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High-grade endometrioid carcinoma arising from uterine serosal endometriosis with focal choriocarcinomatous differentiation and embryonal carcinoma-like morphology: a case report and literature review

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Case Report

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Abstract

Background

Malignant transformation of endometriosis is uncommon and most frequently results in endometrioid carcinoma or clear cell carcinoma. Choriocarcinomatous differentiation arising in endometriosis-associated carcinoma is exceptionally rare, and the clinical characteristics and optimal management strategies remain unclear. We report a rare case of high-grade endometrioid carcinoma arising from uterine serosal endometriosis with focal choriocarcinomatous and embryonal carcinoma-like differentiation.

Case presentation

A 54-year-old postmenopausal woman presented with postmenopausal vaginal bleeding for more than 50 days and rapid enlargement of a pelvic mass. Preoperative serum AFP and CA125 were mildly elevated, whereas serum β-hCG remained persistently below 1 mIU/mL throughout follow-up. After radiological and hysteroscopic evaluation, emergency surgery was performed because of clinical deterioration. A 12-cm pelvic mass invading the sigmoid colon was identified intraoperatively. Histopathological examination demonstrated malignant transformation arising from uterine serosal endometriosis, diagnosed as high-grade endometrioid carcinoma with aberrant p53 immunostaining, accompanied by focal choriocarcinomatous differentiation and focal embryonal carcinoma-like morphology. The patient received five cycles of adjuvant BEP chemotherapy postoperatively. Brain metastasis developed during follow-up and was treated with radiotherapy. Retroperitoneal lymph node metastasis subsequently occurred, and second-line chemotherapy with nab-paclitaxel plus carboplatin was administered. Dynamic serum tumour marker changes correlated with disease burden, whereas serum β-hCG remained negative. Histological confirmation of metastatic lesions was unavailable.

Conclusions

This case highlights that malignant transformation of postmenopausal uterine serosal endometriosis may rarely exhibit divergent differentiation, including choriocarcinomatous differentiation, despite persistently normal serum β-hCG levels. Aberrant p53 expression may be associated with tumour progression and lineage plasticity, although its biological significance requires further investigation. Individualized multimodal surveillance may be considered for this rare entity, as optimal follow-up strategies remain undefined.

1 Introduction

Endometriosis is an oestrogen-dependent chronic inflammatory disorder with a malignant transformation rate of approximately 0.7%–2.5%,which most commonly progresses to ovarian clear cell carcinoma or endometrioid carcinoma[1].Although endometriosis predominantly affects women of reproductive age, malignant transformation may occur in peri- or postmenopausal patients[2, 3].Several mechanisms have been proposed to contribute to endometriosis-associated malignant transformation, including iron-related oxidative stress, genomic instability, alterations in tumour suppressor pathways such as PTEN, ARID1A and TP53, and immune microenvironmental dysregulation[4, 5].Recent single-cell multi-omics studies have demonstrated that TP53 loss-of-function may contribute to cellular lineage stability and facilitates cross-lineage tumourigenesis.Recent multi-omics studies have suggested that TP53 alterations may be associated with tumour heterogeneity and cellular plasticity; however, their contribution to divergent differentiation remains incompletely understood[6].

Herein, we report a rare case of high-grade endometrioid carcinoma arising from uterine serosal endometriosis with focal choriocarcinomatous differentiation and embryonal carcinoma-like morphology. The tumour exhibited an unusual biomarker profile, including persistently negative serum β-hCG despite tissue β-hCG expression. To our knowledge, few cases of endometriosis-associated carcinoma with choriocarcinomatous differentiation have been reported, and longitudinal clinical outcomes remain poorly characterized. This case highlights the diagnostic complexity and clinical challenges associated with this rare form of malignant transformation.

2 Case presentation

A 54-year-old female with natural menopause at age 50 was admitted on June 24,2024,complaining of intermittent postmenopausal spotting vaginal bleeding for over 50 days and rapid enlargement of a pelvic mass within 4 days.She presented with persistent mild lower abdominal discomfort and watery vaginal discharge one week before admission,without dysuria,frequent micturition or tissue discharge.

2.1 Preoperative examinations

1.Laboratory tests: Anaemia was detected with haemoglobin 71 g/L.Serum tumour markers: AFP 106.8 ng/mL(elevated),CA125 54.03 U/mL(mildly elevated),ferritin 1384 ng/mL,and serum β-hCG <1 mIU/mL.

