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OVARIAN MASSES IN CHILDREN

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Masses arising from the ovary are very rare in children. Forty-five patients with ovarian masses presenting to the New Children's Hospital, Cairo University between 1991 and 2000 were studied. All patients were between 20 days and 17years, with a mean age of 5.8 years. Only one case of complex corpus luteum cyst was diagnosed antenatally. Ultrasonography and tomographic scanning were performed for all cases together with hormonal assays in some patients. Surgical intervention was not performed in four cases of follicular cysts.

Among those with benign diseases (34 cases), two had simple cysts, 13 had follicular cysts, a case of corpus luteum cyst, 2 had serous cystadenoma, one had Brenner' s tumor, 3 cases of granulosa cell tumor and 12 cases of benign cystic teratoma.The malignant lesions (11 cases) included 6 cases of immature teratomas , 3 cases of endodermal sinus tumor , one case of dysgerminoma and a case of embryonal carcinoma . Most cases presented with abdominal masses or pains. Isosexual pseudoprecocious puberty occurred in eight patients, torsion resulted in three cases. All patients remained disease-free except two cases: an immature teratoma and an endodermal sinus tumors who died postoperatively .

INTRODUCTION

Ovarian masses represent a range of pathology from highly aggressive malignant tumors to benign cysts. These lesions may have multiple presentations. It has been estimated that gynecologic malignant conditions account for approximately 2% of all types of cancer in children, 60-70% of these lesions arise in the ovary [(1).] Nevertheless, ovarian tumors in young patients represent less than 1% of all ovarian neoplasms [(2)].

Ovarian lesions in girls differ from those in women in terms of clinical, pathologic and prognostic characteristics. The incidence and epidemiologic features may differ and, therefore, the diagnostic and therapeutic approaches must be appropriately altered for the pediatric age group. The concept that the highest incidence of malignant conditions occurs in the youngest patients is undergoing reassessment. The current belief regarding the relative frequency of benign versus malignant neoplasms is also undergoing modification.

The histology of ovarian tumors is extremely varied and their classification stimulated controversy and continuous modification for many years [(3).] As ovarian masses are relatively rare in children and thus their management is occasionally unclear, this study has reviewed the experience with these lesions in order to evaluate their pathology, treatment and outcome.

PATIENTS AND METHODS

Cases presenting to the pediatric Surgical Division with ovarian masses in a nine-year period -1991 through 2000 were studied. Clinical records of the patients were reviewed including the age, the presenting symptoms and any associated endocrine manifestations.

Radiological assessment of the tumor and its extension included both ultrasonography and computed tomography scan with special notification to the presence of calcification, the state of the other ovary and the presence of metastases. The Nussbaum's classification was applied to specify the lesions sonographically into three groups: cystic (when

sonographic findings disclosed that they contained fluid), complex (containing anechoic area intermixed with a clump of echogenic foci) and solid [4]. Chest radiography was performed to detect lung involvement in suspected cases. Antenatal diagnosis using ultrasonography was reported in one case.

In patients showing functional endocrinal manifestations, hormonal assessments e.g. estrogens, follicular stimulating hormone (FSH), luteinising hormone (LH) were performed. Serum assays of protein markers including alpha-fetoprotein (AFP), B-human chorionic gonadotropin (B-HCG) were measured for all germ cell tumors. Lactate dehydrogenase (LDH) was not performed. Their postoperative levels were assessed to assure complete removal of the tumor and detect the development of recurrences or metastases.

Surgical procedures consisted of an exploratory laparotomy with removal of the ovarian mass. Total excision of the mass was performed whenever possible. In suspected benign lesions, every effort was made to spare the ovary even when the mass is very large. If this was not possible, the gonad and the tumor alone were removed leaving the fallopian tube in place unless it is necrotic from torsion.

Suspected malignant tumors were treated with conservative surgical procedures whenever possible. All peritoneal surfaces, the inferior surface of the diaphragm, the omentum, the serosa of the intestine and the mesentery were carefully inspected for metastases. The pelvic and paraortic lymph nodes were palpated and all suspicious nodes were biopsied or removed if possible. The other ovary was carefully inspected and palpated for nodules, any suspicious areas were removed Lesions in which bilateral involvement is known to be common -e.g. mature teratomas - when no suspicious areas were detected, very close follow-up in short-period intervals was adopted with the possibility of performing a second-look operation. The other ovary was not bivalved. Ascitic fluid was collected for cytological evaluation. If no fluid was present, peritoneal washings was obtained.

Histopathologic examination of all specimens was performed. The lesions were classified according to the World Health Organization proposal for the International Histologic Classification of Diseases and its adaptation for oncology [5] into nonneoplastic and neoplastic entities. Cases with simple torsion of the ovary without pathologic lesions were excluded from the study.

Stromal and germ cell tumors were staged according to the clinico-pathologic system adopted by the Children Cancer Group (CCG) and the Pediatric Oncology Group (POG). Immature teratomas were graded according to semiquantitative assessment of the amount of immature tissue in the various histologic sections of the tumor and to the presence and quantity of the neuroepithelial components using Norris et al grading system [6] modified by Joshi [7] with adequate number of blocks taken for histologic examination.

Follow-up that ranged between 6 months and 3.5 years included physical examination, measurement of tumor markers and imaging. All patients were monitored for events and recorded as disease-free (NED), tumor recurrence, second malignancy or died.

