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Case report

Hormonal based treatment of ovarian anaplastic ependymoma with anastrozole

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ABSTRACT

Objective: Ovarian anaplastic ependymoma is a rare gynecologic malignancy that poses diagnostic and treatment challenges. Treatment of sub-optimally debulked disease usually portends poor prognosis. Molecular testing of tumor specimen can identify more specific targets for additional therapy such as estrogen and progesterone receptors (ER/PR).

Case: A 29-year-old woman presented with incidental finding of large bilateral adnexal masses and elevated CA 125. Biopsy proved anaplastic ovarian ependymoma with high ER/PR expression. She underwent sub-optimal surgical debulking followed by adjuvant chemotherapy with bleomycin, etoposide and cisplatin (BEP) which resulted in a partial response. Due to extensive residual disease she has been maintained on anastrozole for over fifteen months without increased tumor burden. Targeted somatic mutation testing was negative for all high risk clinically useful variants.

Conclusion: Aromatase inhibitors may be considered in patients with extra-axial anaplastic ependymoma and can produce prolonged stable disease.

1. Introduction

Traditionally, ependymomas are thought to originate from neuroectodermal tissue, most commonly from spinal tissue or in the cranium. However, rarely, these tumors can proliferate outside the central nervous system. It has been theorized that ependymomas in the pelvis can arise from pluripotent stem cells of müllerian origin or from an established ovarian teratoma (Stolnicu et al., 2011).

Ovarian anaplastic ependymoma is a rare malignancy that poses numerous diagnostic and treatment challenges. Pathologic diagnosis is challenging due to diverse histologic characteristics such as: papillary areas with psammoma bodies, pseudofollicles, trabeculae and microcysts. These features and others can lead to misdiagnosis as papillary serous, struma ovarii, granulosa cell, Sertoli-Leydig cell, and wolffian duct tumors. Although only approximately 30% of intracranial ependymoma are classified as malignant, the lack of a uniform histologic definition of anaplasia makes the prognostic significance controversial (Chamberlain, 2003). Anaplastic features include: hypercellularity, cellular and nuclear pleomorphism, frequent mitosis, pseudopalisading necrosis, endothelial proliferation and the hallmark characteristic perivascular rosettes (Reni et al., 2007). Additionally, treatment is challenging due to the aggressive nature of the malignancy which frequently recurs within a year of optimal cytoreduction.

A review of the literature demonstrates that treatment of extra-axial ependymomas has largely revolved around treatment modalities designed for malignant germ cell tumors including surgical debulking followed by adjuvant chemotherapy and targeted radiotherapy. This traditional first-line approach rests with the dogma that four courses of bleomycin, etoposide and cisplatin (BEP) is effective in treatment of patients with incompletely resected ovarian germ cell tumors and should be given to all such patients (Hinton et al., 2003).

2. Case

A 29-year-old female of middle eastern descent was incidentally diagnosed with a complex left ovarian pelvic mass in February 2015. This finding was identified during a hospitalization in Doha, Qatar for complications from elective breast augmentation. Pelvic ultrasound identified adnexal masses and MRI confirmed suspicion for malignancy. She presented to our facility in April 2015 for a second opinion regarding management. CT of the abdomen and pelvis with and without contrast

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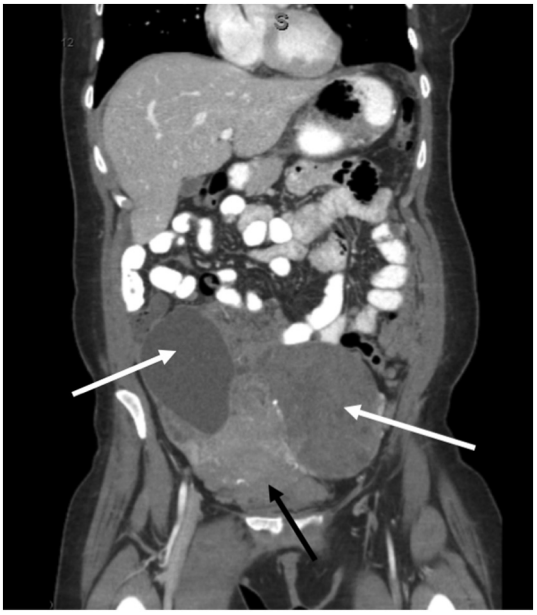

Fig. 1. Ovarian anaplastic ependymoma demonstrated on initial computed tomography (CT) scan at time of diagnosis. Bilateral adnexal masses (white arrows) and bulky pelvic disease (black arrow).

