

A 15-year report of pathological and benign ovarian tumors in teenagers

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Summary

The purpose of this retrospective study was to determine the frequency, clinical aspects and surgical management of ovarian masses in 52 adolescent patients, in whom surgery was deemed necessary, from 1991-2006. We considered age, symptoms, ultrasound investigations, CA 125 levels, family history, operative treatment, surgical complications tumor size, histopathological examinations, pregnancy rate and follow-up. Ovarian lesions in teenagers include a broad array of pathologic diagnoses that have variable and non-specific presenting symptoms. The most common presenting complaint was abdominal pain in 34 (65.4%). Forty-seven patients (90.4%) had benign lesions, two (3.8%) had borderline tumors and three patients had malignant lesions (5.8%). Most of the patients who wanted to conceive subsequently did so. For benign ovarian disorders the operation should be designed to optimize future fertility while in patients with malignancy, complete staging and resection of the lesion should be the first concern.

Key words: Adolescence; Ovarian tumours; Borderline ovarian tumours; Ovarian carcinoma; Surgical treatment.

Introduction

The presence of ovarian tumors in adolescence is of great significance because of the possibility of malignancy and the probable long-term effect on reproduction. Ovarian neoplasms constitute 1-2% of all childhood and adolescent malignancies, and represent the most common gynecological tumor (60-70%) during this period of a woman's life [1, 2]. Ovarian masses span a spectrum of pathology from benign to highly aggressive malignant neoplasms [3]. Non-neoplastic conditions include follicular cysts, corpus luteal cysts, and endometriomas. Neoplastic processes include both benign tumors such as mature cystic teratomas as well as highly malignant tumors. In addition, there are tumors of low malignant potential that frequently follow a benign clinical course [4]. Benign neoplasms and functional cysts are the most common ovarian masses during childhood and adolescence [5]. Surgical intervention may be required depending on the diagnostic evaluation and possible trial of treatment that has failed. Certain conditions require immediate intervention such as possible torsion, medically refractory tub ovarian abscess, and intraabdominal hemorrhage with hemodynamic instability [6]. These problems may, to various degrees, effect the reproductive potential of these women [7-9]. In this report we analyzed cases from a Greek population for preoperative and intraoperative tumor evaluation, operative treatment, staging, follow-up and pregnancy rate.

Material and Method

This is a retrospective study of 52 adolescent girls with a diagnosed ovarian mass between 1/1/1991-31/12/2006. They were referred and evaluated at the Department of Obstetrics & Gynecology and Department of Pediatrics (2 cases) of Democritus University Alexandroupolis in Greece.

The following data were analyzed: age, age of menarche, present symptoms and signs (including the presence of fever and rebound abdominal tenderness or peritonitis, abdominal distension and menstrual disorders), preoperative diagnostic workup, operative procedure, histology of tumor, and postoperative follow-up including pregnancy rate. The following laboratory evaluations were analyzed: white blood count, the levels of beta human chorionic gonadotropin (β -hCG), carcino embryonic antigen (CEA), CA-125 and alpha-fetoprotein (α FP), and the results of further endocrinologic workup, where appropriate. We reviewed all radiology reports including the results of abdominal X-rays, ultrasound (US) scans, computed tomography (CT), nuclear magnetic resonance (NMR) scans, all operative reports, and recorded the size of all ovarian masses as documented at surgery or in the pathology record. US was used to define the size of the lesion and to characterize its gross morphologic condition as solid, simple cyst or complex cyst. A transvaginal sonographic examination, accompanied if necessary by transabdominal examination, was performed on all patients using an (GE-LOGIC™ 400) US machine with color and power Doppler capability, equipped with a 2.5-5.5-MHz convex transabdominal transducer and a 5.5-8.5-MHz transvaginal probe. Size and echostructure of the uterus, endometrial thickness and any irregular findings and intraperitoneal free fluid (pouch of Douglas or ascites) were recorded.

