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NON-EPITHELIAL OVARIAN CANCER: A RETROSPECTIVE ANALYSIS OF 5-YEARS EXPERIENCE IN A TERTIARY CANCER CENTRE

Oncology/Radiotherapy

Dr Parul Gupta* Assistant Professor, Department of Radiation Oncology, SMS Medical College, Jaipur, Rajasthan, India. *Corresponding Author

Dr Sneha Dhillon Department of Radiation Oncology, Gujarat Cancer and Research Institute, Ahmedabad.

ABSTRACT

Background: In this retrospective study, we determine the clinicopathologic characteristics, prognostic factors and treatment outcomes in the patients of non-epithelial ovarian cancers during a five year period. **Method:** Between the year Jan-2014 and Dec-2018, data of malignant non-epithelial ovarian cancer patients was analysed, who were treated at tertiary Cancer Centre from north india for their clinicopathologic characteristics, management and follow-up status. **Results:** Twelve patients with non-epithelial ovarian cancer were analysed, amongst which 7(58%) patients had sex cord stromal tumours and 5(42%) had malignant germ cell tumours (GCTs). The median age at presentation was 55-years (32-65) for sex cord stromal tumours and 30-years (14-35) for germ cell tumours. The patients were staged according to the FIGO ovarian cancer staging system 2014 and majority of patients (57.1%) with sex cord stromal tumours had stage I disease. All patients with sex cord stromal tumours and 20% with GCTs underwent non-fertility sparing surgery. Adjuvant chemotherapy was administered in 29% patients with sex cord stromal tumours and in all patients with germ cell tumours. The chemotherapy regimen used was BEP in all patients. At a median follow-up of 24-months, none of the patients experienced recurrence. **Conclusion:** Non-epithelial ovarian cancers are a rare presentation. The outcomes of patients with GCTs were good irrespective of disease stage with optimal treatment. Sex cord stromal tumours are more indolent with good short-term prognosis but carry significant risks of late relapse. Platinum-based chemotherapy has shown benefits in either with manageable toxicity.

KEYWORDS

Non-epithelial ovarian cancer, Germ cell tumours, Sex cord stromal tumours, malignant tumours

INTRODUCTION

Non-epithelial ovarian cancers are a group of uncommon malignancies which account for 6-10% of all ovarian cancers.[1](Ray-Coquard et al).[1]The most common type of sex cord stromal tumor is granulosa cell tumor [2]Among thenon-epithelial ovarian cancers, mMalignant oOvarian gGerm cell tumourstumours and sSex cord stromal tumourstumours are the two most common types, each of which is further divided into subtypes based according to ontheir histological classification.y[2](Boussios et al)[3] Malignant ovarian gGerm cell tumourstumours account for approximately 5% of all ovarian cancers ,it and is mainly seen in young women and the most common include dysgerminoma, immature teratoma are the most common types.[3]Sex cord stromal tumourstumours of the ovary accounts for 3-5% of all ovarian cancers ,it and is mainly seen in post-menopausal women. The most common type of sex cord stromal tumour is granulosa cell tumor.[4] and the most common type of sex cord stromal tumour is granulosa cell tumour(Kim et al).[4]The signs and &symptoms and signs in patients with non-epithelial ovarian cancer includes lower abdominal pain, feeling of pelvic pressure due to mass effect, menstrual irregularities and abdominal distension in advanced stages.[5](Medina-Franco et al)[2]Diagnostic workup in patients with non-epithelial ovarian cancer includes imaging modalities, pelvic ultrasoundsonography, CT computed tomography scan of the abdomen and pelvis, cChest X RRay, and positron emission tomographyPET-CT S scan in selected cases.[1], lLaboratory studies includesLaboratory studies include complete blood counthemogram ,liver function test and renal function testsand complete biochemical profiling of the patients (Ray-Coquard et al). [1]TumourTumour markers include seruminclude serum alpha fetoprotein, sSerum cancer antigen 125(CA-125), serum Lactate lactate dehydrogenase (LDH), serum βB human chorionic gonadotropin(βB-HCG). CA-125 is usually used as a tumourtumour marker in epithelial ovarian cancer, however, recent studies have also reported elevated levels of CA-125 in non-epithelial ovarian cancers.[52]Presently, The staging system used for nonepithelial ovarian cancer is the 2014FIGO ovarian cancer staging system 2014 is. used for staging of non-epithelial ovarian cancers.

