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Case Report

Lymph node involvement in an ovarian borderline serous tumor: a rare clinicopathologic presentation with management dilemma

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Abstract: Borderline serous tumor (BST), earlier known as atypical proliferative serous tumor, is an ovarian neoplasm of low malignant potential. Extraovarian spread in the form of peritoneal implants is common in these tumors; however, lymph node (LN) involvement is infrequent. The prognostic implication of LN involvement in BST is controversial. We present a case of a 25-year-old female presenting with dull-aching abdominal pain in the left iliac fossa for the past 3 years, which was associated with constipation and abdominal bloating. Her serum Cancer antigen 125 (CA125) level was 841.3 units/ml. Pelvic ultrasonography and magnetic resonance imaging showed a large well-defined, solid-cystic, abdominopelvic mass arising from the right ovary, measuring 21×18×10 cm. The left ovary was also solid-cystic and measured 7×4×3 cm. A provisional clinico-radiologic diagnosis of ovarian malignancy was rendered. The patient underwent bilateral salpingo-oophorectomy with omentectomy and right-sided pelvic and para-aortic lymph node dissection. Histopathology revealed bilateral ovarian BST with involvement of pelvic and para-aortic lymph nodes. This was followed by adjuvant chemotherapy (in view of stage IIIA). She is disease-free at 3 years of regular follow-up. The prognosis and management of BST with LN is not yet fully elucidated. Nevertheless, the finding of such an involvement mandates thorough sampling of the primary ovarian tumor to exclude a possibility of low-grade serous carcinoma with LN metastasis.

Keywords: Borderline serous tumor, atypical proliferative serous tumor, APST, BST, lymph node metastasis, lymph node involvement in BST

Introduction

Borderline serous tumors (BST), previously known as atypical proliferative serous tumors (APST) of the ovary, represent around 15-20% of all ovarian epithelial tumors [1]. These are ovarian neoplasms of low malignant potential. Unlike benign serous tumors of the ovary, approximately one-third of these tumors are associated with an extraovarian spread, most commonly in the form of peritoneal implants [1]. Rarely, lymph node involvement with BST has also been reported [1-3].

According to the recent World Health Organization (WHO) classification of ovarian tumors, the presence of such tumor deposits in lymph nodes of patients with BST should be referred to as involvement by BST and not as metastasis [4]. However, owing to the rarity of this finding and limited nodal sampling in borderline ovarian tumors, many surgical histopathologists are not aware of such phenomenon and may interpret such involvement as metastasis, thereby necessitating additional therapeutic measures. Hence, it is important to be aware that such involvement can be seen in BST and it does not change the primary diagnosis to invasive serous carcinoma.

Case presentation

A 25-year-old unmarried female presented with dull-aching abdominal pain for the past 3 years, which was associated with constipation and abdominal bloating. The pain was non-radiat-

ing, localised to left iliac fossa and was associated with a dragging sensation. Ultrasonography and pelvic magnetic resonance imaging showed a large well-defined abdominopelvic cystic lesion measuring 21×18×10 cm occupying the right hemi-abdomen and extending up to the right hypochondrium. The mass was seen to be arising from right ovary, was predominantly cystic with multiple small eccentric polypoidal solid projections, measuring up to 1.4 cm, along the cyst wall. The mass was displacing the uterus and abutting the dome of the urinary bladder. The left ovary was also solid-cystic and measured 7×4×3 cm. Her serum cancer antigen 125 (CA125) level was 841.3 units/ml.

With a provisional clinico-radiologic diagnosis of ovarian malignancy, the patient was counselled regarding the treatment options and being young and unmarried, she opted for uterine-preservation surgery. Based on the published evidence in the literature regarding the possibility of having successful pregnancy following oocyte donation and low tumor recurrence risk, her uterus was preserved and she underwent bilateral salpingo-oophorectomy with omentectomy and pelvic and para-aortic lymph node dissection [5, 6]. Simultaneously, a peritoneal biopsy was also obtained from a suspicious deposit found intra-operatively. Intraoperative peritoneal washings were also sent for cytological examination along with the surgical specimen. According to the International Federation of Gynecology and Obstetrics (FIGO) surgical staging, the disease was staged Ic.

