

## Pediatric Malignant Ovarian Tumors

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**Abstract:** Pediatric malignant ovarian lesions are not uncommon. In 5 years between 2012 to 2017, 12 patients were diagnosed at GMK Medical College Hospital, Salem and Coimbatore Medical College Hospital, Coimbatore. The mode of clinical presentation, imaging findings, tumor markers, operative details, histopathology reports and follow up of these patients were reviewed. There was varied presentation clinically, abdominal pain being the most common, abdominal mass and other non-specific symptoms were also noted. Among the Histological group, there were 6 dysgerminoma, 4 Mixed germ cell tumor and 2 yolk sac tumor. Adjuvant chemotherapy with BEP regimen was given in high grade malignant tumors. All the patients are currently doing well on follow up. Though malignant ovarian tumor in pediatric population is found to be rare, it has to be considered as a possible differential diagnosis in premenstrual age group with abdominal pain, mass or other non-specific symptoms.

**Keywords:** Malignant ovarian tumor, Dysgerminoma, Mixed germ cell tumor, abdomen pain.

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### I. Introduction

Pediatric ovarian tumors are an uncommon but important form of childhood cancer. Ovarian tumors are the most frequent neoplasms of the female genital tract in childhood<sup>1</sup> and are generally considered to account for approximately 1% of all malignancies in patients ages 0–17 years<sup>2</sup>.

Ovarian masses include neoplastic and non-neoplastic processes. 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.

Ovarian masses whether cystic, solid, or both, generally have been considered rare in the pediatric age group.<sup>1-5</sup> As a group, these lesions span a spectrum of pathology from functional (nonneoplastic) ovarian cysts to ovarian torsion, and from benign to highly aggressive malignant neoplasms. The actual incidence of pediatric ovarian lesions is unknown; however, ovarian neoplasms (which make up about one-half of all ovarian masses in children) are estimated to occur at a rate of approximately 2.6 cases per 100,000 girls per year, and malignant ovarian neoplasms make up about 1% of all childhood cancers.<sup>4</sup> Ovarian masses come to surgical attention in a variety of ways. Patients may present with acute abdominal pain and signs of peritonitis that can be difficult to distinguish from acute appendicitis. Patients may be referred with a large pelvic or abdominal mass and concerns of malignancy. Patients with ovarian lesions may present with precocious puberty, masculinization, or other signs of endocrine disturbance. Some patients with a mass effect from an enlarged ovary experience ureteral compression and hydronephrosis, bowel obstruction, or respiratory insufficiency. More rarely, patients may present with bleeding. Ovarian disorders must be included in the differential diagnosis in any girl who presents for evaluation of abdominal pain, a pelvic or abdominal mass, or gynecologic endocrine disorder.

In this report we review a 5-year experience with the surgical management of ovarian masses in children. It is our goal that such information may help guide the evaluation and surgical management of future children with ovarian disorders.

### II. Material And Methods

A retrospective study was carried out on patients of Department of Pediatric Surgery at GMK Medical College Hospital, Salem and Coimbatore Medical College Hospital, Coimbatore from 2012 to 2017. A total of 12 children of age <12 years with diagnosis of ovarian neoplasm were considered in this study.

**Study Design:** Retrospective study.

**Study Location:** This was a tertiary care teaching hospital based study done in Department of Pediatric Surgery, at GMK Medical College Hospital, Salem and Coimbatore Medical College Hospital, Coimbatore

**Study Duration:** 2012 - to 2017

**Sample size:** 12 children

**Inclusion criteria:**

1. Children <12 years
2. Children with Malignant Ovarian tumors

**Exclusion criteria:**

1. Age >12 years
2. Benign ovarian neoplasm

#### **Procedure methodology**

The institutional ethical committee approval was taken before the commencing this study. The data pertaining to Pediatric ovarian neoplasm were collected and presented to the committee for review and their approval sought. After the approval, we retrospectively reviewed the case files of children who were diagnosed with ovarian neoplasm. Among the study population only children with malignant ovarian neoplasm were considered as the study group. The review data included socio-demographic characteristics such as age, presenting complaints, tumor markers, imaging reports, operative notes, complications, adjuvant chemotherapy and follow up. The written and informed consent in the local language was taken before any surgical intervention were carried out, consent includes usage of data for academic purpose.

#### **Statistical analysis**

Data was analyzed using SPSS version 20 (SPSS Inc., Chicago, IL). Student's *t*-test was used to ascertain the significance of differences between mean values of two continuous variables and confirmed by nonparametric Mann-Whitney test. In addition, paired *t*-test was used to determine the difference between baseline and 2 years after regarding biochemistry parameters, and this was confirmed by the Wilcoxon test which was a nonparametric test that compares two paired groups. Chi-square and Fisher exact tests were performed to test for differences in proportions of categorical variables between two or more groups. The level *P* < 0.05 was considered as the cutoff value or significance.

### **III. Result**

In our study 12 patients were diagnosed with malignant ovarian tumor.

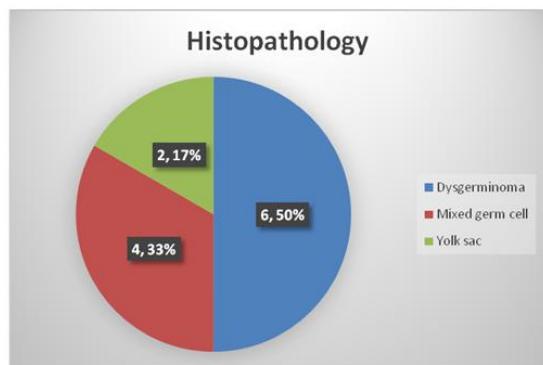
**AGE:** Median age of the study was 10.5 years. Two children were less than 6 years of age.

