TPM Vol. 32, No. S2, 2025
ISSN: 1972-6325
https://www.tpmap.org/

Open Access

ISOLATED PRESACRAL LOW-GRADE ENDOMETRIOID OVARIAN CARCINOMA – A RECURRENCE CASE

[1]KALPANA L, [2]MOHANA PRIYA, [3]DR. RANJITH MARI
[1]POST GRADUATE, DEPARTMENT OF OBSTETRICS AND GYNAECOLOGY , SAVEETHA MEDICAL COLLEGE, SAVEETHA UNIVERSITY, CHENNAI,TAMIL NADU , INDIA
[2]ASSOCIATE PROFESSOR, DEPARTMENT OF OBSTETRICS AND GYNAECOLOGY , SAVEETHA MEDICAL COLLEGE, SAVEETHA UNIVERSITY, CHENNAI,TAMIL NADU , INDIA
[3]SENIOR LECTURER, DEPARTMENT OF PERIODONTOLOGY, SREE BALAJI DENTAL COLLEGE & HOSPITAL, CHENNAI, INDIA

Abstract
Ovarian cancer, primarily epithelial ovarian carcinomas (EOCs), is a leading cause of gynecological cancer mortality. Among EOCs, low-grade endometrioid ovarian carcinoma (LG-EOC) accounts for 10–15% of cases, characterized by a favorable prognosis but significant potential for recurrence. This case discusses a 44-year-old female with recurrent isolated presacral LG-EOC managed with secondary cytoreductive surgery. Diagnosed in 2021, she presented with a multiloculated cystic lesion on surveillance imaging, later confirmed by MRI and PET-CT to exhibit hypermetabolic activity suggestive of recurrence. She underwent successful secondary cytoreductive surgery, achieving optimal debulking without residual disease. Histopathology confirmed low-grade endometrioid carcinoma, and immunohistochemistry showed intact nuclear expression of mismatch repair (MMR) proteins (MLH1, MSH2, MSH6, PMS2), ruling out microsatellite instability-high (MSI-H). This result excluded Lynch syndrome and suggested a competent DNA repair system, influencing her management and prognosis. The patient's postoperative course was uneventful, and she was discharged with instructions for follow-up and genetic counseling. This case highlights the role of meticulous surgical management and histopathological evaluation in recurrent LG-EOC. It also underscores the importance of individualized approaches, particularly in assessing molecular markers like MMR proteins, which guide therapeutic decisions and genetic risk evaluation. Secondary cytoreduction remains crucial for improving survival in recurrent ovarian cancer.

INTRODUCTION

Ovarian cancer remains a leading cause of gynecologic cancer-related mortality worldwide, with epithelial ovarian carcinomas (EOCs) constituting approximately 90% of cases (1). Among EOCs, endometrioid ovarian carcinoma represents a distinct histologic subtype, accounting for 10–15% of cases (2). This subtype is characterized by glandular patterns reminiscent of endometrial carcinoma and is generally associated with a more favorable prognosis compared to high-grade serous carcinomas (3).

Low-grade endometrioid ovarian carcinomas are typically indolent but can present challenges due to their potential for recurrence and resistance to conventional therapies. The management of recurrent disease often involves secondary cytoreductive surgery, aiming to achieve optimal tumor debulking, which has been associated with improved survival outcomes in select patients (3). However, the decision to pursue secondary cytoreduction must be individualized, considering factors such as the extent of disease, patient performance status, and the interval since initial treatment (3).

Histopathological evaluation remains a cornerstone in the diagnosis and management of ovarian carcinomas. The assessment of mismatch repair (MMR) protein expression is particularly pertinent, as deficiencies in MMR proteins can lead to microsatellite instability (MSI), a condition observed in various malignancies, including ovarian cancer (4). MSI status has implications for prognosis and therapeutic strategies, especially concerning the potential efficacy of immune checkpoint inhibitors. In endometrioid carcinomas, MMR deficiency is more prevalent compared to other ovarian cancer subtypes, underscoring the importance of routine MMR protein evaluation in these tumors (4,5).

This case report discusses a 44-year-old female patient with recurrent low-grade endometrioid ovarian carcinoma who underwent secondary cytoreductive surgery. We emphasize the histopathological findings, particularly the intact expression of MMR proteins, and discuss the implications for the patient's management and prognosis.

