Review Article

Borderline Ovarian Tumors

Habeebullah S*, Latha C**

*Professor & HOD, Dept of Obstetrics & Gynaecology, Mahatma Gandhi Medical College & Research Institute, Pondicherry**Professor,Dept of Obstetrics & Gynaecology, JIPMER, Pondicherry.

Dr S.Habeebullah is currently a Professor of Obstetrics and Gynaecology at Mahatma Gandhi Medical college and Research Institute, Pondicherry. He was formerly a senior Professor and Head of Obstetrics and Gynaecologyat JIPMER, Pondicherry. He had his fellowship in fetal medicine from Glasgow. He wrote chapters and co-edited two text books. He has over 70 publications and a resource person for various teaching programs in South India. His fields of interest currently include High risk obstetrics and gynaecological oncology.

Corresponding author - Dr S.Habeebullah - (oghod@hotmail.com)

Chettinad Health City Medical Journal 2018; 7(4): 134 - 136

Abstract

About 15 to 20% of ovarian epithelial tumors are "borderline". Majority of them are serous or mucinous. They pose significant problems in diagnosis as there are no specific clinical features or investigations to ascertain the "borderline" nature. For a frozen section diagnosis an expert pathologist is needed. Surgical staging with radical surgery ensures near 100% survival in stage I. Even in advanced stage without invasive implants survival is excellent. A third of Borderline Ovarian Tumors(BOT) occur in women under 40 years. Fertility sparing surgery in early stage carries good prognosis. Laparoscopic surgery can also be undertaken without adverse effects. There is no role for adjuvant chemo/radiotherapy except probably when there are invasive implants. Prognostic factors include advanced stage at surgery, suboptimal debulking, invasive implants and micropapillary architecture. Long follow up has been recommended as recurrences are reported even after decades.

Key Words: Ovarian tumors, Borderline tumors, Fertility sparing surgery

Introduction

Ovarian tumors are common neoplasms in the lives of women. They are usually classified as benign and malignant. In 1971 FIGO introduced one more variety called "low malignant potential tumors". Subsequently WHO in 1973 named them as "borderline ovarian tumors (BOT).[1] They are unique in the sense that they fulfil the criteria neither for benign nor for malignant. They are neoplasms with higher proliferative activity when compared with benign neoplasms but do not show stromal invasion which is characteristic of invasive malignancy. Though they can occur in any histological type, they are mostly seen in epithelial cancers. Among ovarian cancers, up to 90% are of epithelial origin and 10 to 15 % of epithelial cancers are borderline.

Epidemiology

BOTs are seen in 2.5 / 100,000 women per year. Due to improvement in diagnosis there seems to be increasing number of BOTs. It is also possible that age at menarche, menopause, increased usage of OC pills and hormone therapy, weight gain and infertility may play a role in increasing the incidence.[2] They present 10-15 years before their malignant counterparts. One-third present before age forty.[3] The risk factors include Asian & Caucasian race, nulliparity, obesity, oral contraceptive pill usage, assisted reproductive techniques and smoking. Increased parity and lactation are protective. Tubal ligation is not protective against BOTs.[4] It may be noted that OC pills and tubal ligation are protective against malignant epithelial tumors.

Pathology

Out of BOTs, serous tumours account for 55% and mucinous 40%. Other histological types are rare.

Serous BOTs:They are mostly unilateral but bilateral in 25%. Majority (90%) are unilocular with fine septae. About 70% are in stage I at the time of diagnosis. The serous tumors may be papillary cystic or surface papillary lesions, adenofibroma or cystadenofibroma. There may be peritoneal implants in about 25%. These implants can be noninvasive or invasive.

The presence of a micropapillary architecture in the primary ovarian tumor is a strong predictor of invasive implants.[5]

Mucinous tumors: They may be unilocular or multilocular with fine septations and intramural nodules. They may have peritoneal implants less commonly. They may also be associated with pseudomyxoma. The implants may be secondary to malignancy of appendix. They may have intestinal (90%) or endocervical (10%) type of epithelium. The intestinal type are seen in older women, likely unilateral, multicystic and carry better prognosis. The endocervical type are seen in younger women, mostly unilocular, more commonly bilateral with peritoneal implants and carry poorer prognosis.