On gross examination of the specimen, both the right and left ovaries were enlarged, measuring 15×12×8 cm and 7×4×3 cm, respectively. The outer surface of right ovary was smooth, greyish-white in color with areas of hemorrhage. The cut-surface showed multiple cysts with numerous papillary excrescences arising from the cyst walls. The left ovary showed numerous papillary excrescences over the surface (**Figure 1**). Both the fallopian tubes and omentum were grossly unremarkable. A total of 14 pelvic and 2 right para-aortic lymph nodes were identified grossly with size ranging from 0.5-2 cm in diameter.

Histopathological examination of meticulously selected representative sections from both ovarian specimens revealed several interesting histomorphological characteristics. The tumor displayed an exquisitely organized architecture, predominantly composed of papillary formations, each displaying a distinctive hierarchical branching pattern. These intricate papillae, the hallmark of the tumor, were lined by a ciliated columnar serous epithelium with mild nuclear pleomorphism. The epithelial lining demonstrated conspicuous stratification and cell tufting. Despite exhaustive sampling and rigorous examination, no microinvasive foci were identified within the examined sections, reaffirming the tumour's confined intraparenchymal growth. The absence of micropapillary, solid, or cribriform architectural arrangements in the tumor, were indicative of a favourable prognosis. Importantly, lymphovascular space involvement remained conspicuously absent in all sections examined, underscoring limited propensity of the tumor for vascular dissemination. In addition, representative sections were obtained from the surface of the left ovary of the surface implants (**Figure 1**).

Ten of the 14 pelvic lymph nodes and both the right para-aortic lymph nodes showed presence of lymph node involvement in the form of tumor deposits, seen as cystic spaces lined by eosinophilic serous epithelial cells with small rounded clusters and papillae composed of tumor cells with similar morphology as seen in the ovarian BST. Few psammoma bodies were also noted (**Figure 2**). These tumor deposits were commonly seen in the subcapsular region. Both the fallopian tubes, grossed according to the serial sectioning and extensive examination of the fimbriated end (SEEFIM) protocol, were free of tumor and precursor lesions. Omentum and peritoneal biopsy did not show any metastatic tumor deposits. Peritoneal washings were negative for malignant cells. A final histopathologic diagnosis of borderline serous tumor with pelvic and para-aortic lymph node involvement was rendered. Her FIGO stage was upstaged after histopathologic examination to stage IIIa, owing to the lymph node involvement.

Post-operatively, the patient was clinically stable with serum CA125 levels of 2.57 IU/ml, indicating that a substantial portion of the tumor burden had been eliminated, and that the patient had responded well to the intervention.