For sex cord stromal tumourstumours the surgical approach is similar to epithelial ovarian cancers except in patients with stage I disease who is desirous of fertility, a fertility sparing surgery can be done. With surgery alone the 10-year survival in stage I is 85%, is 50-65% in stage II and 17-33% in stage III-IV. The value of adjuvant chemotherapy is questionabledebatable due to rarity of randomised trials. and pPlatinum containing regimens are the most commonly used regimens in the adjuvant setting.[68]While fFor germ cell tumourstumours a fertility sparing surgery is recommended due to their young age at diagnosis and the chemo-sensitivity of these tumourstumours. The10-year progression free survival for patients with germ cell tumourtumour is up to 82%.[79]The most commonly used adjuvant chemotherapy regimens are platinum based regimens, of which the 5-day course of BEP regimen is the most commonly used.[87]The present is retrospective study was conducted to determine the clinical and pathological features and the treatment received in patients with non-epithelial ovarian cancers.

METHODS

Data of the patients with non-epithelial ovarian cancer, who were registered and treated at tertiary cancer center in north india between Jan-2014 and Dec-2018 was retrospectively collected and analysed for patient their characteristics, clinical presentation, extent of surgery, post-operative adjuvant therapy, management and follow-up status. Relevant information was extracted from the medical records. Patients were included if they had a histopathologically proven sex cord stromal tumour or GCT. Patients with insufficient data were excluded from the analysis. The study was approved by the local ethics committee. Comparisons between patients and disease characteristics were done by Chi-square test.

RESULTS

12-Twelve patients with non-epithelial ovarian cancer were studied from 2014-2018.about Ttheir characteristics, stage of disease and clinical details asre described in Table 1. There were 7(58%) patients with sex cord stromal tumours and 5(42%) patients with malignant germ cell tumours. The median age at presentation was 55-years (32-65) for sex cord stromal tumours and 30-years (14-35) for germ cell tumours. The initial presentation for sex cord stromal tumours and germ cell tumours was abdominal pain in (42.8% for sex cord stromal tumor,and 60% for germ cell tumor)respectively. Majority (85.7%) of patients with sex cord stromal tumour i.e. 86were% were post-menopausal while all patients with germ cell tumour were pre-menopausal. The primary site was gonadal for both sex cord stromal tumours and germ cell tumours. One patient with sex cord stromal tumour had bilateral ovaries involved. The patients were staged according to the 2014 FIGO ovarian cancer staging system 2014 and majority (57.1%)of patients (57.1%) with sex cord stromal tumours had stage I disease. whereas in the germ cell tumors cohort,the stage was not specified in 60% of patients. All patients with sex cord stromal tumours and 20% with germ cell tumours underwent non-fertility sparing surgery. Adjuvant chemotherapy was administered in 298.6% patients with sex cord stromal tumours and in all patients with germ cell tumours. The chemotherapy regimen used was BEP in all patients and majority received four cycles of chemotherapy. At a median follow-up of 24-months, none of the patients experienced recurrence.

DISCUSSION

This five year retrospective study was conducted in the Department of

Radiation Oncology, Pt B D Sharma PGIMS, Rohtak between January 2014 and December 2018. This study included 12-patients with non epithelial ovarian cancer who were registered and treated at our institution.

Non-epithelial ovarian cancers constitute rare neoplasms, constitute about 6-10% of all ovarian cancer and . Iin our institution non-epithelial ovarian cancer also, comprised of 7.6% of all ovarian cancer.[87]The two most common types of non-epithelial ovarian cancer seen was were sex cord stromal tumour and germ cell tumour. Of Among all 157-patients of malignant ovarian cancer who were treated in our institution during the 5-year period, 4.5% of patients had sex cord stromal tumours and 3.2% of patients had malignant germ cell tumour, which is similar to the findings by Kim et al and Ray-Coquard et al.[4,11,4]The median age at presentation for sex cord stromal tumours was 55yearsand for germ cell tumours was 55-years and 30-years respectively. [13]Most (865.7%)of the patients with sex cord stromal tumours i.e. 86% were post-menopausal with a peak in the 4-5th decade while all patients with germ cell tumours were pre-menopausal with age range between 14-35 years, similar to findings reported by Saber et al and Bryket al.[8,97,13,14]The most common initial presentation for both sex cord stromal tumour and germ cell tumours was abdominal pain and menstrual irregularities.[10,116,15]

The number of patients with right sided Thetumorswere and left sided tumours were equalright sided i i.e.n 42.8%,patients,left sided in 42.8% patients andwhilebilateral in 14.3% patients were observed with bilateral with sex cord stromal tumours, similar to the findings by similar to the findings reported by Lee et al,, whereas in germ cell tumours, the majority of tumours were found to be right sided.[3] The most common stage at presentation for sex cord stromal tumours was stage I as estrogen production causes menstrual abnormalities leading to early presentation and early diagnosisin these patients,while in patients with germ cell tumors, the stage was not specified in 60% cases.[3]

CA-125 is most commonly used as a tumour marker in epithelial ovarian cancer, but studies have reported elevated levels of CA-125 in non-epithelial ovarian cancers. A study conducted by Kim et al on 199-patients with malignant ovarianepithelial germ cell tumours found that 70.2% of the patients had elevated preoperative serum CA-125 levels > 35 U/ml and in 19.9% of their patients CA-125 levels were more than 249.5 U/ml, which showed a significant association with poor survival in those patients.[44] In our study, we found thatthethat the levels of serum CA-125 levels were elevated (>35 U/ml) in 34% of patients pre-operatively and in 66% of patients preoperative serum CA-125 levels were not specified. Even though these tumour markers are non-specific, they can provide information about prognosis, response to chemotherapy and recurrence.[44] Therefore, it is advisable that these markers are quantitatively assessed pre-operatively.

