



Fertility preservation in ovary pathologies in pediatric patients

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ABSTRACT

Purpose: To study cases with ovarian torsion or ovarian tumors and hemorrhagic cysts and to review those who underwent ovary sparing surgery in a follow up period of 1 month, 3 months and a1 year.

Methods: A prospective study of 46 youth and adolescent patients, from 6 to 16 years old, were prospectively studied from October 2015 to October 2020, in a single tertiary care children's hospital. All underwent radical or ovary- sparing operative management, due to ovarian torsion or ovarian tumor/cyst. Statistical analysis was performed with SPSS (ve 24 SPSS Inc., Chicago, IL, USA).

Results: Sixteen patients underwent radical surgery, while ovary sparing surgery was performed in thirty three. Overall, 5 were diagnosed with ovarian torsion, 11 with ovarian or fallopian tube torsion due to hemorrhagic cyst or tumor and 30 with ovarian tumor (23 benign and 7 malignant). Benign or malignant etiology was confirmed through biopsy. Ultrasound was used for diagnosis in all patients, while CT scan or MRI only in 18 cases, especially in those with strong indications of tumor pathology. Initial operation was performed laparoscopically in 30% of patients, without any conversion to open surgery. In all patients postoperative ovarian ultrasound imaging was performed 1 and 3 months after surgery. An ultrasound follow-up 12 months postoperatively was performed in 38 patients.

Conclusion: Ovarian-sparing operations are safe for ovarian torsion and benign ovarian tumors and conferred successful clinical outcomes of low recurrence and repeated surgery rates. It is also a viable approach in children and young girls in an attempt to preserve future fertility.

Key words: *Ovarian torsion;ovarian tumors;ovary sparing surgery*

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Introduction

Ovarian surgery in children are rare. The most common pediatric cases in need of surgery are ovarian tumors and ovary or fallopian tube torsion. Overall incidence for ovarian tumors in childhood is estimated 2.6/100,000 girls, depending on patient's age and histological characteristics. Ultrasonography can differentiate ovarian tumors from cystic lesions, a benign and asymptomatic condition. In addition, the incidence of ovarian torsion, fallopian tube torsion or both is estimated 5/ 100,000 girls, 1-20 years old. Sometimes, more often in teenage girls, either hemorrhagic cysts or an ovarian mass (both benign or malignant) could cause an ovarian torsion (1), (2).

Regarding contemporary treatment, there has been a change in practice and most pediatric surgeons nowadays prefer ovarian preservation rather than oophorectomy in order to maintain best chance of fertility in subsequent years. In the majority of ovarian torsion cases, even if the appearance of the ovary at the time of detorsion is not the best indicator for parenchymal viability, ovarian preservation has been advocated. In cases of benign ovarian tumors, the prognosis is excellent following tumor resection within clear margins. If a malignant tumor in the ovary is present, a complete resection with a preservation of the unilateral ovary is usually strongly suggested. Nevertheless, there is an incidence of approximately 23% of a metachronous disease occurring in the other ovary (1), (2).

The aim of the present study is to evaluate the clinical symptoms, diagnosis, management and outcome of ovarian torsion and tumors after ovary sparing surgery in pediatric patients.

Materials and Methods

This is a prospective study over a 5 years period (October 2015- October 2020) in "P. & A. Kyriakou" Children's Hospital. After the institutional review board approval for medical records and pathological slide reviews was obtained, a total of forty six patients, 6 to 16 years old, requiring surgery were included. Their diagnosis varied from ovarian tumors, hemorrhagic ovarian cysts or ovarian and fallopian tube torsion. Patients who did not receive primary treatment or follow-up care at "P. & A. Kyriakou" Children's Hospital were excluded.

Demographic data, patient's history, imaging, operative and histological data were collected, including age, symptoms, physical examination findings, menstrual status, tumor markers, imaging features, operative details (surgical technique and remaining ovarian tissue), biopsy results and follow up ultrasound and relevant clinical data during 1 month, 3 months and 1 year postoperative.