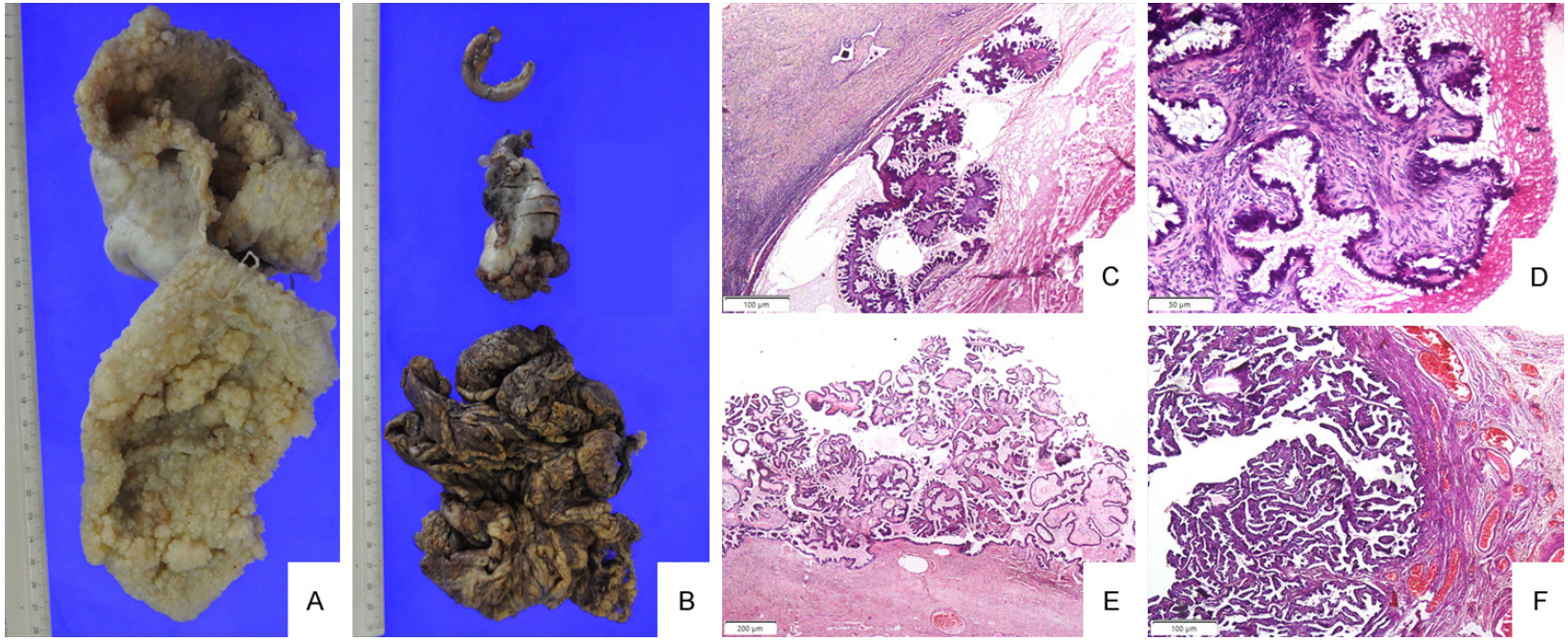

Figure 1. A: Gross image of the right ovary with the presence of papillary excrescences over the cut surface; no solid areas were identified; B: Gross image of left ovary showing papillary excrescences over the surface, along with the omentum, which was grossly unremarkable. The appendix did not show any significant gross pathology; C: The right ovary showed a tumor composed of cells arranged in papillae with a hierarchical branching pattern (Hematoxylin and eosin, 10×); D: These papillae were lined by 2-3 layers of cuboidal to columnar cells with mild atypia and a moderate amount of cytoplasm. Few tufts were also seen (Hematoxylin and eosin, 20×); E: The left ovary showed surface deposits of similar tumor (Hematoxylin and eosin, 4×); F: Both the fallopian tubes were unremarkable (Hematoxylin and eosin, 10×).

