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ORIGINAL ARTICLE
ORİJİNAL ARAŞTIRMA

Treatment Approaches in Ovarian Masses in Children

Çocuklarda Over Kitlelerinde Tedavi Yaklaşımları

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Abstract

Aim: The aim of this retrospective study is to evaluate clinical features, treatment approaches and outcomes of children with ovarian mass.

Material and Method: In our clinic, the oncologic charts of children with a mass in the ovary between 2009 and 2020 were analyzed retrospectively. The patients' demographic features, symptoms and signs, diagnosis, treatments and outcomes were recorded.

Results: The age of 55 patients included in the study ranged from two months to 18 years (median, 12.9 years). While the ages of 38 patients were ≥ 10 years (69%), 17 of them were <10 years (31%). Fifty-one of the patients underwent elective surgery (92.7%), and four had emergency surgery (7.3%). Of the surgeries performed, 28 were salpingo-oophorectomy (51.9%), 23 were oophorectomy (42.6%), and 4 were cystectomy (5.6%). The types of ovarian mass were germ cell tumors (n: 44, 80%), epithelial tumors (n: 4, 7.3%), stromal tumors (n: 3, 5.5%), simple cyst (n: 2, 3.6%), and others (n: 2, 3.6%). Two patients with malignant tumor (one dysgerminoma patient with ataxia telangiectasia, and the other with yolk sac tumor) died while the others were alive.

Conclusion: In children, benign tumors are more prominent and surgical treatment is sufficient. In malignant tumors, overall survival rates have increased with multidisciplinary approaches.

Keywords: Ovary, mass, children, treatment approaches

Öz

Amaç: Bu geriye dönük çalışmanın amacı, over kitlesi olan çocukların klinik özelliklerini, tedavi yaklaşımlarını ve sonuçlarını değerlendirmektir.

Gereç ve Yöntem: Kliniğimizde, 2009 ile 2020 yılları arasında, overde kitle saptanan çocukların dosyaları geriye yönelik incelendi. Hastaların demografik özellikleri, semptom ve bulguları, tanıları, tedavileri ve sonuçları kaydedildi.

Bulgular: Çalışmaya dâhil edilen 55 hastanın yaşı iki ay ile 18 yıl arasında değişiyordu (ortanca, 12,9 yıl). Hastaların 38'inin yaşı ≥ 10 yıl iken (%69), 17'sinin yaşı <10 yıldı (%31). Hastaların 51'inde elektif cerrahi (%92,7), ve dördünde acil cerrahi uygulandı (%7,3). Gerçekleştirilen ameliyatların 28'i salpingo-ooferektomi (% 51,9), 23'ü ooferektomi (% 42,6) ve 3'ü kistektomi (% 5,6) idi. Overdeki kitlelerin tipleri, germ hücreli tümörler (n: 44,% 80), epitel tümörleri (n: 4,% 7,3), stromal tümörler (n: 3,% 5,5), basit kist (n: 2, %3,6), ve diğerleri (n: 2, %3,6) idi. Malign tümörü olan iki hasta (biri ataksi telenjiektazili disgerminoma hastası ve diğeri yolk sac tümörlü) kaybedilirken, diğer hastalar yaşamaktaydı.

Sonuç: Çocuklarda, benign tümörler daha ön plandadır ve cerrahi tedavi yeterlidir. Malign tümörlerde ise multidisipliner yaklaşımlarla genel sağ kalım oranları artmıştır.

Anahtar Kelimeler: Over, kitle, çocuk, tedavi yaklaşımı

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INTRODUCTION

In children, unlike adults, there is not much experience with adnexal masses and generally the limited experience in children is mostly on ovarian tumors (1, 2). The majority of the ovarian masses are benign in children (1-4). Although the most common complaints in ovarian masses are abdominal pain and palpable mass in children, urinary system symptoms such as dysuria or pollakiuria, or gastrointestinal system symptoms such as constipation, or menstrual disturbances such as dysmenorrhea, and menorrhagia or oligomenorrhea can also be presented. It should be kept in mind that precocious puberty, gonadotropin-independent, may be a sign of an ovarian mass, especially in juvenile granulosa cell tumors (1-5). Another interesting presenting complaint may be galactorrhea (6). The ovarian torsions that appear together with ovarian mass that require urgent surgical approach should not be forgotten (7).

