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Case Report

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Management of recurrent adult granulosa cell tumor in a resource-limited setting: a case report and review of systemic therapy evidence

Abstract

Background: Adult granulosa cell tumors (AGCTs) are rare, low-grade malignant ovarian neoplasms of sex cord-stromal origin. They are characterized by an indolent clinical course but possess a significant propensity for late recurrence. Early detection and appropriate intervention are crucial, particularly in resource-limited settings where advanced diagnostic tools and standard chemotherapeutic agents are often constrained.

Case presentation: A 35-year-old nulliparous woman presented with a two-month history of progressive abdominal pain, swelling, and vomiting. Initial imaging suggested a malignant teratoma. Exploratory laparotomy revealed a ruptured left ovarian mass measuring 8×15 cm. Histopathological examination confirmed an adult granulosa cell tumor, staged as FIGO IC2 due to preoperative capsule rupture. Three years post-surgery, she presented with recurrent abdominal swelling. Clinical assessment and imaging confirmed a right ovarian recurrence accompanied by severe ascites. Following emergency surgical debulking, systemic therapy was indicated. Due to the unavailability of Bleomycin in the local setting, a pragmatic chemotherapy regimen of Cisplatin and Etoposide (EP) was initiated. The patient completed six cycles with a favorable clinical response, characterized by the complete resolution of ascites and significant symptomatic improvement.

Conclusion: This case highlights the diagnostic and therapeutic challenges associated with managing recurrent AGCTs in resource-limited environments. It emphasizes the necessity of maintaining a high index of clinical suspicion for recurrence, the critical role of timely surgical debulking, and the pragmatic application of available chemotherapy regimens, such as the EP doublet, when standard protocols are inaccessible.

Keywords: adult granulosa cell tumors, malignant ovarian neoplasms, cisplatin and etoposide, chemotherapy

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Introduction

Ovarian adult granulosa cell tumors (AGCTs) are rare neoplasms, representing approximately 2% to 5% of all ovarian malignancies and the majority of malignant sex cord-stromal tumors.[1] Unlike the more common epithelial ovarian carcinomas, AGCTs typically exhibit an indolent clinical behavior and are often diagnosed at an early stage (FIGO Stage I).[2] However, a defining characteristic of AGCTs is their tendency for late recurrence, which can occur decades after the initial diagnosis, necessitating lifelong clinical surveillance.[3]

The standard management for primary AGCT is surgical staging and resection. For patients with advanced-stage disease or recurrent tumors, systemic therapy is often required. The most widely recommended first-line chemotherapy is the platinum-based combination of Bleomycin, Etoposide, and Cisplatin (BEP).[4] In low- and middle-income countries (LMICs), the management of recurrent AGCT is frequently complicated by systemic healthcare challenges. These include limited access to advanced diagnostic imaging, the unavailability of specific tumor markers such as Inhibin B for monitoring disease status, and frequent shortages of essential chemotherapeutic agents like Bleomycin.[5]

This case report details the management of a recurrent AGCT in a 35-year-old patient in The Gambia. It underscores the importance of strengthening healthcare infrastructure and demonstrates how pragmatic, cost-effective treatment protocols specifically the use of an Etoposide and Cisplatin (EP) regimen can be successfully tailored to resource-constrained environments to achieve favorable clinical outcomes.

Case presentation

Initial presentation and diagnostic pathway

In October 2021, a 35-year-old nulliparous woman presented to the gynecology clinic at the Edward Francis Small Teaching Hospital (EFSTH) in Banjul, The Gambia. She reported a two-month history of progressive abdominal pain, increasing abdominal girth, and recurrent vomiting. Physical examination revealed a hemodynamically stable patient with grade 3 bipedal edema and uniform, tense abdominal distension suggestive of massive ascites.

The diagnostic evaluation proceeded from clinical suspicion to imaging. An initial abdominopelvic ultrasound demonstrated massive ascites and a large, solid-cystic pelvic mass. A subsequent computed tomography (CT) scan suggested a left ovarian malignant teratoma as the primary differential diagnosis. Preoperative laboratory investigations, including complete blood count and basic metabolic panel, were within normal limits. Specific tumor markers for sex cord-stromal tumors, such as Inhibin B, were unavailable in the local laboratory.

Surgical management and staging

The patient underwent an exploratory laparotomy. Intraoperative exploration revealed a ruptured, friable left ovarian mass measuring

approximately 8×15 cm, which had resulted in the accumulation of roughly six liters of ascitic fluid within the peritoneal cavity. The contralateral right ovary, fallopian tubes, uterus, and other intra-abdominal organs appeared grossly normal. A left salpingo-oophorectomy and omentectomy were performed.