2.Imaging: Pelvic MRI revealed a huge mixed-signal pelvic mass measuring 120 × 143 × 138 mm(Figure 1).

A heterogeneous hypervascular pelvic mass (120 × 143 × 138 mm) is visible, attaching to the anterior lower uterine segment and infiltrating the muscular wall of the sigmoid colon. Bilateral ovaries appear grossly unremarkable.

3.Endoscopy and cytology:hysteroscopy under anesthesia demonstrated friable haemorrhagic lesions filling the cervical canal.

Given rapid clinical deterioration and suspected septic shock,emergency surgery was performed.

2.2 Surgical findings and pathological diagnosis

Emergency exploratory laparotomy was conducted on June 28,2024,including total hysterectomy,bilateral salpingo-oophorectomy,en bloc resection of pelvic mass and involved sigmoid colon,descending colostomy,and lysis of intestinal adhesions.Intraoperative findings revealed a 12 × 12 × 10 cm hypervascular malodorous pelvic mass densely adherent to and invading the muscular layer of the sigmoid colon.The tumour attachment site was attached to the anterior lower uterine segment,while bilateral ovaries and fallopian tubes appeared grossly normal.Complete R0 resection was achieved,with tumour-free margins of the proximal/distal colon,cervix and right adnexa.

Initial postoperative pathological evaluation revealed poorly differentiated carcinoma extensively infiltrating the uterine corpus,cervix and left adnexa,with negative colonic resection margins.Expert pathological review confirmed high-grade endometrioid carcinoma originating from serosal endometriosis,complicated by focal choriocarcinomatous differentiation and suspected embryonal carcinoma-like component.

Initial immunohistochemical staining showed partial CK(AE1/AE3) positivity,partial Vimentin positivity,focal PLAP positivity,Ki-67 index ~80%,mutant-type p53,diffuse p16 positivity,partial HNF1-Beta expression,negative Napsin A,negative ER,focal PR positivity,negative SALL4,partial WT1 expression,and intact mismatch repair proteins(MSH2,MSH6,MLH1,PMS2) without microsatellite instability.Supplementary pathological re-review confirmed aberrant/mutation-type p53 immunostaining and focal CK7 expression.Histologically,the differentiated area consisted of multinucleated syncytiotrophoblast-like cells with extensive hemorrhage and necrosis.Immunohistochemically,these cells showed strong β-hCG expression,supporting choriocarcinomatous differentiation(Figure 2).

2.3 Treatment and follow-up

Given the presence of choriocarcinomatous differentiation,postoperative adjuvant chemotherapy with BEP regimen(bleomycin,etoposide,cisplatin) was administered for 5 cycles.

At 15 months postoperatively(September,2025),cranial MRI identified an irregular enhancing lesion with a maximum diameter of 28.45 mm in the right frontal lobe with prominent mass effect,consistent with brain metastasis.Local cranial radiotherapy with a total dose of 50 Gy over 25 fractions was delivered from September 18 to October ,2025,combined with mannitol and corticosteroids for intracranial pressure reduction.

In March 2026,contrast-enhanced whole-abdominal CT detected multiple retroperitoneal soft-tissue lesions suggestive of lymph node metastasis.Local retroperitoneal radiotherapy(50 Gy/25 fractions) was initiated,with 18 fractions completed.Since May 2026,second-line systemic chemotherapy with nab-paclitaxel 300 mg ivgtt d1 q3w plus carboplatin 400 mg ivgtt d2 q3w has been administered.Contrast-enhanced abdominal CT revealed enlarged retroperitoneal lymphadenopathy after first-line BEP chemotherapy;follow-up imaging demonstrated obvious lesion shrinkage after switching to second-line chemotherapy (Figure 3).

Dynamic serial serum tumour markers were monitored throughout surgery,chemotherapy and radiotherapy follow-up,as summarised in Table 1.Serum β-hCG remained persistently low-normal during the entire course,while CA125 fluctuated in parallel with tumour burden and normalised after second-line chemotherapy.Pathological biopsy of brain metastatic lesions was unavailable due to upfront stereotactic radiotherapy;metastatic histology was indirectly evaluated via serial imaging and serum tumour markers only.

