


Ovarian serous borderline tumor with mural nodules of anaplastic carcinoma and omental involvement: A case report

Rare Tumors
Volume 15: 1–5
© The Author(s) 2023
Article reuse guidelines:
sagepub.com/journals-permissions
DOI: 10.1177/20363613231172260
journals.sagepub.com/home/rtu


Paula I Hernandez Acevedo¹, Gloria J Carter², Madeleine Courtney-Brooks³ and Beth Z Clark² 

Abstract

Mural nodules are rarely identified in cystic ovarian neoplasms, and have been categorized into sarcoma-like, sarcomatous, and anaplastic carcinomatous types. Most reports of these mural nodules have been described in mucinous ovarian tumors. In this case report, we describe an ovarian serous borderline tumor with mural nodules composed of high-grade carcinoma with anaplastic features and necrosis, including the morphologic features, immunoprofile, and results of tumor DNA sequencing. Omental involvement was also identified. Recognition of this phenomenon in serous tumors is important, so that thickened areas of cyst wall in ovarian serous tumors will be thoroughly examined.

Keywords

Ovary serous borderline tumor, mural nodules

Date received: 17 January 2023; accepted: 10 April 2023

Case

Informed consent was sought, but unable to be obtained, as the patient was deceased at the time of preparation of the manuscript, and the patient's legally authorized representative was unable to be contacted. This case report is not classified as research by the Human Research Protection Office at the University of Pittsburgh and therefore approval is not required. No Health Insurance Portability and Accountability Act (HIPAA) identifiers or other identifying characteristics are included in this manuscript. The patient, a mid-70s female, presented with longstanding gastrointestinal symptoms and underwent computed tomography (CT) of the abdomen and pelvis, showing a 14 cm cyst probably arising from the right ovary. Physical examination revealed a large cystic smooth pelvic mass on bimanual examination. Pre-operative CA-125 was elevated at 380.6 U/mL, and carcinoembryonic antigen testing was within normal limits. The patient underwent laparotomy, revealing a large cystic mass arising from the right ovary with some adhesions.

Intraoperative rupture was noted during dissection of adhesions. The right adnexal mass was described on gross examination as a previously opened, 15 cm in greatest dimension, uniloculated and cystic mass with minimal papillary excrescences, although abundant thickened areas with tan-white focally hemorrhagic and focally necrotic cut surfaces were identified.

Frozen section diagnosis of the mass was requested, and definitive diagnosis was deferred to permanent

¹Ponce Health Sciences University, Ponce, Puerto Rico

²Division of Breast and Gynecologic Pathology, University of Pittsburgh Medical Center, Magee-Womens Hospital, Pittsburgh, PA, USA

³Division of Gynecologic Oncology, University of Pittsburgh Medical Center, Magee-Womens Hospital, Pittsburgh, PA, USA

Corresponding author:

Beth Z Clark, Division of Breast and Gynecologic Pathology, Department of Pathology, University of Pittsburgh Medical Center, Magee-Womens Hospital, Pittsburgh, PA, USA

Email: clarkbz@upmc.edu



Creative Commons Non Commercial CC BY-NC: This article is distributed under the terms of the Creative Commons Attribution-NonCommercial 4.0 License (<https://creativecommons.org/licenses/by-nc/4.0/>) which permits non-commercial use, reproduction and distribution of the work without further permission provided the original work is attributed as specified on the SAGE and Open Access pages (<https://us.sagepub.com/en-us/nam/open-access-at-sage>).

