CASE REPORT

OPEN ACCESS

A young nulliparous woman with right ovarian serous borderline tumor and left ovarian micropapillary serous carcinoma

Vinita Jaggi Kumar, Dhruv Jain, Asit Mridha, Sidharth Nanda,
Jyotica Jain, Rajesh Kumar Grover

ABSTRACT

Introduction: Serous borderline tumor (SBT) of low malignant potential (LMP) is heterogeneous group, neither wholly benign nor frankly malignant. It usually involves premenopausal age patients, has good prognosis and may recur even after 20 years. Decades later, transformation to low grade serous carcinoma can occur in 7%, mandating prolonged follow-up. Ten and 20 years survival in stage I is 95% and 80% respectively. Micropapillary type and invasive tumor implants warrant treatment like carcinoma and need adjuvant chemotherapy. **Case Report:** We present the case of a 25-year-old nullipara, married for four years who had ovarian cystectomy one year back. She reported to our institute with massive ascites and failure of anti-tubercular treatment of three months. Diagnostic tap revealed cells

suggestive of metastatic adenocarcinoma. Bilateral complex adnexal masses with ascites were seen on computed tomography (CT) scan. CA125 was 191 U/mL. Thorough staging laparotomy i.e., inspection and palpation of abdomen and pelvic organs, ascitic fluid cytology, bilateral salpingo-oophorectomy, and bilateral pelvic and aortocaval lymph nodes sampling up to inferior mesenteric artery level, along with supracolic and infracolic omentectomy, and multiple peritoneal biopsies was carried out. Uterus was preserved. In our patient while right ovarian tumor was the benign type of SBT, the left ovarian tumor was the aggressive micropapillary type of SBT. **Conclusion:** This case emphasizes the need of subclassification of serous borderline tumors showing a broad spectrum of clinical and biological behavior from benign to low grade carcinoma. We suggest that in patients of reproductive age with infertility and adnexal masses, despite malignant cells in ascites, serous borderline tumor should be kept as a differential diagnosis and conservative surgery be offered.

Keywords: Micropapillary serous carcinoma, Typical SBT, Malignant ascites, Staging laparotomy, Low malignant potential tumors

Kumar VJ, Jain D, Mridha A, Nanda S, Jain J, Grover RK. A young nulliparous woman with right ovarian serous borderline tumor and left ovarian micropapillary serous carcinoma. International Journal of Case Reports and Images 2013;4(9):471–476.

doi:10.5348/ijcri-2013-09-359-CR-3

Vinita Jaggi Kumar¹, Dhruv Jain², Asit Mridha³, Sidharth Nanda³, Jyotica Jain⁴, Rajesh Kumar Grover⁵

Affiliations: ¹MBBS, MD, MRCOG, Department of Surgical oncology (Gynecological Oncology Division, Delhi State Cancer Institute (Govt. of NCT), Dilshad Garden, Delhi, India; ²MBBS, MD, Assistant Professor, Department of Onco Pathology, Delhi State Cancer Institute (Govt. of NCT), Dilshad Garden, Delhi, India; ³MBBS, MD, Assistant Professor, Clinical Oncology, Delhi State Cancer Institute (Govt. of NCT), Dilshad Garden, Delhi, India; ⁴MBBS, MD, Associate Professor, Clinical oncology, Delhi State Cancer Institute (Govt. of NCT), Dilshad Garden, Delhi, India; ⁵MBBS, MD, PGDHHM, Director, Radiation Oncology, Delhi State Cancer Institute (Govt. of NCT), Dilshad Garden, Delhi, India.

Corresponding Author: Dr. Vinita Jaggi Kumar, Delhi State Cancer Institute (Govt. of NCT Delhi), Dilshad Garden, Delhi, India; Postal Code-110095; Ph: +91 9560390112; Fax: +91-11-22110505; Email: drvinitakumar@yahoo.co.in

Received: 16 November 2012

Accepted: 1 June 2013

Published: 01 September 2013

INTRODUCTION

Serous borderline tumors (SBT) of ovary are an enigmatic group which are neither wholly benign nor frankly malignant. They occur mostly in premenopausal age group, have favorable prognosis, with 10 years survival rate of nearly 95% for stage 1 tumors. They may recur even after 20 years, hence they are labeled as low malignant potential (LMP) tumors. About half of all LMP tumors are serous tumors [1]. Mean age of borderline serous tumors is 40 years, which is two decades earlier than invasive cancer. [2] According to FIGO and WHO, stromal invasion, defined as destructive infiltrative growth, is the sole criterion used to distinguish SBT from invasive serous carcinomas [2].