Table 1 Serial serum tumour marker levels during treatment and follow-up

tumour marker	25/06/2024	26/06/2024	11/09/2024	03/10/2024	27/10/2024	17/11/2024	17/12/2024	04/03/2025	13/09/2025
β-hCG(mIU/mL)		<1						2	
AFP(ng/mL)	106.8		4.61	6.94	4.47	5.92	4.95	6.49	5.37
CA12-5(U/mL)	54.03		44.02	18.91	9.44	10.05	9.92	14.24	30.9
Ferritin(ng/ml)	1384	>2000	337.2	435.2	535.9	585.111	444		309
CA199(U/mL)									

Abbreviations: β-hCG,beta-human chorionic gonadotropin;CA125,cancer antigen 125;CA199,carbohydrate antigen 199;CA50,carbohydrate antigen 50;CA724,carbohydrate antigen 724;CEA,carcinoembryonic antigen;HE4,human epididymis protein 4;ROMA,risk of ovarian malignancy algorithm;AFP,alpha-fetoprotein;SCC-Ag,squamous cell carcinoma antigen.

3 Discussion

Malignant transformation of endometriosis followed by choriocarcinomatous differentiation represents an extremely rare clinical entity,with only limited case reports published to date.To clarify the clinical discrepancies between the present case and previously reported patients,all retrievable relevant English case reports were summarised(Additional file 1: Table S1).Most previously documented tumours arose from the ovary or colonic serosa, and TP53 alterations were not reported in most cases. In contrast, our case originated from uterine serosal endometriosis. We hypothesise that aberrant p53 expression may be associated with the phenotypic heterogeneity observed in this tumour.Persistently negative serum β-hCG throughout surveillance may be attributed to limited

trophoblastic differentiation or impaired hormone secretion capacity of the tumour.This case also documents complete sequential treatment including first-line chemotherapy,metastasis-directed radiotherapy and second-line chemotherapy with long-term follow-up data,providing clinical references for disease management.

Endometriosis-associated carcinomas arising in different anatomical sites share several common biological features and molecular alterations.The classic Sampson and Scott diagnostic criteria require a clear benign-to-malignant histological transition zone,which is difficult to satisfy clinically[7].Rapid tumour proliferation after malignant transformation often obliterates pre-existing endometriotic lesions,leading to frequent misdiagnosis as primary epithelial carcinoma.In addition to histological continuity, immunohistochemical profiles may provide supportive evidence when assessing tumour origin: retrospective studies have confirmed consistent immunohistochemical profiles of p53,ER,PR,Ki-67 and mismatch repair proteins between EAOC and sporadic epithelial ovarian carcinoma.Endometriosis-associated endometrioid carcinoma typically presents with focal PR positivity,while clear cell subtypes frequently lack hormone receptor expression [8,9],Our patient's immunohistochemical findings match these features: aberrant/mutation-type p53 immunostaining,diffuse ER negativity,focal PR positivity and Ki-67 index up to 80%.Although hormone receptor expression may be reduced in high-grade tumours, the overall immunophenotype remained compatible with endometrioid differentiation.Combined with intraoperative attachment of the tumour attachment site to uterine serosa and residual endometriotic tissue within the lesion,gross and immunohistochemical evidence collectively supported the diagnosis of high-grade endometrioid carcinoma arising from uterine serosal endometriosis.

Comprehensive histological,immunohistochemical and serological evidence supported focal choriocarcinomatous differentiation in this tumour: histologically,sheets of pleomorphic multinuclear syncytiotrophoblast-like cells with extensive haemorrhage and necrosis were observed,with focal areas with embryonal carcinoma-like morphology were observed..Immunohistochemically,syncytiotrophoblast-like cells showed diffuse strong β-hCG staining with concurrent epithelial marker expression and negative germ cell-specific markers,arguing against a primary germ cell tumour,particularly given the patient's postmenopausal status and the absence of germ cell marker expression.[10].Compared with previously reported cases,serum β-hCG remained persistently normal throughout follow-up.Prior literature proposes that limited trophoblastic differentiation or impaired hormone secretion may lead to negative serum β-hCG [11].This finding highlights that follow-up relying solely on β-hCG risks underestimating tumour burden and missing recurrent lesions[12].

