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HISTOPATHOLOGICAL SPECTRUM AND DIAGNOSTIC CHALLENGES OF OVARIAN MALIGNANCIES: A CASE SERIES⁴

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Abstract

Ovarian malignancies comprise a heterogeneous group of neoplasms with diverse histopathological features, biological behavior, and clinical outcomes, making their diagnosis and management particularly challenging. This case series presents fifteen patients with different histological subtypes of ovarian malignancies, including high-grade serous carcinoma, mucinous carcinoma, endometrioid carcinoma, clear cell carcinoma, transitional cell carcinoma, malignant Brenner tumor, carcinosarcoma, granulosa cell tumor, dysgerminoma, yolk sac tumor, immature teratoma, squamous cell carcinoma arising in mature cystic teratoma, and small cell carcinoma of the ovary. Most patients presented with nonspecific symptoms such as abdominal pain, abdominal distension, pelvic mass, early satiety, and weight loss. Radiological imaging and serum tumor markers aided preoperative evaluation; however, definitive diagnosis was established through histopathological examination supported by immunohistochemistry. Comprehensive surgical staging followed by histology-directed adjuvant therapy constituted the primary treatment approach. The series emphasizes the crucial role of meticulous histopathological assessment in distinguishing morphologically similar tumors, identifying rare variants, and guiding appropriate management. Early diagnosis, accurate pathological classification, multidisciplinary treatment, and long-term follow-up are essential to improve prognosis and optimize outcomes in patients with ovarian malignancies.

Keywords: Case series; Histopathology; Immunohistochemistry; Ovarian malignancy; Ovarian carcinoma;.

1. Introduction

Ovarian malignancies are among the most lethal gynecological cancers because they are often diagnosed at an advanced stage due to vague, nonspecific symptoms [1,2]. Although they account for a relatively small proportion of female cancers, they cause a disproportionately high number of gynecological cancer deaths. According to GLOBOCAN 2022, more than 324,000 new cases and 206,000 deaths occur annually, making ovarian cancer the eighth most common cancer among women worldwide [3,4]. Nearly 70% of patients present with advanced-stage disease, resulting in poor survival rates.[5] Ovarian malignancies are a heterogeneous group comprising surface epithelial tumors, germ cell tumors, sex cord-stromal tumors, and metastatic tumors.[6,7] Epithelial ovarian carcinomas account for approximately 90% of malignant ovarian neoplasms, with high-grade serous carcinoma being the most common subtype, followed by mucinous, endometrioid, and clear cell carcinomas. Germ cell and sex cord-stromal tumors occur less frequently and mainly affect younger women, while metastatic tumors represent a smaller but clinically significant proportion.[8,9]

Patients commonly present with abdominal pain, abdominal distension, pelvic discomfort, bloating, early satiety, urinary frequency, and unexplained weight loss.[10] Serum tumor markers including CA-125, HE4, AFP, β -hCG, LDH, and inhibin aid diagnosis but lack sufficient sensitivity and specificity to establish a definitive diagnosis independently.[11,12] Ultrasonography, CT, and MRI are essential for evaluating adnexal masses and staging disease, but imaging alone cannot reliably distinguish histological subtypes, borderline tumors, or metastatic lesions.[13,14,15] Therefore, histopathological examination remains the gold standard, with gross examination, adequate tissue sampling, microscopy, and immunohistochemistry being crucial for accurate tumor classification, grading, staging, and diagnosis of rare variants.[16,17,18] This case series highlights the histopathological spectrum and diagnostic challenges of various ovarian malignancies, emphasizing the pivotal role of histopathology and immunohistochemistry in achieving accurate diagnosis, guiding appropriate treatment, and improving patient outcomes.

2. Case Series

Patient 1

A 56-year-old postmenopausal woman presented with progressive abdominal distension, lower abdominal pain, loss of appetite, early satiety, generalized weakness, and unintentional weight loss over several weeks. She had no significant family history of breast or ovarian cancer. Examination revealed mild cachexia, abdominal distension, a large abdominopelvic mass with shifting dullness (ascites), and bilateral adnexal fullness with restricted mobility. Vital signs were stable.

Investigations showed a markedly elevated CA-125, while routine hematological and biochemical parameters were within normal limits. Contrast-enhanced CT demonstrated bilateral complex ovarian masses, multiple peritoneal implants, omental cake, and moderate ascites, suggestive of advanced epithelial ovarian carcinoma. The patient underwent exploratory laparotomy with optimal cytoreductive surgery, which revealed bilateral ovarian tumors, diffuse peritoneal deposits, omental involvement, and ascitic fluid. Histopathology confirmed high-grade serous ovarian carcinoma (HGSOC) involving both ovaries, and immunohistochemistry supported the diagnosis. She subsequently received platinum-based combination chemotherapy, with satisfactory postoperative recovery, symptomatic improvement, and a progressive decline in serum CA-125 during follow-up. The case highlights the importance of clinical evaluation, radiological imaging, histopathology, and immunohistochemistry for accurate diagnosis and management of advanced ovarian malignancy.

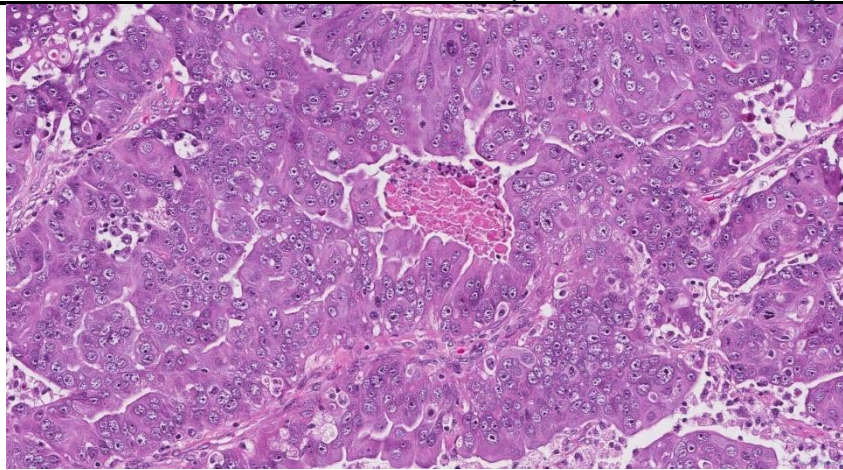


Figure 1 High-grade serous ovarian carcinoma

Patient 2

A 38-year-old nulliparous woman presented with progressively worsening lower abdominal pain and pelvic discomfort. She had a 4-year history of bilateral ovarian endometriotic cysts managed conservatively. Over recent months, she developed increasing pelvic pain and abdominal fullness. She was hemodynamically stable, with a palpable pelvic-abdominal mass, mild tenderness, bilateral adnexal fullness, and no significant family history of ovarian or breast carcinoma.

MRI pelvis revealed a large multiloculated pelvic mass with solid and cystic components extending between the pelvic walls and posterior uterus, suspicious for malignant transformation of endometriosis. Serum tumor markers supported the suspicion of epithelial ovarian malignancy. The patient underwent exploratory laparotomy, total abdominal hysterectomy, bilateral salpingo-oophorectomy, omentectomy, and comprehensive surgical staging. Intraoperatively, a large ovarian mass with extensive pelvic adhesions was identified. Histopathology confirmed FIGO Stage IIIA ovarian clear cell carcinoma arising from endometriosis, showing clear cytoplasm, hobnail cells, and tubulocystic architecture, with a contralateral endometriotic cyst also present. She subsequently received platinum-based chemotherapy and remained under regular oncologic surveillance. The case highlights the rare malignant transformation of endometriosis into ovarian clear cell carcinoma and the importance of early radiological suspicion and meticulous histopathological evaluation for accurate diagnosis and management.