Following are the features of BOTs as suggested by Dietel and Hauptman[6]:

- Multi-layered epithelium (more than 4 cell layers)
- 4 or less mitoses per 10 high-power fields (HPF)
- Nuclear atypia which is mild
- Nuclear/cytoplasmic ratio increased
- Slight to complex branching of epithelial papillae and pseudopapillae
- Epithelial budding and cell detachment into the lumen
- Most importantly "no stromal invasion"

Diagnosis

BOTs pose problems of diagnosis as neither the clinical findings nor radiological findings and tumour markers are of much help in the accurate diagnosis. BOTs like the malignant ovarian tumors, do not produce any specific symptoms. A quarter of them may be asymptomatic and the rest may present with abdominal distension, abdominal pain, abdominal mass, altered bowel habits and bloating.[5] Transvaginal sonography may reveal a complex cystic mass with septations and mural nodule. Doppler may show similar features like malignant tumors (increased vascularity and low PI). CT/MRI can detect advanced disease. Tumor markers like CA-125 may be elevated in 50% cases whereas CEA and CA 19-9 may be elevated in mucinous BOTs. None of the clinical features and investigations mentioned above can reliably predict the borderline nature of these tumors. Even the frozen section reports may be erroneous. Only histopathology confirms the diagnosis.

Staging and surgery

The staging of BOT is same as that of FIGO staging for malignant ovarian tumors. Most of the BOTs are seen in early stage. Surgical staging is mandatory as it is of prognostic value. Diagnosis of BOT at frozen section may be missed unless the pathologist is experienced. It is better to perform a complete staging once histologically a benign disease is unlikely. Though there are controversies regarding the extent of staging, the guidelines include Peritoneal washings, TAH, BSO, omentectomy, excision of deposits, biopsies of peritoneum over bowel, paracolic gutters, diaphragm etc and removal of pelvic and paraaortic lymph nodes. However, it has been found that lymph node involvement is not a prognostic factor; hence their removal can be omitted.[7,8] In mucinous BOTs appendicectomy is performed as it may be a metastasis from appendix.[9] Studies found that most of the BOTs are inadequately staged and the recurrences are seen mostly in this group of patients.

Fertility preservation

Since a third of patients are under 40 years, and the majority present in early stage, they may need fertility preservation. In patients with unilateral tumor, unilateral salpingo-ovariotomy can be performed. Though recurrences are two to four fold more common than radical surgery, they occur in about 10% and may not affect the survival as these recurrences can be successfully treated.[8] Ovarian cystectomy is associated with more recurrences than ovariotomy.The risk of recurrence in the form of invasive cancer is very low. There is no need to biopsy the normal looking contralateral ovary. In bilateral tumors, bilateral ovarian cystectomy or unilateral salpingo-ovariotomy and contralateral ovarian cystectomy can be performed. Currently, more gynecologists prefer laparoscopic surgery as the survival rates are similar with less morbidity.[8] But the controversies include spillage due to rupture of the tumour and port site metastasis. Recurrences following laparoscopic surgery may be related to ovarian cystectomy instead of salpingo-ovariotomy. When laparoscopy is considered, tumor markers have to be normal and one has to ensure that there is no spill by bagging the tumors. Once the family is complete, the completion surgery should be undertaken to reduce the recurrences as they can occur even after decades. In patients attempting conception following fertility sparing surgery, about 50% conceive. There is controversy whether assisted reproductive techniques in these patients result in increased recurrences.

Adjuvant therapy

There is no definite role of adjuvant chemo, radio or hormone therapy in early stage disease. Chemotherapy is recommended when there are invasive implants. Platinum based agents as in ovarian cancers have been tried. Even in advanced disease the results are mixed - some studies showing better survival without adjuvant therapy.[7] Such patients are treated after enrolling in clinical trials.