The necessity of surgical management was determined on the basis of disease extent, patient age, and the need to preserve fertility, after thorough preoperative counseling. A surgical procedure could be considered as ovary sparing (fertility sparing) when the uterus and at least part of one ovary were left in situ. Thus, unilateral salpingo-oophorectomy and unilateral ovarian cystectomy with/without contralateral ovarian cystectomy were all defined as fertility sparing surgeries.

Statistical analysis was performed with SPSS (ve 24 SPSS Inc., Chicago, IL, USA). Chi-square test was used to study the relation between categorical variables. All patients were categorized according to age and pathology and further analyzed with similar univariate and multivariate regressions.

Results

From October 2015 to October 2020, forty six patients, aged 6 to 16 years, met our inclusion criteria and were studied. The cases included 5 ovarian torsions, 10 ovarian and/or fallopian tube torsions due to a hemorrhagic cyst, 15 hemorrhagic cysts bigger than 4-4.5cm in size, 8 unilateral mature teratomas, 1 bilateral teratoma with right ovarian torsion, 5 immature teratomas, 1 serous cystadenoma and 1 granulomatous ovarian tumor (Fig.1,2,3). The average age of girls was 14 +/- 1.5 years (mean age between 6 to 16 years). There were 28 right ovaries with either a torsion, ovarian tumor or hemorrhagic cyst, 15 left ovaries with similar pathologies and 3 bilaterally affected ovaries including 2 mature teratomas and 1 immature teratoma.

Twenty two (43,4%) out of 46 patients (about half of them) were presented as surgical emergencies in the emergency department. All of them the main symptom was acute abdominal pain. Pain that spread into the groin was also mentioned in 82% of the patients, nausea in 70% and vomiting in 89%. Six pat-

ients reported that they had experienced similar pain in the past. Eighteen patients (39.1%) presented with a palpable abdominal mass or a prominent lower abdomen, without any other symptoms. However, fever $>38^{\circ}\text{C}$, as a symptom, was absent during clinical examination.

The diagnosis was obtained in all patients by ultrasound imaging. CT scan or MRI were performed additionally in 18 cases, with indications of tumor presence. Cystic appearance of a mass on ultrasound had a high sensitivity for diagnosis of hemorrhagic cysts, while the presence of solid components increased the suspicion of malignancy and needed further evaluation with CT scan or MRI. In addition, in a case of an ovarian torsion, an increased size of ovaries was seen. However, only in two of them, no blood flow in the ovary was identified in Doppler sonography.

Type of presentation – i.e. whether a patient was presented in the emergency department or not - did not influence the choice of surgery. On the other hand, tumors or cysts were smaller in minimally invasive procedures. Generally, 70% of cases were treated with open procedures and 30% with minimally invasive surgery. None of the laparoscopic operations was converted. Ovaries were removed unilaterally in twelve patients and bilaterally in one patient. Ovary sparing surgery was done in thirty three patients: 11 girls with ovarian torsions with or without hemorrhagic cysts, all girls with hemorrhagic cysts and 7 girls with mature teratoma. In a girl with bilateral mature teratoma, one ovary and two fallopian tubes were preserved. Postoperative complication of superficial and deep/organ surgical site infections, as defined by the American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP) occurred only in 2 patients.

Blood cancer markers were very helpful in order to decide whether to perform an ovary preserving surgery or not. Cancer markers, such as α -fetoprotein, β - human chorionic gonadotropin (β -HCG), CEA and CA-125, were examined in all patients. Both α -fetoprotein and β -HCG were positive only in 4 cases. Positive CEA was found in one girl and positive CEA-125 in two girls. In girls with positive blood cancer markers oophorectomy was performed.