The morphology of each adnexal mass was described according to the following different types of sonographic morphological tumor characteristics:

1) Unilocular cyst: smooth-walled unilocular cyst with clear fluid or dense (echogenic) fluid content.

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2) Cyst with septa: smooth-walled cyst with clear fluid or dense (echogenic) fluid content and only septa inside the cyst.

3) Cyst with papillae: cyst with clear fluid or dense (echogenic) fluid content and papillae.

4) Tumors with fluid/solid content: cyst with clear fluid or dense (echogenic) fluid and solid content.

5) Pure solid tumors: tumors composed of only solid tissue.

The main indication for surgery was the presence of the ovarian mass. The diagnoses of the presence of an ovarian mass were the follows: acute abdominal pain and recurrent abdominal pain despite conservative treatment, abdominal distension and menstrual bleeding. The operative procedure differed based on the size, type of lesion (cystic, solid or mixed) as well as the age of the young woman.

Laparoscopy was performed in 15 cases, while laparotomy was carried out in 37 cases. All the adnexal masses which were suspicious of malignancy at the time of laparoscopy were evaluated by frozen section evaluation intraoperatively. In those cases in which malignancy was suspected laparotomy was performed and the final histological diagnosis was provided postoperatively.

Results

The characteristics of the 52 subjects are presented in Table 1. The majority of operated women 39 (75.5%) were under 17 years of age. The mean age was 16.64 ± 5 SD years (range min 14 - max 19 years). We identified 47 postmenarchal subjects and five premenarchal. The most common presenting complaint was abdominal pain which was present in 34 (65.4%); in 11 of these the suspected diagnosis was appendicitis but a pelvic mass was diagnosed instead. The other presenting symptoms were abdominal distention in ten (19.2%) and menstrual disorders in eight (15.4%) cases, respectively (Table 2). On physical examination ten (19.2%) had abdominal tenderness, 37 (71.2%) had a palpable mass or increased abdominal girth. In another five (9.6%) cases there were no findings on physical examination but the ovarian masses were detected through US. Forty-nine (94.2%) of all operations were non emergency procedures, while three (5.8%) were done as emergency cases. These three patients presented with lower acute and persistent abdominal pain. In two cases the diagnosis was adnexal torsion of paraovarian cyst while in the third case the cause was a ruptured lutein cyst with intrabdominal

Table 1. — Patient characteristics and symptoms.

Age	16.6 ± 5 SD, range min 14 – max 19 years	
Postmenarchal	47	90.4%
Premenarchal	5	9.6%
Non emergency - symptomatic	49	94.2%
Emergency - symptomatic	3	5.8%

Table 2. — Signs and symptoms leading to diagnosis of ovarian mass.

Abdominal pain	34	65.4%
Abdominal distention	10	19.2%
Menstrual disorders	8	15.4%

Table 3. — Preoperative transvaginal (TV) - or transabdominal (TA) ultrasound, CT, MRI.

Ovarian cysts	US	CT	MRI	Mean tumor size cm
Simple	16	–	–	4.8 (min 3.8 - max 8.3)
Complex	27	2	1	5.3 (min 4.6 - max 9.8)
Solid	9	3	3	5.1 (min 3.5 - max 7.5)
Total	52	5	4	

Table 4. — Correlation between CA-125 levels and histological findings.

β hCG > 5 U/ml		AFP > 0.7 U/ml		CEA > 2.5 U/ml		CA-125 > 35 U/ml	
1/1	100%	1/1	100%	1/1	100%	Ovarian cancer	1/1 100%
0/7	0%	0/7	0%	0/7	0%	Endometrioid cysts	2/7 28.57%
2/17	11.76%	2/17	11.76%	2/17	11.76%	Germ cell tumor	4/17 23.52%
0/6	0%	0/6	0%	0/6	0%	Epithelial cysts	1/6 16.67%
0/12	0%	0/12	0%	0/12	0%	Functional cysts	0/12 0%
0/3	0%	0/3	0%	0/3	0%	Paraovarian cysts	0/3 0%
0/2	0%	0/2	0%	0/2	0%	BOT	0/2 0%
0/1	0%	0/1	0%	0/1	0%	Granulosa-cell tumor	0/1 0%
Total	3/49	Total	3/49	Total	3/49	Total	8/49

