Ovarian masses in infant-juvenile age

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ABSTRACT

Introduction. The appropraite surgical treatment to pediatric patients with ovarian lesions are heterogeneous and ovarian preservation is desirable in children. The aim of this study is to the discuss findings related to a set of patients who were operated on for ovarian lesions.

Patients and methods. A retrospective study carried out in 13 years on 56 patients under the age of 17. These patients were divided into 3 groups according to ovarian pathologic diagnosis: 25 with functional (cyts and torsion), 18 with epithelial ovarian lesions and 13 with germ cell tumours. These three groups were compared in terms of menarche, torsion, age, duration, size, pain, mass, vomiting, irregular menstruation, location and operation type.

Results. Follicle cysts, serous cyst adenomas and teratomas were the most common in these groups. The mean age of the patients was 12.18±4.84 years. The most common symptoms and signs were abdominal-pelvic pain (85.7%) and swelling(37.5%). Torsion was seen in 21 patients (37.5%), mean mass size was found to be 10.46±6.55 cm. A salpingo-oophorectomy (SO) was performed in 38 patients and cyst excision (CE) was performed in 18 patients. In premenarcheal cases, torsion was seen more in menarcheal cases and in the functional lesion group. CE was performed more often in the functional and t SO was performed often in the epithelial and germ cells groups.

Conclusion. Torsion and functional ovarian pathologies are thought to be common in premenstrual ages and malign lesions are very rare in all age groups so we recommend ovarian protective surgery should be preferred.

Key words: *ovarian neoplasms, benign, malignancy, surgery, child.*

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INTRODUCTION

Ovarian neoplasms are uncommon and occur in 2.6/100,000 girls per year and malignant neoplasms about 1% of all children cancers. The etiologies of ovarian enlargement in childhood include functional cysts, ovarian torsion and malignant and benign neoplasms.[1] Ovarian lesions come to hospital in a variety of ways. Patients may present with acute abdominal pain and signs of acute appendicitis' with precocious puberty, masculinization, or endocrine disturbance, a pelvic or abdominal mass and concerns of malignancy. The diagnostic study included abdominal ultrasonography(US), Doppler-US and in selected patients magnetic resonance imaging (MRI), computed tomography(CT) and tumor markers(CA-125, AFP, b-HCG). The surgeon have to choose two routes: emergencey surgey for patients with acute abdominal pain and with a mass associated complications(torsion, rupture, hemorrages) and elective surgery for endocrine disturbance, ovarian cysts and mass without abdominal pain.[2,3] Ovarian surgery in childhood can result in compromised future fertility, either from the removal of normal ovarian tissue or from adhesion formation. Therefore, preservation of ovarian tissue as well as minimization of adhesion formation should be surgical goals.[4]

This retrospective study reviews the clinical experience and outcome operative treatment of three different pathologic ovarian masses in children during the past 13-years period.

PATIENTS AND METHODS

This retrospective study was performed only operated 56 patients under 17 years old between January 2004 and December 2016 with a diagnosis of an ovarian mass in our Medical Faculty Hospital of Gazi University. We analyzed the diagnostic exams, abdominopelvic-X ray, US and MRI/CT and tumor markers for masses that were complex or solid with echogenic signs, those with huge size and endocrinologic signs such as precocious puberty. Surgeries were done in emergency or elective

surgery, conforming to clinical presentation. We considered as conservative approach a simple CE, with untwisting if adnexal torsion was associated; the radical approach, instead, consisted in the SO and, if involved, of the fallopian tube.[2,3] Ovarian cysts in fetuses are resolve but they become complicated by intracystic hemorrhage, torsion, incarceration in a hernia, or, rarely, by a mass effect and respiratory distress or hydronephrosis. In general, operation has been advocated only for those cysts that increase in size or persist for ≥4 months. Preoperative risks for malignancy that should be considered include the patient's age, the characteristics of the mass and the tumour's volume. If the surgeon is concerned that a cyst might be malignant, laparotomy should be performed to facilitate intact removal and staging procedures as indicated. Additionally, laparotomy should be considered for functional cysts larger than 8 to 10 cm. The diagnosis and the course of the surgery are usually determined by frozen section examination during the operation for the recognition of ovarian cancer. Therefore, the frozen section diagnosis of ovarian tumours is important, especially in adolescents who may be managed conservatively in order to preserve fertility.[5-9] Simple cysts are routinely observed for resolution, because most are self-limiting and disappear within 4 to 8 weeks. If the cyst causes significant pain, persists beyond 8 weeks, or enlarges with observation, however, surgical management is warranted. Cystectomy, with reservation of the remaining ovary, is the preferred operative management of a functional cyst.[7-9]