Oxidative stress, inflammation and genomic alterations have been proposed to contribute to endometriosis-associated malignant transformation[13].Recent single-cell multi-omics studies have linked TP53 loss-of-function to enhanced tumour cellular lineage plasticity[6].Although aberrant p53 expression was observed in our case, whether this alteration contributed to the unusual choriocarcinomatous differentiation remains unclear. The proposed relationship between TP53 abnormalities and divergent differentiation remains hypothetical and requires validation through genomic and functional studies.

Given the choriocarcinomatous differentiation and concern for germ-cell-like biological behaviour,BEP was selected as an empirical regimen based on the multidisciplinary consideration of the tumour's divergent differentiation pattern;however, evidence supporting this approach in this rare tumour setting is limited[14].However,brain and retroperitoneal lesions suspicious for metastases developed approximately one year after initial treatment.Although metastatic lesions were theoretically suspected to represent trophoblastic spread,persistently normal serum β-hCG provided no serological evidence of active trophoblastic proliferation.Given the primary tumour was predominantly high-grade endometrioid carcinoma,second-line chemotherapy combining nab-paclitaxel and carboplatin(standard platinum-taxane regimen for epithelial gynaecological malignancies) was administered.Significant CA125 reduction and normalisation after second-line therapy suggested a clinical response of the epithelial carcinoma component[15].Pathological biopsy of brain metastasis was unavailable due to upfront stereotactic radiotherapy,precluding precise histological classification of metastatic lesions.

No standardized surveillance or therapeutic guidelines exist for this rare tumour subtype.All clinical decisions for this patient were formulated based on published EAOC guidelines,clinical experience,and combined serial symptoms,imaging and serum tumour marker assessments.This study has several limitations: pathological biopsy of brain metastatic lesions was unavailable,and metastatic histology was inferred indirectly via radiology and serum markers only.Next-generation sequencing(NGS) was not performed to generate full tumour genomic profiles,so direct causal links between TP53 mutation and cross-lineage transdifferentiation cannot be validated,relevant mechanistic conclusions are speculative based on published literature only.Although germ cell tumour markers were negative and the histological context supported somatic carcinoma differentiation, definitive molecular exclusion of a germ cell origin was not performed.In addition,follow-up duration remains limited,and prolonged continuous surveillance is required to characterise long-term recurrence risk,survival outcomes and treatment tolerance.

This case illustrates malignant transformation associated with uterine serosal endometriosis and focal choriocarcinomatous differentiation. The clinical course provides descriptive observations, while the optimal treatment and surveillance strategies remain uncertain.

Declarations

Ethics approval and consent to participate

Ethics approval was not required for this retrospective single-case report according to institutional policies. Written informed consent for publication was obtained from the patient. The study was conducted in accordance with the Declaration of Helsinki.

Consent for publication

Written informed consent for publication of this case report, including clinical information, pathological images and radiological data, was obtained from the patient.

Availability of data and materials

All relevant clinical data are included in the manuscript and supplementary files. Pathological images supporting the diagnosis are included in the manuscript. Additional pathological materials may be available from the corresponding author upon reasonable request and with appropriate ethical approval.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

Li Ziqi: literature retrieval,data curation, writing-original draft;

Xu Ruibo and Xin Man: Conceptualization,Clinical data collection;

Xue Jie: Supervision, writing-review & editing.

All authors read and approved the final manuscript.