bleeding. All the non emergency cases (49) underwent complete preoperative diagnostic work-up, while in the three emergency cases only sonography with Doppler assessment of the ovarian pathology and laboratory examination were performed. Forty patients underwent transvaginal and 12 transabdominal examination because they were virgins. The US findings of the 52 subjects are presented in Table 3. To further evaluate the source of the pelvic mass an abdominal CT scan was performed in five cases (11.5%) and a MRI scan in four cases (7.7%). Serum tumor markers and hormonal status evaluation was performed only in the non emergency cases. CA-125 was normal (< 35 mIU/ml) in 41 patients and elevated in eight patients 15.3%. The preoperative average CA-125 level was 45.1 ± 5.19 mIU/ml. Serum CA-125 levels were elevated in one case of extraovarian ovarian cancer, in two cases of dysgerminoma, two cases of teratoma, one case of mucinous cystadenoma and in two cases of endometrioid cysts (Table 4). The levels of other tumor markers – human chorionic gonadotropin, a-fetoprotein and carcinoembryonic antigen – were normal in all cases, except the two patients with dysgerminoma and the patient with extraovarian ovarian cancer.

Three patients (emergency cases) were operated on for adnexal torsion and the remaining 49 (non emergency cases) had ovarian masses with various conditions. Two of the patients had bilateral lesions (3.8%). The associated cysts were of a functional nature in both cases. From the 52 patients, 15 (28.8%) (Group A = 15) underwent the laparoscopic approach while in 37 patients (71.2%) (Group B = 37) exploratory laparotomy was done. Surgical duration ranged from 30-100 min. The most common laparoscopic procedure was cystectomy in ten patients, aspiration and electrocoagulation of ovarian cysts in four and salpingo-oophorectomy in one. During laparotomy salpingo-oophorectomy was performed in five patients and cystectomy in 32 patients. Histological findings in

Table 5. — Correlation between surgical treatment and histological findings.

Histological findings	Laparoscopy	Laparotomy	Laparotomy after laparoscopy
Functional cysts	12	—	
Granulosa-cell tumor	1	—	
Paraovarian cysts	2	4	
Borderline tumor	—	2	2
Endometrioid cysts	—	7	3
Ovarial cancer	—	1	1
Dermoid cysts	—	10	3
Teratoma	—	5	
Dysgerminoma	—	2	
Epithelial cysts	—	6	
Total = 52	15	37	9

Table 6. — Ovarian cysts, histological findings and age-distribution.

	Histological findings - Age distribution		
1 Germ cell tumors	17	32.69%	16.7 (min 15 - max 19) years
A. Dermoid cysts	10 (19.23%)		
B. Teratoma	5 (9.6%)		
C. Dysgerminoma	2 (3.84%)		
2 Functional cysts	2	23.08%	16 (min 15 - max 17) years
A. Serous cysts	7 (13.47%)		
B. Bleeding cysts	5 (9.6%)		
3 Endometrioid cysts	7	13.47%	16.8 (min 14 - max 19) years
4 Epithelial cysts	12 (3.84%)	6	11.54%
A. Serous cystadenoma	4 (7.69%)		
B. Mucinous cystadenoma	2 (3.84%)		
5 Paraovarian cysts	6	11.54%	16.3 (min 14 - max 18) years
6 Borderline tumor	2	3.84%	18 (min 17 - max 19) years
7 Granulosa-cell tumor	1	1.92%	17 years
8 Ovarian cancer	1	1.92%	19 years