Fifty-six cases were classified as functional, epithelial and germ cell ovarian pathologies after pathologic diagnosis. The age, symptom(s) and sign(s), menarche status, mass size and localization of each patient was analysed. Differences between the informations were compared. Patients' numerical results were stated as mean ± standard deviation(SD). Anova and Chi-Square tests were used to test de differences between the groups; $p < 0.05$ was taken as statistically significant.

RESULTS

The patients' ages ranged from 4 months to 17 years (mean 12.18) (median age= 14 years) Twenty-two of these patients were premenarcheal, while 34 were menarcheal. The duration of complaints ranged from 0 to 365 (mean= 52.05) days. The most common presentation was abdominal/pelvic pain (48 cases), followed by abdominal and pelvic swelling (mass) (21 cases,37.5%), (*Table 1*). Two cases of intrauterine ovarian mass operated for their masses did not disappear or shrinking in the follow-up periods. Elective CE was performed for precocious puberty patient who was 7 years old and had a 2 cm cyst in her right ovary. There was no evidence of endocrinologic and other pathologies. Five patients experienced menstrual irregularity. Some patients had more than one complaint. The masses were mostly unilateral, cystic, or solid/cystic and ranged in size from 2 to 35 cm (mean 10.46). In addition, 2-patients experienced bilateral lesions and the remaining 54 were split equally into right and left side (*Table 1*). Urgent surgery was performed in 19-patients (33.9%) and other patients (n= 37; 66.1%) were operated electively. A SO was performed in 38-patients (only 3 oophorectomies) and CE was performed in 18 patients. Six of the CE were done laparoscopically (*Table 1*).

Patients were divided into three groups: 25 functional, 18 epithelial ovarian lesions and 13 germ cell tumours. Follicle cysts, serous cyst adenomas and teratomas were the most common in these groups, respectively. The findings and parameters of these three groups were compared. There was no difference between the three groups with regard to menarche ($p > 0.05$). However, the age at which the functional group presented with symptoms was younger than in the other groups (11.13 ± 5.35 y) ($p < 0.005$). The size of the mass was also smaller in this group (7.60 ± 3.46 cm) than it was in the other two groups ($p= 0.011$). Ovarian torsion was seen in 21(37.5%) patients. Two cases of cyst-related torsion were diagnosed in intrauterine period and followed. These cases were found to be free floating inside the abdomen due to torsion without any attachments (parasitically) and vascular pedicle without any marker elevations or alterations in size (5 and 7 cm). Torsion was highest in the functional ovarian group (n= 15, 71.4%), followed by the germ cells (n= 5, 23.8%) and epithelial groups (n= 1, 4.8%) ($p= 0.004$, $p= 0.001$, respectively). Torsion was found to be statistically significant in 13, 59.1% of the premenarcheal patients but in only 8, 23.5% of the menarcheal patients ($p= 0.007$). The mean age of the torsion cases was 10.44 years and non-torsion cases was 13.22, regardless of the group ($p= 0.036$). There was no difference between the groups in terms of pain at first visit ($p > 0.05$), whereas swelling was more

frequent in the epithelial and germ cell groups (p= 0.009) (*Table 1*). Ovarian torsion was found to be more frequent, waiting time and mass size were found to be less in premenarcheal patients (p= 0.007, p= 0.004, p= 0.048 respectively). CE was performed more often in the functional group and SO was statistically more prevalent in the other two groups (p= 0.001). In addition, in the premenarcheal group, there was less waiting time than in the menarcheal group (27.68 ± 36.03 and 67.82 ± 98.11 days) (p= 0.004). This situation can be attributed to frequent torsion in premenarcheal girls. In addition, a smaller mass size is seen in premenarcheal girls (7.90 ± 3.98 and 12.11 ± 7.36 cm) (p= 0.048). The mass size in the CE operation was 6.61 ± 2.85 cm and 12.28 ± 7.03 cm in the SO operation, which was statistically significant (p= 0.001). The size of the mass was smaller in functional lesion group than the other two groups (p= 0.011) (*Table 1*).