Case Details

Patient Presentation

A 44-year-old female presented with a known history of low-grade endometrioid ovarian carcinoma, initially diagnosed on April 17, 2021, following evaluation for pelvic pain and menstrual irregularities. She had undergone initial cytoreductive surgery and subsequent follow-up at Isabella Hospital, Mylapore, with regular imaging studies. Over time, recurrent disease was noted during routine surveillance.

History of Present Illness

On November 10, 2022, during a regular follow-up, a multiloculated cystic lesion of size 5.4 cm × 4.9 cm was identified on ultrasound (USG) in the pelvic region. Further imaging with MRI on November 14, 2022, confirmed a suspicious cystic lesion (5.8 × 4.5 × 5.5 cm) in the left hemipelvis, adherent to the vaginal vault and anterior abdominal wall. The lesion was associated with an eccentric solid nodule, raising concerns for disease recurrence. A PET-CT scan on November 11, 2022, demonstrated hypermetabolic activity in the same region with an SUV value of 4.8, suggesting high metabolic turnover and confirming suspicion of recurrent malignancy. No evidence of distant lymph node or visceral metastasis was detected. At this stage, the patient was planned for secondary cytoreductive surgery to optimize tumor removal.

Past Medical History

The patient had a known history of:

- Systemic hypertension, managed with Tab. Telmikind H (40 mg/12.5 mg) and Tab. Cilacar (5 mg).
- Type II diabetes mellitus for 4 years, controlled with Tab. Vinglyn M (5/500 mg).
- Bronchial asthma, intermittently managed with Foracort 200 mg inhaler.

The patient denied any history of coronary artery disease (CAD), kidney disorders, or seizures.

Clinical Examination

On admission, the patient was clinically stable.

- General Examination: Afebrile, alert, conscious, oriented. No signs of lymphadenopathy, cyanosis, or pedal edema.
- Vitals:
  - Blood Pressure (BP): 120/70 mmHg
  - Pulse Rate (PR): 78/min
  - Respiratory Rate (RR): 18/min
  - Temperature: 96.5°F
- Systemic Examination:
  - Cardiovascular: S1, S2 normal; no murmurs.
  - Respiratory: Bilateral air entry present; no adventitious sounds.
  - CNS: No focal neurological deficits.
  - Per Abdomen: Soft; on bimanual examination, a tense cystic lesion was palpable in the pouch of Douglas (POD), more prominent on the left side.

Procedure

The patient underwent secondary cytoreductive surgery on November 18, 2022, under combined epidural anesthesia (EA) and general anesthesia (GA).

- Operative Findings:
  - Frozen pelvis with extensive adhesions involving the anterior abdominal wall, bladder surface, and posterior vaginal vault.
  - The cystic lesion, measuring 5 × 4 cm, was found in the presacral region, adhering posteriorly to the rectum and anteriorly to the vaginal vault.
  - Adhesiolysis was performed meticulously to free the cystic lesion from surrounding structures.
  - Excision of the lesion was achieved with careful dissection, and bowel integrity was maintained despite evidence of minor serosal tears, which were promptly repaired.
  - Blood loss during the procedure was approximately 100 ml; no intraoperative transfusions were required.

Postoperatively, the patient was transferred to the Intensive Care Unit (ICU) for close monitoring.

Postoperative Course

The patient’s postoperative recovery was uneventful:

- On Postoperative Day 1 (POD-1), she was hemodynamically stable with normal blood glucose and vital signs.