Prognosis

The overall survival of BOTs is good with survival of 100% in stage I. In advanced disease without invasive implants 5 year survival of 95% can be anticipated. When there are invasive implants, the survival drops by one-third (66%).[5] Even with invasive implants, one-third of the patients survive for 10 years. The 10 year survival for advanced disease is 65%.[10] Lymph node involvement and histological subtype (serous/mucinous) do not carry any prognostic significance.[8] Advanced FIGO stage, suboptimal debulking, invasive implants and micropapillary architecture carry poor prognosis.[5,8,10,12] Progression to low grade serous carcinoma has been reported after long follow up. Hence, long follow up is advocated.[10]

Conclusion

BOTs are relatively rare epithelial tumors which usually present in early stage and carry excellent long term survival. Though staging laparotomy and radical surgery is the rule, in younger women with early disease fertility sparing surgery can be undertaken without affecting the survival. Minimal invasive surgery also can be undertaken with all its advantages. Adjuvant therapy is usually not advised.

References

1) Sutton GP. Ovarian tumors of low malignant potential. In: Rubin SC, Sutton GP(ed). Ovarian cancer. 2nd ed. Philadelphia: Lippincott Williams & Wilkins; 2001. 399-417.

2) Skírnisdóttir I, Garmo H, Wilander E, Holmberg L. Borderline ovarian tumors in Sweden 1960–2005: Trends in incidence and age at diagnosis compared to ovarian cancer. Int J cancer. 2008; 123(8): 1897-901.

3) Sherman ME, Mink PJ, Curtis R, Cote TR, Brooks S, Hartge Pet al. Survival among women with borderline ovarian tumors and ovarian carcinoma: a population-based analysis. Cancer. 2004; 100(5): 1045-52.

4) Madsen C, Baandrup L, Dehlendorff C, Kjaer SK. Tubal ligation and salpingectomy and the risk of epithelial ovarian cancer and borderline ovarian tumors: a nationwide case–control study. Acta Obstet Gynecol Scand. 2015;94(1): 86-94.

5) Seidman JD, Kurman RJ. Ovarian serous borderline tumors: a critical review of the literature with emphasis on prognostic indicators. Human Pathol. 2000; 31(5): 539-57.

6) Dietel M, Hauptman S. Serous tumours of low malignant potential of the ovary. Diagnostic pathology. Virchows Arch. 2000;436(5):403-12.

7) Camatte S, Morice P, Thoury A, Fourchotte V, Pautier P, Lhomme C et al. Impact of surgical staging in patients with macroscopic stage I ovarian borderline tumors: Analysis of a continuous seriesof 101 cases. Eur J cancer. 2004; 40(12):1842-9.

8) Lenhard MS, Mitterer S, Kumper C, Stieber P, Mayr D, Ditsch Net al. Long-term follow-up after ovarian borderline tumor: Relapse and survival in a large patient cohort. Eur J Obstet Gynecol Reprod Biol. 2009;145(2):189-94.

9) Seong SJ, Kim DH, Kim MK Song T. Controversies in borderline ovarian tumors.J Gynecol Oncol. 2015; 26(4):343-9.

10) Longacre, TA, McKenney, JK, Tazelaar, HD, Kempson RL, Hendrickson MR. Ovarian Serous Tumors of Low Malignant Potential (Borderline Tumors): Outcome-based study of 276 patients with long-term (≥5-Year) follow-up. Am J Surg Pathol. 2005;29(6):707-23.

11) Kane A, Uzan C, Rey A,Gouy S, Camatte S, Pautier Pet al. Prognostic factors in patients with ovarian serous low malignant potential (borderline) tumors with peritoneal implants. Oncologist. 2009; 14(6): 591-600.

12) Yokoyama Y, Moriya T, Takano T,Shoji T, Takahashi O, Nakahara K et al. Clinical outcome and risk factors for recurrence in borderline ovarian tumours. Br J Cancer. 2006; 94(11): 1586–91.