Original Study

Evaluation and Treatment Results of Ovarian Cysts in Childhood and Adolescence: A Multicenter, Retrospective Study of 100 Patients

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A B S T R A C T

Study Objective: To investigate the characteristics of children with ovarian cysts and evaluate treatment strategies.
Design: Retrospective study.
Setting: Eight pediatric endocrinology clinics, Turkey.
Participants: A total of 100 children and adolescents with ovarian cysts.
Interventions: Patient data collected via retrospective chart review. Patients were stratified according to age into 4 groups (newborns, 1-12 months, 1-8 years, and 8-18 years).
Main Outcome Measures: Special emphasis was given to torsion and tumor cases, concomitant diseases, treatment modalities, and problems during follow-up.
Results: Most newborns and infants were asymptomatic with the cysts being discovered incidentally; in girls ages 1-8, symptoms were common, including breast budding (47.1%, 16 of 34) and vaginal bleeding (29.4%, 10 of 34). Girls older than 8 years mostly presented with abdominal pain (31.6%, 12 of 38) and menstrual irregularity (21.1%, 8 of 38). Most of our patients were diagnosed with a simple ovarian cyst, but 9 patients were found to have ovarian tumors. Ovarian torsion was detected in 7 patients; 5 with large and 2 with small cysts ($<$20 mm). Two patients had central precocious puberty (CPP) at presentation and 5 patients developed CPP during follow-up. The surgical intervention rate was high (38%, 38 of 100), but was associated with earlier treatment year, and this association remained significant after adjusting for confounders (P = .035).
Conclusion: Most girls have simple cysts, which have a favorable prognosis without intervention; however, there might be coexisting pathologies or complications such as tumors, torsion, and CPP; hence these patients should be evaluated accordingly and treated with a multidisciplinary approach.
Key Words: Ovarian cyst, Ovarian tumor, Ovarian torsion, Precocious puberty, Aromatase inhibitors

Introduction

Adnexal masses are uncommon during childhood, but their recognition is increasing perhaps as a result of the increasing availability of advanced diagnostic technologies. Finding a mass in a child always raises concern for malignancy, but the most adnexal masses in children are thought to be benign ovarian cysts.[1] Up to 98% of female newborns have small ovarian cysts on ultrasonography (USG), but the prevalence of clinically significant ovarian cysts in this age group is approximately 1 in 2500 live births. In contrast, ovarian cysts are identified in 2%-3% of girls aged younger than 8 years of age when USG is performed for other reasons.[2] Benign and malignant tumors of the ovary, tubo-ovarian abscess (TOA), genitourinary anomalies, and ectopic pregnancy are other diagnoses to be excluded.[1] Ovarian neoplasms are very rare in children but should be considered in the differential diagnosis especially with complex cysts. Germ-cell tumors are the most common ovarian neoplasm in childhood and adolescence with mature cystic teratomas accounting for 55%-70% of cases.[3] These tumors embrace tissues from at least 2 germ layers and can form skin derivatives, teeth, hair, cartilage,

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neural elements, fat, and bone. Juvenile granulosa cell tumors (JGCTs) are malignant stromal tumors that present in childhood, adolescence, and young adulthood with symptoms (such as breast budding, vaginal bleeding, and menstrual irregularity) due to estradiol (E2) production.[3] The diagnosis of McCune-Albright syndrome (MAS) should be considered if there is evidence for peripheral precocious puberty (PPP), polyostotic fibrous dysplasia, and café au lait pigmentation.[4] This disorder, with highly variable clinical features, is caused by the postzygotic activating mutation of the *GNAS1* gene, which encodes the α-subunit of the stimulatory G protein.[5] This mutation leads to ligand-independent activation of cyclic adenosine monophosphate signaling.[6] PPP is the most common endocrinological manifestation of MAS in girls, and is caused by estrogen-producing functional ovarian cysts (FOC).[7]

Previous studies in children with ovarian cyst were predominantly from surgery clinics. Most studies have focused on surgical indications and techniques, and lack long-term clinical follow-up. In this article, we report on a retrospective comprehensive evaluation of 100 children with ovarian cysts. We gave special emphasis to torsion and tumor cases, concomitant diseases, treatment modalities, and problems during follow-up.

