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Original Article:

Borderline Ovarian Malignancies : A Single Institute Retrospective Study.

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Abstract: Background: Borderline ovarian tumors are histologically characterized as epithelial tumors with a stratified growth pattern but without destructive stromal invasion. Little is known about the histological subtypes and outcome, role of fertility sparing surgery and role of postoperative therapy in advanced stage in Indian scenario. While there is ample data in the world literature about this disease, prognosis in Indian patients is largely unknown due to dearth of studies in our setting. **Objective:** To study the demographic profile, clinical features, imaging, treatment and outcome of borderline ovarian tumors. **Methods:** This is a retrospective study of eighty seven patients with pathologically proven diagnosis of borderline ovarian tumor, diagnosed and treated from January 2006 to October 2011 at our institution. Most patients underwent surgical staging which incuded total abdominal hysterectomy and bilateral salphingo-oophorectomy, infracolic omentectomy, bilateral pelvic and para aortic lymphadenectomy. Young patients who had not completed their family underwent fertility sparing surgery. Patients with invasive metastatic implants received adjuvant chemotherapy. The outcome of these patients was correlated with stage, type of peritoneal implant, type of surgical procedure and with histological subtype. **Results:** At a median follow-up of 48 months, 100 percent survival was noted. One patient with stage III disease had recurrence. Conclusions: Borderline ovarian tumors occur at a younger age compared to invasive tumors. In patients with early stage disease who wish to preserve fertility, hysterectomy and contralateral oophorectomy are not necessary. Serous tumors occur at a younger age. They can be associated with invasive peritoneal implants and raised CA125 values. Majority of the serous tumors are bilateral and smaller in size compared to mucinous and endometroid tumors. Raised CA125 values did not correlate with the stage of disease. These patients have an excellent prognosis even in Indian scenario where majority of patients present with big ovarian masses.

Key Words: Borderline ovarian tumor; Retrospective study; CA125

Introduction:
Taylor in 1929 described Borderline ovarian tumors (BOT) as semi malignant ovarian tumors.[1] This subset of lesions has a good prognosis compared to invasive ovarian cancers. BOT account for approximately 15% of ovarian epithelial eoplasms.[2] The sine qua non for the diagnosis is the absence of stromal invasion. Considerable controversy has surrounded the management of these tumors as little is known about the histological subtypes and outcome, role of fertility sparing surgery and role of postoperative therapy in advanced stage disease.

In this study we have correlated outcome with stage, type of peritoneal implants, histological subtype and type of therapy. There are very few studies of outcome of borderline ovarian tumors from India. To the best of our knowledge, this is the largest study of outcome of borderline ovarian tumors from India.

Material and method:
Eighty seven patients were diagnosed to have BOT from January 2006 to October 2011 at our institution. The case records of these patients were analysed in detail for demographic profile, clinical features, imaging, treatment and outcome.

These patients underwent complete surgical staging in our institute which incuded total abdominal hysterectomy and bilateral salphingo-ophorectomy, infracolic omentectomy, bilateral pelvic and para aortic lymphadenectomy. The diagnosis was established on the basis of histopathological examination of post operative specimen. FIGO 2009 staging was followed. The type of peritoneal implant (i.e., invasive, non-invasive) was noted. Post operative platinum based chemotherapy was given for patients with invasive peritoneal implant. Outcome was correlated with stage (early vs. advanced), type of peritoneal implant, type of therapy (completion surgery vs. fertility sparing) and with histological subtype. These patients were followed up every 3 monthly for initial 2 years and 6 monthly thereafter. The outcome was evaluated for all patients using the Kaplan Meier curve (SPSS 19 - SPSS Inc, USA).

Results:
This retrospective study included eighty seven patients treated at our institute. The median age of presentation was 40 years (range 20-70 years). Majority of patients were premenopausal. The most common presenting symptom was abdominal distension, seen in 69% of patients. Ten percent of patients were asymptomatic and were detected incidenatlly by ultrasound imaging done for other indications.

CA125 was raised (>35 IU/ml) in 60 patients. Only 18% (16) patients had a CA125 value of more than 100 IU/ml. Cystic mass with septation was the most common ultrasound finding. Bilateral ovarian masses were noted in 10% patients. Mucinous tumors were larger in size as compared to serous borderline tumors on ultrasound. The tumor was limited to one ovary and commonly manifested as multilocular or unilocular cystic mass.

Of the sixty seven patients operated at our centre, fifty seven underwent complete surgical excision and ten patients underwent fertility sparing surgery. Twenty patients were referred to our centre without complete staging surgery. Staging surgery was carried out in all these patients at our centre. Majority of patients (84) had stage I disease. Only 3 patients had stage III disease. Serous borderline ovarian tumor was the most common histologic subtype. Invasive peritoneal implants were noted in three patients with serous histology. All mucinous and endometroid tumors were confined to ovary at the time of diagnosis.