TABLE 1. *Characteristics of patients (n= 56)*

	Functional lesions (n= 25) 44.6%					**Epithelial tumors (n= 18) 32.1%**						**Germ cell tumors (n= 13) 23.2%**		**Total**
	Corpus luteum cyst	Hemorrgagic cyst	Follucul cyst	Paraovarian cyst	Only Torsion	Serous cystadenom	Mucinous cyst adenom	Mucinous cyst	Serous cyst	Serous	mClear cell carcinoma	Teratoma	mChoriocarcinoma	
Number	6	7	8	1	3	7	6	1	2	1	1	12	1	56
Age	11.13±5.35 Median age=13					13±4.29 Median age=14						13.07±4.48 Median age=15		12.18±4.84 Median age=14
Duration	41.68 ±90.47					49.00±86.03						76.23±52.99		52.03±81.62
Size	7.60 ±3.46$^{\Sigma}$					12.88±8.25						12.61±6.73		10.46±6.556
MRI/CT workings	10					15						11		36
Tumor markers workings	5					16						10		31
Menarche $^{€}$	12/13 48%/52%					7/11 38.9%/61.1%						3/10 23.1%/76.9%		22/34 39.3%/60.7%
Torsion$^{€}$	10/15 40%/60%$^{@}$					13/5 72.2%/27.8$^{@}$						12/1 92.3%/7.7%$^{@}$		35/21 62.5%/37.5%
Mass	21/4 84%/716%					9/9 50%/50%						5/8 38.5%/61.5%		35/21 62.5%/37.5%
Pain	6/19 24%/76%					2/16 11.1%/88.9%						0/13 0%/100%		8/48 14.3%/85.7%
Vomitting	23/2 92%/8%					17/1 94.4%/5.6%						13/0 100%/0%		53/3 94.6%/5.4%
Menstruel irregularity	23/2 92%/8%					16/2 88.9%/11.1%						12/1 92.3%/7.7%		51/5 91.1%/8.9%
Other symptom	22/3 88%-12%					17/1 94.4%-5.6%						13/0 100%-0%		52/4 92.9%-7.1%
Location	L=11(44%) R=14(56%)					L=10(55.6%) R=7(38.9%) B=1(5.6%)						L=6(46.2%) R=6(46.2%) B=1(7.7%)		L=27(48.2%) R=27(48.2%) B=2(3.6%)
Urgent surgery	12					6						1		19
Surgical type$^{\neq}$	SO=11(44%) CE=14(56%)					SO=14(77.8%) CE=4(22.2%)						SO=13(100%) CE=0 (0%)		SO=38(67.9%) CE=18(32.1%)
Urgent Surgery	5	2	1	1	3	3	2	0	1	0	0	1	0	19(33.9%)

Distrubition of 56 ovarian lesions, age (median,mean±SD,year), duration time (mean±SD, day), size (mean±SD, cm), MRI/CT working, tumor markers, workings, menarche status, torsion -/+, mass-/+, pain-/+, vomitting-/+, menstruel irregularity-/+, other symptoms-/+ (intrauterine cyst, weight gaine, precocious puberty), location (right/left/bilaterally), surgical type and urgent surgery of all group.
@,€, ∑, ≠ = p <0.05, M= malignancy.