Tumor markers such as human chorionic gonadotropin (HCG), alpha-fetoprotein (AFP), lactate dehydrogenase (LDH), and inhibin have the clinical utility in childhood germ cell tumors (8). Especially, elevations of AFP in yolk sac tumor, LDH in dysgerminoma, and HCG in choriocarcinoma are very useful in diagnosis, evaluation of treatment response and in follow-up.

Malignant ovarian tumors in children constitute 25% to 35% of all ovarian masses (2, 9). The functional lesions including corpus luteum cyst, hemorrhagic cyst, follicular cyst, paraovarian cyst, and only ovary torsion accounts for about half of all childhood ovarian masses (5, 10). Others are epithelial tumors such as serous cyst adenom, mucinous cyst adenom, mucinous cyst, serous cyst, and germ cell tumor such as mature cystic teratoma, mature teratoma, dysgerminoma, yolk sac tumor, and immature teratoma (5, 10, 11). Different childhood malignant diseases including neuroblastoma, rhabdomyosarcoma, Ewing's sarcoma, rhabdoid tumor, and carcinoid tumor may cause metastatic ovarian tumor in children also (12).

The aim of this study is to evaluate clinical features, treatment approaches and outcomes of children with ovarian mass, retrospectively.

MATERIAL AND METHOD

Approval was obtained from the local ethics committee for this retrospective study (No: 2021/129, Date: 27 Jan, 2021). Written informed consent was not obtained as a retrospective study. This study complies with the guidelines for human studies and was conducted ethically in accordance with the World Medical Association Declaration of Helsinki.

From 2009 to 2020, the oncologic charts of patients who were diagnosed and followed up with an ovarian mass at the department of pediatric hematology and oncology were retrospectively reviewed. The patients with functional lesions including corpus luteum cyst, hemorrhagic cyst, follicular cyst, paraovarian cyst, and only torsion were excluded.

The ages of the patients were recorded as demographic data. The patients were divided into two groups as age <10 years and ≥ 10 years. In addition, the symptoms and findings of the patients at admission, tumor markers at admission, if any; the largest diameter of the mass; surgical findings; diagnosis; treatment approaches and results were recorded.

The main diagnoses of the patients were given as simple cyst, germ-cell tumors, stromal tumors, and epithelial tumors, as definitive diagnosis.

"Federation Internationale de Gynecologie Oncologique" classification system was used for staging except non-Hodgkin lymphoma. For non-Hodgkin lymphoma, Murphy staging system was used.

The BEP chemotherapy protocol containing cisplatin, etoposide and bleomycin was used in patients with germ cell tumors, and the LMB89 protocol was used for non-Hodgkin lymphomas (13).

Statistical analysis

SPSS-15 software (SPSS Inc., Chicago, Illinois, USA) was used for all statistical analyses. According to whether the distribution was normal or not, the mean value and standard deviation or median value plus the minimum and maximum values were used in numerical data. For categorical data, frequency and percentage values were used. Kaplan–Meier survival analysis was used for survival analyses.

RESULTS

In this period, 55 children with ovarian mass were included in the study. The age of the patients ranged from two months to 18 years (median, 12.9 years). In addition, 17 patients (31%) were <10-year-old, while 38 patients (69%) were ≥ 10 years.

The patients' symptoms and signs are summarized in **Table 1**. The most common symptom was abdominal pain (n: 50, 91%). Four patients (7.3%) underwent emergency surgery for ovarian torsion.

The largest tumor diameter ranged from 3 cm to 28.5 cm (median, 11 cm). High AFP levels in 11 patients, high HCG levels in 10 patients and high LDH levels in 12 patients were found. In one of our patients with dysgerminoma, the LDH level was very high (value: 37155 IU/L, N: 125-243 IU/L).