RESULTS

Forty-five patients having ovarian masses were included in the study. Their ages ranged between 20 days and 17 years with a case being diagnosed antenatally. Distribution of the cases according to their pathologic results in relation to their ages is displayed in (Table 1). Fourteen patients were below 4 ears, only one case (7%) was malignant. Thirteen patients were between 4 and 8years, two lesions (15%) were malignant. Those above 8years were 18 cases, 8 tumors were malignant (44%).

Abdominal enlargement with palpable mass (n=28) and intermittent abdominal pain (n=22) were the most common complaint. Isosexual precocious puberty with irregular vaginal bleeding resulted in 8 cases: five patients had functioning follicular cysts and three cases had granulosa cell tumors. Torsion occurred in three cases: simple and follicular cysts were the cause in two patients. A granulosa cell tumor was detected in a third case where torsion occurred while the patient was in hospital scheduled for elective surgery. Gynecomastia was present in a patient aged 17 years reared as a male. He gave a history of previous exploratory laparotomy done in another center where excision of torsion in an ovarian lesion was performed, but no pathological data was available. Other uncommon presenting features included urinary symptoms, constipation and vomiting.

Ultrasonography was performed for all patients, with one case being detected antenatally. It has identified the lesions as ovarian pathology in 36 cases. In the other nine cases, an ovarian cause was a part of other differential diagnosis e.g.: mesenteric, omental or urachal cysts, intestinal duplication etc…. Five of these cases were below one year of age.

Sonographic classification of the masses is summarized in (Table 2). In fourteen cases, the lesions were cystic, none of them was malignant; one case was a benign neoplasm (serous cystadenoma). Nineteen patients had complex masses, seventeen were benign (four of these were nonneoplastic lesions) and two were malignant. Twelve showed a solid mass, three of these were benign and nine were malignant.

Patients presenting with functional ovarian lesions (n=8) were hormonally assessed. Basal serum gonadotropin levels – FSH and LH – were low while those of estradiol were elevated. Their sex hormone binding globulin levels were normal with normal thyroid functions.

The nonneoplastic lesions included 16 cases forming 35% of all ovarian masses; eleven of these were below 8years. Conservative treatment was conducted in four cases of follicular cysts. Simple cystectomy was performed for ten cysts greater than 5 cm in diameter while salpingo-oophorectomy was done for 2 cases with torsion.

In two cases, the cysts were simple with flattened epithelial lining; one of these was complicated by torsion. One case of corpus luteum cyst was diagnosed antenatally in an infant of diabetic mother at 36 weeks gestational age. Sonography revealed a cyst of 3.5 cm with fluid debris. The cyst increased in size with progression of pregnancy and reached 5.5 cm at the time of delivery. Follow-up for one month after delivery, the cyst did not regress in size and was excised. It was lined by luteinized granulosa cells and filled with retracting clots.

Follicular cysts included 13 cases; bilateral lesions were present in two cases, (Fig. 1). Conservative treatment was applied in four cysts less than 5 cm in diameter. In three cases, the children were above 8 years having functional cysts and a case was one month old. On follow-up, these cysts had disappeared completely.

Cystectomy was performed for 8 follicular cysts. In one case where torsion has occurred, salpingo-oophorectomy was mandatory. The cysts were filled with yellow fluid and lined by simple squamous to cuboidal epithelium. No cyst aspiration, fenestration or cyst wall excision were performed.

Functional follicular cysts with endocrine activity occurred in five cases, four of these children were between 8 and 12 years and one case was 5 year-old. Three cases were treated conservatively while cystectomy was performed in two patients (5 and 9-year old), (Fig. 2).

Neoplastic lesions included 29 cases. Sixteen patients were below 8 years, three of them were malignant (19 %) while thirteen were above 8 years, eight were malignant (61%).

Epithelial tumors included two cases of benign unilateral serous cystadenoma aged 6 and 8.5 years. The cysts were unilocular and measured 10 and 13 cm respectively. They had a smooth glistening wall lined by tall columnar ciliated epithelial cells and filled with clear serous fluid with no nodularity or papillary projections. Cystectomy was performed in one case and salpingo-oophorectomy in the other. The patients were followed-up for 1.5 years with no recurrences.

A non-functioning Brenner's tumor was reported in a child 3.5 year-old. The swelling appeared globular mostly firm except a cystic area at one pole filled with opaque viscous yellow-brown to hemorrhagic fluid. Salpingo-oophorectomy with omentectomy was performed as the later was adherent to the tumor. Microscopically it consisted of solid nests of epithelial cells resembling transitional urothelium surrounded by abundant dense fibroblastic stroma with no atypia, (Fig. 3).

Three cases of functioning granulosa cell tumors were included in the study. All of them presented with precocious puberty. Torsion occurred in one case. The sizes of the tumors ranged between 6 -11 cm. They appeared as solid, smooth, lobulated masses gray in color, yellowish in some areas. Histologically small cuboidal to polygonal follicle cells formed anastomosing cords, (Fig. 4). In one case, occasional areas of gland-like structures filled with an acidophillic material (Call-Exner bodies) were observed. A juvenile variant was reported in a one-year-old girl with abundant eosinophilic nuclei and few atypical nuclei.

Salpingo-oophorectomy was performed for all the cases. Upon review, 6 months to 1.5 years postoperatively, all the patients' pubertal signs had resolved and their hormonal levels had normalized with no recurrence of the tumors.

