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The mucinous ovarian cancer: classification and clinical use of cancer biomarkers for diagnosis

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The mucinous ovarian cancer: classification and clinical use of cancer biomarkers for diagnosis

Abstract

The aims of the study were to examine the prevalence of positive mucinous ovarian carcinoma (MOC) at different stages as well as to investigate the age at diagnosis and histological type, and to assess the correlation between the carcinoembryonic antigen/ cancer antigen 125 (CEA/CA 125) tests and the diagnosis of ovarian cancers retrospectively, to promote the prognosis and patient's health outcome. Descriptive a cross-sectional correlational design was used to examine the prevalence of positive ovarian cancer over a period of seven years of follow-up between 2010 and 2016. All study analysis was performed using SPSS version 22. $P<0.05$ was taken to indicate a statistically significant value. We found that about 70% of cases showed elevation of CEA marker and about 95% of them showed elevation of Ca125. The age-specific incidence rate increased greatly in women aged 50 years or older. The majority of the patients had stage III or IV disease. Our study results can be used as a detection method of possible new ovarian cancer cases in an early stage and would provide a quick non-invasive screening method for women with strong risk factors such as old age, smoking, family history, history of other tumors and obesity.

Keywords

serology, Ca125, screening, Mucinous ovarian cancer (MOC), Women, Jordan, CEA

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The mucinous ovarian cancer: classification and clinical use of cancer biomarkers for diagnosis

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ABSTRACT

The aims of the study were to examine the prevalence of positive mucinous ovarian carcinoma (MOC) at different stages as well as to investigate the age at diagnosis and histological type, and to assess the correlation between the carcinoembryonic antigen/ cancer antigen 125 (CEA/CA 125) tests and the diagnosis of ovarian cancers retrospectively, to promote the prognosis and patient's health outcome. Descriptive a cross-sectional correlational design was used to examine the prevalence of positive ovarian cancer over a period of seven years of follow-up between 2010 and 2016. All study analysis was performed using SPSS version 22. $P<0.05$ was taken to indicate a statistically significant value. We found that about 70% of cases showed elevation of CEA marker and about 95% of them showed elevation of Ca125. The age-specific incidence rate increased greatly in women aged 50 years or older. The majority of the patients had stage III or IV disease. Our study results can be used as a detection method of possible new ovarian cancer cases in an early stage and would provide a quick non-invasive screening method for women with strong risk factors such as old age, smoking, family history, history of other tumors and obesity.

Keywords: Mucinous ovarian cancer (MOC), women, Jordan, serology, screening, CEA, Ca125

INTRODUCTION

Ovarian cancer has a high mortality rate among gynecological malignancies of the female reproductive system and is the 5th cause of cancer death in women [1]. In Jordan, ovarian cancer is one of the top ten tumors among Jordanian females and accounts about 2.8%[2]. The annual mortality rate per 100,000 Jordanian people from ovarian cancer has increased by 20.7% since 1990, an average of 0.9% a year, as described by the cancer registry of Jordanian ministry of health in 2013.

The ovarian neoplasms which comprise several histologic types and grades are classified into surface epithelial-stromal tumors, sex cord-stromal tumors, and germ cell tumors. The epithelial neoplasms which are the most common types of ovarian cancer are classified into serous, endometrioid, mucinous, clear cell and undifferentiated subtypes. Mucinous carcinoma of the ovary is a rare ovarian cancer that is distinct from other epithelial subtypes based on specific clinical, histologic, and molecular features accounting about 7% to 14% of all primary epithelial ovarian cancer [3].

Mucinous tumors of the ovary include a spectrum of neoplastic disorders, including mucinous cystadenoma, mucinous tumor of low malignant potential (borderline) and invasive mucinous ovarian carcinoma (MOC). The diagnosis and classification of mucinous tumors has been problematic and controversial. The pathologic diagnosis of MOC to differentiating benign, borderline (low malignant potential), and metastatic tumors from primary invasive MOC is very difficult to determine and challenging, so the true incidence is not clear yet [4]. However; the benign mucinous tumors account for 10–15 % of all benign ovarian neoplasms tumors, borderline (low malignant potential) tumors account for 67 % of tumors not considered strictly benign either potentially malignant and thus are more common than invasive MOC [5].

