Persistent Ependymal Tumor arising from an Immature Ovarian Teratoma: A Rare Case

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Abstract

Primary ovarian ependymoma is a rare neuroectodermal neoplasm that can arise from immature ovarian teratoma. Due to the paucity of this entity, a complete molecular analysis of these tumors has not been done, thus creating a challenge for finding an effective and safe therapeutic treatment. In limited literature, patient with primary ovarian ependymoma showed various responses to an array of individualized therapies ranging from surgeries and chemotherapies. Here, we present a 38-year-old female with persistent ovarian ependymoma with molecular profile similar to traditional central nervous system ependymoma that is irresponsive to multiple cytoreduction and clinical experimental therapies. Therefore, a prompt recognition and reporting of this entity can greatly aid in expanding the understanding and standardization of therapies for this neoplasm.

Keywords: Ependymoma; teratoma; ovarian; immature teratoma

Introduction

Ependymoma is a glial neoplasm with ependymal differentiation that primarily arises in the central nervous system. However, central nervous system (CNS) type tumors can rarely arise from ovarian immature teratoma. First ovarian ependymoma was reported by Kleinman and colleagues in 1984 [1]. Since then, few cases of primary ovarian ependymoma have been reported in literature [2,3]. Primary ovarian ependymoma is thus classified as neuroectodermal tumor arising from pluripotent stem cells from Mullerian origin according to female reproductive tumor classification. Limited studies suggest that there may be a difference in molecular profile of CNS and extra-axial ependymoma [4]. However, a larger cohort consisting of the two entities

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with comprehensive molecular analysis is warranted to clarify the abnormal molecular events leading to these neoplasms.

Case Presentation

Our patient is a 38-year-old female, gravida 0 with a past medical history significant for profound vision loss since age 12 due to retinitis pigmentosa and polydactyly removal at birth and at age 1. She initially presented with multiple pelvic masses with suspicion of omental metastatic disease in May of 2016. Initial tumor marker panel revealed elevated CA(Cancer Antigen) of 379 U/mL, normal CA19-9 (12 U/mL), CEA(carcinoembryonic antigen) of <0.5 ng/mL), and hCG(human chorionic gonadotropin) of <1 ng/mL. Cytology specimen of interventional radiology guided paracentesis showed cellular sample with atypical cells positive for CK(Cytokeratin)7 and negative for homeobox protein CDX-2, CK(Cytokeratin)20, chromogranin, and TTF(Thyroid transcription factor)-1.

Patient underwent laparoscopic diagnostic biopsy and paracentesis with intraoperative impression of suspicious stage III ovarian tumor. Final pathology report showed neoplasm that is histologically and molecularly consistent with ependymoma. Microscopic sections of the abdominal wall and falciform ligament tumor revealed round to oval nuclei with a fine “salt and pepper” chromatin pattern, perivascular pseudo rosette formation, and rare true ependymal rosette formation (Figure 1A-1D). There were areas of elevated mitotic activity, vascular proliferation and necrosis. Multiple architectural patterns, including classical, papillary, and clear cell areas were present. Tumor cells were diffusely positive for Glial fibrillary acidic protein (GFAP) (Figure 1E) with characteristic dot-like Epithelial Membrane Antigen (EMA) positivity (Figure 1F) and focal positivity for CK7 (Figure 1G). Genomic evaluation revealed abnormal gain of 15q11.1q13.1, gain of15q22.2q26.3, gain of chromosomes 4, 7, 8, 9, 10, 12, 14, 16, 18, 20, 21, and X, and loss of chromosomes 6, 17, and 22.

Patient was placed on Bleomycin, Cisplatin, and Etoposide combination chemotherapy from June of 2016 to September of 2016. Bleomycin was later discontinued due to significant pulmonary side effects. Repeat peritoneal biopsy on 09/27/2016 showed persistent disease. Patient was subsequently placed on multiple clinical trials but she was found to be unresponsive to all of them. Repeat peritoneal biopsy (Figure 1H-1I) on 07/01/20 is consistent with persistent disease.

