinoma with immunohistochemistry profile (CK7 +, CK8/18 +, CK20 −, CDX2 −, BRST2 −, TTF1 −) consistent with primary endometrial carcinoma (Fig. 2). Postoperatively, she developed bilateral pulmonary emboli with a saddle embolism component.

The patient was subsequently evaluated for consolidative whole brain radiation (WBRT) vs. stereotactic radiosurgery (SRS) to the postoperative cavity and residual tumor. Due to the size of the postoperative bed, as well as rapid interval post-surgical growth, she was given WBRT followed by chemotherapy (gemcitabine and carboplatin). Residual tumor was left attached to the corpus callosum and pericallosal arteries, as it was thought that aggressive resection of this portion would carry a high risk of post-surgical neurologic morbidity; however about 20 days later, reimaging suggested a continued growth of the residual tumor posteriorly along the corpus callosum and superiorly into the frontal lobes. In February 2014, imaging revealed metastatic lung nodules. As of submission date, she is alive with disease on chemotherapy.

Discussion

USC is an uncommon form of endometrial cancer that rarely metastasizes to the brain. Herein we present a summary of the eight reported cases in the literature; our case report marks the ninth. An extraction of

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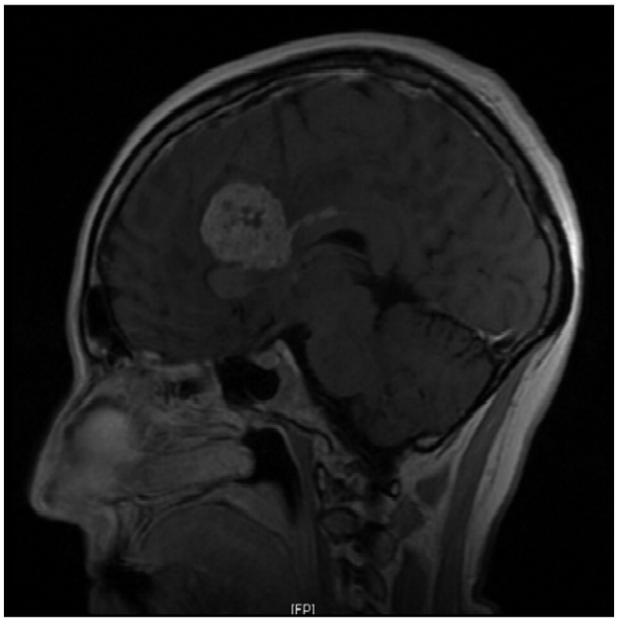

Fig. 1. Preoperative sagittal MRI with IV contrast showing enhancing mass involving the anterior body of the corpus callosum.

clinicopathological features (age, stage, grade, lymphovascular space involvement), time interval to brain metastasis, diagnostic findings (number and location of brain metastases, presence of systemic disease), treatment, and survival is summarized in Table 1 (Petru et al., 2001; Gulsen and Terzi, 2013; Chura JC et al., n.d.; Gien et al., 2004; Talwar and Cohen, 2012; Dietrich et al., 2005; Comert et al., 2012).

Among the nine cases of USC metastatic to the brain, the median age was 69.5 with a median survival of 5 months since diagnosis of brain metastasis. Our case report is the youngest patient at 55 and she is still alive at 12 months, currently undergoing treatment.

The stages of USC were varied, with 4 stage I, 3 stage III, 1 unstaged, and 1 unreported stage. This variation translated into a large interval of diagnosis of brain metastasis from USC, with a median interval of 23 months (range, 0.6 months to greater than 5 years). This is consistent with the previous finding of a median of 17 months (range, 2 to 108 months) for all endometrial carcinoma (Piura and Piura, 2012).

Most of the cancers were high-grade with >50% myometrial invasion and signs of systemic disease at the time of brain metastasis (although 3 cases showed no other sites of metastases). This finding is also similar to Piura et al.'s conclusion that 80% of patients who developed brain metastases from endometrial carcinoma presented with high-grade disease and about half had disseminated disease, although certainly our case series yields far too few numbers to state any definitive conclusions (Piura and Piura, 2012).