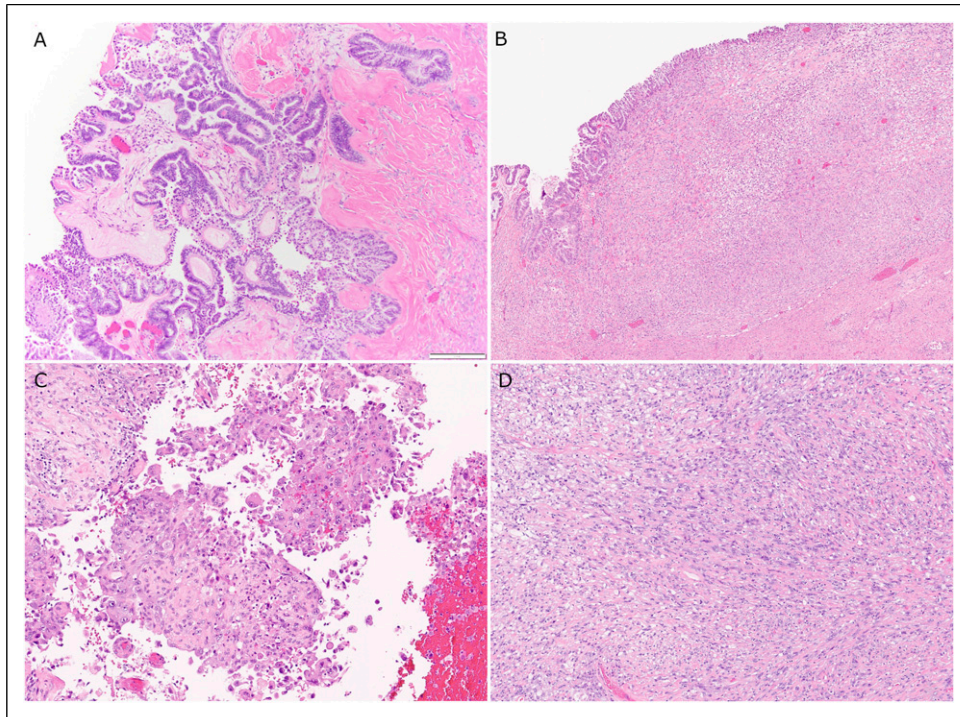


Figure 1. Representative hematoxylin and eosin (h and e) images of the tumor. (a): Focus of epithelial proliferation with stratification, hierarchical branching, and mild nuclear atypia; (b): Nodule composed of spindle cells, abutting serous cyst lining; (c): Focal papillary epithelioid growth pattern within nodule; (d): Nodule with spindle morphology.

histopathologic examination, with a diagnosis of “at least borderline tumor with extensive inflammation and necrosis”. A 3 cm firm white omental nodule was also identified intraoperatively. Staging procedure was ultimately performed, to include total hysterectomy, bilateral salpingo-oophorectomy, omentectomy, pelvic and peritoneal biopsies, and pelvic and para-aortic lymphadenectomy.

Histopathologic examination of the mass demonstrated characteristic features of serous borderline tumor lining the cystic spaces, composed of mostly bland columnar epithelial cells with apical snouts and inconspicuous nucleoli. In some foci, comprising greater than 10% of the serous component of the neoplasm, epithelial proliferation and hierarchical branching were noted (Figure 1(a)). No evidence of mucinous differentiation was identified, and no high-grade nuclear features were noted in the cyst lining cells. Within the wall of the cystic mass, multiple nodules were identified, composed of a spindled and epithelioid proliferation which abutted the serous lining in some areas but did not exhibit a biphasic growth pattern (Figure 1(b)). The epithelioid areas demonstrated cells with enlarged vesicular nuclei, moderate nuclear pleomorphism, and abundant eosinophilic cytoplasm with admixed inflammatory cells predominantly composed of lymphocytes and neutrophils. Focally, the epithelioid cells showed a papillary growth pattern with more marked nuclear pleomorphism

(Figure 1(c)). Other nodules were composed of cells with similar nuclear features; however, the cells showed spindled morphology with some fascicular growth pattern with more conspicuous mitotic figures and multiple foci of necrosis (Figure 1(d)). Tumor involving the omentum showed high-grade features and a predominantly spindled morphology, similar to the tumor seen in Figure 1(d).

Results of immunohistochemical stains performed on the tumor are detailed in Table 1. The serous borderline component of the neoplasm showed an immunoprofile that supported the serous phenotype, including reactivity for estrogen receptor (ER), progesterone receptor (PR), Wilms’ tumor (WT-1), cytokeratin 7 (CK7), and PAX-8. The anaplastic nodules showed reactivity for cytokeratins (AE1/AE3, CK8, and CK7), PAX-8, WT-1 (weak), and showed a mutated pattern for p53. Representative images of the immunoprofile are shown in Figure 2.

Mismatch repair protein immunohistochemistry showed preserved expression of MLH-1, PMS-2, MSH-2, and MSH-6. PD-L1 testing using the 22C3 antibody was reported as positive with a CPS of 40 (Caris Life Sciences). Tumor DNA sequencing (Caris Life Sciences) was reported to show pathogenic variants in KRAS (Exon 2, p.G12D) and TP53 (Exon 4, p.W91) genes. Variants of uncertain significance were also noted in the ATM (Exon 8, p.R337H) and BRAF (Exon 9, p.R389H) genes.