Materials and Methods

This was a multicenter retrospective study of 100 girls with ovarian cysts who received medical care at 8 pediatric endocrinology clinics in the Marmara Region of Turkey between June 1994 and October 2013. Data were derived from the paper patient charts using a structured review of medical records in which patient's age, symptoms at presentation, serum gonadotropin and E2 levels, size and ultrasonographic features of the cyst, treatment modalities, final diagnosis, follow-up time, and problems during follow up-were recorded. Participating centers were asked to review medical records of all patients diagnosed with ovarian cyst. A total of 105 study forms were completed and sent to the principal investigator (N.S.). Four patients were excluded because they had cysts less than 10 mm and 1 patient, with dysgerminoma in 1 gonad and gonadoblastoma in the other, because of her 46,XY karyotype. Patients with ovarian tumors were included, if their initial diagnosis was ovarian cyst.

The study population was stratified into 4 groups on the basis of patient age: group 1 included antenatal and newborn patients, group 2 included patients age 1-12 months (infants), group 3 included patients age 1-8 years (prepubertal ages), and group 4, patients age 8-18 years. The cysts were classified according to size and ultrasonographic features. Cysts with a diameter between 10 and 20 mm were defined as small cysts, between 20 and 40 mm as medium-sized, and greater than 40 mm were defined as large cysts. Anechoic, homogeneous, thin-walled, unilocular and unilaterally located cysts were defined as simple. Complex cysts were defined as those with thick walls with a solid structure and septa, and containing blood clot and debris.[8]

Treatment modalities were investigated by using a cutoff date (before/after 2010). Our rationales for this cutoff date were: (1) almost all studies of pediatric ovarian cysts have been published after 2005 (approximately 80% in PubMed), and increased awareness of ovarian-sparing procedures for children and adolescents; and (2) balanced distribution of our study group before and after this time point (47 vs 53 patients).

Statistical analysis was done with SPSS 15.0 software (SPSS Inc, Chicago, IL). Univariate analysis was performed using the Mann-Whitney *U* and Kruskal-Wallis tests for comparison of continuous variables and the χ^2 test for comparison of percentages. Linear regression was done to evaluate the association between treatment year (before/after 2010) and application of ovarian-sparing procedures. A multiple linear regression model was built to adjust for differences in baseline characteristics. Data are presented as the mean ± SD of the mean and a *P* value of less than .05 is considered significant.

The Istanbul University review board approved the study.

Results

The mean age at diagnosis was 6.9 ± 5.7 years (range, 0-17.9 years). Eighteen patients were diagnosed during the antenatal or newborn period (group 1), 10 in infancy (group 2), 34 at ages 1-8 years (group 3), and 38 patients were identified after the age of 8 years (group 4).

The symptoms at presentation were significantly different among the 4 groups ($P < .001$; Table 1). Most newborns and infants were asymptomatic with the cysts being discovered incidentally, in girls ages 1-8 years, the most common symptoms were breast budding (47.1%, 16 of 34) and vaginal bleeding (29.4%, 10 of 34). Patients older than 8 years most often presented with abdominal pain (31.6%, 12 of 38) or menstrual irregularity (21.1%, 8 of 38).

There was a significant difference between the maximum cyst diameters among patients in the 4 groups ($P = .003$; Table 2), but when cysts were viewed as simple or complex using USG, there was no significant difference among the age groups ($P = .72$; Table 2). Mean luteinizing hormone (LH) and follicle-stimulating hormone (FSH) levels were significantly higher in group 4 ($P < .001$ and $P < .001$, respectively), whereas mean E2 levels were highest in group 3 ($P = .025$; Table 1).

Ovarian Torsion

Ovarian torsion was detected in 7 patients (7%); 4 in group 3 and 3 in group 4. There were no reported cases of torsion in groups 1 or 2 (Table 1). All of the patients with torsion presented with abdominal pain. Most of the cysts in patients with torsion were classified as large (71.4%, 5 of 7), but there were 2 patients with small cysts, and no significant difference was found between the cyst diameters of the children with or without torsion (49.4 ± 24.2 mm vs 40.8 ± 24.8 mm, respectively, $P = .28$). Age at diagnosis, gonadotropin, and E2 levels as well as ultrasonographic features of the cysts were not different