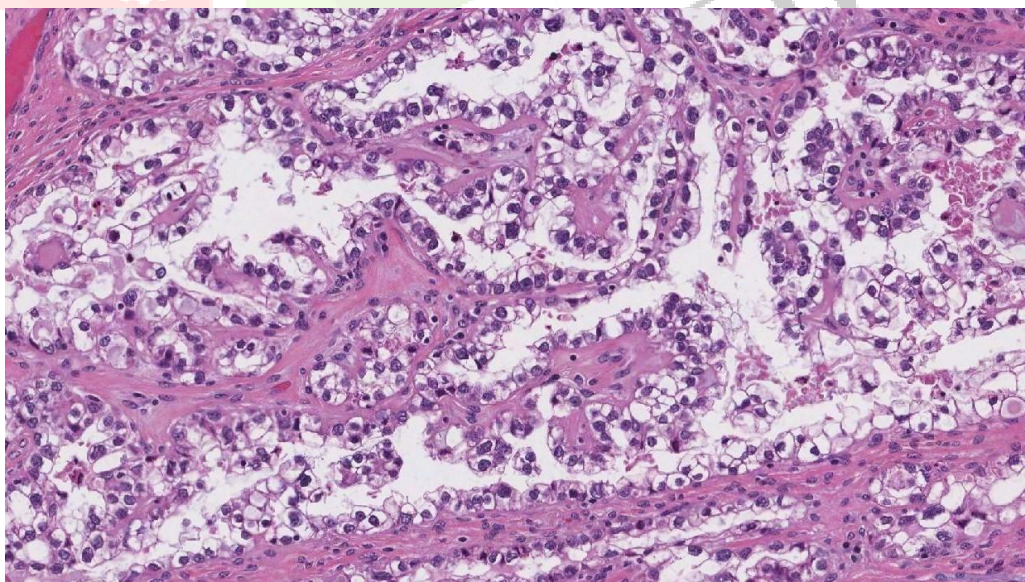


Figure 2 Ovarian clear cell carcinoma

Patient 3

A 52-year-old postmenopausal woman presented with lower abdominal pain, abdominal distension, a palpable pelvic mass (3 months), early satiety, intermittent constipation, and weight loss, with no postmenopausal bleeding or significant family history. Examination revealed a firm irregular pelvic-abdominal mass and a fixed adnexal mass, without inguinal lymphadenopathy.

Investigations showed moderately elevated CA-125 and mildly elevated inflammatory markers. Contrast-enhanced CT demonstrated a large complex ovarian mass with cystic and solid components, calcifications, fat density, and enhancing soft-tissue nodules, suggestive of malignant transformation of a mature cystic teratoma. The patient underwent exploratory laparotomy, total abdominal hysterectomy, bilateral salpingo-oophorectomy, infracolic omentectomy, pelvic lymph node sampling, and surgical staging. Intraoperatively, a large left ovarian tumor with focal capsular disruption and pelvic adhesions was identified, without distant metastasis. Histopathology confirmed well-differentiated squamous cell carcinoma arising within a mature cystic teratoma, showing invasive squamous epithelial nests with keratin pearls and adjacent mature ectodermal elements. The diagnosis was differentiated from metastatic squamous carcinoma by comprehensive histopathological evaluation. The patient received adjuvant platinum-based chemotherapy and remained under close clinical and radiological follow-up. The case highlights the rare malignant transformation of mature cystic teratoma and the importance of thorough histopathological examination of excised ovarian dermoid cysts.

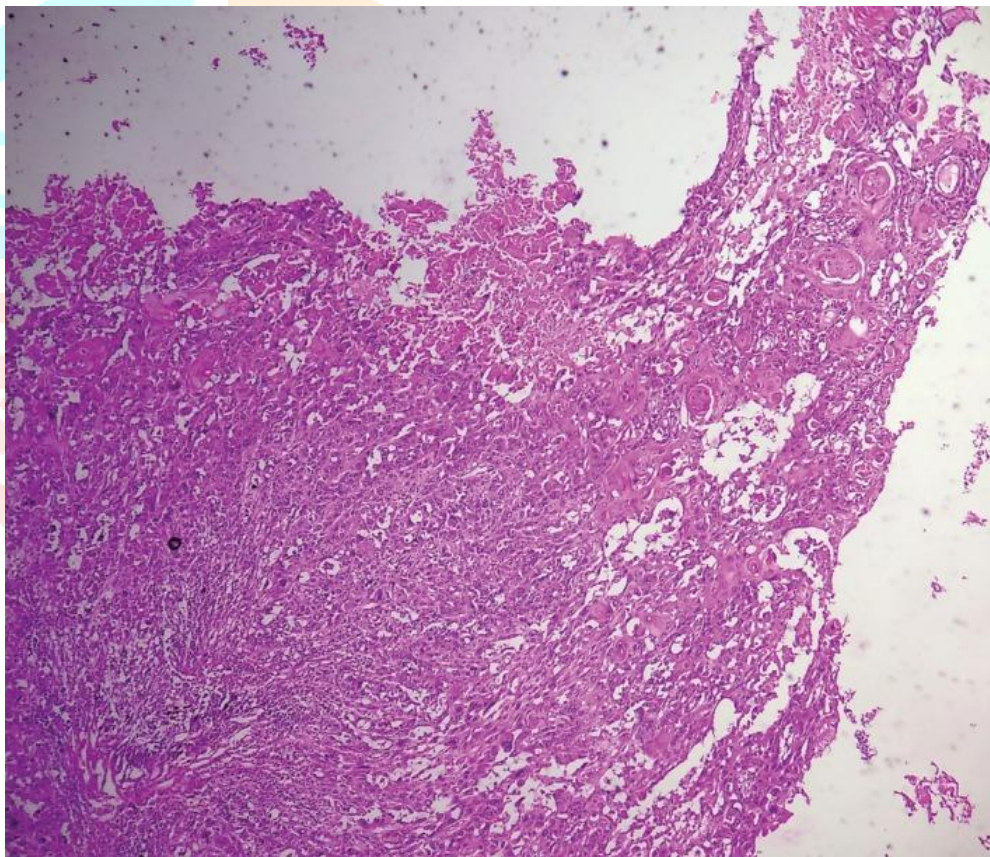


Figure 3 Squamous cell carcinoma arising in mature cystic teratoma

Patient 4

A 29-year-old nulliparous woman presented with lower abdominal pain, abdominal distension, a palpable pelvic mass (2 months), nausea, early satiety, and generalized weakness. She had regular menstrual cycles with no significant medical or family history of gynecological malignancy. Examination revealed a large, firm, non-mobile pelvic mass without ascites or lymphadenopathy.

Investigations showed markedly elevated AFP, while CA-125 and β -hCG were normal. Contrast-enhanced CT demonstrated a large unilateral heterogeneous ovarian mass with solid components, hemorrhage, and necrosis, without distant metastasis, suggestive of a malignant germ cell tumor. The patient underwent fertility-sparing staging laparotomy with unilateral salpingo-oophorectomy, infracolic omentectomy, peritoneal washings, and multiple peritoneal biopsies. Intraoperatively, a large unilateral ovarian tumor with an intact capsule and no gross peritoneal dissemination was identified. Histopathology confirmed a yolk sac

tumor (endodermal sinus tumor), showing a reticular growth pattern, Schiller-Duval bodies, and eosinophilic hyaline globules, while immunohistochemistry demonstrated strong AFP positivity. The diagnosis was differentiated from embryonal carcinoma and other malignant germ cell tumors. The patient received BEP chemotherapy (bleomycin, etoposide, and cisplatin), with a progressive decline in serum AFP, and remained disease-free during follow-up. The case highlights the importance of early diagnosis, histopathology, immunohistochemistry, and timely multimodal treatment in ovarian yolk sac tumors.

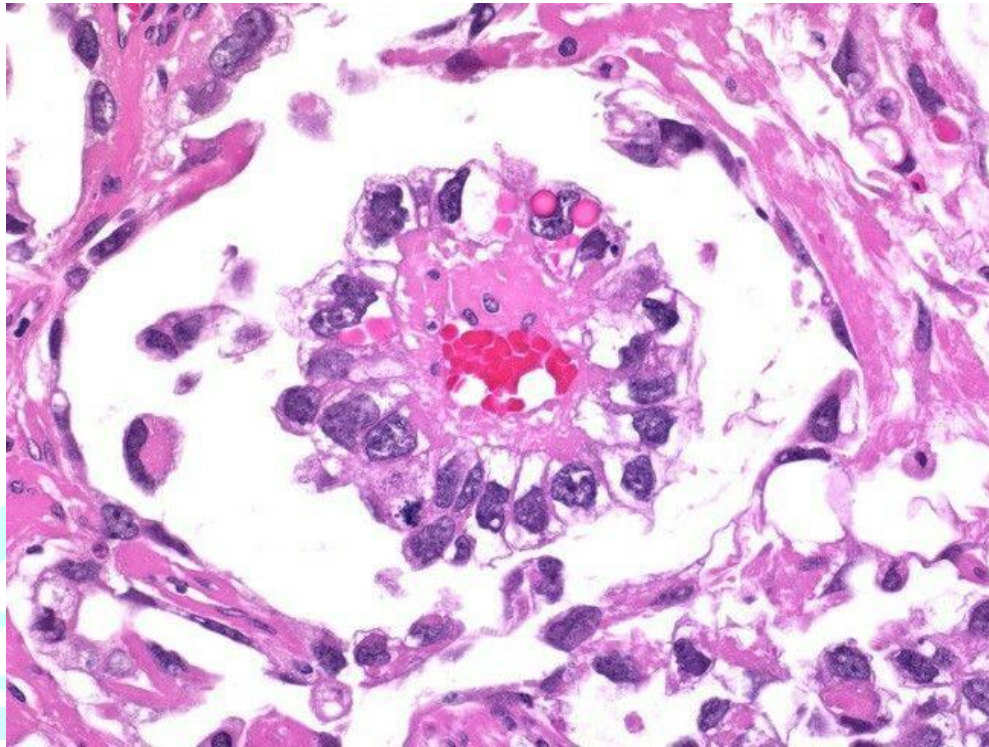


Figure 4 Yolk sac tumor showing Schiller–Duval bodies

Patient 5

A 24-year-old woman presented with lower abdominal pain, abdominal distension, nausea, recurrent vomiting (1 month), generalized weakness, and loss of appetite, with no significant menstrual abnormalities or family history of ovarian or breast malignancy. Examination revealed mild dehydration, a large pelvic-abdominal mass, a fixed unilateral adnexal mass, and no palpable lymphadenopathy.