Histopathological examination of the excised surgical specimen confirmed the diagnosis of an Adult Granulosa Cell Tumor. Based on the 2014 International Federation of Gynecology and Obstetrics (FIGO) criteria, the tumor was staged as IC2, specifically due to the preoperative rupture of the ovarian capsule, which inherently leads to the spillage of tumor cells into the peritoneal cavity.[6]

Recurrence and multidisciplinary management

Three years following her initial surgery, the patient returned to the hospital with a three-month history of recurrent abdominal pain and progressive swelling. Given the presentation of ascites, she was initially referred to the internal medicine department with a working diagnosis of suspected liver cirrhosis or abdominal tuberculosis, conditions highly prevalent in the region. However, a repeat abdominopelvic ultrasound identified a complex, heterogeneous pelvic mass consistent with a right ovarian recurrence, accompanied by severe ascites.

The patient underwent a second emergency exploratory laparotomy for optimal tumor debulking. Following the surgical intervention, the multidisciplinary oncology team convened to discuss systemic therapy options. While the BEP regimen is considered a standard of care for recurrent sex cord-stromal tumors, Bleomycin was unavailable in the national pharmacy supply chain at the time. Consequently, a pragmatic clinical decision was made to initiate a two-drug chemotherapy regimen consisting of Cisplatin and Etoposide (EP).

The patient received six cycles of the EP regimen, administered every 21 days. In the absence of specific biochemical tumor markers like Inhibin B, the treatment response was meticulously monitored through serial clinical examinations, focusing on abdominal girth and symptomatic relief, alongside follow-up ultrasound imaging. The patient demonstrated a complete clinical response, characterized by the total resolution of ascites and the absence of palpable masses. She currently remains under close, regular gynecologic follow-up.

Discussion

Rationale for the selected regimen

The management of recurrent AGCT in resource-limited settings requires a delicate balance between adhering to evidence-based international protocols and adapting to local resource availability. The BEP regimen is widely recognized as an effective systemic therapy for sex cord-stromal tumors.[4] However, the unavailability of Bleomycin; a frequent logistical challenge in LMICs necessitated the utilization of the EP doublet in this case.

Both Etoposide and Cisplatin are potent antineoplastic agents against SCSTs. The EP regimen has been historically utilized as a viable alternative in clinical scenarios where Bleomycin toxicity (such as pulmonary fibrosis) is a significant concern, or when the drug is simply inaccessible.[7] Recent systematic reviews evaluating the response to systemic therapies in ovarian AGCTs indicate that while the objective response rate (ORR) to chemotherapy may be modest (approximately 30%), the disease control rate (DCR)—which includes patients achieving stable disease—is moderate, approaching 58%.[8] Achieving stable disease is a highly relevant clinical endpoint in AGCT management, as it offers the benefit of postponing further clinical deterioration and prolonging the interval between necessary surgical interventions, thereby reducing overall patient morbidity.[8]

Decision-making without advanced diagnostic tools

Inhibin B is established as a highly sensitive and specific serum marker for monitoring AGCT recurrence and evaluating treatment response.[9] In healthcare settings where such advanced biochemical markers are unavailable, clinical decision-making must rely heavily on fundamental medical practices. High-quality, serial physical examinations are paramount for monitoring changes in abdominal girth and detecting the re-emergence of pelvic masses. Furthermore, the utilization of serial ultrasound imaging serves as a cost-effective and accessible modality for detecting early anatomical recurrence. This case underscores the necessity of surgical vigilance; prompt operative intervention is critical when clinical and imaging findings suggest recurrence, even in the absence of confirmatory biochemical markers.

Contribution to existing evidence

This report contributes to the sparse literature regarding the management of rare ovarian tumors in West Africa and other resource-constrained regions.[10] It clearly demonstrates that even in the absence of "gold standard" diagnostic and therapeutic tools, favorable patient outcomes can be achieved. Timely surgical debulking remains the absolute cornerstone of management for recurrent AGCT disease.[11] Furthermore, the pragmatic application of chemotherapy, specifically demonstrating that the EP regimen can be an alternative, is crucial for clinicians operating in similar environments. However, as this is a single case report, the effectiveness of the EP regimen in recurrent AGCT cannot be generalized, and larger case series are needed.

Importantly, this case highlights the concept of clinical stewardship. It emphasizes the critical need for healthcare providers to maintain a high index of suspicion for recurrence in patients with a history of AGCT, regardless of the time elapsed since the primary diagnosis. Misdiagnosing late recurrences as more common regional pathologies, such as cirrhosis or tuberculosis, can delay life-saving surgical and systemic interventions.

Conclusion

Adult Granulosa Cell Tumors present unique and complex challenges in resource-limited settings due to their rarity, the necessity for long-term clinical monitoring, and frequent supply chain constraints for standard chemotherapeutics. This case illustrates a favorable short-term clinical outcome using a strategic combination of aggressive surgical debulking and pragmatic, adapted chemotherapy (such as the EP regimen). It serves as a call to action for increased awareness among clinicians in LMICs to accurately identify late recurrences and avoid misdiagnoses. Ultimately, strengthening local pathology services, improving access to basic tumor markers, and ensuring a consistent supply of essential chemotherapeutic agents remain vital.

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Conflicts of interest

There is no competing interests between the authors.

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