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References

1. Giannini A, Massimello F, Caretto M, Cosimi G, Mannella P, Luisi S, et al. Factors in malignant transformation of ovarian endometriosis: a narrative review. Gynecol Endocrinol. 2024;40(1):2409911. 10.1080/09513590.2024.2409911.
2. Moraru L, Mitranovici M-I, Chiorean DM, Moraru R, Caravia L, Tiron AT et al. Adenomyosis and its possible malignancy: a review of the literature.Diagnostics. 2023;13(11):1883. 10.3390/diagnostics13111883
3. Szubert M, Kozirog E, Wilczynski J. Adenomyosis as a risk factor for myometrial or endometrial neoplasms–review. Int J Environ Res Public Health. 2022;19(4):2294. 10.3390/ijerph19042294.
4. Chen F, Zhu M, Li W. Advances in research on malignant transformation of endometriosis-associated ovarian cancer.Front Oncol. 2024;14:1475231. 10.3389/fonc.2024.1475231
5. Hablase R, Kyrou I, Randeva H, Karteris E, Chatterjee J. The Road to malignant transformation from endometriosis to endometriosis-associated ovarian cancers(EAOCs): an mTOR-Centred review. Cancers(Basel). 2024;16(11):2160. 10.3390/cancers16112160.
6. Wang X, Mei Y, Wang X, Wu H, Wang R, Zhang P, et al. Dissecting cross-lineage tumourigenesis under p53 inactivation through single-cell multi-omics and spatial transcriptomics. Clin Transl Med. 2025;15(9):e70461. 10.1002/ctm2.70461.
7. Chiaffarino F, Cipriani S, Ricci E, Esposito G, Parazzini F, Vercellini P. Histologic subtypes in endometriosis-associated ovarian cancer and ovarian cancer arising in endometriosis: a systematic review and meta-analysis. Reprod Sci. 2024;31:1642–50. 10.1007/s43032-024-01489-9.
8. Wang H, Chen C, Wang D, Zhu Y, Chen P. Correlation of clinicopathological and prognostic characteristics between endometriosis-associated and primary ovarian cancer.BMC. Cancer. 2023;23(1):1210. 10.1186/s12885-023-11641-4.
9. Bas-Esteve E, Pérez-Arguedas M, Guarda-Muratori GA, Acién M. Acién P.Endometriosis and ovarian cancer: their association and relationship.Eur J Obstet Gynecol Reprod Biol X. 2019;3:100053. 10.1016/j.eurox.2019.100053
10. Wakahashi S, Sudo T, Nakagawa E, Ueno S, Muraji M, Kanayama S, et al. Endometrioid adenocarcinoma with high-grade transformation with serous and choriocarcinomatous differentiation - a case report. J Cancer. 2012;3:14–8. 10.7150/jca.3.14.
11. Dietel J, Bartholdt E, Hänel C, Horn L-C. .Serous carcinoma of the endometrium with choriocarcinomatous differentiation: a case report and review of the literature indicate the existence of 2 prognostically relevant tumour types. Int J Gynecol Pathol. 2006;25(3):247–51. 10.1097/01.pgp.0000215294.45738.a4.
12. Mangla M, Palo S, Kaur H, Kanikaram PK, Rahiman EA. Prognostic significance of trophoblastic differentiation and β-hCG secretion in somatic malignancies of uterine corpus: a systematic review with. survival Anal Oncoscience. 2025;12:96–106. 10.18632/oncoscience.625.
13. Samartzis EP, Labidi-Galy SI, Moschetta M, Uccello M, Kalaitzopoulos DR, Perez-Fidalgo JA, et al. Endometriosis-associated ovarian carcinomas: insights into pathogenesis,diagnostics,and therapeutic targets—a narrative review. Ann Transl Med. 2020;8(24):1712–1712. 10.21037/atm-20-3022a.
14. Renz M, Friedlander M, Berek JS. Cancer of the ovary,fallopian tube,and peritoneum: 2025 update. Int J Gynaecol Obstet. 2025;171(S1):6–35. 10.1002/ijgo.70282.
15. Bai L, Chen Y, Han L, Zheng A, Mo X. Uterine choriocarcinoma coexistence with endometrioid adenocarcinoma: a case report and literature review. BMC Womens Health. 2023;23(1):252. 10.1186/s12905-023-02377-1.

Figures

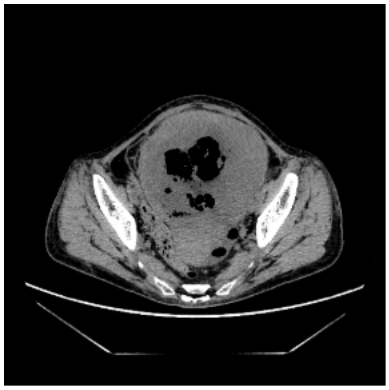


Figure 1

Axial view of preoperative pelvic contrast-enhanced MRI.

A heterogeneous hypervascular pelvic mass (120 × 143 × 138 mm) is visible, attaching to the anterior lower uterine segment and infiltrating the muscular wall of the sigmoid colon. Bilateral ovaries appear grossly unremarkable.