Investigations showed marked hypercalcemia, mildly elevated CA-125, and otherwise normal laboratory findings. Contrast-enhanced CT demonstrated a large unilateral heterogeneous ovarian mass with solid components, hemorrhage, and central necrosis, without distant metastasis, suggestive of a rare ovarian malignancy. The patient underwent exploratory laparotomy with unilateral salpingo-oophorectomy, infracolic omentectomy, peritoneal washings, multiple peritoneal biopsies, and surgical staging. Intraoperatively, a large unilateral ovarian tumor with an intact capsule, minimal peritoneal deposits, and no contralateral ovarian involvement was identified. Histopathology confirmed small cell carcinoma of the ovary, hypercalcemic type (SCCOHT), showing small hyperchromatic cells, brisk mitotic activity, extensive necrosis, and follicle-like spaces. Immunohistochemistry excluded lymphoma, metastatic neuroendocrine carcinoma, primitive neuroectodermal tumor, and other small round cell tumors. The patient received adjuvant platinum-based chemotherapy, with normalization of serum calcium after surgery, and remained under close surveillance because of the tumor's aggressive nature and high recurrence risk. The case highlights that hypercalcemia in a young woman with an ovarian mass should raise suspicion for SCCOHT, with histopathology and immunohistochemistry being essential for definitive diagnosis.

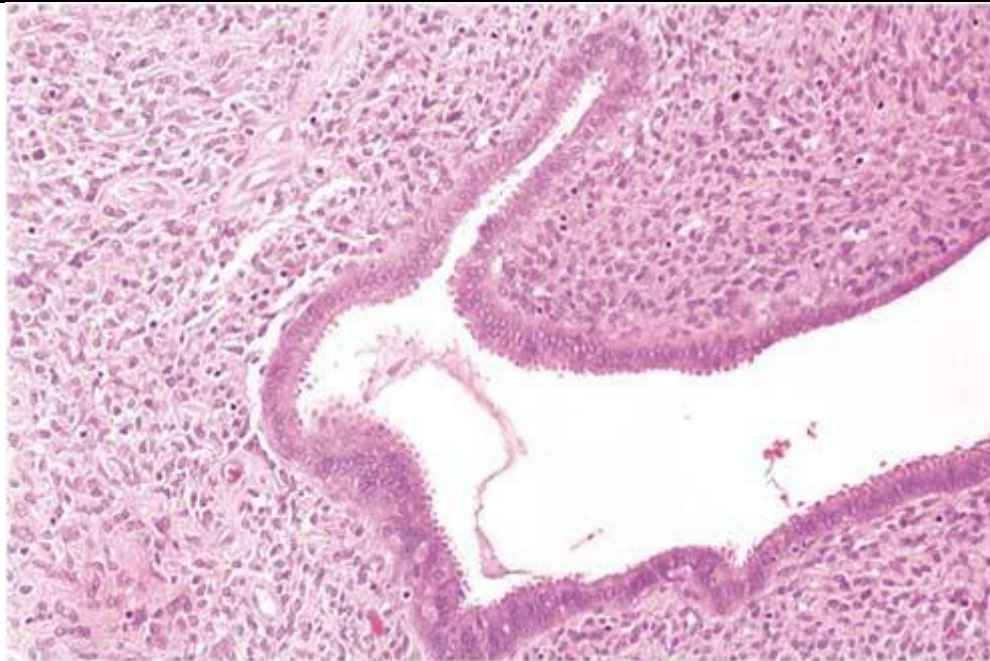


Figure 5 Small cell carcinoma of the ovary, hypercalcemic type

Patient 6

A 46-year-old multiparous woman presented with abdominal distension, intermittent lower abdominal pain, irregular vaginal bleeding (4 months), pelvic pressure, and generalized fatigue, with no significant medical or family history. Examination revealed a ~10 cm firm mobile pelvic mass without ascites or lymphadenopathy.

Investigations showed mildly elevated CA-125 and increased serum inhibin-B, suggestive of a sex cord–stromal tumor. Transvaginal ultrasonography demonstrated a predominantly solid ovarian lesion, while contrast-enhanced MRI revealed a well-circumscribed unilateral ovarian mass with solid and cystic components, without metastasis or peritoneal dissemination. The patient underwent exploratory laparotomy, total abdominal hysterectomy, bilateral salpingo-oophorectomy, infracolic omentectomy, and surgical staging. Intraoperatively, a unilateral encapsulated ovarian tumor without gross extra-ovarian disease was identified. Histopathology confirmed an adult granulosa cell tumor, showing diffuse, trabecular, and microfollicular patterns with Call-Exner bodies and coffee-bean nuclei. Immunohistochemistry was positive for inhibin- α , calretinin, FOXL2, and SF-1, confirming the diagnosis and differentiating it from endometrioid carcinoma and other sex cord–stromal tumors. The patient recovered uneventfully and remained under long-term oncological surveillance because of the risk of late recurrence. The case highlights the importance of histopathology and immunohistochemistry for accurate diagnosis and management of adult granulosa cell tumors.

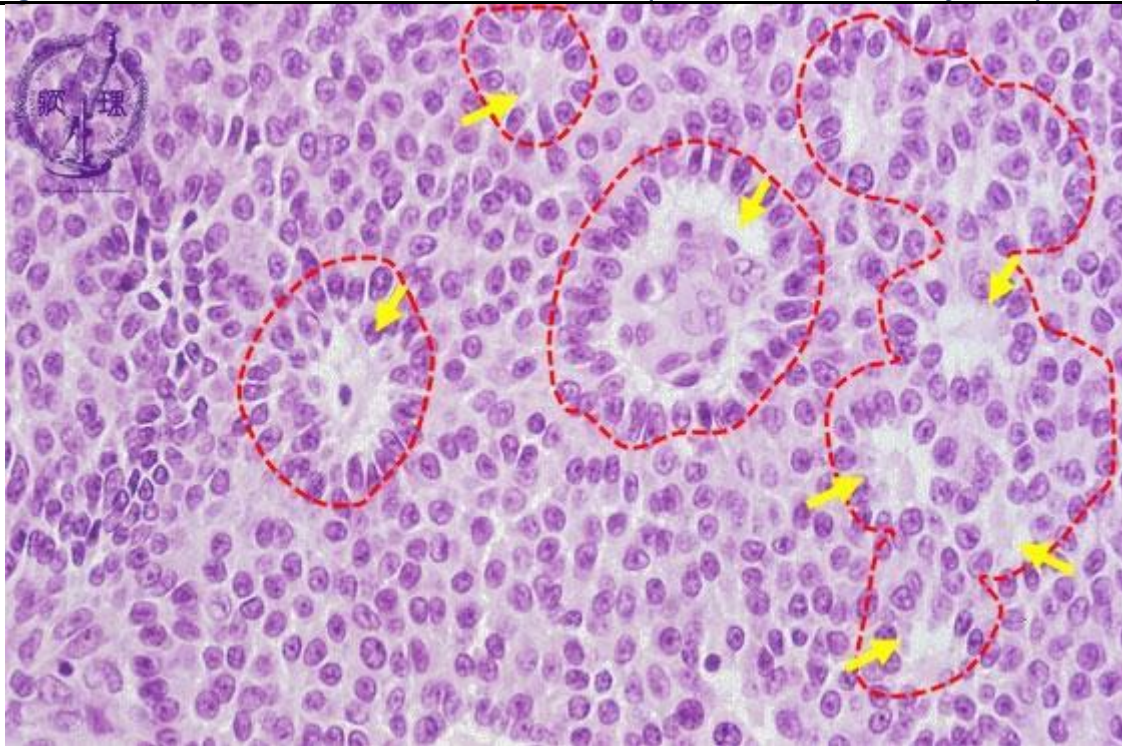


Figure 6 Adult granulosa cell tumor with Call-Exner bodies

Patient 7

A 62-year-old postmenopausal woman presented with abdominal enlargement, lower abdominal discomfort, anorexia, early satiety (3 months), intermittent constipation, and a 6 kg weight loss (2 months), with no postmenopausal bleeding or gastrointestinal malignancy. Examination revealed a large cystic pelvic-abdominal mass, mild ascites, and a large adnexal mass, without palpable lymphadenopathy.