Furthermore, SBT have been subclassified into benign and malignant types according to their biologic behavior. Micropapillary serous carcinoma (MPSC) is a proliferative, serous, ovarian neoplasm, characterized by a micropapillary pattern. Though it lacks destructive infiltrative growth, yet it behaves as a low-grade invasive carcinoma, hence is more aggressive than a typical ovarian serous borderline tumor. They are also associated with extraovarian invasive peritoneal implants and more frequent recurrences than in typical ovarian serous borderline tumors. [3] In absence of invasive implants, MPSC does not imply unfavourable prognosis, and is much closer in its biologic behaviour to SBT than to serous carcinomas, hence it is retained in LMP category [4, 5]. Typical SBT as well as those with noninvasive implants are placed at lower end of proliferative spectrum.

We present the case of a patient who presented with massive ascites and bilateral ovarian tumors who was taken up for laparotomy and on surgical staging was diagnosed as bilateral borderline ovarian tumors in stage 1C with typical non-invasive SBT in right ovary and more aggressive non-invasive micropapillary type SBT in left ovary.

CASE REPORT

On 24th June 2010, a nulliparous female, aged 25 years, married for four years, presented with progressive abdominal distension due to massive ascites (Figure 1). There was no history of fertility inducing drugs but one year back, she had undergone ovarian cystectomy in a private hospital, the details of which were not available. There was loss of appetite and weight but no history of hormone intake. She had hypomenorrhea. There were no signs and symptoms of bowel disturbance or any family history of cancer. On examination, she was emaciated with hugely protuberant abdomen due to ascites. There was mild bilateral pedal edema but no lymphadenopathy, or hepatosplenomegaly. Vague mass was palpable in suprapubic area. Perspeculum examination showed, normal cervix displaced backwards. On bimanual pelvic examination, uterus was not felt separately but

incorporated in bilateral adnexal masses, which were felt through both fornices. A large tumor about 6x5 cm, hard to feel was impacted in pouch of douglas. Rectal mucosa was smooth and mobile. Investigations revealed normal hepatic, renal and hematological profile. Preoperative serum Ca125 (marker for ovarian carcinoma) was 191 U/mL, CEA (colon carcinoma), CA19.9 (gallbladder and pancreatic carcinoma) and CA 72.4 (pancreatic and gastric carcinoma), β -hCG (germ cell tumor of ovary), AFP (hepatobiliary malignancy and germ cell tumor of ovary) were normal. Contrast computed tomography (CT) scan revealed huge ascites with bilateral, complex, solid cystic adnexal heterogeneous mass, which measured 8x10 cm on the right side and 7x8 cm on the left side. Uterus, liver, gallbladder, spleen, pancreas, both kidneys, bones and joints were normal. No significant retroperitoneal lymphadenopathy was seen. Computed tomography scan was suggestive of bilateral ovarian tumors with ascites.

First diagnostic ascitic fluid tap revealed clear yellow, serous fluid with atypical cell clusters suspicious of malignancy, while second tap was suggestive of metastatic adenocarcinoma (Figure 2). Adenosine deaminase (ADA) test which is indicative of tubercular etiology was performed in the ascitic fluid. Its value was in the normal range, thus ruling out abdominal tuberculosis.

Upper gastrointestinal tract endoscopy revealed grade 1 esophageal varices, at the lower end at 3' O clock position. Stomach and duodenum were normal. Colonoscopy could not be done due to improper bowel preparation. Endometrial biopsy revealed secretory endometrium with no evidence of malignancy and PAP smear was normal.

On 25th July 2010, after informed consent the patient underwent staging exploratory laparotomy. Surgery included inspection and palpation of abdomen and pelvic organs, ascitic fluid cytology, bilateral salpingo-oophorectomy, bilateral pelvic and aortocaval lymph nodes sampling up to inferior mesenteric artery level, along with supracolic and infracolic omentectomy, and multiple peritoneal biopsies. Both the fallopian tubes were also removed, however, uterus was preserved.