Table 1. Immunohistochemistry results with antibody clone and vendor information.

Antibody (clone, vendor)	Serous borderline tumor component	Anaplastic carcinoma component
ER (SP1, ventana)	Positive	Negative
PR (SP1, ventana)	Positive	Negative
P53 (DO-7, leica biosystems)	Wild-type reactivity	Strong nuclear reactivity
CK8 (35 beta H11, leica microsystems)	Positive	Positive
CK20 (KS20-8, roche/Ventana biocare)	Negative	Negative
CD10 (56C6, CellMarque)	Negative	Positive
HNF-1B (polyclonal rabbit, sigma-aldrich)	Weakly positive	Weakly positive
Beta HCG (polyclonal rabbit, roche/Ventana biocare)	Negative	Negative
CD34 (QBend/10, roche/Ventana biocare)	Negative	Negative
CK7 (OV-TL 12/30, roche/Ventana biocare)	Positive	Most positive
AE1/AE3 (AE1/AE3, leica microsystems)	Positive	Positive
Desmin (DE-R-11, roche/Ventana biocare)	Negative	Focally positive
RCC (PN-15, ventana)	Negative	Negative
PAX-8 (polyclonal rabbit, CellMarque)	Positive	Positive
WT-1 (WT49, leica microsystems)	Positive	Weakly positive
PI6 (E6H4, leica)	Patchy reactivity	Essentially negative
PLAP (polyclonal rabbit, signet)	Negative	Negative
Inhibin (RI, dako)	Negative	Negative

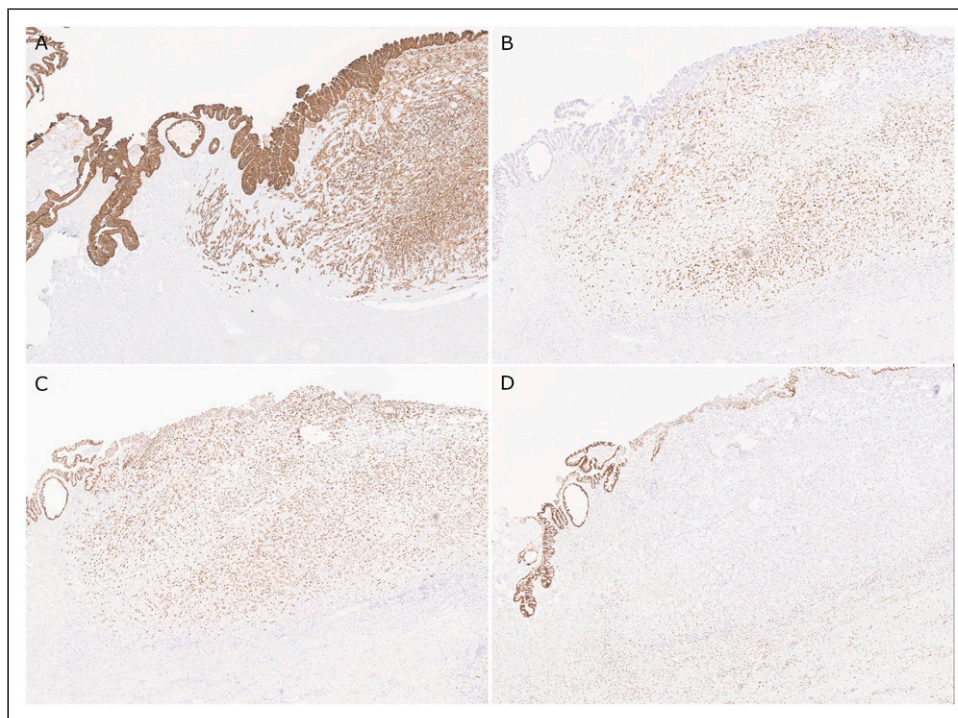


Figure 2. Immunoprofile of serous cyst lining and anaplastic nodule. (a): Cytokeratin eight shows diffuse reactivity in cyst lining and nodule; (b): p53 shows wild-type reactivity in serous component, but diffuse strong nuclear reactivity in anaplastic nodule; (c): PAX-8 shows diffuse reactivity in cyst lining and nodule; (d): WT-1 shows strong nuclear reactivity in cyst lining but only weak expression in anaplastic nodule.