At median follow up of forty eight months (range 12 months-66 months) all patients with stage I disease were alive irrespective of the type of surgery performed. There was 100 percent survival with either fertility sparing surgery or complete surgical staging. There were 3 patients with stage III disease. All these 3 patients had invasive implants and received adjuvant chemotherapy with single agent carboplatin, One patient had recurrence. There was no statistical significant relationship between histology and outcome (p = 0.35) or with type of surgical procedure performed.

Table 1: Clinical features	
Total number of patients	87 (100%)
Clinical Presentation	
Mass per abdomen	60 (69%)
Pain abdomen	12 (14%)
Asymptomatic	15 (17%)
Parity	
Nullipara	05 (06%)
Primipara	14 (16%)
Multipara	68 (78%)
Menopausal State	
Pre	51 (59%)
Post	36 (41%)
USG features	
Cystic mass with solid areas	11
Cystic mass with septations	65
Bilateral masses	9
Ascitis	2
Investigation	
CA125 > 35IU/ml	60

Table 2: Histopathological features			
	Serous	Mucinous	Endometroid
Number of cases(87)	47	36	04
Median age	35	42	40
Bilateral disease (9)	6	1	2
Median size of tumor	1100ml	1300ml	800ml
Invasive implant (3)	3	-	-

Table 3: Outcome	
Surgery	
Conservative	10 (11%)
Complete	57 (66%)
Operated elsewhere (completion surgery)	20 (23%)
Histology	
Serous	47 (55%)
Mucinous	36 (41%)
Endometroid	04 (04%)
Chemotherapy	3 (3.5%)
Recurrence	1 (1.1%)

Discussion:
The separation of ovarian neoplasms into benign, borderline and malignant forms is crucial, because the pathology and outcome for each of these entities is markedly different. In general, borderline tumors are characterized as neoplasms exhibiting cellular proliferative changes greater than the benign form of the same type of tumor, but not showing destructive invasion of the ovarian stroma.

As seen in our study, patients with borderline ovarian tumors are younger than those with invasive ovarian carcinoma.The same has been reported from other studies.[3] Thus, this tumor frequently affects women with a desire to preserve child bearing potential. In Indian scenario, majority of patients present late with bulky disease. The mean diameter in the present study was 11.2 cms (range 6-36cms) which is much larger compared to western literature.[4]

Ten percent of patients were asymptomatic and were diagnosed sonographically. The present rise in incidence of borderline tumors may partly be due to increased diagnostic procedures performed. Increasing use of oral contraceptive

pills[5] and use of fertility drugs[6] may also partly explain the observed rise in borderline ovarian tumors. More than 60% patients of BOT had raised CA125 levels in our study. Similar incidence has been reported in other studies as well.[7] Raised CA125 was commonly associated with serous tumor.However the rise did not correlate with stage of disease. One patient with stage III with invasive peritoneal implants disease had a recurrencewhich was primarily detected by raised CA-125.

In patients with stage I disease, no recurrence was noted when either fertility sparing surgery or complete comprehensive surgical staging was performed. This has been reported in other larger studies as well.[8,9] Patients with early stage disease have excellent prognosis, and in these who wish to preserve fertility, uterus and the contralateral ovary may be preserved.

In patients with advanced stage disease, only patients with invasive peritoneal implant had poor prognosis. Other factors which have an increased risk of invasive recurrence are controversial: these include micropapillary patterns in serous borderline ovarian tumour[10] and intraepithelial carcinoma in mucinous borderline tumor.[11]

Comparing the histology of serous, mucinous and endometroid tumors have different presentation (Table 2). Serous tumors occur at a younger age, are commonly bilateral and smaller in size compared to mucinous and endometroid tumors. Raised CA 125 was commonly seen in serous histology. Other larger studies have reported similar statistics.[12,13] All primary mucinous and endometroid tumors are confined to the ovary at time of diagnosis; an advanced stage mucinous tumor at first diagnosis should be evaluated as possible metastasis from other sites, particularly the gastrointestinal tract. In the present study appendicectomy was perfomed in all mucinous tumours as a part of surgical staging.

Conclusion

Borderline ovarian tumors occur at a younger age compared to their invasive counterpart. In patients with early stage disease who wish to preserve fertility, uterus and the contralateral ovary may be preserved. Serous tumors occur at a younger age and may be associated with invasive peritoneal implants and raised CA125.They are smaller in size compared to mucinous and endometroid tumors. Raised CA125 did not correlate with the stage of disease.Long-term surveillance is necessary to document and treat late recurrences. The pathologist has a crucial role in the diagnosis of borderline nature of ovarian tumours and in identification of high-risk criteria. These patients have an excellent prognosis even in Indian scenario where majority of patients present late with bulky disease.

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