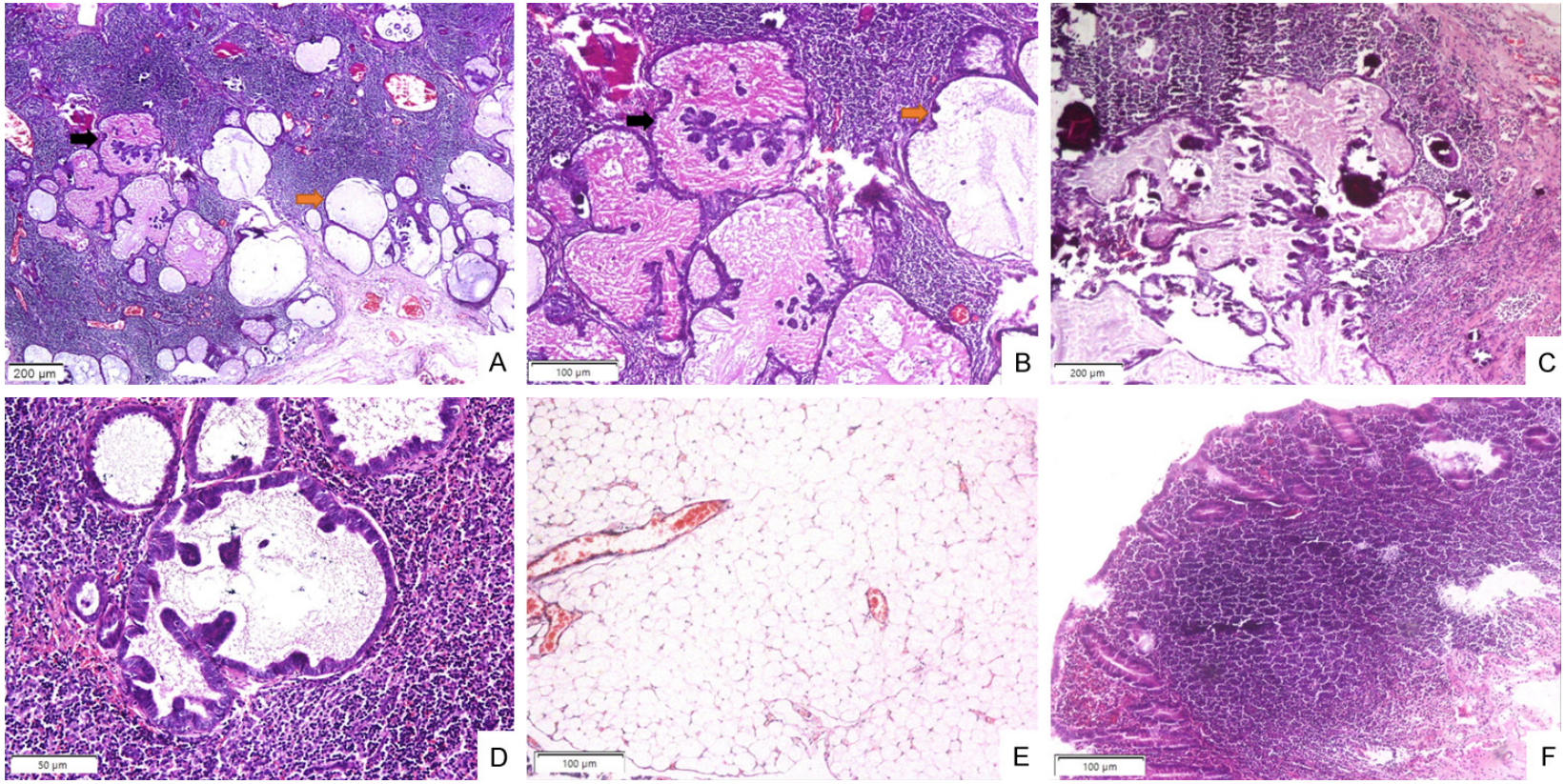

Figure 2. A: Lymph node showing endosalpingiosis (orange arrows) and deposits of borderline serous tumor (BST) (black arrow) (Hematoxylin and eosin, 2×); B: Endosalpingiosis shows single layer lining and BST deposits are lined by 2-3 cell layers of serous epithelial cells with mild nuclear atypia, eosinophilic cytoplasm and presence of detached cell tufts (Hematoxylin and eosin, 10×); C: Focal psammomatous calcifications around the BST deposits (Hematoxylin and eosin, 4×); D: BST deposits were lined by 2-3 cell layers with presence of detached cell tufts and mild nuclear atypia (Hematoxylin and eosin, 20×); E: Omentum was free of tumor (Hematoxylin and eosin, 10×); F: Appendix was microscopically unremarkable (Hematoxylin and eosin, 10×).