Final pathologic stage was International Federation of Gynecology and Obstetrics (FIGO) Stage IIIC due to omental involvement. The patient received adjuvant combination chemotherapy with carboplatin and paclitaxel. Unfortunately, intraabdominal recurrence in the liver and pelvic peritoneum was identified on imaging approximately 5 months following the surgical resection of the mass, treated with bevacizumab and doxorubicin. No significant response to treatment was identified on follow-up CT imaging 2 months later. The patient expired soon thereafter.

Discussion

The differential diagnosis of ovarian cystic lesions is broad, and can include physiologic entities, simple epithelial cysts with a variety of lining cell types, borderline tumors, and malignant tumors. Borderline tumors show epithelial proliferation that falls short of a malignant diagnosis, and a diagnosis of carcinoma is generally reserved for epithelial neoplasms that demonstrate frank stromal invasion, confluent growth pattern, or unequivocal high-grade nuclear features. The most common types show a serous or mucinous epithelial lining. Mural nodules, since first described by Prat and Scully,¹ have been well-documented in the literature in mucinous tumors, despite their rarity. To be considered a mural nodule microscopically, these lesions should demonstrate little, if any, focal admixture with the associated tumor.² These mural nodules have been divided into reactive sarcoma-like, anaplastic carcinoma, and sarcomatous nodules.³ Reactive sarcoma-like nodules are difficult to diagnose, but may be well-circumscribed, may show a prominent inflammatory reaction, do not have associated necrosis or vascular invasion, and may have a better prognosis.⁴ Anaplastic carcinoma nodules usually show reactivity for some cytokeratins by immunohistochemistry, while sarcomatous nodules typically do not.

The pathogenesis of mural nodules in cystic ovarian epithelial neoplasms is poorly understood. In a prior case report of ovarian mucinous carcinoma with anaplastic carcinoma mural nodules in a 20-year-old, continuity between the epithelial element and sarcoma-appearing element was described, suggesting dedifferentiation and epithelial to mesenchymal transformation of the mucinous carcinoma.⁵ In a recent study of 13 ovarian mucinous tumors with associated mural nodules, 12 of the cases showed genetic evidence of clonality between the mural nodule(s) and associated mucinous tumor, including in sarcoma-like mural nodules, although no single recurrent genetic alterations were identified to suggest a “trigger” for mural

nodule development.⁶ Desouki, et al. reported a case of a mucinous ovarian adenocarcinoma with mural nodule of anaplastic carcinoma showing identical K-RAS mutations in each component, suggesting a form of dedifferentiation of the mucinous carcinoma.⁷ A K-RAS mutation (c.35G > A p.G12A) was also previously reported in both the mucinous and anaplastic carcinoma nodule components of an ovarian mucinous tumor with a mural nodule.⁸

In contrast to mural nodules associated with mucinous ovarian tumors, only very rare examples have been described in cystic ovarian tumors with a serous phenotype. Baergen, et al., described a case with bilateral serous cystadenocarcinoma with peritoneal involvement, in which one ovary showed sarcomatous mural nodules, with positive vimentin, but negative cytokeratin, EMA, and desmin by immunohistochemistry.² Gungor, et al., published a report of a 54-year-old with ovarian serous borderline tumor with both sarcomatous and sarcoma-like mural nodules.⁹ Parker, et al. described a high-grade abdominal recurrence of a serous borderline tumor (SBT) with noninvasive implants that showed sarcomatoid-type carcinoma with microscopic foci of better differentiated tumor that resembled the primary SBT; however, the spindled and high-grade areas were not identified in the primary tumor.¹⁰

In our case, mucinous differentiation was not identified in the epithelial component. The epithelial cyst lining showed cuboidal to columnar cells with focal cytoplasmic clearing and hierarchical branching characteristic of an SBT. No high-grade nuclear features were identified in the cyst lining cells. Immunohistochemical stains showed a characteristic profile of serous phenotype, including expression of CK7, ER, PR, and WT-1, with negative CK20 and wild-type p53 expression pattern. Based on the morphology and unusual nature of the histologic findings, carcinosarcoma (malignant mixed Mullerian tumor) was considered in the differential diagnosis, but a true biphasic growth pattern was not present and the cyst lining component was not frankly malignant. Adenosarcoma could also be considered in the differential diagnosis, but again, this lesion did not show a biphasic growth pattern, the epithelial component showed significant proliferation not usually present in adenosarcoma, and the tumor was predominantly cystic. The presence of KRAS and TP53 mutations is also of interest, as serous borderline tumors and low-grade serous carcinomas of the ovary can show KRAS mutations, while TP53 mutations are more often identified in high-grade serous carcinoma and carcinosarcoma, although the significance of this finding is unclear because the testing was performed at

an outside laboratory and it is unclear if tumor microdissection was performed.

