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Original Article

Age-stratified analysis of tumor markers and tumor characteristics in adolescents and young women with mature cystic teratoma

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Abstract

Background: Serum tumor markers are widely used for the preoperative evaluation of an adnexal mass. Elevations of cancer antigen (CA) 125 and CA 19-9 have been reported in patients with mature cystic teratoma (MCT). The aim of the study is to investigate the relation of serum tumor markers with tumor characteristics in young women with MCT.
Methods: We conducted a retrospective review of 157 patients under the age of 35 who underwent laparoscopic surgery for ovarian MCT. Patients were divided into two age groups: Group I (n = 80): adolescents/young adults (aged 13−25 years) and Group II (n = 77): women aged 26−35 years. Data were analyzed for serum tumor markers, tumor size, and bilaterality.
Results: The rates of elevated CA 125 and CA 19-9 were 10.7% and 31.5%, respectively, for Group I, and 13.9% and 26.5%, respectively, for Group II. The bilaterality rate was higher in Group II compared to Group I (19.5% vs. 8.8%, respectively, $p = 0.04$). Serum CA 125 and CA 19-9 elevations were not related to tumor size in Group I. In Group II, elevated levels of CA 125 were also unrelated to tumor size. However, significant elevation in CA 19-9 levels was observed when tumor size was larger than 4 cm in this age group ($p = 0.004$). Elevated CA 125 and CA 19-9 levels were not significantly associated with the presence of bilateral MCT in either group.
Conclusion: The results of our study indicate that elevations of CA 19-9 are associated with larger tumor size in women aged 26−35 years, but not in adolescents/young adults. However, elevated serum CA 125 levels are not related to tumor size in either age group.
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Keywords: Adolescents; Mature cystic teratoma; Tumor marker; Tumor size; Young women

1. Introduction

Mature cystic teratomas (MCTs) are the most common germ cell neoplasms and account for 25%−40% of all primary ovarian tumors.[1] Although they can be seen at any age, more than 80% of MCTs are diagnosed during reproductive years.[2] Ovarian MCTs contain well differentiated ectodermal, mesodermal, and endodermal layers of germ cells. Malignant transformation in a teratoma has been reported to occur in 1−3% of cases, especially in postmenopausal women.[3] These tumors are bilateral in 10−15% of patients.[4]

Ovarian MCTs are often an incidental finding during routine pelvic examination or imaging procedures. About 20% of patients experience complications such as torsion, rupture and infection.[4] Ultrasonography is the main diagnostic tool and ultrasound features are usually pathognomonic for MCTs.[5] Additionally, serum tumor markers including cancer antigen (CA) 125 and CA 19-9 can provide additional information for the diagnosis of MCTs which is very important for surgical planning.[6−8] Since the peak incidence is reported in young women, the surgical treatment of MCTs usually focuses on preserving ovarian tissue and future fertility.[9] Laparoscopic surgery has become a widely preferred procedure in the

Conflicts of interest: The authors declare that they have no conflicts of interest related to the subject matter or materials discussed in this article.

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management of MCT, especially in young women. It is a safe and effective treatment modality and provides many benefits over open surgery, including reduced risk of pelvic adhesions and operative morbidity.[10,11]

In the literature, several studies focused on the relationship between serum tumor markers and tumor characteristics in MCT.[6,8,12−16] The majority of these studies included all age groups with ovarian teratoma. However, it has been suggested that younger women with ovarian MCT may show different clinical presentations and tumor sizes when compared with older patients.[17] Furthermore, tumor markers are most often measured in older women, due to the concern of malignancy, and there is scarce data about tumor markers in young patients with MCT. The aim of this study was to investigate the levels of serum tumor markers and tumor characteristics in young age groups who underwent laparoscopic surgery because of ovarian MCT. We further analyzed the association of the tumor markers with tumor size and bilaterality.

2. Methods

This retrospective chart review study included all patients aged 35 years or younger who underwent laparoscopic surgery for MCT at the Reproductive Endocrinology Unit of Zekai Tahir Burak Women's Health Education and Research Hospital, between January 2012 and June 2016. Data were obtained from hospital records after exclusion of the following conditions: 1) pregnancy, 2) concomitant pelvic pathology such as myoma or endometriosis, 3) malignant transformation of teratoma or other types of malignant ovarian lesions, and 4) severe hepatic or renal diseases. The study was approved by the institutional review board of the hospital. This study was conducted in accordance with the principles outlined in the Declaration of Helsinki.