Germ cell tumors formed a large group in the study (n=23). Teratomas were the most frequent histopathologic type of this group (n=18).On radiography, calcification was detected in 17 cases (74 %). Mature forms occurred in 12 patients with their ages ranging from 2.5 to 12 years. The sizes of the lesions varied between 6 to 14 cm, all of them were cystic. None of these tumors had developed torsion. Inspection of the peritoneum did not reveal any nodules. With follow-up - which ranged between 6 months to 2 years - recurrence did not develop nor another tumor had aroused in the other ovary, (Fig. 5,6).

Malignant germ cell tumors included 11 cases; their ages ranged from 3 to 17 years. Immature teratomas occurred in six cases, (Fig. 7). Tumors with mixed histologic types resulted in three cases: two cases of endodermal sinus tumors (6 and 12 year-old), (Fig. 8) and a case of embryonal carcinoma (9 year-old). The malignant components were coexisting with immature teratoma. Pure forms included a case of dysgerminoma (17 year-old) and a three year-old girl with endodermal sinus tumor. All the cases were unilateral. Gross retroperitoneal lymph node enlargement (>2 cm) was observed in three cases. The pelvic peritoneum was involved in a case of yolk sac tumor. Liver metastases developed in two cases. Abdominal pain and a palpable mass were the commonest presenting features. No endocrinologic manifestations were elicited in these cases.

AFP levels were raised in all cases of endodermal sinus tumors and a case of immature teratoma. The published age-adjusted normal values were used to define the increase of these levels [8]. Those of B-HCG were slightly elevated only in the patient with dysgerminoma. Gynecomastia, severe hypospadias and bilateral impalpable gonads were detected in the case of dysgerminoma with a scar of a previous left paramedian laparotomy incision. Chromosomal analysis revealed a karyotype of 46 XX. The huge mass was seen infiltrating a near-by uterus, which was, excised on-block with the tumor, (Fig. 9). On microscopy, the resection margins were free of tumor cells. The testosterone level was very low for age (0.3 ng/ml) with increased estrogen / testosterone ratio.

Treatment of germ cell tumors was initially achieved by surgical excision of the mass. No preoperative adjuvant therapy was given. Complete removal of the mass was performed in all cases. In mature teratomas, the tumor was excised with trial to conserve any ovarian tissue present. The capsule was incised circumferentially several centimeters from the attachment of each cyst to the suspected hilum. In seven cases, recognizable ovarian tissue could be identified in the hilum. In all cases, the adjacent fallopian tube was spared.

Salpingo-oophorectomy was performed for all malignant germ cell tumors (n=11). The uterus was excised en-block with the tumor only in the case of dysgerminoma. Complete omentectomy was performed in four cases. None of the masses had ruptured during operative removal.

Patients with completely resected stage T1 germ cell tumors (n=13) were treated according to the watch-and-wait strategy that included frequent controls of the tumor markers. No recurrences were reported. Adjuvant therapy was added in tumors stage T2 (n=2), T3 (n=6) and T4 (n=2). Radiotherapy (3000 rads) was only given in the case of dysgerminoma. Multiagent chemotherapy using three cycles of cisplatinum (P, 20 mg/m2) , etoposide (E, 80 mg/m2) and bleomycin (B, 15 mg/m2) was started three weeks after surgery. Two patients- an endodermal sinus tumor and an immature teratoma – died from recurrence and progression of the disease 6 and 8 months later. The other patients with germ cell tumors remained disease free with a follow-up period that ranged between 1.5 and 3.5 years.

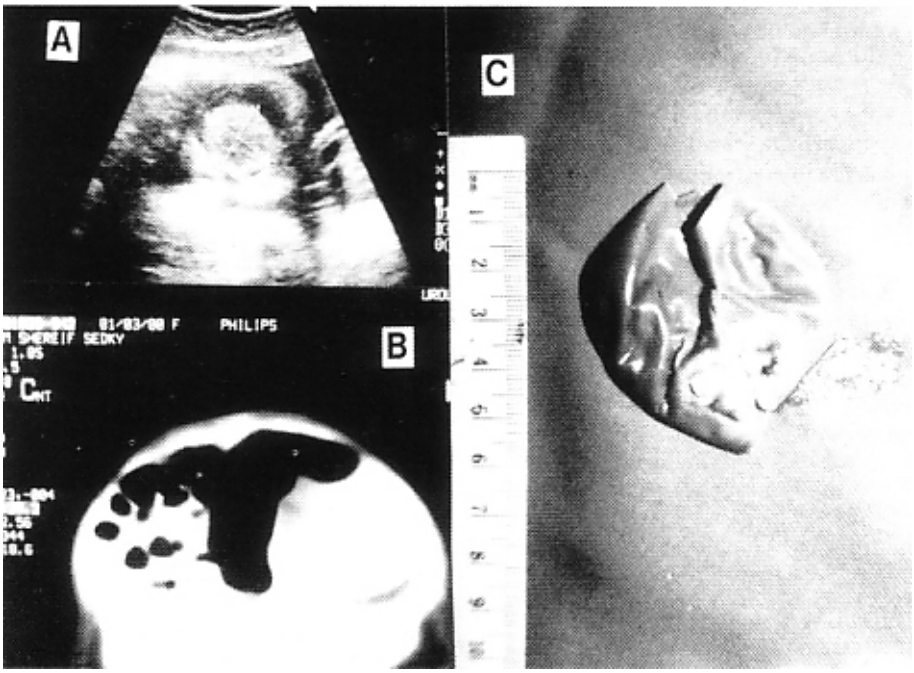

Fig (1):