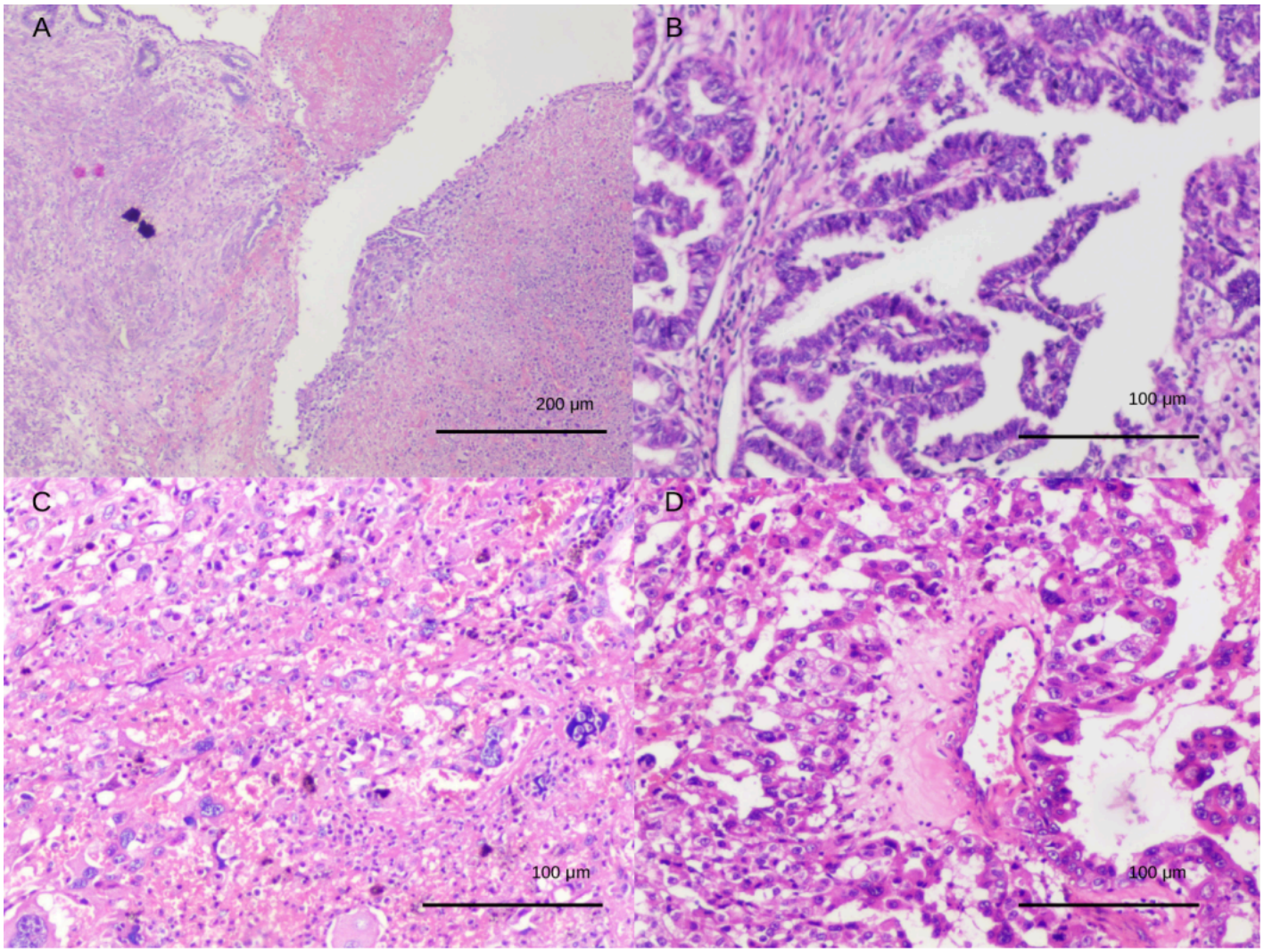


Figure 2

Histopathological features of the lesion on hematoxylin and eosin (H&E) staining

(A) Low magnification (40×) showing the transition zone between endometriotic focus and malignant tissue.(B) High-grade endometrioid carcinoma (100×). (C) Focal areas exhibiting choriocarcinomatous morphology (100×).(D) Regions with embryonal carcinoma-like morphology (100×).Scale bars: 200 μm (A,B; 40× magnification); 100 μm (C,D; 100× magnification).