Investigations showed elevated CA-125 and CEA. Transvaginal ultrasonography demonstrated a large multiloculated cystic ovarian mass with thick septations and papillary projections, while contrast-enhanced CT revealed a 20 cm unilateral multilocular cystic ovarian tumor with enhancing mural nodules, suspicious for mucinous ovarian carcinoma, with metastatic gastrointestinal mucinous adenocarcinoma as the main differential diagnosis. The patient underwent exploratory laparotomy, total abdominal hysterectomy, bilateral salpingo-oophorectomy, infracolic omentectomy, appendectomy, pelvic lymph node sampling, and comprehensive surgical staging. Intraoperatively, a large multiloculated mucin-filled ovarian mass was identified without gross gastrointestinal malignancy or distant metastasis. Histopathology confirmed FIGO Stage IA primary mucinous ovarian adenocarcinoma, showing complex glandular and papillary architecture with stromal invasion. Extensive tumor sampling and immunohistochemistry confirmed a primary ovarian origin and excluded metastatic colorectal adenocarcinoma. The patient received adjuvant platinum-based chemotherapy, recovered uneventfully, and remained disease-free on follow-up. The case highlights the importance of histopathology, extensive sampling, immunohistochemistry, and clinicoradiological correlation in distinguishing primary ovarian mucinous carcinoma from metastatic mucinous tumors.

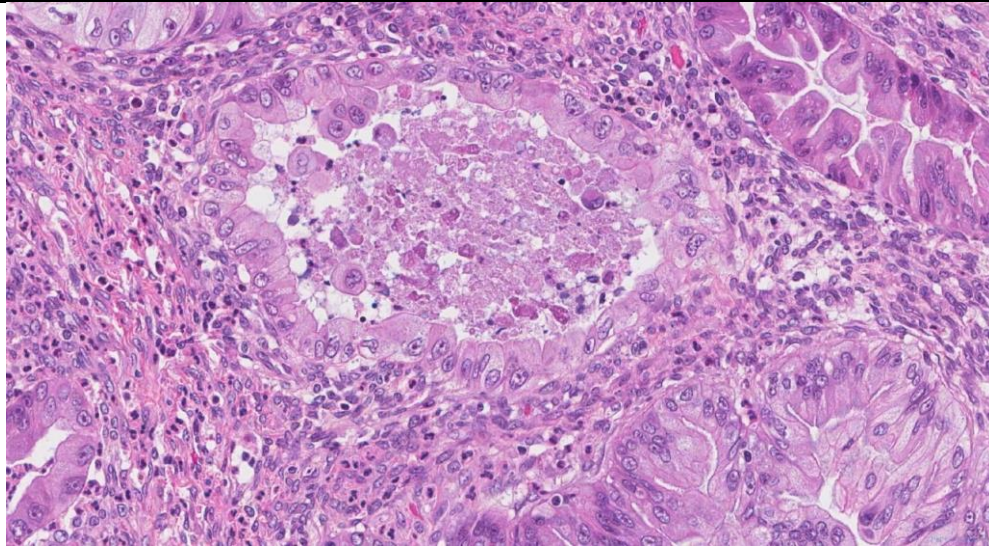


Figure 7 Primary mucinous carcinoma

Patient 8

A 58-year-old postmenopausal woman presented with abdominal distension, persistent lower abdominal pain, constipation, loss of appetite (4 months), abdominal fullness, and occasional nausea, without vaginal bleeding or urinary symptoms. She had no significant medical or family history of gynecological malignancy. Examination revealed a 15 cm fixed left adnexal mass without significant ascites or lymphadenopathy.

Investigations showed elevated CA-125 and SCC antigen. Transvaginal ultrasonography demonstrated a heterogeneous ovarian mass with cystic areas, calcifications, and irregular solid nodules, while contrast-enhanced CT revealed a predominantly cystic ovarian lesion with fat density, calcifications, and enhancing mural nodules, suggestive of malignant transformation of a mature cystic teratoma. The patient underwent exploratory laparotomy, total abdominal hysterectomy, bilateral salpingo-oophorectomy, infracolic omentectomy, pelvic lymphadenectomy, and comprehensive surgical staging. Intraoperatively, a large unilateral ovarian tumor with focal capsular irregularity and pelvic adhesions was identified, without distant metastasis. Histopathology confirmed squamous cell carcinoma arising within a mature cystic teratoma, showing invasive keratinizing squamous epithelial nests with adjacent mature ectodermal structures. The diagnosis was differentiated from metastatic squamous carcinoma through histopathological evaluation and clinicoradiological correlation. The patient received adjuvant platinum-based chemotherapy and remained recurrence-free during initial follow-up. The case highlights that malignant transformation of mature cystic teratoma, although rare, should be suspected in postmenopausal women with rapidly enlarging ovarian masses, with histopathology being essential for definitive diagnosis.

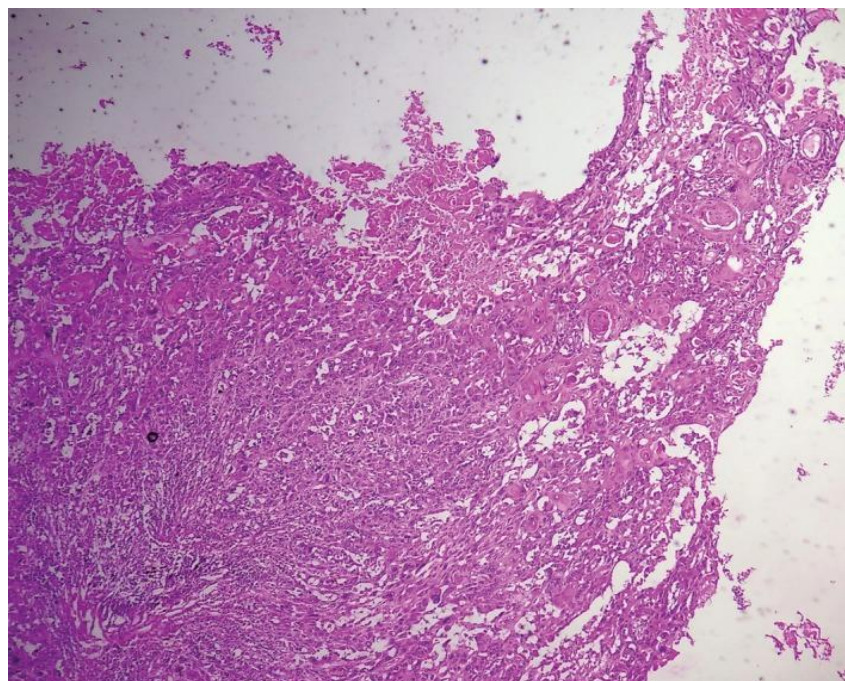


Figure 8 Squamous cell carcinoma

Patient 9

A 55-year-old postmenopausal woman presented with lower abdominal pain, abdominal bloating, early satiety, pelvic discomfort (3 months), fatigue, and a 5 kg weight loss (2 months). She had obesity and hypertension, with no family history of ovarian or endometrial carcinoma. Examination revealed a left adnexal mass without ascites or lymphadenopathy.

Investigations showed moderately elevated CA-125. Transvaginal ultrasonography demonstrated a complex unilateral ovarian mass, while contrast-enhanced MRI revealed a well-defined heterogeneous ovarian lesion without distant metastasis. Differential diagnoses included endometrioid carcinoma, clear cell carcinoma, and borderline epithelial ovarian tumor. The patient underwent exploratory laparotomy, total abdominal hysterectomy, bilateral salpingo-oophorectomy, infracolic omentectomy, pelvic lymph node sampling, and complete surgical staging. Intraoperatively, a 12 cm unilateral ovarian mass with focal endometrial thickening and no gross peritoneal dissemination was identified. Histopathology confirmed FIGO Grade 2 endometrioid adenocarcinoma of the ovary, showing back-to-back endometrioid glands with adjacent endometriosis. Immunohistochemistry was positive for PAX8, ER, PR, and CK7 and negative for WT-1, confirming primary ovarian endometrioid carcinoma and excluding high-grade serous carcinoma. The diagnosis was differentiated from metastatic endometrial adenocarcinoma through clinicopathological correlation. The patient received adjuvant platinum-based chemotherapy, with normalization of CA-125 and no recurrence on follow-up. The case highlights the importance of histopathology and immunohistochemistry for accurate diagnosis and management of ovarian endometrioid carcinoma.

