Case Report

Progression of serous ovarian tumor of low malignant potential to invasive serous carcinoma: a case report

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Abstract

Serous borderline ovarian tumors (SBOTs) represent group of tumors with cellular atypia and absent stromal invasion. Many studies support that SBOTs share similar molecular and genetic alterations with low-grade serous carcinomas, while high-grade serous carcinomas have a distinct pathway to carcinogenesis. Here we present a 55-year-old woman who underwent exploratory laparotomy and maximal debulking for SBOT. First recurrence was SBOT while second recurrence was low-grade invasive serous carcinoma. Recent molecular studies showed that molecular alterations detected in SBOTs were also present in low-grade serous carcinomas. In this manner, ovarian low-grade serous carcinomas are thought to evolve in a step-wise fashion from benign serous cystadenoma to SBOT and finally low-grade invasive serous carcinoma.

Key words: Borderline ovarian tumor, ovarian tumor, invasive serous carcinoma, serous

Introduction

The synonym “borderline” was adopted in 1973 by WHO, represents group of tumors with cellular atypia and absent stromal invasion, invasive and non-invasive peritoneal implants were described following years [1]. Micropapillary pattern in histologic specimens is the first prognostic factor described for serous borderline ovarian tumors (SBOT); this pattern is related with bilateral tumors, peritoneal implants and advanced stage disease. There is strong molecular evidence demonstrating similarity between low-grade invasive serous carcinoma and SBOTs with micropapillary pattern [2]. Peritoneal implants are mostly non-invasive in 85% of cases, and invasive in the remaining patients [3]. Sometimes it is difficult to classify peritoneal implants as invasive or non-invasive even for the expert gynecopathologists. Micropapillary pattern is a poor prognostic factor, but it seems that prognosis is related with high incidence of invasive peritoneal implants rather than micropapillary pattern itself.

Another prognostic factor for SBOTs is stromal micro-invasion. It is defined as the presence of individual or clusters of neoplastic cells cytologically similar to those of the non-invasive tumor and none should exceed 10 mm². Recurrence rates and invasive nature of recurrences are more common in the presence of stromal micro-invasion [4]. Many studies support that SBOTs share similar molecular and genetic alterations with low-grade serous carcinomas, while high-grade serous carcinomas have a distinct pathway to carcinogenesis.

Case presentation

A 55-year-old woman presented with 6 months history of abdominal swelling on the right side. Her physical examination was unremarkable. Abdominal ultrasound showed right adnexal mass, 19 x 15 cm in diameter with solid mural nodules. Abdominopelvic computerized tomography supported ultrasound findings. Serum Ca-125 level was 14.8 U/ml. Biochemical, hematologic and coagulation parameters were in normal range. An explorative laparotomy with frozen section was performed. In exploration, a cystic mass was noted originating from the right ovary with a smooth surface (20 cm in diameter). Frozen section study of right adnexa showed borderline serous tumor components. Visceral and parietal peritoneal surfaces were negative for implants. Since 20% of tumors reported...
as “borderline” during frozen section and revised as “invasive carcinomas” in the final histopathological report, a staging procedure including hysterectomy, contralateral salpingo-oophorectomy, peritoneal biopsies, bilateral pelvic and para-aortic lymphadenectomy were performed. There was no macroscopic tumor residue left. Final pathology result was SBOT with microinvasion. Microinvasion less than 2 x 1 mm was positive in one area (Figure 1).

Figure 1

Figure 1 Atypical serous tumoral cells and stromal microinvasion. Floating cell clusters represents papillomatous pattern (H&E staining)

Peritoneal washing, peritoneal biopsies and 64 dissected lymph nodes were negative for tumoral invasion or implantation. It was decided to observe the patient with 3-months intervals.

After 10 months, from the first operation, the disease recurred in the pelvis. A cystic mass with thin walls and multisepae was noted on the left side of the pelvis, 6 x 5 cm in diameter. The patient was observed for 2 months for possible lympho-cyst formation. Two months later, the cyst enlarged to 7.5 cm and a new 7 x 4 cm cystic mass was formed in the opposite side of the pelvis and serum Ca-125 level was 14.2 U/ml. A second surgery was planned for disease recurrence. The mass was strictly adhered to right external iliac artery, and maximal debulking could not be achieved; however, optimal cytoreduction was achieved with residual tumor less than 1 cm. Final pathology of the specimens was consistent with SBOT again (Figure 2).

During expectant management, the disease recurred on the abdominal wall 5 months after the second operation. Invasive tumoral conglomerate strictly adhered to small intestine and rectus fascia on anterior abdominal wall was noted during laparotomy. Tumoral excision with bowel resection and anastomosis was performed. Pathologic result of the tumor was low-grade invasive serous carcinoma (Figure 3).