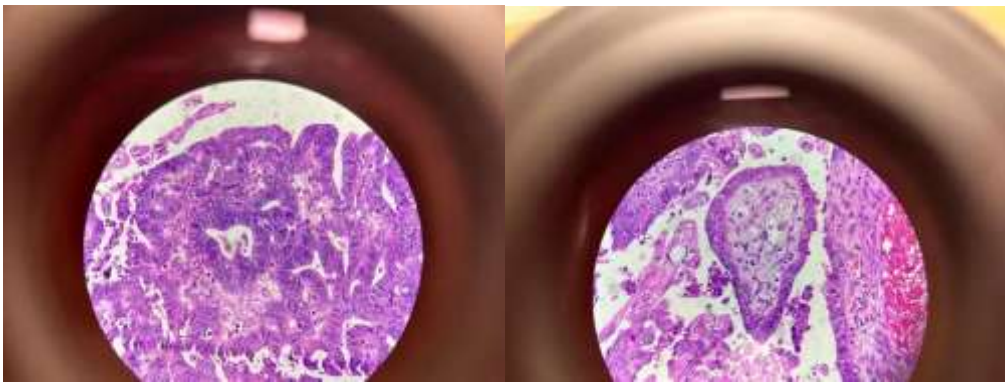
- On POD-2, the patient's Abdominal Surgical Drain (ASP) output reduced, and catheter care was managed.
- By POD-3, the drain was removed, and wound dressing revealed good healing with no signs of infection.
- Postoperative imaging confirmed the absence of residual tumor.

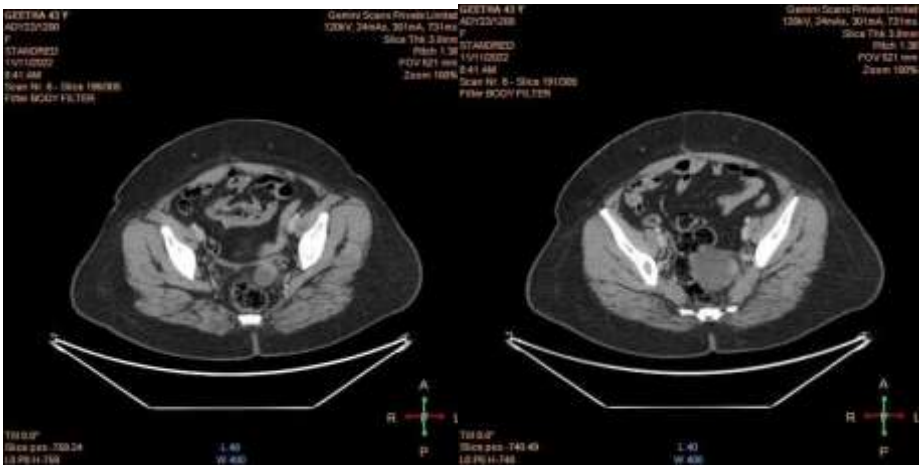
The patient received supportive medications, including intravenous antibiotics, analgesics, and proton pump inhibitors. She was mobilized early, and on discharge, she was stable and tolerating a soft diet.

Histopathology and Immunohistochemistry

The excised specimen was sent for histopathological evaluation.

- Macroscopic Findings: Cystic lesion wall measuring 5 × 4 cm.
- Microscopic Findings: Consistent with low-grade endometrioid ovarian carcinoma.
- Immunohistochemistry (IHC):
  - MLH1: Intact nuclear expression
  - MSH2: Intact nuclear expression
  - MSH6: Intact nuclear expression
  - PMS2: Intact nuclear expression





The findings demonstrated no loss of nuclear expression of MMR proteins, indicating a low probability of microsatellite instability-high (MSI-H). This result suggested a competent DNA mismatch repair system, ruling out Lynch syndrome or hereditary predisposition.

Follow-Up and Prognosis

The patient was discharged on November 23, 2022, with instructions for routine follow-up and further genetic counseling to rule out any hereditary predisposition. A follow-up PET scan and clinical examination were planned after 4 weeks.

DISCUSSION

Low-grade endometrioid ovarian carcinoma (LG-EOC) is a rare histological subtype of epithelial ovarian cancer, comprising approximately 10–15% of ovarian malignancies. Compared to high-grade serous ovarian carcinoma, LG-EOC demonstrates a more indolent clinical course but retains a significant risk of recurrence, especially in patients with advanced-stage disease or suboptimal primary cytoreduction (1,2). The presented case of a 44-year-

old female with recurrent LG-EOC highlights critical aspects of surgical management, histopathological evaluation, and postoperative considerations.

Role of Secondary Cytoreduction in Recurrent Disease

In ovarian cancer management, secondary cytoreductive surgery plays a pivotal role in patients with isolated recurrent disease, provided that complete tumor debulking can be achieved. The Arbeitsgemeinschaft Gynäkologische Onkologie (AGO) DESKTOP III trial has demonstrated that patients undergoing secondary cytoreduction with no residual disease exhibit significantly improved progression-free survival (PFS) and overall survival (OS) (3). In this case, the patient underwent extensive adhesiolysis and excision of the cystic lesion, with meticulous preservation of bowel and bladder integrity. The achievement of optimal cytoreduction (no visible residual disease) likely improves the patient's long-term prognosis.