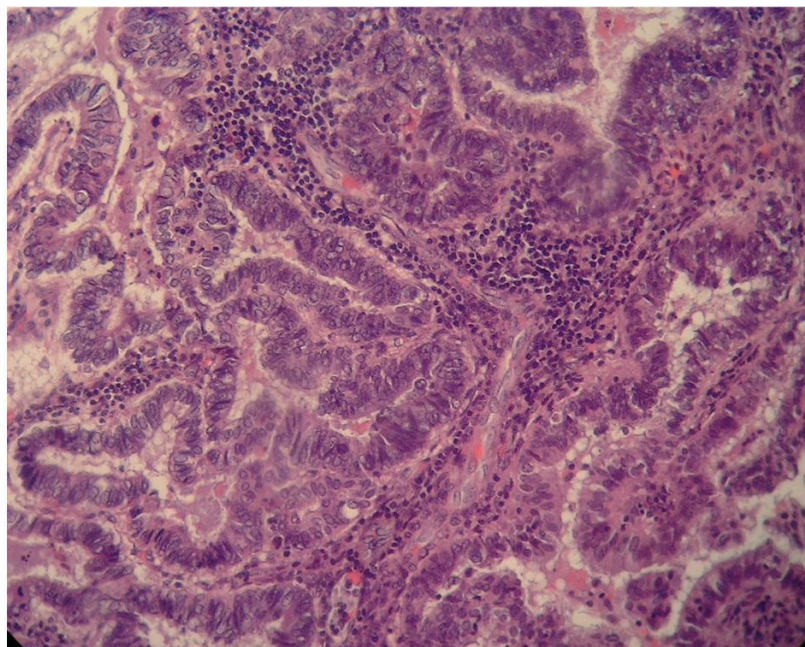


Figure 9 Endometrioid carcinoma

Patient 10

A 49-year-old postmenopausal woman presented with persistent lower abdominal pain, abdominal distension, pelvic heaviness (4 months), early satiety, fatigue, and intermittent nausea, with a history of pelvic endometriosis and no family history of ovarian or breast malignancy. Examination revealed mild pallor, a firm pelvic-abdominal mass, a left adnexal mass, and mild ascites.

Investigations showed mild anemia, significantly elevated CA-125, and normal renal and liver function tests. Transvaginal ultrasonography demonstrated a large unilateral complex ovarian mass, while contrast-enhanced CT revealed a heterogeneous ovarian lesion with irregular enhancing solid areas, moderate ascites, and pelvic peritoneal deposits, suggestive of epithelial ovarian malignancy. The patient underwent exploratory laparotomy, total abdominal hysterectomy, bilateral salpingo-oophorectomy, infracolic omentectomy, pelvic lymphadenectomy, peritoneal biopsies, and optimal cytoreductive surgery. Intraoperatively, a large unilateral ovarian tumor with capsular rupture, pelvic adhesions, and superficial peritoneal implants was identified, without hepatic or splenic metastases. Histopathology confirmed ovarian clear cell carcinoma, showing tubulocystic, papillary, and solid patterns with clear cytoplasm, hobnail cells, and adjacent endometriosis. Immunohistochemistry was positive for HNF-1 β , Napsin A, CK7, and PAX8.

and negative for WT-1, confirming the diagnosis and differentiating it from endometrioid carcinoma and metastatic clear cell renal cell carcinoma. The patient received adjuvant platinum-based chemotherapy, with declining CA-125 levels and satisfactory clinical improvement, and remained under regular oncological follow-up. The case highlights the importance of histopathology and immunohistochemistry for accurate diagnosis of ovarian clear cell carcinoma.

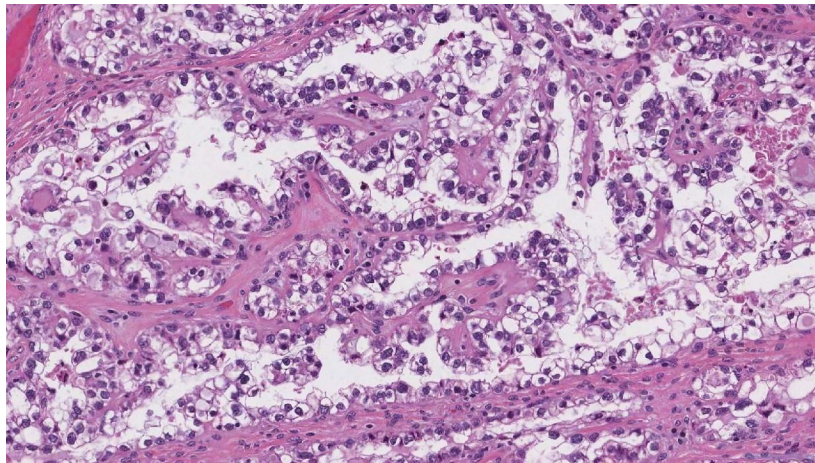


Figure 10 Ovarian clear cell carcinoma

Patient 11

A 61-year-old postmenopausal woman presented with abdominal distension, dull lower abdominal pain, pelvic pressure (3 months), early satiety, decreased appetite, and a 4 kg weight loss (6 weeks). She had controlled hypertension with no history of gynecological malignancy. Examination revealed mild pallor, a firm irregular pelvic-abdominal mass, and moderate ascites, without lymphadenopathy.

Investigations showed mild anemia, markedly elevated CA-125, and normal liver and renal function tests. Transvaginal ultrasonography demonstrated a predominantly solid ovarian mass, while contrast-enhanced CT revealed a heterogeneous unilateral ovarian tumor with moderate ascites, without distant metastasis. Differential diagnoses included transitional cell carcinoma (TCC), high-grade serous carcinoma, and malignant Brenner tumor. The patient underwent exploratory laparotomy, total abdominal hysterectomy, bilateral salpingo-oophorectomy, infracolic omentectomy, pelvic lymphadenectomy, peritoneal biopsies, and optimal cytoreductive surgery. Intraoperatively, a 13 cm unilateral ovarian tumor with capsular involvement and multiple small peritoneal implants was identified, without bowel or upper abdominal involvement. Histopathology confirmed primary ovarian transitional cell carcinoma (TCC), showing papillary and solid nests of malignant transitional-type epithelial cells with stromal invasion and no benign Brenner tumor component. Immunohistochemistry was positive for CK7, PAX8, WT-1, and EMA, confirming the diagnosis and differentiating it from metastatic urothelial carcinoma and malignant Brenner tumor. The patient received adjuvant platinum- and taxane-based chemotherapy, with declining CA-125 and no disease progression during follow-up. The case highlights the importance of histopathology and immunohistochemistry for accurate diagnosis and management of primary ovarian transitional cell carcinoma.

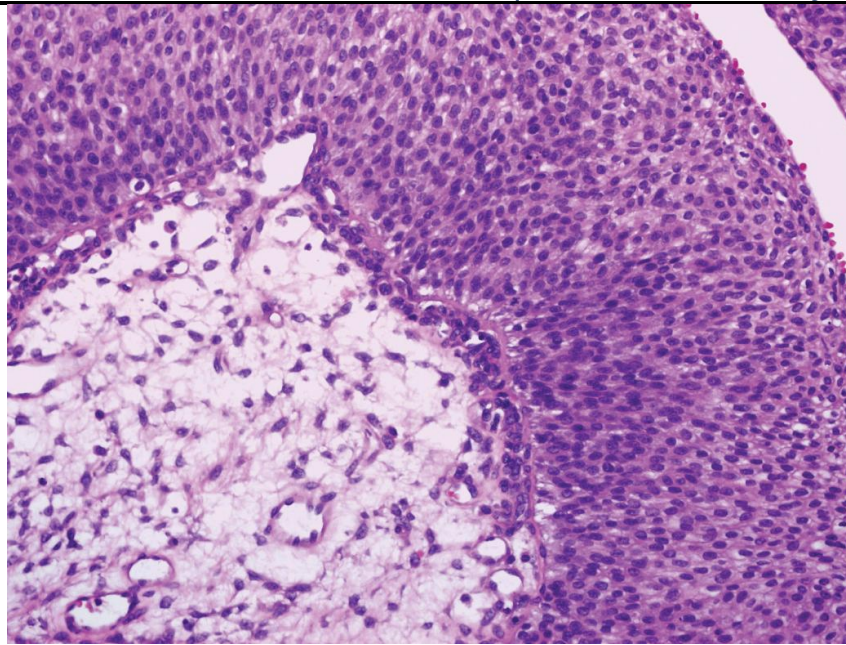


Figure 11 Primary transitional cell carcinoma

Patient 12

A 65-year-old postmenopausal woman presented with abdominal distension, intermittent lower abdominal pain, urinary frequency, pelvic discomfort (4 months), early satiety, and generalized fatigue, with controlled diabetes, hypertension, and no significant family history. Examination revealed a firm pelvic-abdominal mass, a large left adnexal mass, and mild ascites, without lymphadenopathy.

