Comprehensive Analysis of Ovarian Serous Borderline Tumors: Lymph Node Involvement and Implants - A Case Report

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ABSTRACT

Objective: Ovarian serous borderline tumors (SBTs) are a distinct subtype of ovarian tumors that exhibit characteristics intermediate between benign tumors and invasive ovarian cancers. These tumors may display cellular changes suggestive of malignancy but do not meet all the criteria for full malignancy.

Case: This article presents the case of a 55-year-old female who presented to the clinic with complaints of pain and swelling in the lower abdominal quadrant. Upon examination, multiloculated mass lesions were found in the bilateral adnexa, and the patient was diagnosed with Borderline (low malignant potential) serous tumor. The patient underwent total abdominal hysterectomy, bilateral salpingo-oophorectomy, partial omentectomy, and peritoneal implant excision. Additionally, pelvic lymph node resection was performed, and abdominal lavage fluid was collected. The tissue sections were examined under a light microscope, revealing epithelial-lined papillae with a complex structure resembling the columnar fallopian tube epithelium, showing hierarchical branching. The patient was diagnosed with Borderline (low malignant potential) serous tumor, omental implants, and lymph node involvement.

Conclusion: The presence of lymph node involvement and implants in ovarian SBT necessitates thorough surgical exploration and may impact the choice of therapies. Therefore, early detection and accurate staging are crucial in determining prognosis and treatment strategy.

Keywords: Ovary, Serous tumor, Borderline, Omental implant

INTRODUCTION

Ovarian serous tumors encompass a spectrum of tumors, including benign, borderline (low malignant potential), and malignant variants (1). Ovarian serous borderline tumors (SBTs) are a distinct subtype of ovarian tumors that exhibit characteristics intermediate between benign tumors and invasive ovarian cancers. These tumors are considered to have a low potential for malignancy and have a slightly higher potential for recurrence and progression than benign tumors, hence being termed "low malignant potential ovarian serous tumors." The incidence of ovarian borderline tumors is relatively low compared to other types of ovarian tumors (2). The terms Borderline, Indeterminate, and Low Malignant Potential are used interchangeably to describe different stages of ovarian tumors that have varying degrees of cellular atypia and growth potential. They are often used when the tumor's features are not clearly benign or malignant (3). Ovarian SBTs can exhibit cellular changes suggestive of malignancy but do not fulfill all the criteria for full malignancy. They are microscopically subclassified into conventional SBTs and micropapillary/cribriform SBTs (4).

This article presents the case of a patient who presented to the clinic with complaints of pain and swelling in the lower abdominal quadrant. Upon examination, multiloculated mass lesions were identified in the bilateral adnexa. The patient underwent surgery, and the diagnosis of a Borderline (low malignant potential) serous tumor was confirmed.
CASE

A 55-year-old female patient presented to the clinic with complaints of pain and swelling in the lower quadrant of the abdomen and loss of appetite. Pelvic ultrasonography revealed bilateral mass lesions of 15 x 12 cm in the right adnexa and 16x12 cm in the left adnexa, with multiloculated, thick septa with 1.5 and 1 cm papillary projections. The patient was taken into operation with the preliminary diagnosis of ovarian cancer. The patient underwent total abdominal hysterectomy, bilateral salpingo-oophorectomy, and the tissue was sent for a frozen procedure. Intraoperative omental implants and peritoneal implants were observed. Partial omentectomy and peritoneal implant excision were performed. The frozen result was reported as a serous borderline ovarian tumor. Additionally, the patient underwent pelvic lymph node resection, and abdominal lavage fluid was collected. The tissues were placed in 10% formaldehyde solution and sent to the pathology laboratory.

In the macroscopic examination, a polyp with a diameter of 1.2 cm was observed in her endometrium. In the right ovary, a mass measuring 15x12x11 cm with a smooth, shiny outer surface was identified. Upon cross-section, numerous cystic structures were visible, the largest of which measured 0.5 cm in diameter and contained yellow-clear fluid. The cyst wall measured 1-2 mm in thickness, with a smooth and brightly colored inner surface. A tumor exhibiting similar characteristics to the one in the right ovary, measuring 16x12x11 cm, was also found in the left ovary. When the sections were examined under a light microscope, epithelial-lined papillae with a complex structure resembling the columnar fallopian tube epithelium, showing hierarchical branching, were observed. Ciliated cells were occasionally seen. The papillary stroma was generally observed to be cell-poor, edematous and sometimes hyalinized fibrous. The epithelial cells were slightly atypical, hyperchromatic and sometimes multi-row, and tufting was observed in some areas. Tumor infiltration was observed in two lymph nodes. Tumor implants were present on the uterus serosal surface and omentum. With these findings, the following diagnoses were given:

**Right and left ovaries**: Proliferative (Borderline, indeterminate, low malignant potential) serous tumor. Capsule invasion: not seen, Right Tuba: Regular structure.