Secondary cytoreduction is particularly beneficial in cases like LG-EOC due to its slow-growing nature and relative resistance to systemic chemotherapy. Several retrospective studies have indicated that surgical resection of isolated recurrences can lead to durable remission, especially in patients with localized disease and good performance status (3,6). The absence of distant metastases in this patient, as confirmed by PET-CT, made her an ideal candidate for surgical intervention.

Histopathology and Immunohistochemistry in Prognostication

The histopathological analysis confirmed the diagnosis of recurrent LG-EOC with no high-grade features. Immunohistochemistry (IHC) for mismatch repair (MMR) proteins—MLH1, MSH2, MSH6, and PMS2—demonstrated intact nuclear expression, indicating a low probability of microsatellite instability-high (MSI-H). This result is clinically significant as MMR deficiency, commonly associated with Lynch syndrome, occurs more frequently in endometrioid carcinomas than in other ovarian cancer subtypes (4).

The absence of MSI-H in this case has important therapeutic implications. MMR deficiency predicts responsiveness to immune checkpoint inhibitors, such as pembrolizumab, in various malignancies, including endometrioid cancers (4,7). However, for patients with intact MMR protein expression, as in this case, the utility of immunotherapy is limited, and traditional management strategies such as surgery and chemotherapy remain the mainstay.

Genetic Counseling and Surveillance

Although the patient's MMR status was normal, recurrent endometrioid ovarian carcinoma warrants a careful evaluation for potential hereditary syndromes. Germline testing for BRCA1/2 mutations and Lynch syndrome (MLH1, MSH2, MSH6, PMS2, and EPCAM genes) remains essential in patients with recurrent or early-onset disease (7). Identifying such mutations may inform future surveillance strategies and guide treatment for the patient and her family members.

In terms of surveillance, patients with LG-EOC require close monitoring due to the high risk of recurrence. Routine imaging, physical examinations, and serum CA-125 levels are integral components of follow-up care (2,3). In this patient, a follow-up PET scan and clinical evaluation were planned to assess for any signs of residual or recurrent disease.

Zhao and colleagues reported a case of low-grade endometrioid carcinoma of the ovary associated with undifferentiated carcinoma, highlighting the aggressive nature of the undifferentiated component. The patient presented with a pelvic mass and underwent surgical resection, followed by histopathological analysis that revealed the coexistence of low-grade endometrioid and undifferentiated carcinoma components. This finding emphasized the importance of thorough pathological evaluation, as the undifferentiated carcinoma component significantly influenced prognosis and treatment planning. The case underscored the need for personalized management in complex histopathological scenarios (8). Alcid and Shahin presented a case series involving four patients with low-grade serous ovarian carcinoma, providing insights relevant to low-grade endometrioid ovarian cancers. The patients, aged between 31 and 58, underwent cytoreductive surgery followed by chemotherapy and hormonal therapy. Despite initial treatment success, over 80% of patients experienced disease recurrence, demonstrating the persistent challenges in managing low-grade ovarian cancers. This report emphasized the critical role of effective maintenance therapies and close surveillance in managing recurrences (9).

Cheng and colleagues described a case of recurrent estrogen receptor-positive endometrial carcinoma treated with combination endocrine therapy using tamoxifen and megestrol acetate. The patient achieved prolonged disease control with minimal toxicity, suggesting the potential of endocrine therapy for hormonally driven malignancies. While focused on endometrial carcinoma, the findings are applicable to similar histological subtypes, including low-grade endometrioid ovarian carcinoma, offering an alternative therapeutic avenue for recurrent cases with hormonal receptor positivity (10).

Tewari and colleagues discussed findings from the ongoing ALEPRO trial, which investigates the combination of abemaciclib, a CDK4/6 inhibitor, with letrozole in estrogen receptor-positive rare ovarian cancers, including low-grade endometrioid ovarian carcinoma. Preliminary results suggest promising efficacy, with the potential to

offer a targeted approach for recurrent cases that are otherwise resistant to traditional treatments. This trial highlights the growing role of personalized medicine and targeted therapies in the management of rare ovarian cancer subtypes (11).

