Gynaecological Cancer

A Tertiary Cancer Center Experience of 52 Cases of Primary Ovarian Mucinous Adenocarcinomas

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Abstract

Background Primary mucinous epithelial ovarian adenocarcinoma (mEOC) constitutes a small percentage (2–5%) of ovarian cancer. Our aim is to understand the clinicopathological characteristics and survival results of patients with mEOC after a long-term follow-up.

Materials and Methods This is a retrospective study of primary mEOC cases treated at a tertiary cancer center in India, from January 1, 2005, to December 31, 2012.

Results Out of 958 malignant ovarian tumors, 52 (5.43%) were mucinous adenocarcinoma. Nearly 71.2% of cases were of early-stage disease, and the remaining were of advanced-stage disease. After a follow-up period of 63 months (range: 1–138 months), the 5-year actuarial overall survival for stages I, II, III, and IV was 92.5, 70, 38.5, and 0%, respectively. Among advanced-stage tumors, half of them progressed without undergoing cytoreductive surgery and died.

Conclusion Most of the mEOC cases present in early stages and have good clinical outcome. Patients with advanced-stage disease do not respond well to standard chemotherapy regimens in use and have poor survival figures. The use of primary cytoreduction should be considered in the place of interval cytoreduction for advanced mEOC.

Keywords

- cytoreductive surgery
- mucinous adenocarcinoma
- neoadjuvant chemotherapy
- ovarian cancer

Introduction

Primary mucinous epithelial ovarian adenocarcinoma (mEOC) constitutes a small percentage (2–5%) of ovarian cancers, with distinct clinicopathological characteristics when compared with the more common serous histology.^{1,2} The representation of mEOC in large clinical trials exploring the role of therapeutic interventions is small; for example, 1.6% in the Gynecologic Oncology Group (GOG) 182 trial.³ This subset of tumors has a low response to primary chemotherapy. There is no gold standard method to distinguish unequivocally between mEOC and mucinous carcinomas metastatic to the ovary.

Materials and Methods

This is a retrospective study of a series of primary mEOC diagnosed and treated at a premier tertiary care center in India,

from January 1, 2005, to December 31, 2012. The archived case records were studied in detail, including the clinical history and examination, imaging, endoscopy, biopsy, and histopathological reports. The following parameters were collected: age, date of admission, presenting complaints, menopausal status, parity, laterality, size of the tumor, stage of disease, serum tumor markers (cancer antigen 125 [CA-125] and carcinoembryonic antigen), use of neoadjuvant chemotherapy (NACT), date of surgery, presence of malignant ascites, peritoneal disease, whether appendectomy was done or not and the histopathological finding of the appendix, lymph nodal dissection and the nodal status, pathological stage, grade of tumor, adjuvant chemotherapy, recurrence, date of last follow-up, and status at follow-up. Data were analyzed using simple statistical tools such as median values and SPSS version 22.0 (IBM Corp., Armonk, New York, USA). Kaplan–Meier plots were used to estimate the survival distribution.

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Results

A total of 958 malignant ovarian tumors were treated at our institute during this period, out of which 758 were malignant epithelial ovarian cancers, 98 were germ cell cancers, 30 were sex cord stromal tumors, and 48 were not classified.

Mucinous ovarian adenocarcinomas constituted 52 (5.43%) cases. Thirty-seven (71.2%) patients presented with early-stage disease, out of which 27 (51.9%) were in stage I and 10 (19.3%) were in stage II. Advanced-stage disease comprised 15 (28.8%) patients, of whom 13 (25%) were in stage III and 2 (3.8%) were in stage IV (►Table 1).

The most common presenting complaints were abdominal distension and pain. The distribution was almost equal between premenopausal and postmenopausal women. Among the patients with early-stage tumors, 86.5% underwent primary surgery, whereas 13.5% received NACT. Stage IC and II tumors received adjuvant chemotherapy. Nearly 80% of the patients with advanced-stage disease received NACT, whereas the remainder 20% underwent primary cytoreduction. It was observed that among the 12 patients with advanced-stage disease who received NACT, 6 (50%) progressed to chemotherapy and died without having cytoreductive surgery. One patient had secondary cytoreduction. The chemotherapy regimens used were paclitaxel and carboplatin doublet, single-agent carboplatin, cisplatin and cyclophosphamide doublet, and liposomal doxorubicin and carboplatin doublet for six cycles.

The median duration of follow-up was 63 months (range: 1–138 months). The 5-year actuarial overall survival (OS) for stages I, II, III, and IV disease was found to be 92.5, 70, 38.5, and 0%, respectively (►Table 2).

The age of the patient was found to be important in relation to the prognosis for the disease. For the age group 60 years or more, the 5-year OS was 33.3% as opposed to 75.9% for those aged <60 years ($p = 0.004$). When the patients aged under 30 years were considered, they were found to have a 5-year and 10-year OS of 100 and 100% as compared with 64.1 and 48.3%, respectively, for those aged 30 years or more ($p = 0.01$).