The follow up results of treatment in 38/46 patients were evaluated from 1 month to 1 year. Eight out of 46 patients were operated during the last 10 months. Postoperative ovarian imaging was routinely

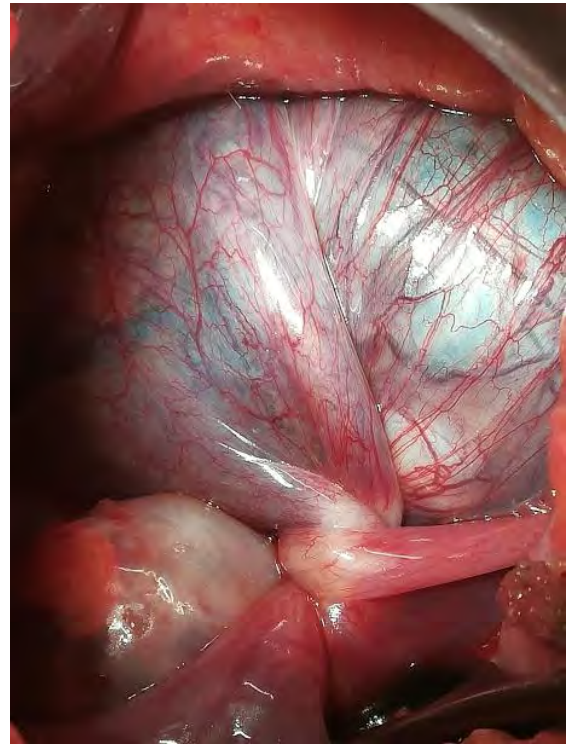


Figure 1: *Ovarian torsion*



Figure 2: *Immature ovarian teratoma*



Figure 3: *Mature ovarian teratoma*

scheduled in 1 and 3 months after surgery in all patients. Thirty eight patients were also examined by ultrasound 1 year postoperatively. In patients with previous ovarian torsion, the ovarian tissue structure and function was evaluated as normal. Doppler test revealed also normal ovary blood flow in all of these patients. Only in 2 out of 25 girls with hemorrhagic ovarian cysts, postoperative ultrasound revealed multifollicular ovaries and they were referred to pediatrician for further evaluation. In addition, children with mature teratomas, who underwent ovary sparing surgery seem to have also normal ovarian tissue for their age, without any fertility problems. Two of them are now adults with normal sexual life. Thirty out of thirty three patients who underwent ovary sparing surgery, open or laparoscopic, seem to have 100% functional preservation of ovarian tissue after 1 to 5 years postoperatively.

Discussion

In the past it was common clinical practice to remove an ischemic (blue-black) ovary without an effort to relieve the torsion or an enlarged ovary in order to avoid leaving part of a malignant tumor. Oophorectomy has been associated with negative long-term consequences. It increases the risk of early menopause and premature ovarian failure, which are associated in adulthood with impaired sexual health, low bone density, neurological and cardiac disease. Increased awareness of these potential negative effects of oophorectomy has led to changes in the management of ovarian pathologies. Nowadays an ovary sparing surgery is performed safely almost always, with satisfactory results regarding the future fertility of young girls (3), (4).

Ovarian detorsion without oophorectomy in the pediatric population was first described in 1985. Ovarian torsion occurs usually secondary to a cystic or solid ovarian mass. In most of the cases the cause is a hemorrhagic cyst, with negative cancer blood markers (α -fetoprotein, β -HCG, CEA, CA-125), thus ovary sparing surgery should be performed. On the other hand, if malignancy is suspected, a biopsy during the operation must be taken, and, if malignancy is confirmed, oophorectomy must be performed in a second-look operation. Ovaries without malformations account only about 25-68% of the total number of torsion cases. In our study benign tumors that cause an ovarian torsion accounted for 11 of 46 cases, 1 was mature ovarian teratoma, whereas hemorrhagic cysts were 10 and and torsions without any ovarian malformations were only 5

(0.1%). This is consistent with other studies demonstrating that ovarian torsion due to ovarian malignancy is extremely rare, with an estimated incidence of 0,5-8% (2), (3), (5).