In a previous study in Jordan for assessment of the knowledge and awareness of Jordanian women about ovarian cancer showing that patients came with most symptoms as the

following: extreme fatigue (43.2%), back pain (42.4%) and persistent pain in pelvic area (40.7%) and the most commonly known risk factor was smoking (68.4%) [8]. Definite diagnosis is essential for appropriate treatment, failure to diagnose benign or borderline histology results in inaccurate treatment, and failure to identify other ovarian disease as metastatic leads to a missed diagnosis of a gastrointestinal primary and incorrect therapy [6]. The early detection of ovarian neoplasms is hampered by the lacking of appropriate tumor markers and of clinically significant symptoms until the disease reaches an advanced stage. For the same reasons, ovarian cancer has the highest fatality-to-case ratio of all gynecological malignancies and the worst prognosis [7].

The aims of the study were to examine the prevalence of positive MOC at different stages as well as to investigate the age at diagnosis and histological type, and to assess the correlation between the carcinoembryonic antigen/ cancer antigen 125 (CEA/CA 125) tests and the diagnosis of ovarian cancers retrospectively, to promote the prognosis and patient's health outcome, because early diagnosis carries a high survival rate reaching 93%.

Materials and Methods

A Descriptive cross-sectional correlation design was used. Data were collected from women diagnosed of ovarian cancer over a period of seven years of follow-up (between 2010 and 2016) with convenience obtained list of women's hospital admission number (ID) from the admission office. Inpatients and outpatients were recruited if they had a diagnosis of current or had a recurrent mutinous cancer. Both malignant and borderline diagnoses were recruited. Only the principal investigator and the associated research team had access to the de-identified data set.

Power analysis estimated a sample of 150 participants to achieve the power of 0.95 which represent the chance of finding an association between study variables, and effect size of 0.3 to represent the likelihood of detecting an association between the pathology testing and other predictors at alpha level of 0.05 to incorrectly rejecting the null hypothesis [8].

The participants' pathology profile, laboratory testing and diagnosis report were collected retrospectively. Each subject was assigned an identification number to collect the needed data retrospectively. Participants' information was kept confidential in a secure encrypted Excel and SPSS computer file. The principal investigator and the associated research team only had access to the de-identified data file.

Data was coded and handled by the principal investigator and kept in a password protected computer file for data entry and analysis. Permission to access data file was given to certified research team member who participated in data entry or analysis. The principal investigator created a code book to use during data entry and analysis. The investigator did not withdraw any additional blood or pathology samples from the study participants. For the purposes of this study, the results of previously performed laboratory samples were collected.

Inclusion Criteria

The pathology reports of female patients who had been diagnosed as mucinous ovarian tumors either benign, borderline or malignant types were collected. The patients could be menopausal, premenopausal or either young. Peritoneal fluids were also sent for diagnosis to pathology lab to determine if these are positive or negative in ovarian cancer because they will affect the stage of the tumor and the prognosis. Then we correlated them with the serologic markers such as CA125 and carcinoembryonic antigen (CEA).

Exclusion Criteria

We excluded any patient who had endometriosis, fibroids, acute pelvic inflammatory disease, menstruation, the first trimester of pregnancy or known case of tumor such as hepatic or pancreatic in origin because these conditions also elevate the serologic markers described above, that will give false positivity.

Statistical analysis

To achieve the study objectives, the researcher used descriptive statistics of percentages, means, medians and standard deviations to identify the prevalence of ovarian cancer at different stages. All study analysis was performed using SPSS version 22. $P<0.05$ was

taken to indicate a statistically significant value.