A- ***Antenatal ultrasound at 36 weeks showing a left-sided cyst containing non-homogenous retracting clot.***

B- ***Postnatal CT scan.***

C- ***Cut section of the cyst filled with debris and clots.***

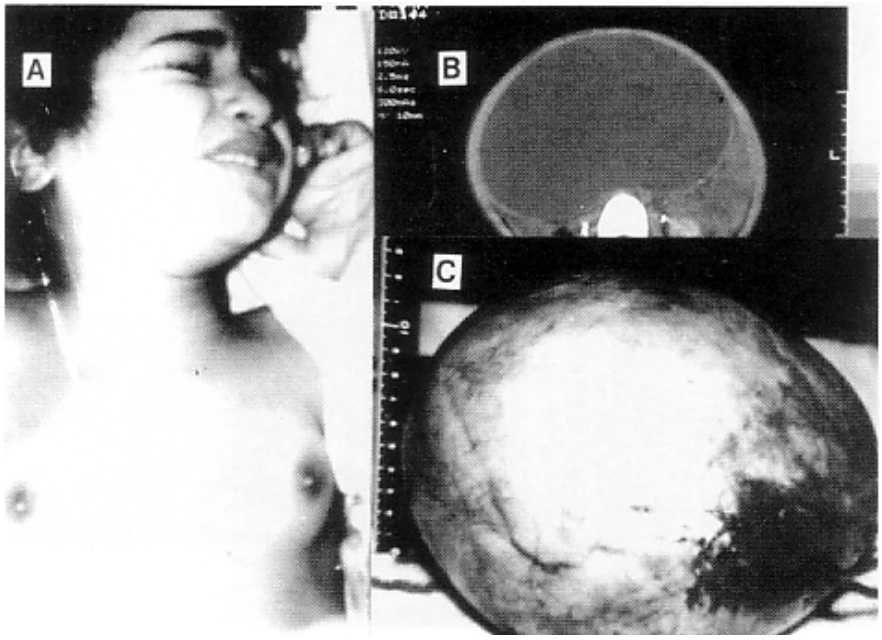

Fig (2):

A- *Premature thelarche in a 5-year old girl having a functional ovarian cyst.*

B- *CT scan of a right-sided follicular ovarian cyst.*

C- *Gross appearance of the huge follicular cyst after surgical excision.*

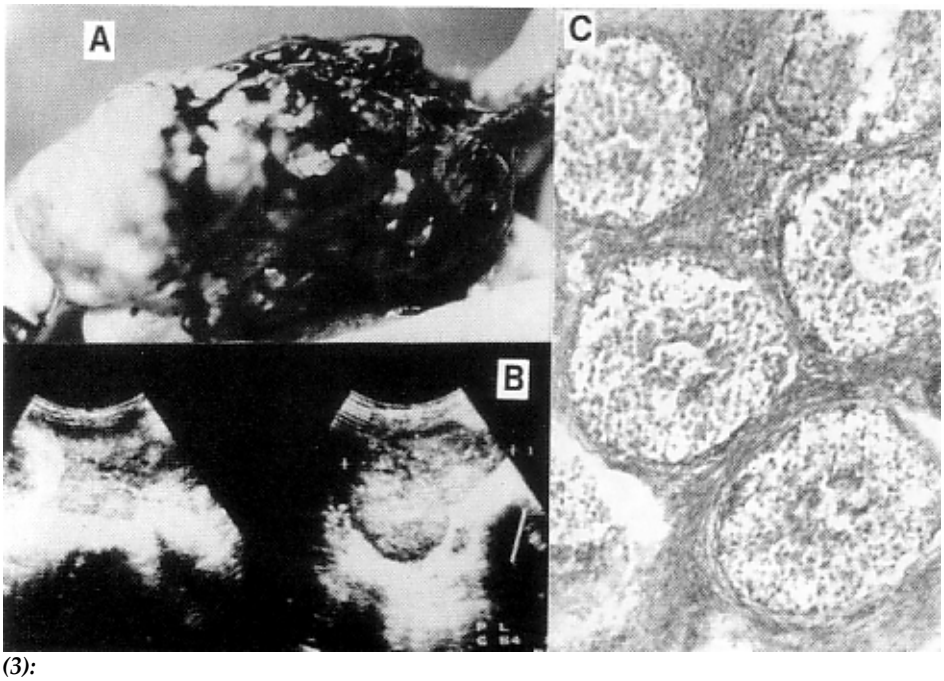

Fig (3):

A- *Operative view of a Brenner's tumor with the omentum adherent to the mass in a girl 3.5-year old.*

B- *Abdominal ultrasound showing the tumor with a heterogeneous echogenesity.*

C- *Micrograph of the tumor showing the characteristic nests of closely packed epithelial cells. (H & E x40).*