correlation with surgical management are shown in Table 5. In nine patients of Group B after initial diagnostic laparoscopy, the procedure was converted to laparotomy in three patients with Stage 4 endometriosis and extensive bowel adhesions, in three patients with large-volume dermoids, and in three patients with suspicious ovarian and peritoneal implants. Tumorectomy with salpingo-oophorectomy was performed in five cases with suspicious results on frozen section (two borderline tumors, BOT, two dysgerminomas and one granulosa cell tumor) and in one more case of extraovarian carcinoma on frozen section. Excision of the ovarian cyst was performed in 42 patients, while cyst aspiration only was done in four cases. After removal of the ovarian masses and satisfactory hemostasis in 36 cases the ovarian bed was not sutured. In six cases the wound in the ovary was closed with repair sutures, initially using PDS (polydioxanone) 4/0, and later with either PDS 2/0 or 4/0. A histologic diagnosis was obtained in every patient. Forty-seven patients (90.38%) had benign lesions, two had borderline tumors (3.85%) and three patients (two dysgerminoma and one ovarian cancer) had malignant lesions (5.77%). The two BOTs consisted of two epithelial tumors. Histological findings in correlation with age distribution of the ovarian tumors are shown in Table 6. Of the 52 study

Cysts and histological findings

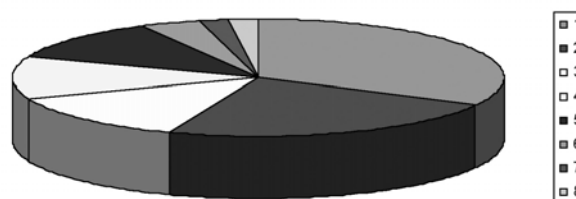


Figure 1. — Ovarian cysts and histological findings.

patients, 13.47% (7) had endometrioid cysts, 13.47% (7) had serous cysts, 9.6% (5) had bleeding cysts, 19.23% (10) had dermoid cysts, 9.6% (5) had teratomas, 11.53% (6) had para ovarian cysts, 3.84% (2) had mucinous cystadenomas, 7.69% (4) had serous cystadenomas, 1.92% (1) had a granulosa cell tumor, 3.84% (2) had borderline ovarian serous cystadenomas, 3.84% (2) had dysgerminomas and 1.92% (1) had invasive carcinoma. The most common ovarian masses detected were germ cell tumors (32.69%) and functional cysts (23.08%) (Figure 1).

In the six histologically suspicious cases the final histological examination confirmed two borderline epithelial ovarian tumors, two dysgerminomas in Stage IA, one granulosa sertolli cell tumor, and only one metastasis to the ovary, a Stage IVb carcinoma. The ovarian carcinoma was a mixed tumor in which only partial tumor excision was performed whereas in the other five cases salpingo-oophorectomy and, if needed, extirpation of peritoneal implants was the treatment of choice. The patient with an extraovarian primary tumor had a low symptomatic ovarian mass in the left ovary which was discovered with bimanual abdominal examination one week before the operation. During the surgery she was found to have extensive intraabdominal metastases from an occult primary extraovarian tumor with histological characteristics of primary ovarian cancer. This lesion was composed of epithelioid cells containing clear or focally granular pale cytoplasm with slightly enlarged hyper chromatic nucleoli. Tumor infiltrating lymphocytes, mitoses or endothelial-lined space invasion, increased proliferative activity and tumor necrosis were also identified. Immunohistochemically, tumor cells stained positively for monoclonal antibodies EMA (epithelial membrane antigen), pankeratins, CEA and negative for CLA (common leukocyte antigen), myosin, vimentin, desmin, actin, cytokeratins 8-18-19, NSE, and S-100 protein. No additional treatment was recommended in this patient because she had generalized metastases.

Concerning the two presenting dysgerminomas, Stage IA ovarian tumors, one of them lacked extensive infiltrative invasion but the other one was associated with unexpectedly aggressive behavior. In the latter case postoperative radiation was administered. This patient received six rounds of first-line adjuvant chemotherapy with platinex. During a four-year follow-up and postsurgically, the patient who initially had Stage 1A dysgerminoma disease developed recurrent tumor.