Table 1. The patients' symptoms and signs at admission

Symptom/Signs	n (%)
Abdominal pain	50 (91)
Palpable mass	11 (20)
Menstrual disturbances	2 (3.6)
Enuresis	1 (1.8)
Weight loss	1 (1.8)
Constipation	1 (1.8)
Anorexia	1 (1.8)

While 51 of the patients underwent elective surgery (92.7%), four had emergency surgery (7.3%). The operations of the patients were performed by a pediatric surgeon (n = 45), a gynecologist (n = 9) and a general surgeon (n = 1). Of the surgeries performed, 28 were salpingo-oophorectomy (51.9%), 23 were oophorectomy (42.6%), and four were cystectomy (5.6%). Lymph node dissection was performed in three patients (5.5%) and these were performed by gynecologists.

The types of ovarian mass were germ cell tumors (n: 44, 80%), epithelial tumors (n: 4, 7.3%), stromal tumors (n: 3, 5.5%), simple cyst (n: 2, 3.6), and others (n: 2, 3.6) (**Table 2**).

Table 2. The tumor types of the children with ovarian mass

The tumor types	n (%)
Germ-Cell tumors	44 (80)
Benign	
Mature cystic teratoma	25 (45.5)
Mature teratoma	1 (1.8)
Malign	
Dysgerminoma	10 (18.2)
Yolk Sac tumor	7 (12.7)
Immature teratoma	1 (1.8)
Epithelial tumors	4 (7.3)
Benign	
Mucinous cystadenoma	2
Borderline	
Serous borderline tumor	1
Mucinous borderline tumor	1
Stromal tumors	3 (5.5)
Benign	
Serous cystadenofibroma	2
Malign	
Juvenile granulosa cell tumor	1
Simple cyst	2 (3.6)
Others	2 (3.6)
Non-Hodgkin lymphoma	2

Fourteen patients received chemotherapy. Twelve patients with germ cell tumors received the BEP protocol, while two patients with non-Hodgkin lymphoma received the LMB89 protocol. Two patients with malignant tumor died, the others were alive. Of these two patients who died, the patient with yolk sac tumor died with progressive disease. In the other patient with ataxia telangiectasia and dysgerminoma who died, central nervous system tumor developed as a secondary cancer approximately two years later and however, the guardian of the patients refused any treatment. As a result, this patient died due to a central nervous system tumor (14). Overall survival rate was 80.8% with median follow-up time 2.5 years (range, 1.5 months - 14 years) (**Figure 1**).

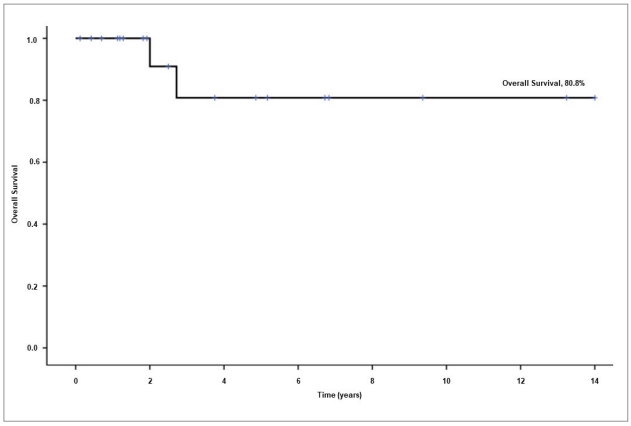

Figure 1. The overall survival of patients with malignant ovarian mass

DISCUSSION

In children, it should be kept in mind that, although most of the adnexal masses are benign unlike adults, approximately 1% may be malignant (15). In addition, almost all adnexal masses arise from the ovaries (1-5). In children, ovarian masses can be classified as functional lesions, simple cysts, epithelial tumors, stromal tumors, germ cell tumors, metastatic tumors and others, and 45% of them are functional lesions (5). Herein, the aim is to evaluate clinical features, treatment approaches and outcomes of children with ovarian mass, retrospectively. In our study, a significant portion of our patients were benign in nature, and most of the patients with malignancy had germ cell tumors.