Two patients who underwent fertility-preserving surgery were alive without any evidence of disease at 97 and 41 months of follow-up, respectively. One of them delivered

a healthy baby, whereas the other patient had polycystic ovarian disease and did not conceive. No statistically significant difference was observed in the survival outcome based on whether the serum CA-125 level was elevated or normal. The tumors that were >13 cm and those that were unilateral fared much better than those <13 cm and bilateral tumors or in cases where the laterality remained undetermined. Grade 1 and 2 tumors had better survival than grade 3 tumors ($p = 0.03$) (►Table 3).

Discussion

The population-based Madras Metropolitan Tumour Registry covers 4.65 million people. The age-standardized ratio for carcinoma ovary per 100,000 population in Chennai is 8.2 as compared with 6.1 in the world.⁴

Mucinous adenocarcinomas of ovary are more often diagnosed at an early stage due to which the OS is better compared with that of serous carcinomas.⁵ In this study, 71.2% of tumors were in the early stages of disease, with a 5-year OS of 86.2%. In contrast, when the disease presents at an advanced stage, the survival is worse, probably owing to lesser sensitivity to platinum-based chemotherapy.^{2,6} In our study, the patients with advanced-stage disease had a 5-year OS of 28%.

The mucinous histology is uncommon.² In our study, over a period of 8 years, only 52 cases were found comprising 5.43% of the total cases. This makes randomized controlled trials of adequate statistical power exploring therapeutic options, such as chemotherapy regimens, a daunting task.

There is no foolproof method to distinguish between primary mucinous adenocarcinomas of the ovary and mucinous adenocarcinomas metastatic to the ovary, although many

Table 1 The results of the various clinical characteristics studied

Characteristics	Values
Median age at presentation (years)	45 (15–73)
For early-stage disease (years)	42 (15–65)
For advanced-stage disease (years)	46 (36–73)
Medium serum CA-125 levels (IU/mL)	52.5
For early-stage disease (IU/mL)	47.1 (3.7–2,700)
For advanced-stage disease (IU/mL)	87.5 (20.7–8,490)
Median size of tumors (cm)	20 (6–30)
For early-stage disease (cm)	20 (6–30)
For advanced-stage disease (cm)	24 (9.9–33)

Abbreviation: CA-125, cancer antigen 125.

Table 2 The survival outcomes in the early and advanced stages

Stage group	3-y OS (%)	5-y OS (%)	10-y OS (%)
Early (I and II)	89.2	86.2	69.0
Advanced (III and IV)	33.3	28.0	20.0

Abbreviation: OS, overall survival.

Table 3 Survival outcome for various subgroups based on tumor characteristics

Subgroup	5-y OS (%)
<13 cm	74.8
>13 cm	33.3
Unilateral	80.5
Bilateral	60.0
Undetermined	0
Grade 1	75.0
Grade 2	84.0
Grade 3	41.7

Abbreviation: OS, overall survival.

algorithms using size and laterality as criteria and several immunohistochemical markers have been used over time to aid in the distinction.^{1,7-9} These are in addition to the several morphological characteristics, such as surface involvement of ovary, a nodular growth pattern, presence of signet ring cells, hilar involvement, an expansile or infiltrative growth pattern, presence of complex papillae, and necrotic luminal debris, which have been described to make the differentiation.¹⁰

In our study, the mucinous adenocarcinomas have been deemed to have primarily arisen from the ovary based on the clinical history and examination, imaging and endoscopy, and histological features of the tumor.

mEOC responds poorly to platinum-based chemotherapy compared with its serous counterparts.² In our study, it was observed that 6 (50%) out of the 12 patients with advanced-stage disease, who received NACT with the standard platinum-containing regimens, progressed and died due to disease without getting cytoreductive surgery. This probably makes us understand that the mucinous ovarian adenocarcinomas can be considered for upfront complete cytoreductive surgery. However, such a comparison has not been made in our retrospective study, in which one-fifth of the advanced-stage mEOC underwent primary cytoreduction as opposed to the remaining 80% receiving NACT.

We understand that there are certain drawbacks to our study. Immunohistochemical studies were not performed, even though it was understood that they could have helped in differentiating between the primary and secondary tumors. This was because the use of these tests has several limitations and does not completely eliminate misclassification. Besides, Zaino et al reported that the median survival did not differ significantly between the groups interpreted as primary or metastatic to the ovary for stage III and IV disease.¹¹ We have also not compared the mucinous ovarian adenocarcinomas head-on with the other histologies for the same study period.

Conclusion

Most of the mEOCs present in early stages and have good clinical outcomes. Patients with advanced-stage disease do not respond well to standard chemotherapy regimens in use

and have poor survival figures. The use of complete primary cytoreduction should be considered strongly in the place of interval cytoreduction for advanced mEOC

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None.

Conflicts of Interest

There are no conflicts of interest.

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