**Uterus**: Surface epithelial implants, endometrial polyp, and psammoma bodies in the uterine serosa.

Omentum, Peritoneum: Epithelial implants, psammoma bodies.

**Left pelvic lymph node**: Tumor infiltration in 2 lymph nodes. Reactive hyperplasia in 2 lymph nodes.

**Right pelvic and para-aortic lymph nodes**: Reactive hyperplasia in 3 and 2 lymph nodes, respectively.

**Abdominal washing fluid**: tumor-free, mesothelial cells, erythrocytes.

![Figure A: Epithelial-lined papillae (Hematoxylin and Eosin 40).](image)

![Figure B: Epithelial-lined papillae with a complex structure resembling the columnar fallopian tube epithelium, showing hierarchical branching (Hematoxylin and Eosin 200).](image)

![Figure C: Slightly atypical, hyperchromatic and sometimes multi-row, and tufting epithelial cells, the papillary stroma is cell-poor, edematous and hyalinized (Hematoxylin and Eosin 400).](image)

![Figure D: Lymph node implants with glands lined by bland cuboidal cells (Hematoxylin and Eosin 200).](image)

![Figure E: Uterus serosal surface implants (Hematoxylin and Eosin 100).](image)

![Figure F: Omental epithelial implants and psammoma bodies (Hematoxylin and Eosin 100).](image)
DISCUSSION

Although the terminology regarding ovarian SBT has evolved over time in the literature, it can still cause confusion. Ovarian SBT was used synonymously with “atypical proliferative serous tumor” according to the 2014 WHO classification (1). According to the WHO classification of female genital tumors, 2020, serous borderline tumor is currently the only recommended term for primary ovarian tumor (5). In addition, “Atypical proliferative serous tumor”, “Serous tumor of low malignant potential”, “Semi malignant serous tumor”, Noninvasive LGSC / micro papillary SBT terminology no longer recommended (1), which were used as synonyms for SBT in the literature. Micro papillary/cribriform SBT is no longer considered synonymous with non-invasive LGSC by definition according to the 2020 WHO (5).

Extra-ovarian involvement is usually seen in the omentum, peritoneal surface of organs, and abdominal wall (6). Rare organ involvements such as the brain and endometrial involvement has been reported in rare cases in the literature (7, 8). Endometrial implant was not observed in our case. In our case's histological examination, papillary structures with fibrous stroma, which are covered with a single layer or complex epithelial proliferations were observed. Epithelial cells appeared tall and columnar in shape with mild to moderate nuclear atypia. Occasionally, psammoma bodies consisting of dense small, round calcifications were observed. With these findings, our case was diagnosed as a conventional ovarian SBT.

Tumor stage, implants and micro papillary pattern are important in prognosis. Early stage disease (ovary confined, constituting a majority of patients) has survival comparable to that of the general population (9).

Systematic lymph node (LN) dissection is not part of the standard surgical procedure of ovarian SBT as the recurrence and survival rate for patients with affected or not affected LNs have been reported to be similar (10). When evaluated in this respect, the fact that lymph node dissection was performed in our case can be considered as overtreatment. Adjuvant chemotherapy was not applied to our patient because it was not indicated (11). In these tumor types, epithelial implants outside the primary tumor site are important in pathological evaluation. The presence of implants may contribute to tumor staging and may be important for treatment planning. In our case, in addition to implants being observed on the uterus and serosal surfaces, implants were also observed in the omentum.

There are 2 types of implants: noninvasive and invasive. It is important that implants are invasive and non-invasive. Invasive implants are more common in micro papillary type ovarian SBT and have a significant impact on tumor recurrence (12). Invasive implant now classified as extra-ovarian Low Grade Serous Carcinoma. Noninvasive implant has two histologic subtypes: epithelial and desmoplastic noninvasive implants.

In ovarian SBT, Lymph node involvement (LNI) is not associated with poor prognosis, but retroperitoneal node involvement is still staged as N1. Lymph node involvement comprises single cells, small clusters, micro papillae or macro papillae and cribriform glands located in nodal sub-capsular sinuses or parenchyma. Cytological lymph node involvement is similar to conventional SBT. Intra-sinusoidal cells have no prognostic effect (13). If lymph node infiltration is accompanied by desmoplasia and destruction of lymph node architecture it should be classified as LGSC (1). According to both UICC and FIGO classifications, the T stage is affected by the presence of peritoneal implants, similar to the staging of invasive carcinoma (14). In contrast, lymph node involvement by ovarian SBT is not considered metastatic disease and is classified as pN0, and the benign nature of these lesions should be mentioned in the pathology report (1). In our case, metastasis was detected in only two lymph nodes in the right pelvic region, among 3 right pelvic lymph nodes, 4 left pelvic lymph nodes and 2 para-aortic lymph nodes. Metastatic epithelium was non-invasive.

