Primary Ovarian Ependymoma: A Diagnostic Challenge Resolved by Immunohistochemistry. A Case Report

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DOI: https://doi.org/10.68050/JAMS.2026.573

Received: 21 Sept 2026; Accepted: 22 Sept 2026; Published: 23 September 2026

ABSTRACT

Primary ovarian ependymoma is an exceptionally rare tumor, a distinct nosological entity separate from central nervous system metastases, for which no standardized therapeutic recommendations exist. We report the case of a 25-year-old young woman admitted with abdominal and pelvic pain, in whom a computed tomography (CT) scan revealed a large bilateral ovarian tumor mass. Microscopic examination of the resection specimens, with confirmation by an expert reference center, revealed characteristic perivascular pseudorosettes and ependymal rosettes, with no associated teratomatous elements. Immunohistochemical studies showed positivity for glial fibrillary acidic protein (GFAP), estrogen receptors (ER), and progesterone receptors (PR), focal expression of epithelial membrane antigen (EMA), and a Ki-67 proliferation index of 10%. Negativity for cytokeratins, Inhibin, and WT1 ruled out the main differential diagnoses. A thorough neurological evaluation and brain/spinal imaging excluded a central nervous system primary, confirming the primary ovarian origin. Classified as stage III bilateral ovarian ependymoma, the patient underwent cytoreductive surgery followed by adjuvant chemotherapy. This case illustrates that, although exceptionally rare, primary ovarian ependymoma must be considered a differential diagnosis in young women presenting with an ovarian mass, and highlights the crucial role of collaboration with expert pathology reference centers for an accurate diagnosis.

Keywords: Ovarian ependymoma; Rare ovarian tumor; Immunohistochemistry; Young woman; Cytoreductive surgery.

INTRODUCTION

Primary ovarian ependymoma is a rare tumor belonging to the group of extra-axial primitive neuroectodermal tumors. It is characterized by ependymal differentiation analogous to that observed in central nervous system (CNS) tumors. It is an exceptional entity, documented primarily by isolated case reports or small series. This rarity considerably limits the establishment of standardized diagnostic and therapeutic recommendations, rendering its classification and management heterogeneous and non-consensual.

CASE REPORT

We report the case of a 25-year-old patient with no significant pathological history, who consulted in May 2015 for the discovery of an abdominal mass. The clinical examination confirmed the presence of a palpable mass in the left iliac fossa. The imaging work-up was revealing. An abdominal CT scan showed a large abdominopelvic mass associated with peritoneal carcinomatosis. A pelvic magnetic resonance imaging (MRI) was then performed, revealing a large, bilateral, multiloculated ovarian mass with solid and cystic components and areas of hemorrhagic remodeling. This mass measured 20 x 18 x 8 cm and showed massive and heterogeneous enhancement after contrast injection. It displaced the uterus anteriorly and the small intestines

posteriorly, without obvious signs of invasion of neighboring organs. A large-volume ascites was also present. Serum tumor markers, particularly CA 125, CEA, and AFP, were within normal limits.

The patient was managed surgically with the goal of maximal cytoreduction. Anatomopathological examination of the surgical specimen revealed a tumor with characteristic ependymal differentiation. Microscopically, numerous perivascular pseudorosettes (Fig1) and true ependymal rosettes were observed, (Fig 2) associated with tumor cells showing eosinophilic fibrillary cytoplasm and elongated nuclei**.** Nuclear atypia was mild to moderate and mitotic activity was low / 2 mitoses per 10 HPF. Areas of necrosis were absent. Extensive sampling of the specimen did not reveal any mature or immature teratomatous elements or other germ cell components.