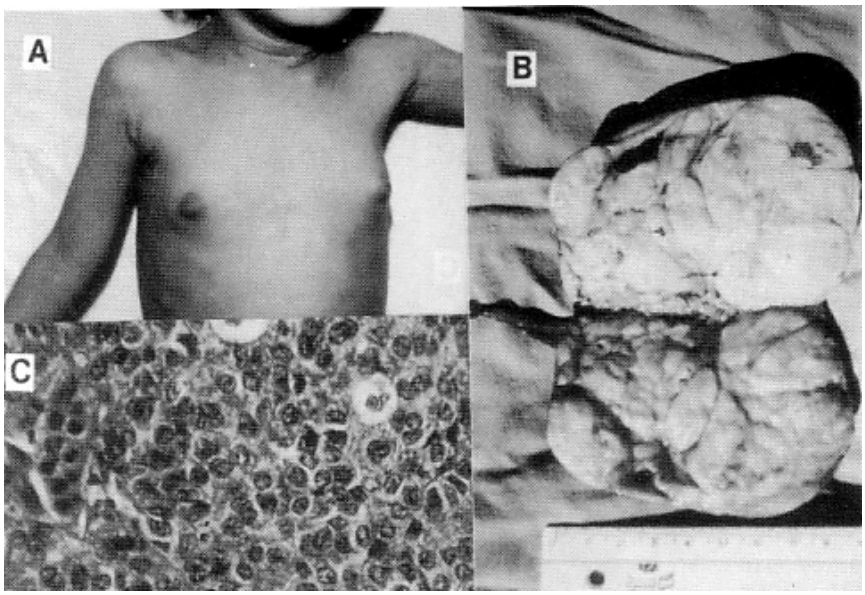

Fig (4):
A- *A premature thelarche in a 2.5-year old girl with functioning granulosa cell tumor.*
B- *Cut section of the tumor.*
C- *Histopathology of the tumor showing cuboidal- to-polygonal epithelial- appearing follicle cells. (H & E x100).*

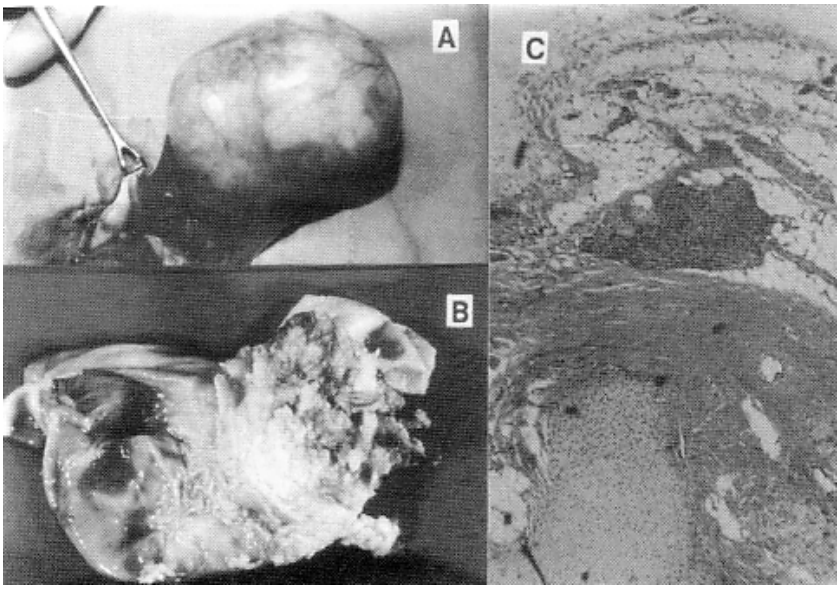

Fig (5):
A- *Mature teratoma of the left ovary in child aged 2.5 years; the right ovary is seen normal.*
B- *Cut section of the tumor. hairs and intestinal mucosa.*
C- *Histopathology of the tumor showing cartilage, fat and sympathetic ganglia (H & E x 40).*

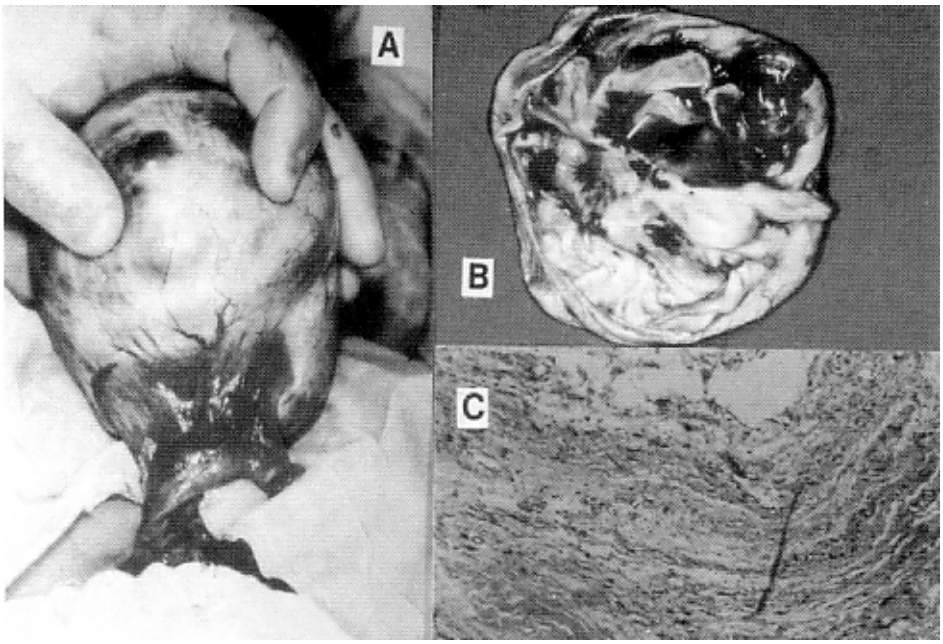

Fig (6):