Table 7. — Correlation between ultrasound and histopathological findings of ovarian cysts.

Histopathological findings	Ultrasound findings		
	Simple	Complex	Solid
Germ cell tumor		12	5
Functional cysts	9	3	
Endometrioid cysts	1	4	2
Epithelial cysts	1	4	1
Paraovarian cysts	3	3	
Borderline tumor	2		
Sex-cord stromal tumor			1
Cancer		1	
Total	16	27	9

In the rare case of a 16-year-old girl with a granulosa cell tumor, the preoperative US finding was a solid, predominantly cystic, hypoechoic tumor and the CA-125 level measured normal. Tumor size was Stage I at presentation and was 5.0 cm or less in mean size. No symptoms of premature pubarche, thelarche, menarche, or hirsutism were observed. Hormonal laboratory (FSH, LH, estradiol, progesterone) analysis revealed values in normal levels.

A mature cystic teratoma or dermoid cyst, seen in 15 patients, was the commonest benign neoplasm, and 74.6% of these girls were under 17 years old. Three girls had malignant ovarian neoplasms, two of which were germ cell in origin. Malignant neoplastic ovarian lesions were commonly greater than 5 cm in diameter. The greatest tumor diameter (about 10 cm) appeared in epitheloid cysts. Lesions < 5 cm in postpubertal girls were significantly more likely to be non-neoplastic, functional cysts. Endocrine manifestations include early or precocious puberty and virilization, which were not encountered in our patients.

There was a great diversity of US patterns and histological results, especially for borderline tumors and one case of endometrioid cyst (Table 7). An interesting case was found in the endometrioid cyst group; a 14-year-old girl with normal menstruation, normal development of secondary sexual characteristics and chronic pelvic pain. The karyotype was normal (46XX) and her urinary system was normal as well. Laparoscopy revealed a double uterus with a rudimentary left horn, normal left ovary, and a cystic mass in the right ovary, but the left fallopian tube was distended and filled with chocolate-like fluid. The cystic mass, rudimentary left uterine horn and left fallopian tube were immediately excised.

Two postoperative complications were noted. The first was bleeding in the place of the trocar installation, in one graft on the trocar site after laparoscopic extraction of one endometrioid-type tumor, and the second one was fever postoperatively after dermoid cyst enucleation per laparotomy. Important clinical information concerning complications were not reported. The overall complication rate of surgically managed adnexal masses was very low. Fifty patients are under our follow-up and are in remission, alive with no evidence of disease after a mean follow-up of 36 months. Only two patients died; the first

one had extraovarian cancer and died three weeks postoperatively due to rapid progression of the disease, and the second one with dysgerminoma died in the fourth year of the treatment as a result of liver metastases related to the ovarian pathology. Forty-four patients tried to conceive during a period of four to 36 months after surgery. Our overall intrauterine pregnancy rate was 72.7% (32/44) in women aged from 17 to 21 years; of these, one 20-year-old patient had an ectopic pregnancy (2%; 1/32). All of these intrauterine pregnancies (31) went to term and no fetal abnormalities or other problems were reported.