Discussion

Prognostic factors for SBOTs have been identified. The most important prognostic factors are “invasive peritoneal implants” and peritoneal residual disease. Other debatable factors are micropapillary pattern and stromal microinvasion. Nodal spread and conservative surgery are not recognized as prognostic factor [5]. In our case, there is only one poor prognostic factor, the stromal microinvasion in the first surgery and the disease recurred one year later. The other poor prognostic factor for our patient was residual peritoneal disease after second surgery. The disease recurred 4 months after the second surgery. Shih et al. reported that 3-year disease free survival was 71% in patients with residual disease, compared with 89% in whom without [6]. In a series of 96 BOT patients, recurrence rate was found 10.4% and the majority of the recurrences were treated with conservaive surgery initially [7].

Figure 2

Figure 2 Pathologic specimen of the second operation shows SBOT histology with micropapillary pattern, pseudostratification and absent stromal invasion. (H&E staining)

Epithelial ovarian tumors can be classified into two categories: type 1 tumors include low-grade serous carcinomas, mucinous, endometrioid and clear cell carcinomas seem to develop from their precursor lesions; SBOTs in a stepwise manner, while type 2 tumors include high-grade serous carcinomas that don’t share the same pathway and their possible precursor lesions have not been identified yet [8]. Several evidences now indicate that type 2 tumors may originate from the epithelium of the fibril portion of the fallopian tube. Recent molecular studies showed that molecular alterations detected in SBOTs were also present in low-grade serous carcinomas [9].
Microsatellite instability is one of the pathways that SBOTs and invasive serous carcinomas share. A progressive increase in the degree of allelic imbalance was observed during progression from non-invasive to invasive serous carcinoma. Ostemberg et al. proposed that a subset of SBOTs could be related to the progression to serous carcinoma. They identified a group of common genetic alterations that SBOTs and low-grade serous carcinomas share [10]. In addition to this data, low-grade serous carcinomas and SBOTs share the same K-Ras and BRAF mutations, while p53 mutation is common in high-grade serous carcinomas and it seems that SBOTs are more related to low-grade serous carcinomas [11]. In this manner, ovarian low-grade serous carcinomas are thought to evolve in a step-wise fashion from benign serous cystadenoma to SBOT and finally low-grade invasive serous carcinoma.

Hogg et al. found 2 recurrences as grade 1 serous carcinoma without a borderline component among 46 SBOTs [4]. Gershenson et al. found median time to recurrence as 19.5 months in SBOT patients [12], while it was 12 months in our case despite no macroscopic residual tumor during the first operation showing poor prognostic nature of the disease. Stromal microinvasion is accepted as a prognostic factor but there is no consensus about microinvasion criteria, especially in size. According to the literature, tumors up to 5 mm of microinvasion have demonstrated an excellent prognosis [13]. There is conflicting data about microinvasion and disease prognosis. Seidman et al. [14] and Hogg et al. [4] concluded that stromal microinvasion were not poor prognostic factors for survival and disease recurrence, however Longacre et al. found that microinvasion was strongly associated with decreased survival and high recurrence rates as in low grade serous carcinomas [15]. Ferrero and colleagues reported microinvasive pattern as a risk factor for disease recurrence [16]. Recurrence rates were 12.7% and 21.4% for non-invasive SBOTs and micro invasive SBOTs, respectively but no statistical significance had been reached. However, progression free survival was significantly shorter in micro invasive SBOTs. There were no invasive recurrences in 209 SBOT patients. There is continuing debate on prognostic factor of stromal microinvasion in the literature. It seems that large, prospective studies are needed to determine the prognostic factor of stromal microinvasion in SBOTs. In contrast to all previous reports, in a recent large retrospective study the authors concluded that, the risk of recurrence was not related to the histological subtypes of the tumor nor to the use of complete staging surgery [17].

There were no peritoneal implants (either invasive or non-invasive) in the pathologic specimens of all three operations in the patient described. The second recurrence was SBOT and the third was invasive serous carcinoma. However, the recurrence was within the rectus muscle on the abdominal wall during the third operation. The recent consensus is that pathologists should define recurrences as either recurrent SBOT, or serous carcinoma [13]. As the progression model proposed by Shih and Kurman [13] has been accepted widely, close and long-term follow-up is mandatory after surgical treatment of SBOTs.

In conclusion, SBOTs can recur as invasive low-grade serous carcinomas during the follow-up period. Intensity of surgical staging is one of the main issues in the management of SBOTs; thus, conservative procedures such as cystectomy or fertility sparing surgery should be reserved for young women desiring future childbearing. On the other hand, women who had completed their fertility (as in our patient) should be surgically treated just as epithelial ovarian cancer regarding to debulking concept. Patients with poor prognostic factors such as micropapillary pattern, stromal microinvasion and peritoneal residual disease should be closely followed-up for probable recurrences.

Conflict of interest statement
The authors declare no conflict of interest.
References