Interestingly, in the youngest case in the literature, a 13-year-old patient diagnosed with bilateral clear-cell carcinoma underwent a bilateral SO, retroperitoneal lymph node dissection and hepatic resection at different times. Her main complaint was abdominal pain in first admission. Her preoperative CA-125 level was 5543,9 U/ml (normal=0-35). After the post surgical period detected high levels of CA 72-4 (129,7 U/ml (normal (0-4)), liver metastasis was discovered at the 18-month follow-up, and an irregular hepatectomy was done. The patient died aged 21. CA 72-4 is specific for gastrointestinal and mamarian tumors. But it elevates after metastatic and recurrent ovarian tumor.[10]Another interesting case was followed in another centre for obesity and excessive weight gain in a 16-year-old girl. Since the patient had gained 20 kg in 3 years, diet and exercise was suggested. However, because of the cystic mass discovered in her US, she was referred to our clinic. MRI revealed a giant cystic mass extending into the xiphoid process and filling the abdominal area. This pure cystic lesion did not contain septa. Tumour markers (b-HCG, AFP, CA-125) were at normal levels, 17 litres of fluid were aspirated from the left ovary and a salpingo-oophorectomy was done. Histopathologic diagnosis was a mucinous ovarian cyst.

In 13 of the germ cell tumours, only one was a choriocarcinoma, while 12 of them were teratomas. This 16-year-old patient had complained of a 4-months abdominal swelling. She applied for hospital due to increased complaints, decreased urination and weakness. Abdominal MRI and US revealed a giant cystic and solid mass with vascular elements between bladdr to inferior level of liver. Her CA-125 and b-HCG were elevated (106.4 U/ml [normal= 0-35] and 1146.9 mIU/ml, respectiveley). US guided diagnostic biopsy was performed because of advanced tumor originating from right over. Her diagnosed was choriocarcinoma and preoperative 4 cycles of BEP (bleomycin, etoposide and cisplatin) chemotherapy was given and tumor removed with SO. The patient is in remission and now she is 24 years old.

Abdominal X-rays showed the presence of bone and tooth particles in the germ cells tumours of 2 patients. In one patient, the markers and US were normal, but hairballs were found in the cyst during the laparoscopic cystectomy and conversion open surgery and left SO was done. In our series, all teratoma patients except one AFP elavation and the others tumour marker levels were normal. CA 125 and CA 72-4 levels were useful in the medication and follow-up of the clear-cell sarcoma patient.

DISCUSSION

Although ovarian malignancy is relatively rare in children and constitutes only 1% of all childhood malignancies, ovarian masses in childhood do have a 10% malignancy rate.[11] Neoplastic lesions, which may be benign or malignant, are generally categorized according to their cell of origin: epithelial, germ cell, sex cord-stromal, or metastatic.[12] Since we have only one sex cord-stromal tumour in our series, we wanted to distinguish between the 56 cases of epithelial, germ cell and functional ovarian lesions and compare their characteristics. Epithelial neoplasia in chidren is very rare but remains part of the differential diagnosis of any ovarian mass.[13] Deprest et al. reported that 19.3% of all ovarian tumours were epithelial in origin, and in the majority of these-15.9% of tumours in all patients from the 10 series- were malignant.[14] Diamond et al. cited a 9.8% malignancy rate for all subtypes of ovarian tumours and an even lower rate of 2.4% for malignant epithelial carcinomas.[15] Authors have postulated that hormonal stimulation may trigger the development of this tumours. All epithelial tumours in patients aged < 14 years were benign, whereas the 8 malignant epithelial tumours occurred in patients aged > 15 years.[16] However, in our series, 7 of the 18 epithelial tumours were found in premenarcheal patients.

Malignant clear-cell sarcoma of the ovary, especially in an adolescent patient, is a rare disorder. Our 13-year-old patient diagnosed with bilateral clear-cell sarcoma is the youngest case in the literature. The higher rate of epithelial ovarian tumours in this series (32.1%) may be explained by the fact that our centre is a tertiary clinic and complicated cases are referred to us.