All patients underwent preoperative pelvic ultrasonography for assessment of ovarian pathology. When sonographic findings were indeterminate, computed tomography or magnetic resonance imaging was also performed. Blood samples were taken for the determination of preoperative serum levels of CA 125, CA 19-9, alpha-fetoprotein (AFP), and carcinoembryogenic antigen (CEA) in the early stage of the follicular phase. Women with gastrointestinal symptoms and elevated CA 19-9 levels were referred to a gastroenterologist. Serum levels of CA 125, CA 19-9, AFP and, CEA were measured with the Accesss 2 Immunoassay system (Beckman Coulter Ireland, Inc. Mervue, Galway). The cut-off value for both CA 125 and CA 19-9 was 35 IU/mL. The upper normal limits for AFP and CEA were 9 ng/mL and 3 ng/mL, respectively. The intra-assay coefficients of variation for CA 125 and CA 19-9 were 1.7% and 6.4%, respectively. The inter-assay coefficient of variation was 6.0% for CA 125 and 5.7% for CA 19-9.

All operations were performed by two expert laparoscopists. Maximum tumor diameter was used for quantification of tumor size and was determined by review of the preoperative imaging studies and operative records. For cases with bilateral ovarian MCT, tumor size was calculated as the sum of the maximum diameters of left and right tumors. All patients underwent laparoscopic surgery and cystectomy was performed. Postoperatively, histopathological examination was performed by experienced pathologists and the diagnosis of MCT was confirmed. For analytical purposes, the study population was divided into two age groups. Group I consisted of adolescents/young adults (aged 13−25 years), which is consistent with the World Health Organization's definition of young people,[18] and Group II included women aged 26−35 years. The clinical characteristics including patient age, preoperative measurements of CA 125 and CA 19-9, tumor size, and bilaterality were recorded.

A sample size calculation was done according to previously published data.[12] We estimated that a total sample size of 140 patients would be required to show a 15% increase in mean tumor size in patients with elevated CA 19-9 levels (alpha of 5% and power of 90%) by using the open-source software R, version 3.0.1. Statistical analysis was performed using SPSS for Windows (version 11.5, Chicago, IL, USA). Continuous data were presented as mean ± standard deviation (SD) or median with range, and were analyzed by Mann−Whitney *U* test. Categorical data were expressed as number and percentage and were compared by Pearson's chi-square or Fisher's exact test when applicable. Pearson's correlation was used to evaluate the relationship between CA 19-9 levels and tumor size. A p-value < 0.05 was considered statistically significant.

3. Results

During the study period, medical records of 172 patients 35 years of age or younger who underwent laparoscopic surgery for a presumed ovarian MCT were reviewed. Of these, 8 had additional pelvic pathology (myoma or endometriosis). In 5 patients, diagnosis of dermoid cyst was not confirmed on histopathological examination and 2 had malignancy on the final pathology report. Therefore, these 15 patients were excluded and a total of 157 patients were enrolled in the study: 80 patients were in Group I and 77 were in Group II. The mean age of all patients was 25.6 ± 5.6 (range, 13−35) years and the mean tumor size was 6.6 ± 2.8 (range, 2−16) cm. The bilaterality rate was 14% (22/157). The serum levels of CA 125 were examined in 147 patients, CA 19-9 in 141 patients, AFP in 126 patients, and CEA in 127 patients. Since only a small number of patients had elevated serum levels of AFP and CEA (n = 3, 2.4% and n = 4, 3.1%, respectively), we analyzed the association of the serum levels of CA 125 and CA 19-9 with tumor size and bilaterality. There were 8 patients (10.7%) with elevated CA 125 levels in Group I and 10 (13.9%) in Group II. Elevation of CA 19-9 levels was detected in 23 patients (31.5%) in Group I and 18 (26.5%) in Group II. No statistically significant differences were found between the groups with regard to mean tumor size, serum CA 125 and CA 19-9 levels, and the rate of elevated tumor markers. However, the bilaterality rate was higher in Group II compared to Group I (19.5% vs. 8.8%, respectively, $p = 0.04$). The clinical characteristics of the groups are represented in Table 1.

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