Similar to epithelial ovarian cancers, surgery remains the first approach in non-epithelial ovarian cancers. Fertility sparing surgery is recommended in germ cell tumours because of their early presentation, chemo-sensitivity and high cure rates.[12,1311,12]In our the present study, we found that all patients with sex cord stromal tumours underwent non-fertility sparing surgery, while 80% of patients with germ cell tumours underwent fertility sparing surgery, which, is similar to the findings reported by Kempf et al.[1410]Post-operative chemotherapy was administered in 28.6% of patients with sex cord stromal tumour similar to the findings reported by Llee et al while all patients with germ cell tumours received adjuvant chemotherapy.[35]

Platinum based regimen is the chemotherapeutic regimen of choice in adjuvant setting, the most widely used regimen being BEP regimen. The optimum number of cycles has not been established, it is recommended to give 3-cycles of BEP regimen in patients with completely resected disease and 4-cycles in patients with macroscopic residual disease.[87]In our studyretrospective analysis, all patients received BEP regimen, with majority of patients receiveding 4-cycles of chemotherapy.

Our study has also some limitations. Like most published studies, our sample was small and it was a retrospective study. Some statistical analyses were limited due to low numbers. The rarity of this disease leads to the need for a very long time period for the accumulation of cases.

CONCLUSION:

Non-epithelial ovarian cancers are a rare presentation but remain highly curable malignancy. The outcomes of patients with GCTs were good at all the stages of disease with optimal treatment. Sex cord stromal tumours are more indolent with good short-term prognosis but carry a significant risk of late relapses. Administering platinum-based chemotherapy has shown benefits with manageable toxicity.

DECLARATIONS

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Conflict Of Interest: *None declared*

Ethical Approval: *Not required*

Table 1: Patient Characteristics, Disease Status And Treatment Details

Characteristics	Sex cord stromal tumours (n=7)	Germ cell tumours (n=5)	Total (n=12)
Total	7	5	12 (100%)
Median age (range) years	55 (32-65)	30 (14-35)	43 (14-65)
Rural/ Urban	1 Urban 6 Rural	1 Urban 4 Rural	
Presentation			
Abdominal pain	3 (42.8%)	3 (60%)	6 (50%)
Menstrual irregularities	3 (42.8%)	2 (40%)	5 (42%)
Abdominal distension	1 (14.3%)	0	1 (8%)
Menopause			
Yes	6 (85.7%)	0	6 (50%)
No	1 (14.3%)	5 (100%)	6 (50%)
Parity			
Multiparous	7 (100%)	1(20%)	
Nulliparous	0	4(80%)	
Primary site			
Gonadal	7 (100%)	5 (100%)	12(100%)
Extra gonadal			0 (0)
Tumour Laterality			
Left ovary	3 (43%)	1 (20%)	4 (34%)
Right ovary	3 (43%)	4 (80%)	7 (58%)
Bilateral	1 (14%)	0	1 (8%)
Stage			
I	4 (57%)	0	4 (34%)
II	0	0	0 (0)
III	1 (14%)	1 (20%)	2 (16%)
IV	0	1 (20%)	1 (8%)
Not specified	2 (29%)	3 (60%)	5 (42%)

Pre-operative CA-125 levels			
Elevated	1 (14%)	3 (60%)	4 (34%)
Not specified	6 (86%)	2 (40%)	8 (66%)
Metastasis	0	0	0
Surgery			
Fertility sparing	0	4 (80%)	4 (34%)
Non-fertility sparing	7 (100%)	1 (20%)	8 (66%)
Chemotherapy			
Yes	2 (29%)	5 (100%)	7 (58%)
No	5 (71%)		5 (42%)
First line Chemotherapy regimen			
BEP	2 (29%)	5 (100%)	7(58%)
Others			
Number of cycles of chemotherapy			
Four	1(14%)	4 (80%)	5 (42%)
Five	0	1 (20%)	1 (8%)
Six	1 (14%)	0	1 (8%)
Treatment modality			
Surgery only	5 (71%)	0	5 (42%)
Surgery +chemotherapy	2 (29%)	5 (100%)	7 (58%)
Median duration of follow up	24 months		

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