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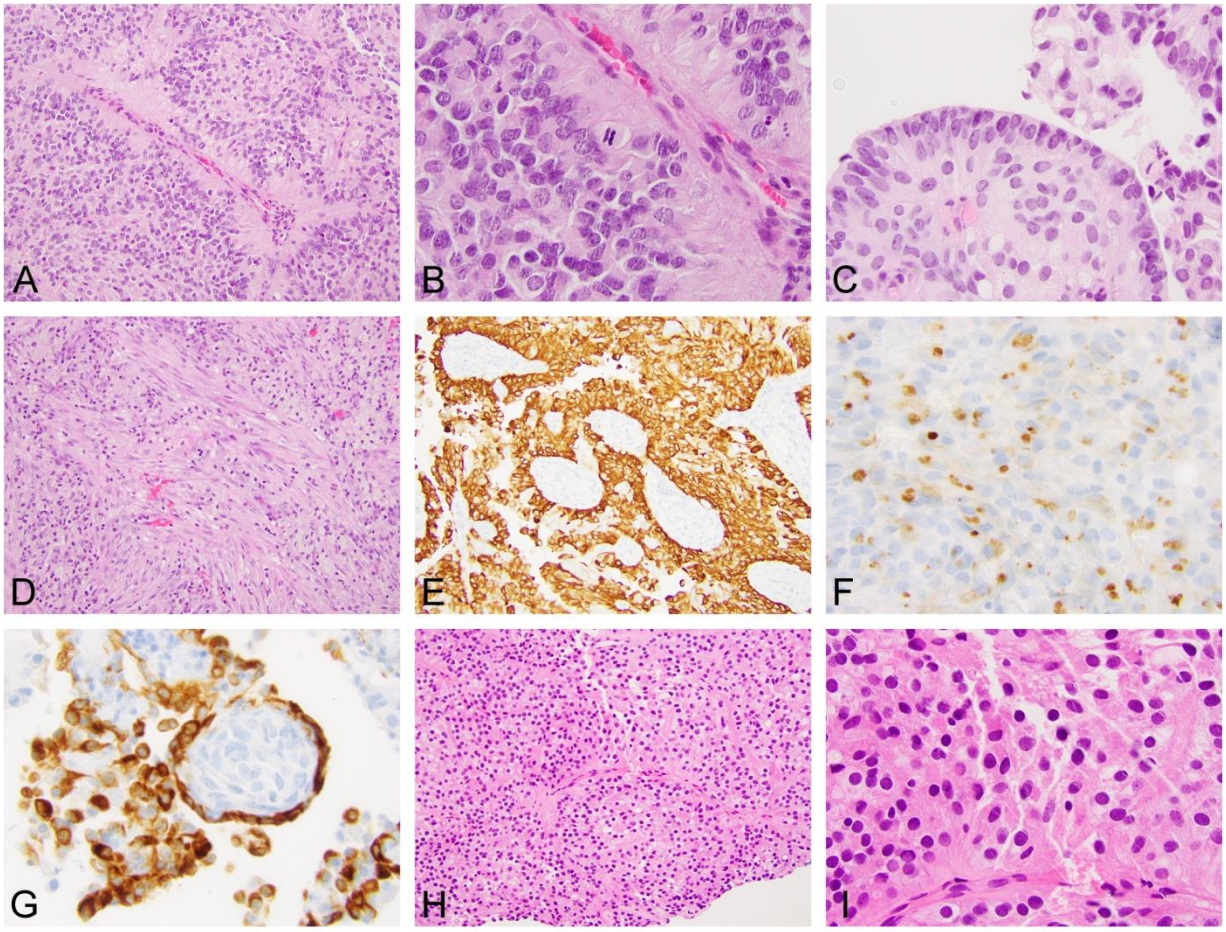

Figure 1: H&E sections from initial biopsy (A, B, C and D) highlight a solid tumor with cells having round to oval nuclei and stippled chromatin, perivascular pseudo-rosette, and rare true ependymal rosette formation. Tumor cells show diffuse positivity for GFAP (E), characteristic dot-like positivity for EMA and focal positivity for CK7 (G). Repeat peritoneal biopsy (H and I) showed persistent disease.

Discussion

Ependymoma is a glial neoplasm with ependymal differentiation that primarily arises in the central nervous system. However, central nervous system (CNS)-type tumors can rarely arise from ovarian immature teratoma. First ovarian ependymoma was reported by Kleinman and colleagues in 1984 [1]. Since then, few cases of primary ovarian ependymoma have been reported in literature [2-4]. Primary ovarian ependymoma is thus classified as neuroectodermal tumor arising from pluripotent stem cells from Mullerian origin according to female reproductive tumor classification. Ependymoma arising in immature teratoma can be molecularly distinct from its CNS counterpart despite its histological resemblances [4]. The comprehensive molecular

analysis of our case revealed genetic abnormalities that are compatible with CNS ependymoma suggesting a larger cohort consisting of the two entities with comprehensive molecular analysis is warranted to fully characterize the two seeming distinct entities. Due to the rarity of this entity and lack of complete molecular analysis of these neoplasms, there is no standardized therapeutic treatment available for ovarian ependymoma. The treatment of extra-axial ependymomas is currently individualized, which can include surgical debulking with adjuvant chemotherapy, surgical approach combined with adjuvant chemotherapy and radiation [4], or treated with approved or clinical experimental chemotherapies [4]. These different therapeutic approaches have shown various degrees of success likely due to different onset disease stages and extent of the tumor involvement [1-6]. Some cases of ovarian ependymoma can be satisfactorily treated with surgery without chemotherapy. It is therefore important to be able to differentiate primary ovarian ependymoma from CNS ependymoma. Our patient had a molecular profile similar to CNS ependymoma and it might have contributed to the reason why she didn't respond initially to the conventional approach of treating extra-axial ependymomas with surgical debulking and chemotherapy. A larger cohort with comprehensive molecular analysis is warranted to clarify the abnormal molecular events leading to these neoplasms.

Conclusions

Encountering a low metastatic potential CNS tumor extra-axially should prompt investigation of a possible associated germ cell tumor. An accurate and rapid recognition and reporting of neuroectodermal tumors arising from gynecologic tract with comprehensive molecular analysis of the primary tumor and recurrence is vitally important for expanding the knowledge of these extra-axial CNS tumors and searching for an effective standardized therapy.

Conflicts of interest: None

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