Usually, the visual appearance of a twisted ovary, with a grossly enlarged size, dark blue or black color and profound signs of ischemia, should not be taken by the surgeons as a definite prognostic sign for future ovarian functioning failure, if left in place after detorsion. Several studies including large numbers of such cases have demonstrated satisfactory ovarian function on follow-up ultrasound examination. After 4 to 6 weeks ovaries have shown reduced size, normal blood flow and follicle formation. In one of these studies, more than 70% of reviewed ovaries, preserved by detorsion, had visible follicles present on follow up ultrasound. Another study has shown that 4-6 weeks after detorsion a dramatic decrease in volume occurs, as well as increase in blood flow and signs of folliculogenesis both in premenarchial and menarcheal girls seen in ultrasonography. In our patients, an ultrasonography was performed 1 and 3 months after the ovary sparing surgery. A complete functional preservation of ovarian tissue has been proved (2), (5).

The goal of surgical treatment in ovarian neoplasms is cure. However, in children the majority of those are benign. Ovary sparing surgery entails removal of the tumor only, leaving the surrounding normal ovarian tissue in place (oncectomy) or preserving the contralateral ovary, fallopian tube and uterus, considering the potential for fertility as well as the future hormonal health of the young patients. The critical step is to be accurate in preoperative risk stratification that can discriminate between benign and malignant ovarian tumors. Patient history, physical examination, imaging studies such as ultrasonography, computed tomography (CT scan) and MRI could help with preoperative risk stratification. In our study ultrasonography, CT or MRI scan and blood cancer markers were performed in all patients with suspected malignancy. The latter were very helpful in the decision making of performing an ovary preserving surgery or not (3), (6), (7).

Following this strategy in the operating room one could achieve an increase in the fertility rate for children with a history of ovarian teratoma during their adulthood period. The ovarian tissue that remains after the removal of the teratoma, no matter how small it looks macroscopically, contains many viable follicles, capable of hormones production and contribution in the

reproduction process.

Laparoscopic ovarian biopsies performed in girls, 11-34 years old, have proved that each mm² of ovarian tissue contains 35 primary ovaries, reinforcing the theory of ovary sparing surgery. The risk of malignancy in the remaining healthy ovarian tissue is very low (0.17-2%). Such rare cases have been reported in women over the age of 40 who underwent surgery at this age for ovarian teratoma. The incidence rate of malignant teratomas in children and adolescents reported in the international literature is very small (1-2%). According to several studies the technique of preserving ovarian tissue can be safely applied in cases of patients with ovarian teratoma who are accidentally found on an imaging test or they present with acute symptoms due to ovarian torsion. In our study 9 girls with mature ovarian teratoma are included, 1 presented with bilateral teratoma and torsion of the right ovary. Both ovaries were preserved in 7 of these cases, whereas in the bilateral teratoma case the right ovary was untwisted and preserved (8), (9), (10).

Ovary sparing surgery is also very important in case of unilateral benign pathology because benign ovarian neoplasms have a 10-23% reported risk for developing a second neoplasm (benign or malignant) in the contralateral ovary. In our group of patients, one child with a right mature ovarian teratoma was referred 14 months after the first successful operation for management of a left sided mature ovarian teratoma. Left ovary sparing surgery was performed (4).

Conclusion

Ovary sparing surgery should be performed by pediatric surgeons in the majority of ovarian torsion cases, following detorsion of affected ovary, regardless of its increased volume or the level of ischemia. The same technique should be used in the management of benign ovarian tumors, where the pediatric surgeon should find the right balance between complete tumor resection and maximal fertility preservation. However, long term follow up is very important, for further evaluation of the ovarian function and possibility of torsion recurrence or a malignancy development in the already affected or the contralateral ovary.

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