Investigations showed mild normocytic anemia, moderately elevated CA-125, normal CEA, and normal liver and renal function tests. Transvaginal ultrasonography demonstrated a predominantly solid ovarian mass with cystic degeneration and calcifications, while contrast-enhanced CT revealed a heterogeneous ovarian tumor with calcified foci. Differential diagnoses included malignant Brenner tumor, transitional cell carcinoma, and high-grade serous carcinoma. The patient underwent exploratory laparotomy, total abdominal hysterectomy, bilateral salpingo-oophorectomy, infracolic omentectomy, pelvic lymphadenectomy, peritoneal washings, and comprehensive surgical staging. Intraoperatively, a 14 cm unilateral ovarian tumor with focal capsular involvement was identified, without upper abdominal metastasis. Histopathology confirmed malignant Brenner tumor, showing malignant transitional-type epithelial cells with stromal invasion alongside benign and borderline Brenner tumor components. Immunohistochemistry was positive for CK7, GATA3, uroplakin III, and p63, with focal PAX8 expression, confirming the diagnosis and differentiating it from primary ovarian transitional cell carcinoma and metastatic urothelial carcinoma. The patient received adjuvant platinum-based chemotherapy, recovered uneventfully, and showed normalization of CA-125 with no recurrence during follow-up. The case highlights the importance of extensive histopathological sampling and immunohistochemistry for accurate diagnosis of malignant Brenner tumor.

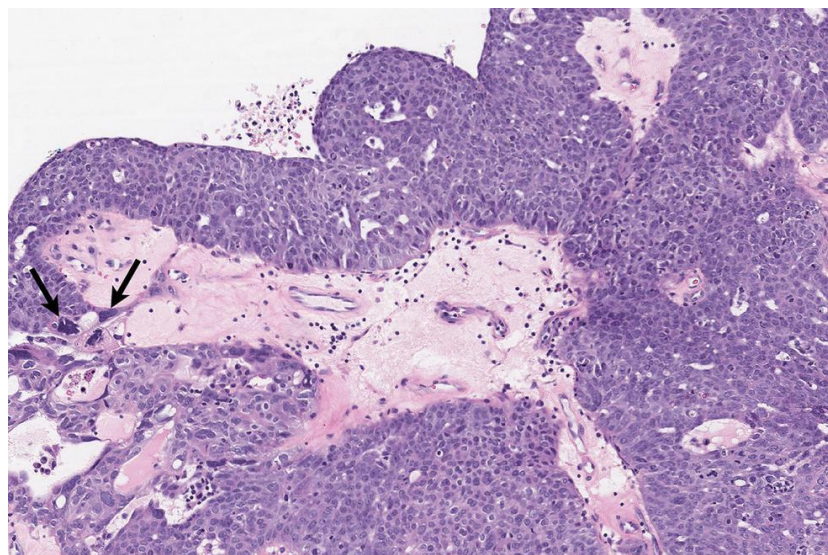


Figure 12 Malignant Brenner tumor

Patient 13

A 67-year-old postmenopausal woman presented with progressive abdominal distension, diffuse lower abdominal pain, anorexia, significant weight loss (4 months), fatigue, early satiety, and occasional constipation, with no abnormal vaginal bleeding. She had hypertension and type 2 diabetes mellitus, with no family history of gynecological malignancy. Examination revealed moderate ascites, a large irregular pelvic-abdominal mass extending above the umbilicus, and fixed bilateral adnexal masses, without palpable lymphadenopathy.

Investigations showed mild normocytic anemia, markedly elevated CA-125, and normal liver and renal function tests. Transvaginal ultrasonography demonstrated a large heterogeneous ovarian mass with solid, cystic, and necrotic areas. Contrast-enhanced CT revealed bilateral complex ovarian masses, omental thickening, moderate ascites, and multiple peritoneal nodules, suggestive of advanced epithelial ovarian malignancy, with differential diagnoses including carcinosarcoma, high-grade serous carcinoma, and metastatic ovarian disease. The patient underwent exploratory laparotomy with optimal cytoreductive surgery, including total abdominal hysterectomy, bilateral salpingo-oophorectomy, infracolic omentectomy, pelvic lymphadenectomy, and resection of peritoneal metastatic deposits. Intraoperatively, bilateral ovarian tumors, omental involvement, extensive pelvic adhesions, and widespread peritoneal implants were identified. Histopathology confirmed ovarian carcinosarcoma (malignant mixed Müllerian tumor) with high-grade serous carcinomatous and spindle cell sarcomatous components. Immunohistochemistry showed cytokeratin (AE1/AE3) positivity in epithelial elements and vimentin positivity in mesenchymal components, confirming the biphasic tumor and differentiating it from poorly differentiated epithelial ovarian carcinoma and metastatic uterine carcinosarcoma. The patient received adjuvant platinum- and taxane-based chemotherapy, showed a decline in CA-125, and remained under close oncological surveillance. The case highlights the importance of histopathology and immunohistochemistry in diagnosing ovarian carcinosarcoma.

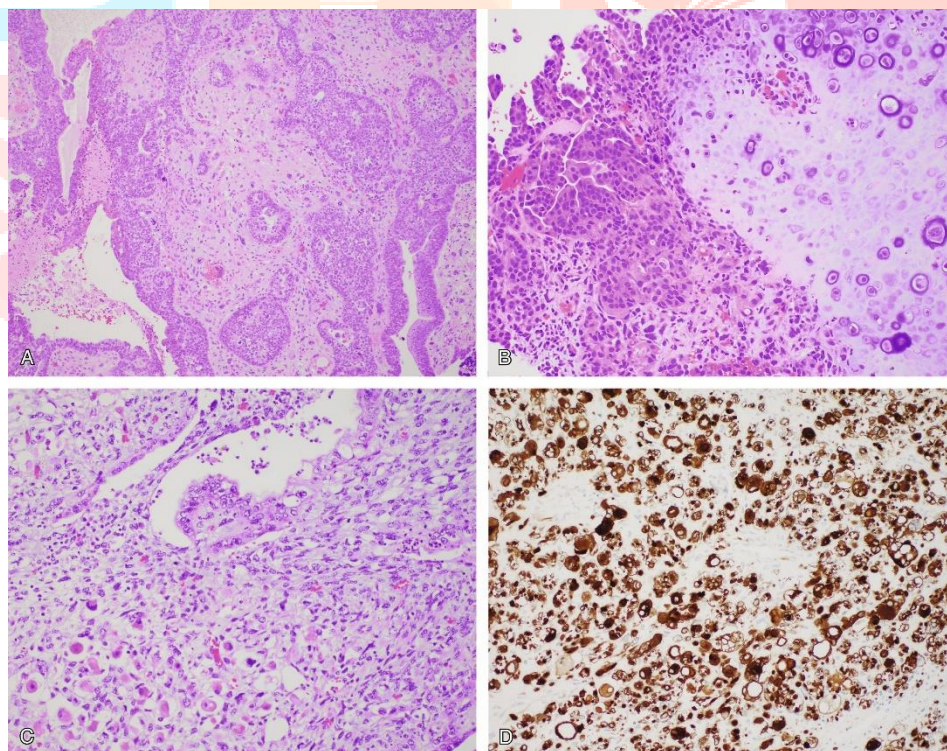


Figure 13 Ovarian carcinosarcoma

Patient 14

A 21-year-old nulliparous woman presented with rapidly increasing abdominal distension, lower abdominal pain, nausea, early satiety (6 weeks), abdominal fullness, and generalized weakness, without menstrual irregularities or abnormal vaginal bleeding. She had no significant personal or family history of gynecological malignancy. Examination revealed a large mobile pelvic-abdominal mass, with no ascites or lymphadenopathy.