Peroperatively, six liters of clear, straw colored ascites. On gross appearance uterus was normal, no normal, ovary seen. The ovaries were replaced by ovarian tumors. The ovarian tumors were separate but together they were impacted in the pelvis. Moreover, the left ovarian tumor was adherent to the sigmoid mesentery. The plane of cleavage was maintained. Liver, under surface of diaphragm, abdominal and pelvic peritoneum, ileal mesentery, stomach, small and large intestines and omentum were normal. Left pelvic lymph nodes and para-aortic lymph nodes were palpable and enlarged and were thoroughly dissected, while on the right side they were not enlarged and were palpated to be normal. Hence, right nodes sided were only sampled.

Histopathology revealed right ovary to be 5.4x5.0 cm, multicystic with solid papillary fronds, without any breach of capsule (Figure 3). Left ovary was 6.5x5.8 cm and similar to the right ovary (Figure 3). Right ovarian

tumor did not show any destructive stromal invasion. Mild nuclear atypia with low mitosis and psammoma bodies were seen (Figure 4). It was labeled as non-invasive serous borderline tumor, of typical type following WHO classification. While no stromal invasion was there in left ovarian tumor as well, there were foci of fused solid areas and occasional mitosis, in foci of >5 mm in length (Figure 5). It was labeled as non-invasive SBT, micropapillary type (micropapillary serous carcinoma). Omentum, appendix, peritoneal biopsies, pelvic and para-aortic lymph nodes were devoid of metastasis or implants.

Immediate postoperative recovery was uneventful. Drain was kept until stitch removal on postoperative day-12 as there was substantial amount of fluid from the drain. Postoperatively her CA 125 was 5.89 U/mL. Subsequent to discussion with our clinical oncology team, decision of adjuvant chemotherapy, was taken to give, keeping in view the biologic behavior of micropapillary type of left ovarian tumor. Postoperative recovery was uneventful but after first cycle of chemotherapy she developed parietal wall abscess. The abscess burst through the surgical stitch line and drained massive amount of pus which tested sterile on culture. Tests for tuberculosis performed on the pus were negative. Wound was debrided and left to heal by secondary intention. After this initial delay, she uneventfully completed six cycles of three weekly chemotherapy with carboplatin and paclitaxel. Currently, she is disease free for one and half years with latest report of CA 125 of 4.32 U/mL and normal CT scans of abdomen and pelvis.

DISCUSSION

Micropapillary serous carcinoma (MPSC) is a proliferative, serous ovarian neoplasm which is without destructive infiltrative growth but still behaves as a low-grade invasive carcinoma and hence considered as an in situ form of serous carcinoma [6]. In the absence of invasive implants, MPSC has favorable prognosis with

Figure 2: Ascitic fluid cytology showing atypical cells suggestive of metastatic adenocarcinoma. (H&E, x400)

Figure 3: Showing right ovary (5.4x5.0 cm), left ovary (6.5x5.8 cm). Both were multicystic, with solid papillary fronds without any breach of capsule.

Figure 4: Photomicrograph showing typical non-invasive serous borderline tumor in right ovary, depicting thick papillae, heirarchical branching, no destructive stromal invasion, mild nuclear atypia, low mitosis and psammoma bodies. (H&E, x200)

Figure 1: Massive abdominal distension with ascites.

Figure 5: Showing non-invasive SBT, micropapillary type (micropapillary serous carcinoma) in left ovary with complex papillae, non-hierarchical branching, foci of fused solid areas and cribriform pattern, occasional mitosis in area of >5 mm in length but no destructive stromal invasion.

biologic behavior similar to serous borderline tumors [7, 8].

Twenty-six cases of MPSC were identified in a review of 400 cases of ovarian SBT. None of the stage 1 patients had recurrence, but in higher stages 50% died of the disease. Twenty-four (92%) of MPSC cases were SBT associated. It was concluded that micropapillary type of SBT may progress to invasive carcinoma in some instances [8]. Drescher et al. studied significance of DNA content and nuclear morphology as prognostic factors to predict aggressiveness of borderline ovarian tumors and to guide adjuvant chemotherapy. [9]

Clinical presentation of LMP tumors is with abdominal distension, pain, and pelvic mass which is same as that of malignant tumors. Young patients have associated infertility or pregnancy. History of infertility increases the risk of LMP tumors with odds ratio (OR) of 1.9, while use of infertility drugs has OR of 4. [10] In patients with serous borderline tumors, after ovarian cystectomy, 8–15% patients have recurrence in the ipsilateral or contra lateral ovarian tissue. Bilaterality or synchronous and metachronous tumors are common and seen in about 40% patients [10].