**Signs and Symptoms at Presentation:** More than half of our patients presented with abdominal pain, few with mass and other nonspecific symptoms. Two children presented with precocious puberty at the age of 5 years. All 12 patients had unilateral pathology. Diagnostic imaging, including abdominal ultrasonogram and abdominal computed tomography, Magnetic resonance imaging was performed in these patients. All patients received surgery. Twelve patients had received unilateral salpingo-oophorectomy. The pathologic diagnoses Dysgerminoma was seen in 6 patients (50%) and mixed germ cell tumor in 4(33%). Two children with yolk sac tumor(17%)(figure 1).

The serum AFP and Beta-hCG were tested by radioimmunoassay. We found that seven patients had high AFP levels. There were four patients who had high  $\beta$ -hCG levels (range, 25-190 mU/mL). One patient had normal AFP and  $\beta$ -hCG levels.

In our study all malignant tumors were germ cell tumors, all patients received chemotherapy with platinum-based regimens (bleomycin, etoposide, and cisplatin regimen). Number of cycles for chemotherapy was ranging from two to six. No major toxicity and no treatment-related deaths were noted. Two children with yolk sac tumor had relapse with elevated tumor markers and she received further chemotherapy with cisplatin, ifosfamide, and etoposide for six cycles and had no evidence of disease till the date of analysis.

**Figure 1 – Tumor Pathology**



#### IV. Discussion

We reviewed our experience with ovarian tumors in children and found a malignancy rate of 40%, similar to those that were previously observed. Reported rates of malignancy vary by study. Our study was confined to age group less than 12 years were previous studies in majority include adolescent age group as well. The patients all had a fairly large size of the tumor with compression symptoms, these large size tumorstends to intraabdominal mass rather than pelvic, making it difficult to identify organ of origin.

In our study, the median age at presentation was 10.5 years. The presenting symptoms are often nonspecific. The most common presenting symptoms in our patients were abdominal pain, followed by abdominal fullness and abdominal mass. Patients will become acutely symptomatic if they undergo hemorrhage, torsion, or rupture<sup>3,4</sup>. All malignant tumors presented were unilateral lesion. Metastasis at diagnosis and bilateral involvement were rare, consistent with other reports. Most malignant ovarian tumors in childhood are germ cell tumors. In our study 50% of the tumor were dysgerminoma and 33% were Mixed germ cell tumor and 17% yolk sac tumor. Literature it states that Germa Norris and Jensen<sup>5</sup> reviewed 353 ovarian tumors in young females and found germ cell tumors composed 80% of the preadolescent malignant ovarian tumors. Hassan et al<sup>6</sup> reported germ cell tumors comprised 49.1% of all malignant ovarian tumors in girls through age 19. Schultz et al found that 67.5% of pediatric malignant ovarian tumors were germ cell tumors. In our study, all were germ cell tumours.

Tumor markers are important for evaluating malignant ovarian tumors for diagnosis, relapse, and follow-up. Various tumor markers have been used for monitoring the clinical status of malignant germ cell tumors, including

AFP, Beta-hCG, human placental lactogen, pregnancy-specific b1 glycoprotein, fibronectin, transferrin, a-antitrypsin, carcinoembryonic antigen, alkaline phosphatase, lactatedehydrogenase, cancer antigen-125, and neuron-specific enolase.<sup>7,8</sup> Among these tumor markers, AFP and Beta-hCG are the most used. AFP can be used as a tumor marker for endodermal sinus tumor, embryonal carcinoma, and malignant mixed germ cell tumor. Elevated levels of Beta-hCG can be seen in some patients with pure dysgerminoma, mixed germ cell tumor, embryonal carcinoma, and ovarian choriocarcinoma. In our study, expect one patient all had elevated tumor markers among them two had grossly elevated AFP levels(>10000ng/ml). Most patients in our study had AFP levels declined to normal range within 3 months after treatment.

The treatment of ovarian tumors is complete surgical staging, followed by chemotherapy in cases beyond Stage I. Total tumor resection when possible is recommended by all studies, and salpingo-oophorectomy is the suggested surgical resection because cancer cells may spread to the fallopian tube through ovarian lymphatics.

The combination of cisplatin, etoposide, and bleomycin has been used with excellent cure rates. Rogers et al reported patients with Stage I tumors had 6-year OS and event-free survival of 95.1% and 95.1%, respectively, and patients with Stage II disease had OS and event-free survival of 93.8% and 87.5% when treated with four cycles of cisplatin, etoposide, and bleomycin. In the St. Jude's experience, the response to treatment of malignant ovarian tumors of low stage was excellent when compared with patients with advanced disease.

In addition to achieving higher cure rates, platinum-based combination therapies were reported to be able to preserve normal menstrual function and maintain fertility with healthy offspring. In order to find validation this statement, we would need long follow-up and disease-free survival rate to analyze.

We also assessed various factors, including age, histology, stage, and levels of tumor marker, to see their impact on prognosis. There was no conclusive result, which might be because of the limited patients in the study group. Cushing et al reported that AFP greater than 10,000 ng/mL and Beta-hCG greater than 5000 mU/mL at diagnosis were unfavorable prognostic factors, whereas Murugaesu et al stated that increasing stage and elevated AFP and Beta-hCG at the time of diagnosis were independent adverse prognostic factors and elevated AFP during treatment meant increased risk of treatment failure.

## V. Conclusion

Pediatric malignant ovarian tumor is a highly curable disease if not in the advanced stage at presentation. Considering malignant ovarian tumor as the differential diagnosis of young girls with abdominal pain or with other non-specific abdominal symptoms is utmost important. Limitation being the small study group and short follow-up period. Longer follow-up is required to assess the disease-free survival rate.

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