A- *Operative view of a mature ovarian teratoma in a girl aged 12 years.*

B- *Cut section of the tumor.*

C- *Histopathology of the tumor showing stratified squamous epithelium with pigmented cells of neural crest origin (H & E x40).*

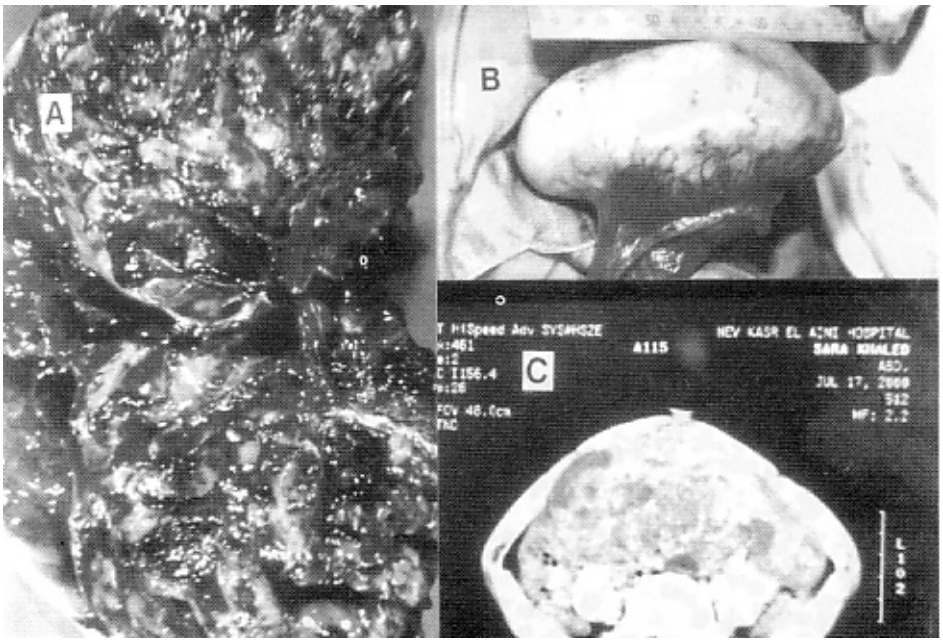

Fig (7):

A- *An immature teratoma of the right ovary in a girl aged 7 years.*

B- *CT scan of the mass showing areas of calcification and necrosis.*

C- *Cut section of the mass showing areas of hemorrhage and necrosis.*

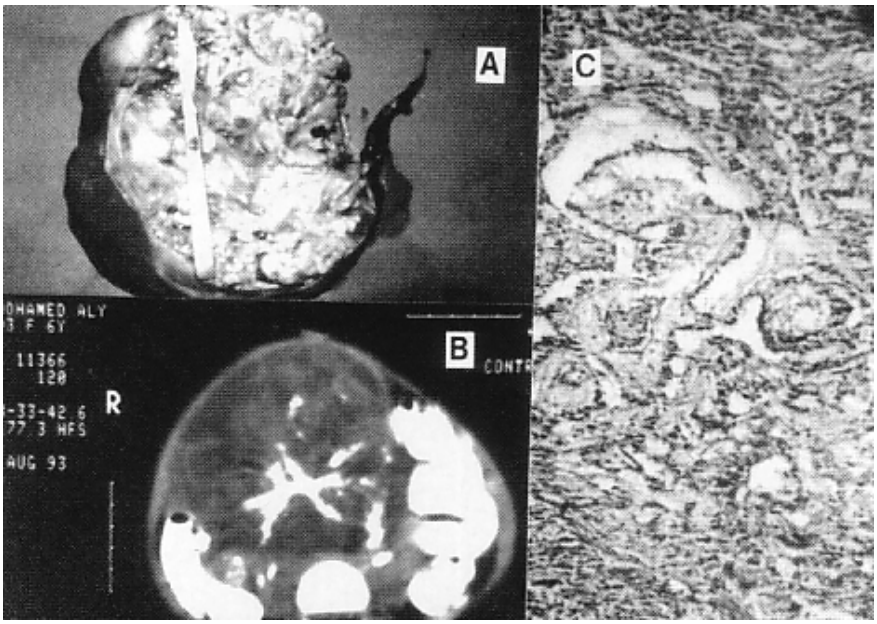

Fig (8):

A- *Cut section of a mixed immature teratoma with foci of endodermal sinus tumor.*

B- *C T scan of the tumor showing areas of calcification.*

C- *Histopathology of the tumor showing reticular areas formed of a loose meshwork lined by flat cells, rounded pseudopapillary processes with central vessels (H & E x40).*