Results and discussion

The results of our study revealed that 126 cases are classified as benign (85%),16 cases as borderline (10%) and 8 cases as malignant (5%) (Table 1). The rate at which women are diagnosed with ovarian cancer has been slowly falling over the past 20 years. These tumors occur most commonly in premenopausal women, as well as postmenopausal patients. The age at diagnosis of MOC which seems to be younger than the other epithelial ovarian cancer, is usually described between ages 20–50 years [9], However; the mean age provided by our study was 50 (standard deviation, ±16 years). Table 1 shows the distribution of ovarian cancers based on classification and patient characteristics.

Table (1): Distribution of ovarian cancers based on classification and patient characteristics

Variable	Frequency (%)
Classification total	150 (100)
Benign	126 (85%)
Borderline	16 (10%)
Malignant	8 (5%)
Age total	150 (100)
<15	1 (0.6)
15-25	7 (4.7)
25-40	10 (6.7)
40-54	90 (60)
55-64	35 (23.4)
65+	7 (4.6)
Stage total*	13(100)
0	0
I	1(7.7)
II	3 (23)
III	5 (38.5)
IV	4 (30.8)
Cyst side total	150 (100)
Right	53 (35.4)
Left	97 (64.6)
*Only the malignant subtype is included	

About 70% (9 out of 13 cases) of the invasive MOC were diagnosed in advanced stages (stage III or VI), because of lacking of an early screening method for ovarian cancer. However; in another study, 17 % of patients with MOC were stage II or higher at the time of diagnosis, the remainder were diagnosed at stage1 [10]. Most of the mucinous tumors are unilateral, as showed by our results in which 83% of our patients had unilateral tumor. This result is also seen in a large retrospective series and a SEER database analysis have both shown that 79 % of mucinous tumors are unilateral and borderline mucinous ovarian tumors were less likely bilateral (7 %) [11]. Most of the cases showed left sided predominate (64.6%). Positive result of cytological peritoneal fluid was 95% in the malignant subtype, however: the benign and borderline cases exhibited negative results 100% (p= 0.04).

Mucinous cystadenomas usually occur as a large, multiloculated cystic mass filed with mucus-containing fluid. The mean size at presentation was 8 cm as showing by our study, but the invasive one was extremely larger. The large size can itself sometimes suggest a mucinous histology. Specimen integrity was divided into capsule intact (60%), capsule ruptured (35%) and fragmented (5%). The diagnosis of ovarian cancer depends on clinical features, ultrasound imaging and serum biomarker cancer antigen 125 (CA125) [12]. CA-125 is tumor marker or biomarker that may be elevated in the blood of some patients with specific types of cancers, or other conditions that are benign including endometriosis, fibroids, hemorrhagic ovarian cysts, acute pelvic inflammatory disease, menstruation and first trimester pregnancy. Carcinoembryonic antigen (CEA) is the most useful serum tumor marker to identify MOC preoperatively and to follow the progress of a patient with MOC postoperatively [13]. We found that about 70% of cases showed elevation of CEA marker and about 95% of them showing elevation of Ca125 (p=0.045). Although these markers are not specific but may be used in women with risk factor as screening method to detect mucinous ovarian tumor in early stage. In this study, the management and the survival rate of all patients were not recorded so can't be mentioned in our study.

CONCLUSIONS

Our study results can be used as detection method of possible new ovarian cancer cases in an early stage and would provide a

quick non-invasive screening method for women with strong risk factors such as old age, smoking, family history, history of other tumors and obesity. In our country, the lack of reliable screening modalities has restricted the opportunities for early diagnosis and cancer detection, leading to a significant proportion of women worldwide presenting at an advanced stage of the disease. Due to this late presentation, available treatments are ineffective, and the majority of patients relapse following treatment-induced regression. Until recently, all epithelial ovarian cancers have been eligible for the same clinical trials, and treatment recommendations have been generalized to specific subtypes. Although the clinical decision making and prognostic information have been applied in a similar fashion to all subtypes, there is a difference in clinical behavior, outcomes and survival rate between MOC and other more common histologic subtypes. Patients with advanced mucinous ovarian cancer have a worse response to chemotherapy compared with patient with other histologic subtypes of epithelial ovarian cancer which their survival rate is also better than MOC [3].

CONFLICT OF INTRESTS

The authors report no conflicts of interest in this manuscript

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