Based on the morphologic features and immunoprofile of both the cyst lining component and the cells comprising the mural nodules, this case appears to represent an exceedingly rare example of anaplastic carcinomatous mural nodules involving a serous borderline tumor of the ovary.

Conclusion

Although very rare, mural nodules can be seen in serous ovary cystic tumors. The anaplastic carcinomatous component was identified in the omentum and likely contributed to the unfavorable outcome reported in this patient. It is important to recognize this phenomenon in order to perform adequate tissue sampling of thickened areas of the wall of the ovarian tumor, and in histologic examination to arrive at the correct diagnosis.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

ORCID iD

Beth Z Clark  <https://orcid.org/0000-0001-5965-8294>

References

1. Prat J and Scully RE. Ovarian mucinous tumors with sarcoma like mural nodules. A report of seven cases. *Cancer* 1979; 44: 1332–1344
2. Baergen RN and Rutgers JL. Mural Nodules in common epithelial tumors, of the ovary. *Int J Gynecol Pathol* 1994; 13: 62–72. DOI: [10.1097/00004347-199401000-00008](https://doi.org/10.1097/00004347-199401000-00008)
3. Vang R, Khunamornpong S, Kobel M, et al. WHO classification of tumours - mucinous borderline tumour, *Pan Afr Med J* 2020; 41; 50–52
4. Bagué S, Rodríguez IM and Prat J. Sarcoma-like mural nodules in mucinous cystic tumors of the ovary revisited. *Am J Surg Pathol* 2002; 26: 1467–1476. DOI: [10.1097/0000478-200211000-00009](https://doi.org/10.1097/0000478-200211000-00009)
5. Tsuruchi N, Kaku T, Kinoshita H, et al. Ovarian mucinous cystadenocarcinoma with sarcoma-appearing mural nodule of anaplastic carcinoma. *Gynecol Oncol* 1993; 50: 259–263. DOI: [10.1006/gyno.1993.1204](https://doi.org/10.1006/gyno.1993.1204)
6. Chapel DB, Lee EK, Da Silva AFL, et al. Mural nodules in mucinous ovarian tumors represent a morphologic spectrum of clonal neoplasms: a morphologic, immunohistochemical, and molecular analysis of 13 cases. *Mod Pathol* 2021; 34: 613–626. DOI: [10.1038/s41379-020-0642-9](https://doi.org/10.1038/s41379-020-0642-9)
7. Desouki MM, Khabele D, Crispens MA, et al. Ovarian mucinous tumor with malignant mural nodules. *Int J Gynecol Pathol* 2015; 34: 19–24. DOI: [10.1097/PGP.000000000000105](https://doi.org/10.1097/PGP.000000000000105)
8. Shao Y, Liu Q, Shi H, et al. Ovarian mucinous tumors with mural nodules: immunohistochemical and molecular analysis of 3 cases. *Diagnostic Pathology* 2020; 15: 35. DOI: [10.1186/s13000-020-00956-6](https://doi.org/10.1186/s13000-020-00956-6)
9. Gungor T, Altinkaya SO, Akbay S, et al. Malign mural nodules associated with serous ovarian tumor of borderline malignancy: a case report and literature review. *Arch Gynecol Obstet* 2010; 281: 485–490. DOI: [10.1007/s00404-009-1180-3](https://doi.org/10.1007/s00404-009-1180-3)
10. Parker RL, Clement PB, Chervover DJ, et al. Early recurrence of ovarian serous borderline tumor as high-grade carcinoma: a report of two cases. *Int J Gynecol Pathol* 2004; 23: 265–272. DOI: [10.1097/01.pgp.0000130049.19643.f6](https://doi.org/10.1097/01.pgp.0000130049.19643.f6)