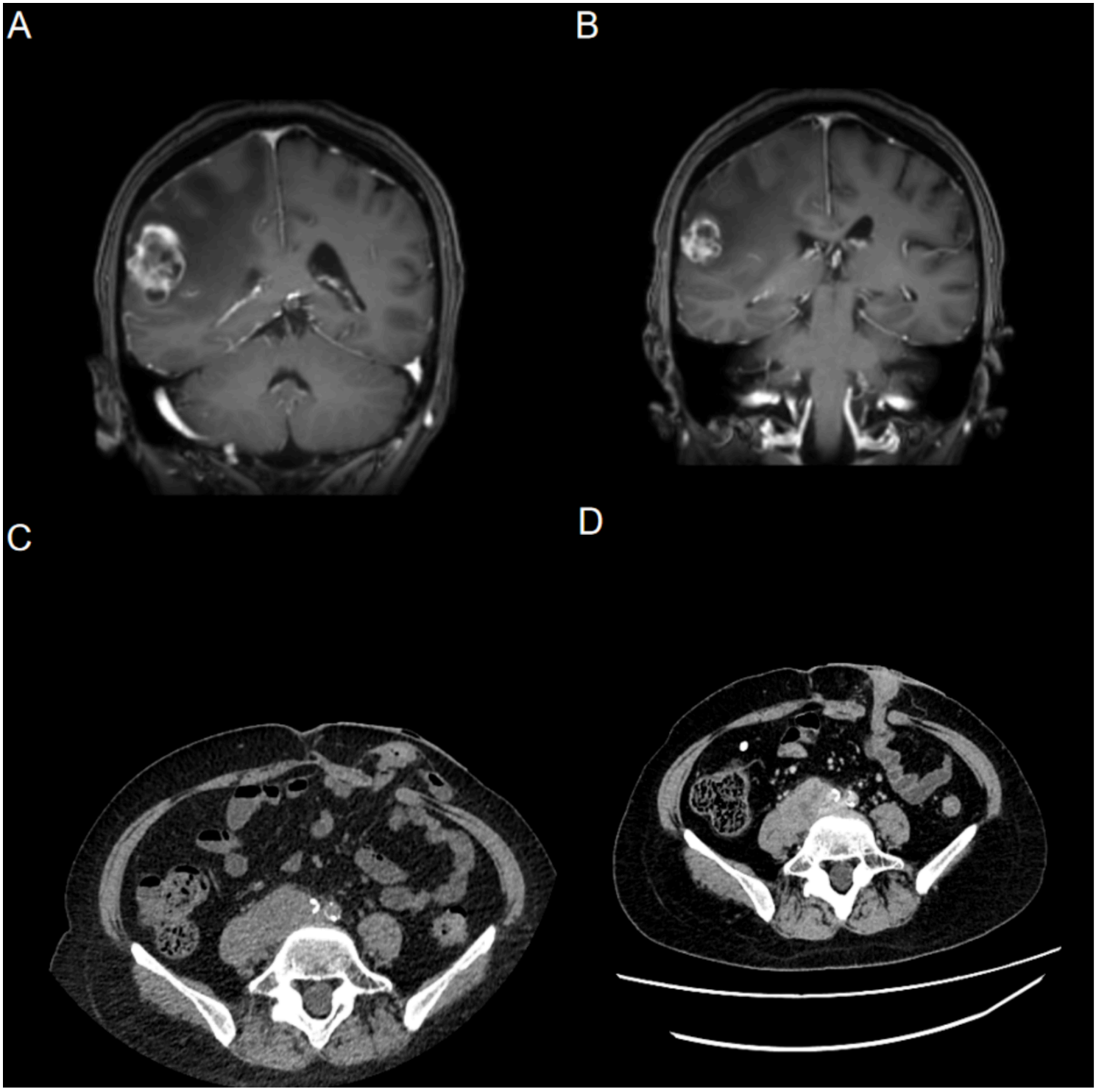


Figure 3

Imaging findings of metastatic lesions before and after chemotherapy.

(A,B) Coronal contrast-enhanced brain MRI. (A) Baseline scan showing a contrast-enhanced metastatic lesion (white arrow) in the right frontal lobe with perilesional edema after BEP chemotherapy. (B) Follow-up brain MRI performed in September 2025 after albumin-bound paclitaxel plus carboplatin therapy, identifying newly developed intracranial metastatic tumour. (C) Baseline CT revealing enlarged retroperitoneal metastatic lymph nodes (white arrow). (D) Post-treatment follow-up CT demonstrating treatment response of retroperitoneal lesions indicated by the white arrow.

Supplementary Files

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