revealed bilateral adnexal masses measuring approximately 14 x 11 cm on the right and 8 × 5.5 cm on the left which appeared inseparable from the uterus, extensive peritoneal carcinomatosis including a 6.3 cm implant in the hepatorenal space, supra and infracolic omental involvement and bilateral pleural effusions (Fig. 1). Tumor marker screen revealed significantly elevated CA-125 of 875 U/mL. In May 2015 she underwent diagnostic laparoscopy with a preoperative presumptive diagnosis of metastatic ovarian cancer. Resulting laparoscopic predictive score was 12 out of 14 (Fagotti et al., 2006). Peritoneal and omental biopsies of suspicious implants were also performed at that time. Review of the final pathology revealed anaplastic ependymoma of extra-axial type. Microscopic examination showed glioneoplasm with formation of prominent perivascular pseudorosettes and focal solid or papillary pattern. Moreover, psammoma bodies were present. The tumor had marked hypercellularity, nuclear atypia and elevated mitotic activity. Immunohistochemical stains revealed tumor cells positive for glial fibrillary acidic protein (95% strong), estrogen receptor (90% strong), progesterone receptor (90% strong), S-100 (focal), WT-1 (focal), P53 (rare) and PAX-8 (patchy), and negative for Sal-like protein 4 (SALL4). Characteristically, the immunostain of epithelial membrane antigen (EMA) exhibited perinuclear dot-like pattern in some well differentiated tumor cells (Liang et al., 2016) (Fig. 2). In June 2015 she underwent uncomplicated exploratory laparotomy, bilateral salpingo-oopherectomy, bilateral ureterolysis and infracolic omentectomy with debulking of approximately 90% of disease. The uterus was left in situ due to extensive adhesive disease and concern for injury to the bladder during dissection. Postoperatively she underwent four cycles of bleomycin, etoposide & cisplatin (BEP) adjuvant chemotherapy. CT scan in September 2015 revealed evidence of residual disease. Molecular testing was performed with a 50-gene somatic mutation analysis panel using PCR-based next generation sequencing developed by the Molecular Diagnostic Laboratory at M.D. Anderson Cancer Center and was negative for all high risk clinically useful variants (Appendix 1). She was started on anastrozole 1 mg daily. The most recent CT chest, abdomen and pelvis performed December 2016 reveals stable peritoneal carcinomatosis. CA-125 levels have also normalized and correlate with disease regression as exemplified (Fig. 3).

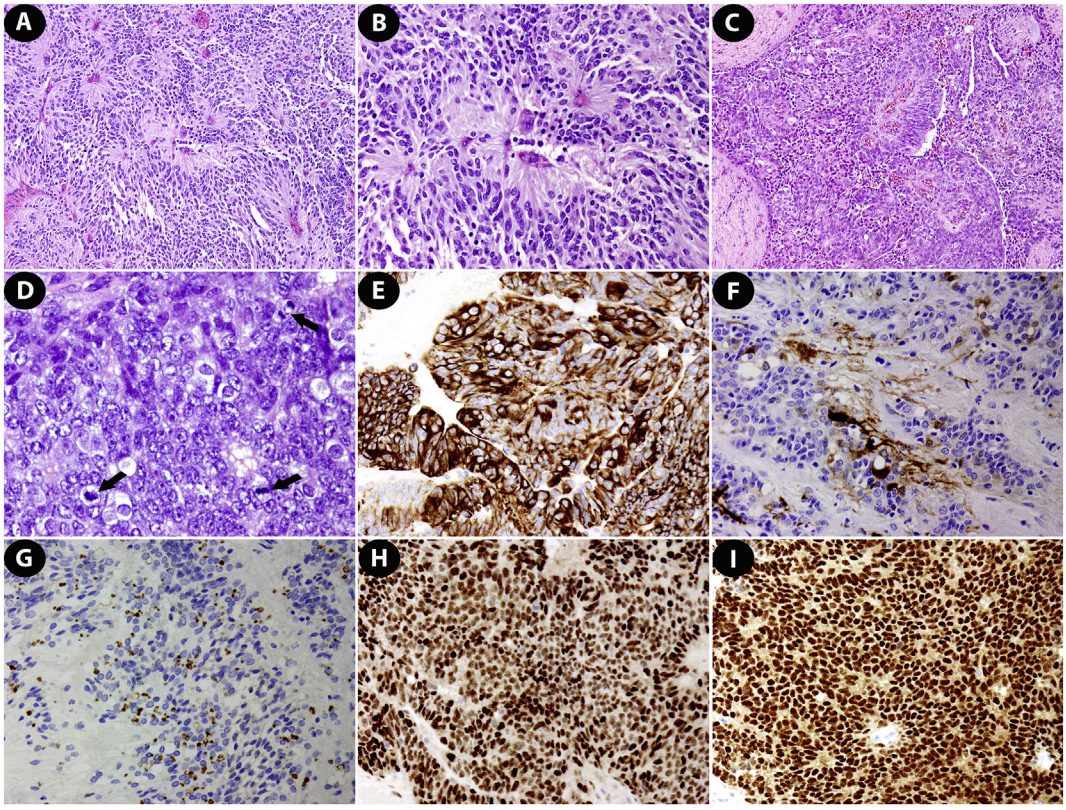

Fig. 2. The anaplastic ependymoma exhibited perivascular pseudorosettes (A & B), papillary (C), and solid architectural patterns with multiple mitotic Figures (D, black arrows). Tumor cells were positive for glial fibrillary acidic protein (E), S-100 (F), epithelial membrane antigen (G), ER (H) and PR (I). A–D, hematoxylin & eosin; E–I, immunohistochemistry; A & C: 100×; B & E–I: 200×; D: 400×.