Conclusion

This case report highlights the clinical complexity and multidisciplinary management required for recurrent low-grade endometrioid ovarian carcinoma. Secondary cytoreductive surgery remains a cornerstone in the management of such cases, particularly when complete tumor debulking is achievable, as it significantly improves progression-free and overall survival. Histopathological evaluation, including immunohistochemistry for mismatch repair (MMR) protein expression, provides critical insights into the tumor's molecular characteristics, influencing both prognosis and therapeutic decision-making. The intact expression of MMR proteins in this patient ruled out microsatellite instability and indicated no immediate need for immunotherapy, underscoring the importance of personalized treatment strategies. This case also emphasizes the role of genetic counseling and surveillance to identify potential hereditary syndromes, which may guide future management for the patient and their family. With advancements in targeted therapies, including hormonal agents and CDK4/6 inhibitors, novel therapeutic approaches hold promise for recurrent low-grade ovarian cancers, particularly those driven by estrogen receptor positivity. Overall, this report underscores the need for individualized, evidence-based care to optimize outcomes in this rare and challenging malignancy.

REFERENCES

1. Prat J. Ovarian carcinomas: five distinct diseases with different origins, genetic alterations, and clinicopathological features. *Virchows Arch*. 2012;460(3):237-49. doi:10.1007/s00428-012-1203-5.
2. Seidman JD, Horkayne-Szakaly I, Haiba M, Boice CR, Kurman RJ, Ronnett BM. The histologic type and stage distribution of ovarian carcinomas of surface epithelial origin. *Int J Gynecol Pathol*. 2004;23(1):41-4. doi:10.1097/01.pgp.0000101080.35393.16.
3. Harter P, du Bois A, Hahmann M, et al. Surgery in recurrent ovarian cancer: the Arbeitsgemeinschaft Gynäkologische Onkologie (AGO) DESKTOP OVAR trial. *Ann Surg Oncol*. 2006;13(12):1702-10. doi:10.1245/s10434-006-9058-0.
4. Pal T, Permuth-Wey J, Kumar A, et al. Systematic review and meta-analysis of ovarian cancers: estimation of microsatellite-high frequency and characterization of mismatch repair deficient tumor histology. *Clin Cancer Res*. 2008;14(21):6847-54. doi:10.1158/1078-0432.CCR-08-0191.
5. Rambau PF, Vierkant RA, Intermaggio MP, et al. Association of p16 expression with prognosis varies across ovarian carcinoma histotypes: an Ovarian Tumor Tissue Analysis consortium study. *J Pathol Clin Res*. 2018;4(4):250-61. doi:10.1002/cjp2.108.
6. Zang RY, Li ZT, Tang J, et al. *Secondary cytoreductive surgery for patients with relapsed epithelial ovarian carcinoma: who benefits?* Cancer. 2004;100(12):2266-75. doi:10.1002/cncr.20288.
7. Konstantinopoulos PA, Norquist B, Lacchetti C, et al. *Testing for homologous recombination repair gene mutations in ovarian cancer: ASCO guideline*. J Clin Oncol. 2020;38(30):3645-56. doi:10.1200/JCO.20.01980.
8. Zhao C, Shen D, Huang X, et al. Low-grade endometrioid carcinoma of the ovary associated with undifferentiated carcinoma: a case report and literature review. Int J Clin Exp Pathol. 2014;7(7):4765-9.
9. Alcid D, Shahin M. Management and outcomes of patients with low-grade serous ovarian cancer: insights from a case series. Int J Cancer Res Oncol. 2018;4(4):100052.
10. Cheng M, Sun L, Zhang Z, et al. Combination endocrine therapy in recurrent estrogen receptor-positive endometrial carcinoma: a case report and review. Front Oncol. 2023;13:1249370. doi:10.3389/fonc.2023.1249370.
11. Tewari KS, Monk BJ, Vergote I, et al. ALEPRO trial: abemaciclib and letrozole in recurrent estrogen receptor-positive rare ovarian cancers. Int J Gynecol Cancer. 2024; early online. doi:10.1136/ijgc-2023-005189.