In our patient there was bilateral involvement of ovaries; the tumors in right and left ovary were separate. While right ovary had benign type of typical borderline serous tumor, the left ovary had noninvasive borderline serous tumor of micropapillary type, which as the literature suggests is a more aggressive subtype. Preoperatively ascitic fluid cytology did have malignant cells, however there were no implants detected in the peritoneal lining.

About 80% of low malignant potential (LMP) tumors are diagnosed in stage 1. Some have extraovarian tumor implants on peritoneal surface of pelvis or abdomen or both. Though some consider these implants to represent metastasis, yet others consider them to represent synchronous extraovarian proliferations arising from surface coelomic epithelium as a result of multifocal field change. Spontaneous regression of extraovarian foci has been reported following resection of ovarian primary tumor. [11]

These extraovarian tumor implants could be invasive or non-invasive. Serous borderline tumors with invasive implants and micropapillary type of ovarian serous borderline tumors are aggressive subgroups and are classified as carcinomas. They are associated with poor prognosis and are treated with adjuvant chemotherapy. [4, 11]

The LMP or borderline neoplasms have 10 years survival rate of 95% for stage 1 patients. [2] Overall survival is 90–95% at 5 years and 80% at 20 years. In another study, disease-specific survival was >95% for patients with lowstage (stage I) tumors and approximately 65% for patients with highstage (stage II–IV) tumors.

Thus, although both the typical type of borderline serous tumors and micropapillary type of serous borderline tumors appear to be noninvasive histologically, the former tumor is benign, while the latter behaves like a low grade carcinoma. Poor prognosis for MPSC prompts clinicians to use adjunctive chemotherapy [4]. According to FIGO and WHO, stromal invasion defined as destructive infiltrative growth is the sole criterion used to distinguish SBT from invasive serous carcinomas. An aggressive subgroup of proliferative serous lesions with micropapillary projections are named as micropapillary serous carcinoma (MPSC). These tumors and SBT with invasive implants may be associated with malignant behavior [5].

Serous borderline tumors have a very favorable prognosis, but complete surgical staging and prolonged follow-up are advised because pelvic recurrence and occasionally transformation to invasive carcinoma may occur, albeit over delayed period of time. Designation of benign subgroup of SBTs as “atypical proliferative tumors” is not recommended because it discourages complete surgical staging and follow-up. Advanced stage tumors with noninvasive implants are common and behave in a benign fashion, and can be safely treated conservatively.

Although histologically ovarian MPSC lack stromal invasion and therefore are qualified by FIGO and WHO guidelines for inclusion in borderline category, clinically they behave more aggressively than typical serous borderline tumors. Hence, the SBTs associated with invasive implants and SBT-MPSC could behave as low grade carcinoma and their management should be seen in this light.

Various subtypes of serous borderline tumors are summarized in Table 1. [12]

Table 1: Classification of serous borderline tumors. [7, 12]

Terms	Typical serous borderline tumor (SBT) without invasive implants (Serous tumors of LMP)	Typical serous borderline tumor with invasive implants	Micropapillary serous carcinoma with or without invasive implants
Synonym	Atypical proliferative serous tumor		Low grade (invasive) or non-invasive micropapillary serous carcinoma
Clinical behavior	Benign	Low grade malignant	Low grade malignant
Histopathology	1. No stromal invasion 2. Heirarchial pattern of branching	1. No stromal invasion 2. Heirarchial pattern of branching 3. Invasive implants present	1. No stromal invasion 2. Micropapillary pattern with small uniform filiform papillae, with cores having no stroma 3. At least one confluent area 5 mm in greatest dimension in at least one slide. 4. Extraovarian invasive or non-invasive implants
Prognosis	Good	Aggressive as compared to typical ovarian SBT	May progress to invasive carcinoma
Molecular biology	Mutations of kras and braf/erb2 mutations		Mutations of kras and braf and loss of 1p36 and loss of CDKN2A/B
Implants	Not seen	Invasive implants present	Extraovarian invasive implants are more frequent
Recurrences	Not frequently seen	Late recurrences may occur	Invasive recurrences are more frequent

Abbreviation: LMP - Low malignant potential

CONCLUSION

We suggest, that in cases in reproductive age group with infertility and adnexal masses, despite presence of malignant cells in ascites we should keep serous borderline tumors in mind and offer conservative surgery.