In view of FIGO Stage IIIa, the patient was counselled in detail regarding the treatment options and risk and benefits of adjuvant therapy [7, 8]. She opted for adjuvant chemotherapy and was administered 6 cycles of paclitaxel and carboplatin. She is asymptomatic and disease-free at 36 months of follow-up.

Discussion

Borderline serous tumors are ovarian epithelial neoplasms of low malignant potential. They are characterized by epithelial proliferation with tufting, mild to moderate nuclear atypia and low mitotic activity without any evidence of stromal invasion. Lymph node involvement is uncommonly described in BST. Though the exact incidence is unknown, various authors have reported it to be ranging from 7-21%. The most commonly involved lymph nodes include retroperitoneal, para-aortic and pelvic lymph nodes [2, 3, 9-11].

Lymph node dissection is not routinely recommended in patients with BST. However, Camatte et al., recommended lymphadenectomy in patients with serous tumors who have LN enlargement [12]. Though the exact pathogenesis of LN involvement in BST is not known, 2 mechanisms have been proposed. One hypothesis proposes that tumor cells shed off from the primary ovarian tumor or tumor cells transported via lymphovascular channels result in peritoneal deposits and LN deposits respectively. Another possible mechanism is transformation of mullerian cells on peritoneal surface and lymph node endosalpingiosis into BST via field effect into peritoneal implants and LN deposits of BST respectively [2]. A few researchers have tested for *KRAS* and *BRAFV600E* mutations in the primary tumor, peritoneal implants (n=13) and lymph node deposits (n=3) of BST. They found that the mutational status of the implants and LN deposits was similar to that of the primary ovarian tumor, indicating their monoclonal origin and supporting their origin from the primary ovarian tumor itself [13].

Benign mullerian inclusions (BMIs) and endosalpingiosis (ES) may be observed in lymph nodes of approximately 20% females with gynaecologic neoplasms and pose a diagnostic challenge as these may closely mimic LN involvement by BST. Although these entities have morphologic resemblance, they have different prognostic significance. There are subtle cytoarchitectural features that may help in differentiating these lesions. Benign mullerian inclusions and ES usually exhibit microcystic architectures and are lined by single layer of ciliated epithelial cells with no/minimal pleomorphism. Mitotic activity and stromal invasion are always absent in BMIs and ES [14]. In contrast, BST involvement is seen in the form of nests or papillae with epithelial tufting, multilayering, nuclear stratification, mild nuclear atypia and low mitotic activity without any surrounding desmoplasia [2].

Although LN involvement may be seen in patients with BST, nevertheless, in all such cases, it is extremely important to adequately and appropriately sample the tumor to rule out a possibility of low-grade serous carcinoma with lymph node metastasis, as the prognosis and therapeutics differ significantly.

Though the exact significance of LN involvement in BST remains unclear, few authors have reported higher recurrence rates in patients with LN involvement, though they observed that the overall survival was not affected significantly [5]. In similar lines, Qian et al., found LN deposits in 17/112 patients with BST on whom lymphadenectomy was performed [3]. Kaplan Meir curves did not show any significant correlation between LN involvement and 5-year disease free survival. Additionally, they observed that the probability of lymph node metastasis was higher in cases with bilateral ovarian involvement, higher FIGO stage, presence of invasive peritoneal implants and higher numbers of LNs dissected [3]. However, few authors have proposed that >1 mm confluent, nodular involvement without any intervening lymphoid tissue, may be considered as an adverse prognostic factor [15]. Notwithstanding these diverging observations, the clinical management of such patients is largely conservative owing to the indolent behavior of BST [16].

Conclusions

To conclude, LN involvement in BST is rare phenomenon and the surgical histopathologists need to be aware of its occurrence so that such borderline serous tumors are not misdiagnosed as serous carcinomas in view of the lymph nodal spread and subjected to unnecessary toxic chemotherapy regimens.

Disclosure of conflict of interest

None.

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