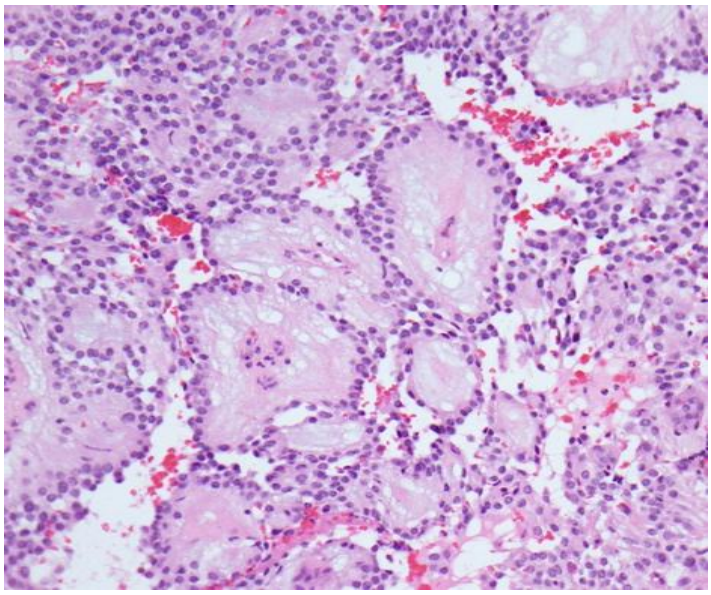

Figure 1: H&E stain showing perivascular pseudorosettes

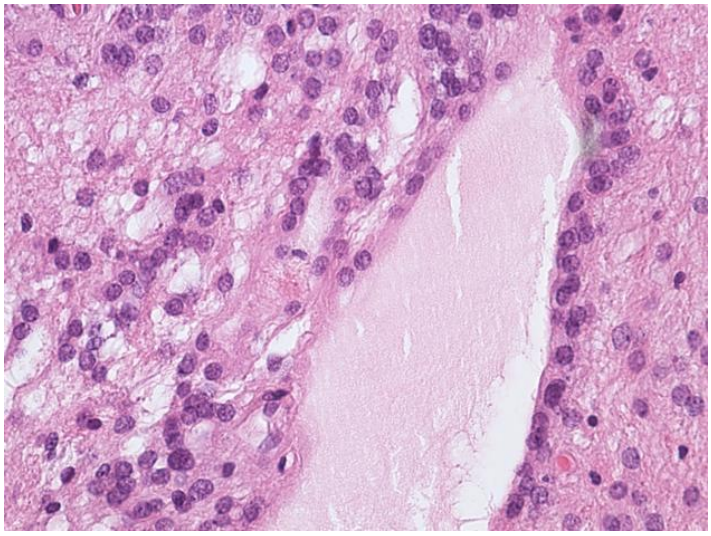

Figure 2: True ependymal rosettes on H&E staining

Immunohistochemical studies, supplemented by expert review, allowed for the definitive diagnosis. Tumor cells showed strong and diffuse positivity for GFAP, confirming glial differentiation, as well as positivity for ER and PR. EMA expression was focal and dot-like (Fig 3) . The Ki-67 proliferation index was approximately 10%. To exclude differential diagnoses, additional markers were performed: the tumor was negative for cytokeratins (AE1/AE3), ruling out an epithelial carcinoma (such as small cell carcinoma); negative for Inhibin, excluding a sex cord-stromal tumor; and negative for WT1, ruling out a serous carcinoma.

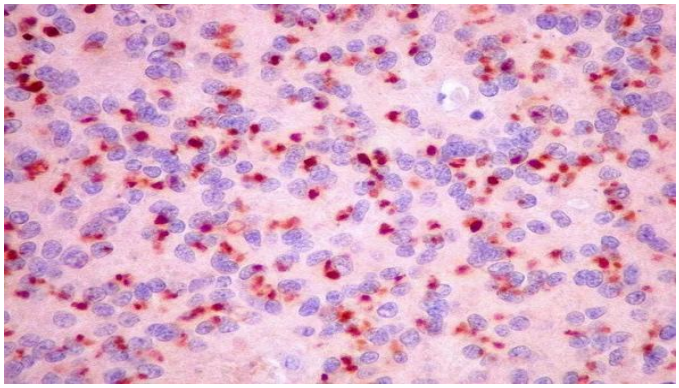

Figure 3: EMA immunostaining (focal dot-like positivity)

To definitively exclude a metastatic ependymoma from the central nervous system, a thorough neurological assessment was performed (unremarkable), and brain and whole-spine MRI scans showed no evidence of a primary CNS tumor.