The quantity and location of lesions in the nine cases reviewed varied considerably. A third of brain metastatic lesions were solitary, a third were multiple, and a third were unreported. Given that the route of spread is primarily hematological when metastatic to the brain, the lesions demonstrated wide spatial distribution.

The treatments for brain metastasis include: WBRT, excisional surgery (i.e. craniotomy), radiosurgery, and chemotherapy. While metastatic brain tumors are the most common intracranial tumor (typically from the lung, breast, renal, and gastrointestinal cancers), treatment varies according to lesion number, accessibility, and overall prognosis. There is no standard of care for USC brain metastasis given the paucity of cases, although general principles from neurosurgery may be followed. Traditionally, solitary brain lesions would undergo resection followed by WBRT and multiple lesions would receive WBRT (Piura and Piura, 2012). In the present case series, 3 patients underwent surgical resection (1 with a solitary lesion, 1 resected one of three lesions that was causing mass effect, and 1 unspecified lesion) (Petru et al., 2001; Gulsen and Terzi, 2013; Chura JC et al., n.d.). Only 1 patient underwent radiosurgery as part of multimodal therapy and 5 patients underwent WBRT.

Chemotherapeutic regimens for brain metastasis are difficult to select because of the paucity of data for endometrial cancer and the likelihood of concomitant systemic disease—5 of the 9 case reports had

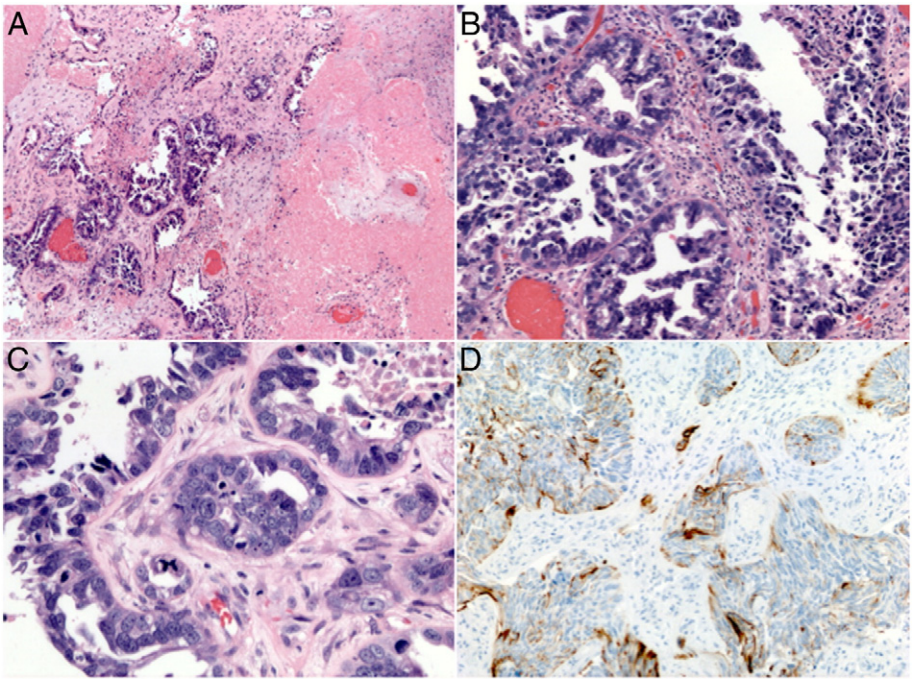

Fig. 2. (A) Microscopic low-power view showing brain parenchyma infiltrated by carcinoma and extensive areas of necrosis (H&E, ×40). (B) Medium-power view showing tumor forming glandular structures and a pseudopapillary arrangement of the tumor cells (H&E, ×200). (C) High-power view showing highly pleomorphic tumor cells and one atypical tetra-polar mitotic figure (blue arrow, H&E, ×400). (D) Tumor cells with positive cytokeratin-7 immunohistochemical stain (CK7, ×200).