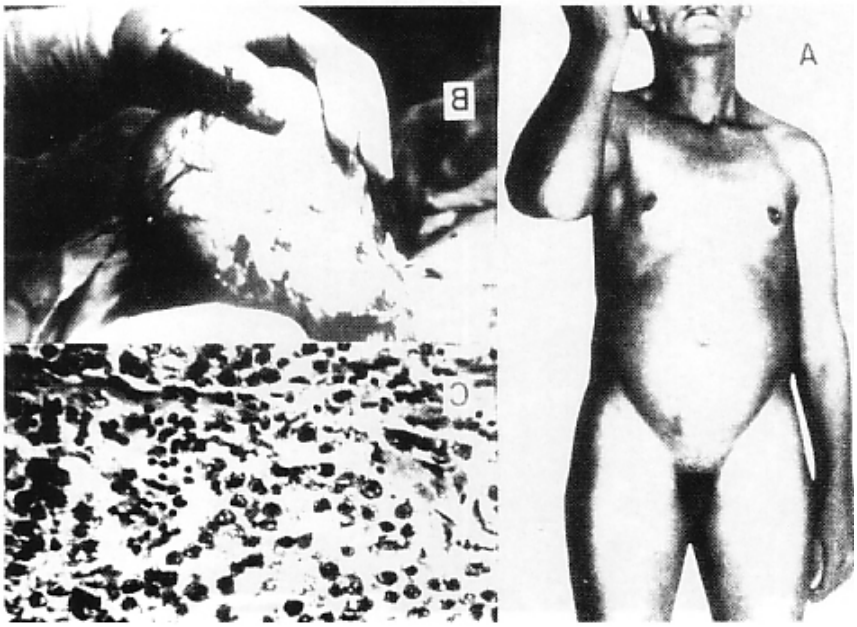

Fig (9):

A- *External appearance of a 17-year old patient reared as a male showing enlargement of the breasts, phallus of good size and an old scar of a left paramedian incision.*

B- *Intraoperative view of the huge tumor.*

C- *Histopathology of the dysgerminoma tumor showing well-defined nests of tumor cells with clear cytoplasm separated by fibrous strands containing numerous lymphocytes (H & E x 100).*

CLASSIFICATION	*TUMOR* Type	N	*AGE* Antenatal	0 - 1m	1m-1y	1 - 4 y	4 - 8 y	8 - 12 y	12 - 17 y	*No*
NON NEOPLASTIC	-Simple cyst	2	-	-	1	1	-	-	-	16
	-Follicular cyst	13	-	2	2	1	3	5	-	
	- Corpus luteum cyst	1	1	-	-	-	-	-	-	
NEOPLASTIC	EPITHELIAL									
	- Serous cystadenoma	2	-	-	-	-	1	1	-	3
	- Brenner's tumor	1	-	-	-	1	-	-	-	
	SEX CORD - STROMAL									3
	- Granulosa cell tmor	3	-	-	1	1	1	-	-	
	GERM CELL TUMORS									
	- Teratoma	18								
	- mature 12		-	-	-	2	6	3	1	
	- immature 6		-	-	-	-	1	4	1	23
	- Dysgerminoma	1	-	-	-	-	-	-	1	
	- Endodermal sinus tumor	3	-	-	-	1	1	1	-	
	- Embryonal carcinoma	1	-	-	-	-	-	1	-	
TOTAL		45	1	2	4	7	13	15	3	45

Table (1) *: Age distribution and histologic classification of the ovarian masses.*

ECHOGENICITY	*PATHOLOGY* *Type*	*N*	*TOTAL*
CYSTIC	- Simple cyst	2	14
	- Follicular cyst	11	
	- Serous cystadenoma	1	
COMPLEX	- Follicular cyst	2	19
	- Corpus luteum cyst	1	
	- Serous cystadenoma	1	
	-Brenner's tumor	1	
	- Mature teratoma	12	
	- Immature teratoma	2	
SOLID	- Granulosa cell tumor	3	12
	- Immature teratoma	4	
	- Endodermal cell tumor	3	
	- Dysgerminoma	1	
	- Embryonal carcinoma	1	

Table (2) : ***Sonographic classification of the ovarian masses and its pathologic correlation.***

STAGE	TUMOR	AGE	GRADE	N	MANAGEMENT			OUTCOME				FOLLOW UP
					Surgery	Chemotherapy	Radiotherapy	NED	Recurrene	2nd malig.	Died	Period
I	MT	1 - 12 y	-	12	O	-	-	12	-	-	-	6m - 3.5y
	IT	9y	1	1	SO	PEB	-	1	-	-	-	1.5y
II	IT	10y	1	1	SO	PEB	-	1	-	-	-	2y
	IT	8y	2	1	SO	PEB	-	1	-	-	-	1.5y
III	IT	7y	2	1	SO	PEB	-	1	-	-	-	2.5y
	IT	12y	2	1	SO+Om	PEB	-	1	-	-	-	3y
	Dys	17y	-	1	HSO	PEB	3000 rads	1	-	-	-	1.5y
	EST	6y	-	1	SO	PEB	-	1	-	-	-	1.5y
	EST	12y	-	1	SO	PEB	-	1	-	-	-	2y
	EC	6y	-	1	SO+Om	PEB	-	1	-	-	-	1.5y
IV	IT	3y	3	1	SO+Om	PEB	-	-	1	-	1	8m
	EST	4y	-	1	SO+Om	PEB	-	-	1	-	1	6m

Table (3) *: Staging, management and outcome of ovarian germ cell tumors.*

MT = mature teratoma, IT = immature teratoma, Dys = dysgerminoma, EST = endodermal sinus tumor, EC = embryonal carcinoma, O = oophorectomy, SO = salpingo-oophorectomy, HSO = hystero-salpingo-oophorectomy, Om = omentectomy, P = cysplatinum, E = etoposide, B = bleomycin

DISCUSSION

Although ovarian tumors are rare in children, they should be considered in the differential diagnosis when a girl presents with abdominal symptoms and a mass. Ehren et al reported 63 children with ovarian tumors in a 21-year-period [9]. Brown et al reviewed 91 patients less than 18 years old with ovarian masses between years 1979 and 1990[10].