LNI needs to be distinguished from hyperplastic mesothelial cells and benign glandular inclusions (Müllerian inclusion cysts or endo salpingiosis). McKenney et al. described four histologic patterns of nodal involvement (15). Clusters of cells, individual cells, or simple non-branching papillae within the nodal sinus or parenchyma characterize the most frequent pattern seen in 90% of patients. The second pattern, designated “intra glandular,” is characterized by complex intra glandular papillary proliferation that shows secondary and tertiary branching. Aggregates of epithelial cells with prominent eosinophilic cytoplasm characterize the third pattern. The least common pattern is characterized by prominent micro-papillary architecture. These different patterns can present in the LN sinuses or parenchyma. In our case, it was observed as cell groups within the lymph node sinuses and as simple non-branching papillae. No involvement was observed in the lymph node parenchyma.

Ovarian SBT differential diagnostic includes serous cystadenoma/cyst adenofibroma, low grade serous carcinoma, endometrioid borderline tumor, seromucinous borderline tumor, mesothelial hyperplasia, well-differentiated papillary mesothelioma, endosalpingiosis and primary peritoneal SBT (16).

Serous cystadenoma / cystadenofibroma does not have architectural complexity in the form of papillae, micro papillae, cribriform or nesting. If proliferation constitutes <10% of the overall tumor, it is diagnosed as serous cystadenoma / cystadenofibroma with focal epithelial proliferation. If epithelial proliferation is >10% of the tumor it is called serous borderline tumor. Serous cystadenoma/cystadenofibroma has a similar heterogeneous population of secretory / ciliated cells but without atypia or mitosis.

Low-grade serous carcinoma is characterized by any single focus of invasion with nuclear features of borderline tumor measuring ≥ 5 mm in greatest linear extent (invasive LGSC). If any single focus of invasion with nuclear features of low-grade serous carcinoma is < 5 mm in greatest linear extent defined as micro-invasive LGSC. Otherwise, if the focus of invasion is > 5 mm it is referred to as invasive LGSC.

Endometrioid borderline tumor arises from / associated with endometriosis. It can have papillary structures but not in a hierarchically branching configuration. The Luminal surface
of endometrial glands is non-ciliated and, not exfoliated, hob nailing or tufting like SBT. Squamous, squamous morular, or mucinous metaplasia may be present, which is extremely rare in both low- and high-grade serous neoplasms.

Seromucinous borderline tumor have hierarchically branching edematous papillae but in contrast to SBT, these have a prominent stromal acute inflammatory infiltrate. It is lined by endocervical type mucinous but occasionally ciliated to indifferent cells.

In mesothelial hyperplasia, diffuse sheets to papillary proliferations of monotonous mesothelial cells restricted to serosa and demarcated from underlying stroma are observed. Variable cellular atypia with rare mitoses is found. Both can be PAX8, WT1 positive but SBT is negative for calretinin, D2-40

Tubulopapillary architecture (uniformly short / blunted rather than hierarchically branching papillae) with bland cuboidal monolayered mesothelial lining is observed in well differentiated papillary mesothelioma. Psammoma bodies associated with both. Immunoprofile is similar to mesothelial hyperplasia.

Endosalpingiosis is limited to simple glandular structures lined by a monolayer of cells similar to fallopian tube epithelium with neither atypia nor cellular crowding/tufting

Primary peritoneal SBT can be multifocal and is histomorphologically identical to epithelial or desmoplastic noninvasive implants of ovarian SBT.

According to the FIGO guidelines, complete surgical staging of epithelial ovarian tumors comprises hysterectomy, bilateral salpingo-oophorectomy, omentectomy, peritoneal washing with cytology, and resection of peritoneal lesions, systematic peritoneal biopsies, and paraaortic lymphadenectomy (17). But standard treatment of ovarian SBT includes complete surgical resection and surgical staging including omentectomy, peritoneal biopsies, and cytology of peritoneal washings. Appendectomy is added in case of mucinous borderline tumor (18).

CONCLUSION

The presence of lymph node involvement and implants in ovarian SBT necessitates thorough surgical exploration and may impact the choice of therapies so the early detection and accurate staging are crucial in determining the prognosis and treatment strategy. The management of ovarian SBT with lymph node involvement and implants requires a multidisciplinary approach to prevent overtreatment or under treatment. The long-term outcomes and recurrence rates of patients with ovarian SBT and lymph node involvement, particularly those with implants, remain areas of ongoing investigation in the field of gynecologic oncology. Further research is needed to better understand the molecular characteristics and genetic factors associated with the development of implants in ovarian borderline serous tumors.

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Ethical approval: The present study was conducted strictly following the principles outlined in the Declaration of Helsinki. Informed consent was obtained from the participants of this study.

REFERENCES