In the presence of residual tumor mass, adjuvant chemotherapy was initiated, combining vincristine, dactinomycin, cyclophosphamide, and doxorubicin. Clinical and radiological evaluation after three cycles showed stable disease. However, tumor progression was observed after the fifth cycle. A second-line chemotherapy regimen, combining carboplatin and paclitaxel, was then initiated, again achieving stable disease after four cycles. Facing a new increase in abdominal volume, the patient underwent a second surgical intervention for the resection of residual lesions. Histological examination confirmed the recurrence of the ovarian ependymoma. Post-operative CT and MRI scans revealed no measurable residual lesions. A third-line treatment with bevacizumab and temozolomide was initiated. The patient is currently under clinical and radiological surveillance.

DISCUSSION

Histogenesis and Histological Features The exact histogenesis of primary ovarian ependymomas remains a subject of debate. Three main hypotheses are considered: aberrant somatic differentiation of totipotent germ cells, neuroectodermal differentiation within ovarian teratomas, or, more rarely, direct ependymal differentiation from ovarian stromal cells. Histologically, the tumor faithfully reproduces the morphological characteristics of ependymomas of the central nervous system. The presence of true ependymal rosettes and perivascular pseudorosettes, associated with tumor cells with eosinophilic fibrillary cytoplasm and elongated nuclei, is a key diagnostic feature. The potential for malignancy, which can range from indolent to aggressive behavior, is conditioned by the degree of nuclear atypia and mitotic activity.

Contribution of Immunohistochemistry (IHC) Immunohistochemical study is fundamental for confirming the diagnosis and ruling out differential diagnoses. The profile of an ovarian ependymoma is characterized by strong expression of glial markers, particularly GFAP and vimentin, supporting its neuroectodermal origin. Expression of Epithelial Membrane Antigen (EMA) may be observed but is often focal and inconsistent. Conversely, the negativity of ovarian epithelial markers is equally crucial. Negativity for cytokeratins (AE1/AE3) helps to exclude an epithelial carcinoma, while negativity for Inhibin and WT1 allows for the exclusion of a sex cord-stromal tumor and a serous carcinoma, respectively, which are the main differential diagnoses (Figure 1).

Differential Diagnosis The differential diagnosis for an ovarian mass in a young woman is broad. IHC is therefore essential to distinguish ependymoma from other tumors that may present morphological or radiological similarities. The main differential diagnoses include serous carcinoma (usually WT1+, CK+), small cell carcinoma (AE1/AE3+, EMA+), and sex cord-stromal tumors (Inhibin+, FOXL2+). The immunohistochemical profile of our case (GFAP+, focal EMA+, CK-, Inhibin-, WT-) allowed for the definitive confirmation of the diagnosis of primary ovarian ependymoma.

Molecular Aspects and Perspectives Molecularly, data remain limited due to the extreme rarity of this entity. However, some forms of ovarian ependymomas share genetic alterations with extra-cranial ependymomas, particularly abnormalities in the NF2 pathway. Transcriptomic profiles similar to those of spinal-type ependymomas have also been reported. The accumulation of such molecular data through international collaborations will be essential in the future to better understand the biology of this tumor and identify potential therapeutic targets.

Clinical Implications and Management Clinically, ovarian ependymoma mainly affects young or middle-aged women and most often presents as a pelvic mass. Its biological behavior is unpredictable, justifying multidisciplinary management and prolonged follow-up. The rarity of this tumor explains the lack of a therapeutic consensus, making the treatment strategy, which combines cytoreductive surgery and chemotherapy, largely empirical, as illustrated by our case.

CONCLUSION

Primary ovarian ependymoma must be recognized as a distinct nosological entity, although related to ependymomas of the central nervous system. It shares a common glial differentiation while presenting its own specific clinical and biological features. A better understanding of its molecular foundations, particularly through large-scale genomic and epigenomic analyses, is essential to elucidate whether it represents an ectopic location of the same tumor continuum or a biologically independent entity. To this end, the publication of rigorously documented cases and the establishment of international registries are essential to refine the classification, prognosis, and therapeutic strategies for this rare tumor.

Conflict of Interest: The authors declare that they have no conflicts of interest related to this article.

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