Discussion

One of the major problems in adolescent gynecology is the presence of an ovarian tumor [10]. Although tumors in this age group are less frequently observed than in adult women, they require immediate and careful investigation. The causes of ovarian enlargement in adolescence include functional cysts, paraovarian cysts, benign neoplasms, ovarian torsion and malignant neoplasms. The vast majority of ovarian masses which occur in children and adolescents have no malignant characteristics [11-13]. Physiological or functional ovarian cysts are the most common ovarian lesions seen in the pediatric age group and malignant neoplasms are rare [14, 15]. Ovarian teratomas (OTs) may be of mature or immature morphologies. Mature cystic teratomas (MCTs), often referred to as dermoid cysts, are the most common germ cell tumors of the ovary in women of reproductive age [16]. Ovarian cancer on the other hand, although rare in this age group, is the most common genital tract malignancy [17, 18]. Despite their rarity the incidence of malignant or premalignant degeneration of neoplasms is higher than in adult women [19, 20]. Ovarian malignant neoplasms in young girls and teenagers are unusual [21]. The most frequent histological subtypes found are those derived from germ cells, followed by epithelial cysts and sex-cord stromal tumors [22]. Sex-cord stromal tumors consist of epithelial (granulosa-Sertoli cells) and mesenchymal elements in a variety of combinations. Granulosa cell tumor is the most common subtype, presenting as the juvenile form in young females. It is of low malignant potential and is adequately treated only with salpingo-oophorectomy [23]. Malignant germ cell tumors account for approximately 20% of ovarian masses in children and adolescents [24]. This was also confirmed in our study. In three malignant cases histopathological assessment showed the following results: two dysgerminomas, and one extraovarian ovarian cancer which was a mixed tumor. Clinical and therapeutical particularities differentiate them from the same tumors of older women [25]. Clinical symptoms are generally not helpful in distinguishing benign from malignant masses. Ovarian masses often present with abdominal complaints that can mimic other diseases, in particular, appendicitis [26]. The most early common clinical features in our patients were abdominal pain pelvic mass and abnormal vaginal bleed-

ing. Patients with large tumors were admitted with compression symptoms or abdominal distension. In our study the appearance of acute symptoms in the non-emergent cases is usually attributed to emergency reasons such as adnexal torsion, torsion of the adnexa with paraovarian cyst and ruptured lutein cysts with ovarian bleeding. It is important in these serious conditions to begin treatment at an early stage without the risk of future decreased fertility. In 30% of the patients, there is torsion of a normal adnexa, while the majority of the cases are associated with ovarian pathology [27, 28]. In our study the torsion was associated with normal adnexa. The use of sonography, Doppler US, and abdominal CT and/or MRI scans may give important additional information to the preoperative detection of ovarian cyst pathology [29-31]. This was confirmed in our patients but it was not possible preoperatively to determine if the ovarian lesion was benign or malignant. Consideration should be given to order preoperatively ovarian tumor markers, to help with intraoperative management and pathology diagnosis [32]. Serum CEA, alpha-fetoprotein and beta-hGC are routine tests for organic tumors. The most common cause of chronic pelvic pain in adolescents is endometriosis, affecting up to 70% of girls with chronic pelvic pain unresponsive to medical management (oral contraceptives and no steroidal anti-inflammatory drugs) [33]. Endometrioid cysts occur more rarely compared to diffuse endometriosis in adolescents [34, 35]. Early diagnosis and medical management may prevent the development of the disease [36]. Intraoperatively, in five patients with endometrioid cysts diffuse pelvic endometriosis was detected and in two cases endometriomas. Paraovarian cysts can show a wide range of sonographic features. Their risk of malignancy is low if no papillary projections are detected at transvaginal sonography, but when mural proliferations are present, a borderline tumor can be found at pathological examination [37]. The characteristic laparoscopic differentiation of ovarian cysts is the crossing of vessels over them [38]. Paraovarian cysts are not always benign; two previous studies reported a malignancy rate of 2-2.6% [39, 40]. Ovarian cystic tumors are the most frequent ovarian disease in adolescence. Although the majority of ovarian masses during this period are benign, the possibility of encountering an unexpected ovarian malignancy could not be excluded. In the absence of effective systemic medical treatment, immediate surgery is recommended. During surgical treatment of ovarian tumors in young girls, consideration should be given to the preservation of future fertility [41-43]. In cases of low malignant potential, tumor is possible in that particularly cystectomy increases the risk for disease recurrence, but recurrence does not affect survival. Conservative treatment can retain the potential for spontaneous pregnancy [44]. From our results, we conclude that fertility following successful conservative treatment of adnexal cysts is very high. Cyst enucleation was the most commonly applied procedure either with laparoscopy or with laparotomy. Oophorectomy or salpingo-oophorectomy is the safest treatment only when malignancy is suspected.

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