In large simple cysts or mature ovarian teratomas, there is little or no tendency for malignant degeneration or coexistence of malignant cells. In the light of a potential bilateral incidence of 12%, conservative therapy would seem more appropriate than open or laparoscopic SO. Collectively, teratomas constitute half of all ovarian neoplasms and only 1% of these are malignant immature teratomas.[9,17-19]

A mean age of 16.3 ± 2.2 years was found in Zhang et al.'s 521 disease series. Ninety-two of these patients had non-neoplastic lesions, 382 were benign and 47 were malignant ovarian

lesions. Abdominal pelvic pain and menstrual disorder were the most common symptoms in these patients, while torsion was found in 48 patients (9.2%). However, they were not separated by patient groups.[20] In Oltmann's 424 patient series, the mean age was 12.5±0.26 years, the malignancy rate was 11% and 114 of these patients had torsion (26%).[1,21] The mean age of the torsion patients was 10 ± 0.53. Four of the torsion patients' tumours were malignant (3.5%) and 26 were benign (24%), while the remainder were functional lesions (72.5%). This result supports the hypothesis that torsion is seen at an early age. Malignancy was observed to be 11% in a 424 ovarian mass series and 1.8% in 707 ovarian torsions.[21] Our malignancy rate(n= 2) is 3.57%. It is therefore understood that ovarian tissue protection must first be achieved.

The primary symptom of benign and functional pathologies was pain, while in malignant pathologies it was pain accompanied by swelling in Zhang's series.[20] In our groups, swelling were detected 61.5% in the germ cell and 50% in the epithelial cells, respectively, and only 16% in the functional ones. This result was consistent with the literature and the average mass size was 7.6 cm in the functional group and 12 cm in the other two groups. In Oltmann's series, cut-off values were given as 8 cm of the mass for malignant lesions, while Zhang was found in the benign neoplasm of 9.0 ± 5.7 cm and 17.3 ± 8.6 cm in the malignant ones.[1,20] However, the first time in the literature, as the ovarian pathologies in our series separated into 3 groups, the ovarian tumour diameters of epithelial and germ cell tumours were found to be close to each other and 12 cm above; the functional group was 7.6 cm, respectively, to be statistically small. Most commonly, the preoperative diagnosis was an abdominopelvic mass. Consideration should be given to order preoperatively ovarian tumour markers to help with intraoperative management and pathological diagnosis.

The treatment for ovarian torsion was usually oophorectomy. However, several investigators have found no evidence to support this fear in their review of the literature, and now detorsion is advocated as an option. Ovarian function has been shown to recover after detorsion in adults although no data are available in children.[5,6,9] If a cystic area is present in the twisted ovary, then a cystectomy can be performed in an attempt to save the ovary and to prevent another torsion. Of course, this procedure is technically challenging because of the small size of the ovaries in premenarcheal patients. The ovarian volume from birth to 5 years of age varies between 0.75 and 0.86 cm.[3,4]

The remaining 25 functional ovarian lesions were functional ovarian cysts which were larger than 5 cm and not reducing in size. There were cysts with ovarian torsion in 7 patients and the ovaries were protected by detorsion and cystectomy without doing an oophorectomy. Simple cysts are routinely observed for resolution, because most are self-limiting and disappear within 4 to 8 weeks. If the cyst causes significant pain, persists beyond 8 weeks, or enlarges with observation, however, surgical management is warranted. Cystectomy, with reservation of the remaining ovary, is the preferred operative management of a functional cyst in women of reproductive age. Most functional cysts can be removed laparoscopically.[4,5,9]

In this series, patients with functional lesions were treated with CE (56%), CE was done in only 22% of the epithelial group and SO was done in all of the germ cell patients.

Oophorectomies were performed because of ovarian necrosis due to torsion and due to the acute abdominal pain and torsion experienced in emergency cases, due to the inability to detect intact ovarian tissue in the epithelial or germ cell tumour.

In the Oltmann series, the malignancy rate was 22% in patients aged 1 to 8 years and 10% in patients over 8, whereas ages in our series age of two malignant cases were 13 and 17 years respectively.[1] This difference may be related to the relatively small number of patients included in our study.

In premenstrual age, cystic ovarian (functional) lesions and torsion should be considered as frequent and malign lesions are very rare in all age groups of children so we recommend ovarian protective surgery should be preferred. ■

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