Our case suggests that MPSC and typical type of SBT represent two ends of a broad spectrum of clinical and biologic behaviour seen in low malignant potential ovarian tumors. The MPSC are associated and probably arise from SBT and may account for few cases of SBT which progress to invasive carcinoma. There is the need of subclassification of serous borderline tumors.

Author Contributions

Vinita Jaggi Kumar – Conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Final approval of the version to be published

Dhruv Jain – Conception and design, Analysis and interpretation of data, Critical revision of the article, Final approval of the version to be published

Asit Mridha – Acquisition of data, Drafting the article, Final approval of the version to be published

Sidharth Nanada – Conception and design, Drafting the article, Final approval of the version to be published

Jyotica Jain – Analysis and interpretation of data, Critical revision of the article, Final approval of the version to be published

R K Grover – Conception and design, Critical revision of the article, Final approval of the version to be published

Guarantor

The corresponding author is the guarantor of submission.

Conflict of Interest

Authors declare no conflict of interest.

Copyright

© Vinita Jaggi Kumar et al. 2013; This article is distributed under the terms of Creative Commons attribution 3.0 License which permits unrestricted use, distribution and reproduction in any means provided the original authors and original publisher are properly credited. (Please see www.ijcasereportsandimages.com/copyright-policy.php for more information.)

REFERENCES

1. Russel P, Merkur H. Proliferating ovarian “epithelial” tumours: a clinico-pathological analysis of 144 cases. *Aus NZ J Obstet Gynecol* 1979;19(1):45–1.

2. Epithelial borderline tumors of the ovary. Age distribution. Annual report gynaecological cancer. FIGO 1994:22.
3. Piura B, Rabinovich A, Yanai-Inbar I. Micropapillary serous carcinoma of the ovary: Case report and review of literature. *Eur J Gynaecol Oncol* 2000;21(4):374–6.
4. Seidman JD, Kurman RJ. Subclassification of serous borderline tumors of the ovary into benign and malignant types. A clinicopathologic study of 65 advanced stage cases. *Am J Surg Pathol* 1996;20(11):1331–45.
5. Prat J, De Nictolis M. Serous borderline tumors of the ovary: a long-term follow-up study of 137 cases, including 18 with a micropapillary pattern and 20 with microinvasion. *Am J Surg Pathol* 2002 Sep;26(9):1111–28.
6. Kurman RJ, Trimble CL. The behaviour of serous tumors of low malignant potential: Are they ever malignant? *Int J Gynecol Pathol* 1993;12(2):120–7.
7. Seidman JD, Kurman RJ. Subclassification of serous borderline tumors of the ovary into benign and malignant types. A clinicopathologic study of 65 advanced stage cases. *Am J Surg Pathol* 1996;20(11):1331–45.
8. Burks RT, Sherman ME, Kurman RJ. Micropapillary Serous Carcinoma of the Ovary: A Distinctive Low-grade Carcinoma Related to Serous Borderline Tumors. *Am J Surg Pathol* 1996;20(11):1319–30.
9. Drescher CW, Flint A, Hopkins MP, Roberts JA. Prognostic significance of DNA content and nuclear morphology in borderline ovarian tumors. *Gynecol Oncol* 1993;48(2):242–6.
10. Lim-Tan SK, Cajigas HE, Scully RE. Ovarian cystectomy for serous borderline tumors: a follow up study of 35 cases. *Obstet Gynecol* 1988;72(5):775–81.
11. Hopkins MP, Kumar NB, Morley GW. An assessment of pathologic features and treatment modalities in ovarian tumors of low malignant potential. *Obstet Gynecol* 1987;70(6):923–9.
12. Jaffery D Seidman, Kathleen R Cho, Brigitte M Ponnet, Robert J Kurman. Surface epithelial tumors of the ovary. In: Robert J Kurman, Lora Hedrick Ellenson, Brigitte M Ronnett editors. *Blaustein's. Pathology of the Female genital tract*. 6th ed. USA, Springer 2011:679–85.

Access full text article on
other devices

Access PDF of article on
other devices