Although the symptoms at the time of diagnosis may be variable in children with ovarian mass, the most commons are abdominal pain and palpable mass, also the ovarian mass should be kept in mind in children with menstrual disturbances or ovary torsion (1-5). Similarly, abdominal pain and palpable mass were the most common complaints in our patients. However, on rare occasions, menstrual disturbances, urinary system symptoms such as enuresis, gastrointestinal system symptoms such as constipation, weight loss, and anorexia were other symptoms.

Generally, AFP, HCG and LDH are commonly used tumor markers. Significant elevation of AFP is seen in yolk sac tumor, while mild elevations may be seen in immature or mature teratoma. Treatment response should also be monitored, taking into account the appropriate half-life

for that age, especially in patients with elevated AFP (8, 16). Another important tumor marker is HCG. High HCG level is usually seen in choriocarcinoma. However, mild HCG elevations can be seen in dysgerminoma and sometimes in yolk sac tumor. Both AFP and HCG elevations are generally seen in mixed germ cell tumors. Another important tumor marker that is sometimes forgotten is LDH. A marked elevation of LDH can be detected in mature or immature teratoma or yolk sac tumor, especially in dysgerminoma. In our patients, high AFP levels in 11 patients, high HCG levels in 10 patients and high LDH levels in 12 patients were found. In one of our patients with dysgerminoma, the LDH level was very high.

General treatment approach for ovarian masses in children is surgery. While only cystectomy is performed for ovarian cysts larger than five cm, salpingooforectomy or oophorectomy is preferred for other masses (1-5, 11, 17, 18). Lymph node dissection is not the preferred approach in children with malignant ovarian mass. In our study, except for four patients, all patients underwent elective surgery. Emergency surgery was performed in four patients due to ovarian torsion. The most preferred surgical intervention was salpingooforectomy or oophorectomy. Lymph node dissection was performed in three patients and primary operations of these patients were performed by gynecologists.

Ovarian tumors other than functional ovarian lesions in children, can be classified as simple cysts, epithelial tumors, stromal tumors, germ cell tumors, metastatic tumors and others (1-5, 10). In the study by Sonmez et al (5), functional lesions (44.6%), epithelial lesions (32.1%) and germ cell tumors (23.2%) were seen in order of frequency. In children, epithelial tumors are often benign and cystadenoma is the most common. Rarely, borderline tumor or more rarely malignant tumor may occur (10). In germ cell tumors, it is usually immature teratoma, dysgerminoma, yolk sac tumor, juvenile granulosa cell tumor, and mixed germ cell tumor at varying rates in different studies (11, 19). In our study, functional lesions were excluded. Germ cell tumors are important part of our patients (80%). According to the literature, the possible reason for this high rate is the complete recording of all benign ovarian masses such as "mature cystic teratoma" due to its close relationship with the pediatric surgery department. Dysgerminomas and yolk sac tumors were the most common malignant ovarian tumors.

In children, the most experience with chemotherapy is in malignant germ cell tumors. For many years, the BEP protocol containing cisplatin, etoposide and bleomycin or the JEB protocol containing carboplatin, etoposide and bleomycin have been preferred. In our study, BEP protocol was preferred, except for two patients with non-Hodgkin lymphoma and the JEB protocol was preferred in a patient with dysgerminoma due to the accompanying ataxia telangiectasia (14).

Success rates are good, depending on the stage, especially in germ cell ovarian tumors. In our study, the overall survival rate is 80.8%. One patient with ataxia telangiectasia was died. This patient was lost because of the development of a second cancer due to telangiectasia.

CONCLUSION

Most of the ovarian masses in childhood are benign. Harmonious collaboration is important in diagnosis and treatment of both benign and malignant ovarian masses.

ETHICAL DECLARATIONS

Ethics Committee Approval: Local Ethic Committee of XXX University, Faculty of Medicine (No: 2021/129, Date: 27 Jan, 2021).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: External double-blind referee assessment.

Conflict of Interest Situation: The authors have no conflicts of interest to declare.

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