Investigations showed mildly elevated AFP, while CA-125 and β -hCG were normal. Transvaginal ultrasonography demonstrated a large heterogeneous ovarian mass with solid tissue, cystic spaces, and

calcifications, while contrast-enhanced CT revealed an 18 cm unilateral ovarian lesion with fat, calcification, and immature soft-tissue components, suggestive of a malignant germ cell tumor. Differential diagnoses included immature teratoma, yolk sac tumor, and mixed germ cell tumor. The patient underwent fertility-sparing staging laparotomy with unilateral salpingo-oophorectomy, omentectomy, peritoneal washings, and multiple peritoneal biopsies. Intraoperatively, a large encapsulated ovarian mass without contralateral ovarian involvement or distant metastasis was identified. Histopathology confirmed Grade II immature teratoma, showing mature derivatives of all three germ cell layers with immature neuroectodermal tissue, immature cartilage, and primitive mesenchymal elements. Immunohistochemistry supported the diagnosis and excluded other malignant germ cell tumors. The patient received adjuvant BEP chemotherapy (bleomycin, etoposide, and cisplatin), recovered uneventfully, and showed no residual or recurrent disease on follow-up. The case highlights the importance of histopathological grading and immunohistochemistry for appropriate treatment, fertility preservation, and prognosis in immature ovarian teratoma.

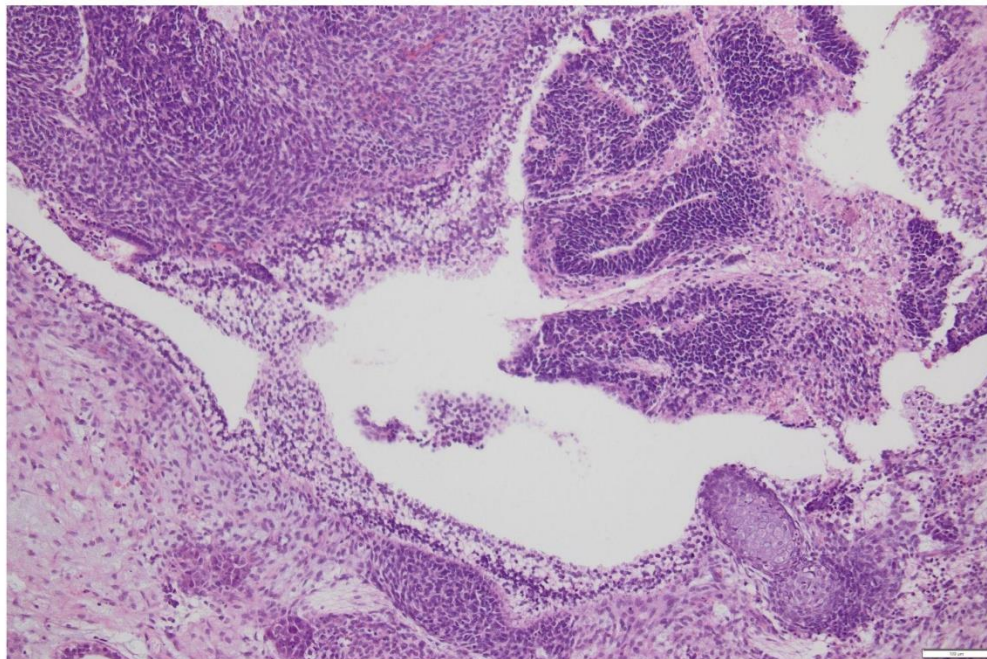


Figure 14 Immature teratoma

Patient 15

A 19-year-old unmarried woman presented with lower abdominal pain, abdominal distension, a palpable abdominal mass (2 months), nausea, decreased appetite, and generalized weakness, without menstrual irregularities or abnormal vaginal bleeding. She had no significant medical or family history of ovarian or breast malignancy. Examination revealed mild pallor, a large pelvic-abdominal mass, and no significant ascites or lymphadenopathy.

Investigations showed mild anemia, markedly elevated LDH, while AFP and β -hCG were normal. Transabdominal ultrasonography demonstrated a large predominantly solid ovarian mass, while contrast-enhanced CT revealed a 16 cm unilateral solid ovarian tumor without distant metastasis, suggestive of a malignant ovarian germ cell tumor. The patient underwent fertility-sparing staging laparotomy with unilateral salpingo-oophorectomy, infracolic omentectomy, peritoneal washings, and multiple peritoneal biopsies. Intraoperatively, a large encapsulated ovarian tumor with an intact capsule and no gross peritoneal dissemination was identified, while the contralateral ovary and uterus were preserved. Histopathology confirmed ovarian dysgerminoma, showing large polygonal cells with clear cytoplasm, prominent nucleoli, and lymphocyte-rich fibrous septa. Immunohistochemistry was positive for OCT3/4, SALL4, PLAP, and c-KIT (CD117), confirming the diagnosis and differentiating it from lymphoma, metastatic melanoma, and other germ cell tumors. The patient received adjuvant BEP chemotherapy (bleomycin, etoposide, and cisplatin), with normalization of LDH and no recurrence on follow-up. The case highlights the importance of histopathology and immunohistochemistry for accurate diagnosis and fertility-preserving management of ovarian dysgerminoma.

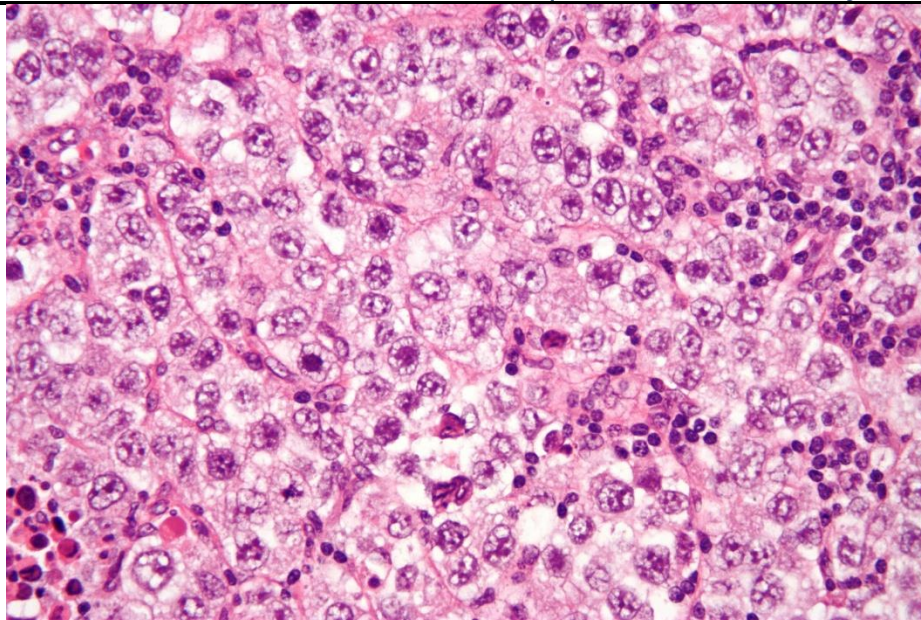


Figure 15 Dysgerminoma

3. Discussion

The present case series demonstrates the broad histopathological spectrum of ovarian malignancies and the diagnostic challenges across different histological subtypes. The cases included epithelial tumors (high-grade serous, mucinous, endometrioid, clear cell, transitional cell, malignant Brenner tumor, and carcinosarcoma), germ cell tumors (dysgerminoma, yolk sac tumor, immature teratoma), sex cord-stromal tumors (granulosa cell tumor), and rare malignancies such as squamous cell carcinoma arising in mature cystic teratoma and small cell carcinoma of the ovary. Despite advances in imaging and tumor markers, histopathology remains the gold standard because many ovarian tumors share overlapping clinical and radiological features.

Most patients presented with abdominal pain, abdominal distension, early satiety, pelvic mass, and weight loss, consistent with Mondal et al. [19], analyzed 957 ovarian neoplasms and found abdominal pain and swelling to be the most common symptoms, with epithelial tumors being the predominant subtype. Pilli et al. [20] similarly reported that 70.9% of 282 ovarian tumors were epithelial, followed by germ cell and sex cord-stromal tumors, with serous carcinoma as the most common malignant epithelial subtype, findings comparable to the present series.

Although several patients showed elevated CA-125, AFP, LDH, inhibin, and SCC antigen, these markers alone were insufficient for diagnosis. Jha and Karki [21] also reported that while tumor markers and ultrasonography aid preoperative evaluation, definitive diagnosis depends on meticulous histopathological examination, with epithelial tumors predominating overall and germ cell tumors occurring mainly in younger women. The present series also highlights rare ovarian malignancies, including clear cell carcinoma, malignant Brenner tumor, carcinosarcoma, dysgerminoma, immature teratoma, and squamous cell carcinoma arising in mature cystic teratoma, which posed significant diagnostic challenges. Similar findings were reported by Gupta et al. [22], emphasized that extensive tissue sampling and careful histopathological evaluation are essential to distinguish these tumors from metastatic or borderline lesions.

Table 1. Clinical Characteristics of Patients Included in the Case Series

Patient	Age (Years)	Clinical Presentation	Radiological Findings	Histopathological Diagnosis	Treatment	Outcome
1	56	Abdominal distension, pain, early satiety	Bilateral ovarian masses with ascites	High-grade serous carcinoma	Cytoreductive surgery + platinum chemotherapy	Improved on follow-up
2	38	Pelvic pain, abdominal fullness	Complex cystic-solid ovarian mass	Clear cell carcinoma associated with endometriosis	TAH + BSO + chemotherapy	Disease-free during follow-up
3	52	Pelvic mass, abdominal pain	Complex ovarian mass with calcifications	Squamous cell carcinoma arising in mature cystic teratoma	Surgical staging + chemotherapy	Stable during follow-up
4	29	Abdominal pain, pelvic mass	Large unilateral solid ovarian tumor	Yolk sac tumor	Fertility-sparing surgery + BEP chemotherapy	Complete clinical response
5	24	Abdominal pain, nausea, vomiting	Large unilateral solid ovarian mass	Small cell carcinoma (hypercalcemic type)	Surgery + platinum chemotherapy	Close surveillance required
6	46	Irregular bleeding, abdominal pain	Solid unilateral ovarian mass	Adult granulosa cell tumor	TAH + BSO	No recurrence on follow-up
7	62	Abdominal distension, weight loss	Multiloculated ovarian cystic mass	Primary mucinous carcinoma	Surgical staging + chemotherapy	Improved
8	58	Abdominal pain, pelvic mass	Dermoid cyst with mural nodules	Squamous cell carcinoma in mature cystic teratoma	Surgery + chemotherapy	Stable
9	55	Pelvic pain, abdominal bloating	Complex unilateral ovarian mass	Endometrioid carcinoma	Surgical staging + chemotherapy	Disease-free
10	49	Abdominal distension, pelvic heaviness	Complex cystic-solid ovarian lesion	Clear cell carcinoma	Cytoreductive surgery + chemotherapy	Improved
11	61	Abdominal pain, ascites	Predominantly solid ovarian mass	Transitional cell carcinoma	Surgery + platinum-taxane	Stable

					chemotherapy	
12	65	Pelvic discomfort, abdominal mass	Solid ovarian tumor with calcifications	Malignant Brenner tumor	Surgery + chemotherapy	No recurrence
13	67	Weight loss, ascites, abdominal pain	Bilateral ovarian masses with peritoneal deposits	Ovarian carcinosarcoma	Cytoreductive surgery + chemotherapy	Under surveillance
14	21	Abdominal distension, pelvic mass	Large heterogeneous ovarian mass	Immature teratoma	Fertility-sparing surgery + BEP chemotherapy	Disease-free
15	19	Abdominal pain, palpable abdominal mass	Solid unilateral ovarian tumor	Dysgerminoma	Fertility-sparing surgery + BEP chemotherapy	Excellent recovery

The present cases also highlighted the critical role of immunohistochemistry (IHC) in challenging diagnoses. Markers including WT-1, PAX8, CK7, HNF-1 β , Napsin A, inhibin, calretinin, AFP, PLAP, OCT3/4, SALL4, and CD117 were instrumental in differentiating primary ovarian malignancies from metastatic lesions and morphologically similar tumors. This is consistent with Mankar and Jain [23], reported that IHC significantly improves diagnostic accuracy, particularly in poorly differentiated epithelial, sex cord-stromal, and germ cell tumors.

The series also demonstrated associations between ovarian malignancies and precursor lesions. Clear cell and endometrioid carcinomas were associated with endometriosis, while squamous cell carcinoma arose within a mature cystic teratoma. Similar findings were reported by Sharadha et al. [24], emphasized the importance of careful gross examination and extensive histological sampling to identify precursor lesions and malignant transformation.

Most patients underwent comprehensive surgical staging followed by platinum-based chemotherapy, while fertility-sparing surgery was successfully performed in selected young patients with malignant germ cell tumors. Ahmad et al. [25] similarly reported that treatment depends on histological subtype, tumor stage, and patient age, with excellent outcomes in germ cell tumors managed by fertility-preserving surgery and platinum-based chemotherapy, whereas high-grade epithelial tumors require aggressive cytoreductive surgery and adjuvant chemotherapy. Overall, this case series reinforces the importance of integrating clinical evaluation, imaging, serum tumor markers, histopathology, and immunohistochemistry for accurate diagnosis of ovarian malignancies. Although imaging provides valuable preoperative information, histopathology remains the definitive diagnostic modality, guiding treatment, prognostic assessment, and long-term follow-up. Early diagnosis, meticulous pathological evaluation, and multidisciplinary management are essential for improving patient outcomes.

Table 2. Histopathological Spectrum and Diagnostic Challenges of Ovarian Malignancies

Patient	Tumor Category	Histopathological Features	Immunohistochemical Markers*	Major Diagnostic Challenge
1	Surface epithelial	High-grade serous carcinoma	WT-1, PAX8, CK7	Differentiation from metastatic serous carcinoma
2	Surface epithelial	Clear cell carcinoma	HNF-1 β , Napsin A, PAX8	Differentiation from endometrioid carcinoma
3	Germ cell-derived transformation	Squamous cell carcinoma in mature cystic teratoma	p63, CK5/6	Identification of malignant transformation
4	Germ cell	Yolk sac tumor	AFP, SALL4	Differentiation from mixed germ cell tumors
5	Rare ovarian malignancy	Small cell carcinoma (hypercalcemic type)	SMARCA4 (loss), CK	Distinction from other small round-cell tumors
6	Sex cord-stromal	Adult granulosa cell tumor	Inhibin- α , Calretinin, FOXL2	Differentiation from endometrioid carcinoma
7	Surface epithelial	Mucinous carcinoma	CK7, PAX8	Excluding metastatic gastrointestinal carcinoma
8	Germ cell-derived transformation	Squamous cell carcinoma in dermoid cyst	p63, CK5/6	Differentiation from metastatic squamous carcinoma
9	Surface epithelial	Endometrioid carcinoma	ER, PR, PAX8	Distinguishing from endometrial primary carcinoma
10	Surface epithelial	Clear cell carcinoma	HNF-1 β , Napsin A	Differentiation from metastatic renal cell carcinoma
11	Surface epithelial	Transitional cell carcinoma	CK7, WT-1	Distinguishing from malignant Brenner tumor
12	Surface epithelial	Malignant Brenner tumor	GATA3, p63, CK7	Differentiation from transitional cell carcinoma
13	Mixed epithelial–mesenchymal	Ovarian carcinosarcoma	Cytokeratin, Vimentin	Identification of biphasic tumor components
14	Germ cell	Immature teratoma	SALL4, AFP (focal)	Accurate grading based on immature neuroepithelium

15	Germ cell	Dysgerminoma	OCT3/4, PLAP, CD117, SALL4	Differentiation from lymphoma and other germ cell tumors
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Conclusion

This case series highlights the broad histopathological spectrum of ovarian malignancies and the diagnostic challenges associated with their management. Patients commonly presented with abdominal pain, abdominal distension, pelvic mass, early satiety, and weight loss, leading to delayed diagnosis. The series included high-grade serous, mucinous, endometrioid, clear cell, transitional cell, malignant Brenner tumor, carcinosarcoma, granulosa cell tumor, dysgerminoma, yolk sac tumor, immature teratoma, squamous cell carcinoma arising in mature cystic teratoma, and small cell carcinoma of the ovary, demonstrating the marked heterogeneity of ovarian cancers. Although imaging and serum tumor markers aided preoperative evaluation, they were insufficient for definitive diagnosis because of overlapping features among tumor subtypes. Histopathology, supported by immunohistochemistry using markers such as WT-1, PAX8, CK7, HNF-1 β , Napsin A, inhibin, calretinin, SALL4, OCT3/4, and CD117, remained essential for accurate tumor classification, identification of rare variants, differentiation from metastatic lesions, and staging.

The findings emphasize the importance of comprehensive surgical staging, individualized treatment, and multidisciplinary management. Early diagnosis, combined with meticulous histopathological evaluation, enables appropriate therapeutic planning and improves prognosis. Overall, histopathology remains the gold standard for diagnosing ovarian malignancies and plays a crucial role in guiding treatment, prognostic assessment, and long-term follow-up.

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