Historical surveys demonstrated that increased age is associated with an increased incidence of ovarian lesions and a decreased risk of malignancy [11]. On the contrary, the present study showed that the risk of malignancy increased with age : the incidence of malignant lesions among the reported ovarian masses was 7% (n=1/14) in children younger than 4 years, 15% (n=2/13) in children 4 to 8 years of age and reached 44% (n=8/18) in those over 8 years of age. Among the neoplastic lesions (n=29), the incidence of malignancy increased from 19% in patients less than 8 years (n=3/16) to 61% in those above that age (n=8/13). This was in accordance with the more recent reports that confirmed that malignant ovarian tumors were more frequent in older children [12]. Brown et al detected 3% incidence of malignancy in patients prior to 8 years and 33% after that age [10]. La Vecchia et al reported an incidence of malignancy of 6 % of the neoplasms in children younger than 5 years of age, 21 % in children 5 to 9 years of age and 73 % in children 10-14 years of age, [2].

Previous reports have estimated that approximately one third of the children with ovarian masses will have nonneoplastic lesions [13,14]. Similarly the current study reported 35 % incidence of such lesions (n= 16/45) , follicular cysts formed the majority (81%) of cases.

In a review of 55 ovarian cysts and tumors in infants and children by Towne et al, 84% were germ cell tumors[15]. In a ten-year experience by Imai et al, 48% of 114 ovarian neoplasms in children and adolescents were germ cell tumors [16]. Browne et al reported 43% of 91 ovarian masses in patients younger than 18 years of age were germ cell tumors, more than half were malignant [10].

In the present study, germ cell tumors formed 51% of all reported ovarian masses (n=23/45), 48% of these were malignant (n=11/23). They represented 79 % (n=23/29) of the reported neoplastic lesions. Mature teratomas formed 41 % (n=12/29) of all neoplastic tumors in the series. Stromal and epithelial tumors formed 10 % each (n=3/29). These results were in concordance with that of Gangir et al who stated that they reported only 47 children with malignant ovarian tumors in the past 15 years. Of these 47 patients, 85% had germinal tumors, 10.6 % were stromal tumors and 4.4% epithelial tumors [17].

Before the introduction of ultrasonography, ovarian cysts in neonates were thought to be rare and could only be diagnosed postnatally. Only 71 cases were reported before 1976 [18]. The recent literature bounds in series from around the world of asymptomatic ovarian cysts diagnosed before birth [19,20]. In the present study, only one case of complex corpus luteum cyst with hemorrhage inside was diagnosed antenatally which emphasized the importance of screening for such lesions before delivery with close contact between obstetricians and pediatric surgeons in their management.

As several series reported that cysts under 5 cm may resolve spontaneously and are associated with low risk of torsion [21], only lesions above such size were operated upon in the current study. All cysts less than 5 cm in diameter (n=4) had resolved spontaneously with no recurrence.

In the present study, ultrasonography was accurate in identifying the origin of the lesions as "ovarian" in 80% of cases. This might be due to the difficulty to visualize the ovaries in very young patients. The application of Nussbaum's et al sonographic classification of fetal ovarian cysts [4] was extended to include all ovarian masses at different ages and the data were correlated to the pathological results. The implication of these results on the strategy of management in these cases was studied.

Complex cysts were removed regardless of their size as it was proved that among the 19 complex cysts recorded in the study, teratomas (n=14) and epithelial tumors (n=2) were diagnosed. This recommendation has been also reached by many authors [22]. Brandt et al stated that complex ovarian cysts should be removed because neoplasia cannot be ruled out. They reported that among 170 antenatally diagnosed ovarian cysts that were removed,, three cystadenomas and two teratomas were identified [21] .

As the stimulus for the formation of neonatal ovarian cyst is chorionic gonadotropin that stimulates the fetal ovary during pregnancy [23], the complex corpus luteum cyst diagnosed antenatally in the study resulted in a baby whose mother was diabetic with expected larger placenta and high concentrations of these hormones.

Most of the older literature recommended salpingo-oophorectomy in newborns [21]. In our study, ovarian cystectomy was performed in all cases as supported by all recent series except in a single serous cystadenoma operated upon early in the study where shelling out the cyst was not easy and in two cases of torsion where salpingo-oophorectomy was performed. Some authors suggested laparoscopic puncturing or fenestration of the cysts and the patient is followed up with serial ultrasound. Recurrence could be treated by repeated aspiration or surgical removal [18, 24]. This concept was not adopted in the present study. Mizumo et al reported two cysts that returned to their previous size few days following aspiration in a study that included 16 cases [20].

In the current study, estimation of the serum levels of the tumor markers in germ cell neoplasms was helpful in identifying and managing this group of tumors. All cases of endodermal sinus tumors (2 mixed with immature teratoma and one pure form) had elevated levels of AFP compared to the age-related normal values.[8]. It was also elevated in one case of immature teratoma although no foci of yolk sac were detected in the histopathologic examination. .These levels has raised four months after their postoperative decrease in a case of endodermal sinus tumor that developed local recurrence. Marina et al in a POG and CCG intergroup study on immature teratomas reported 8 of 31 patients with pure lesions had elevated serum levels of AFP [25].

Gobel et al explained the occasional elevation of B-HCG levels in cases of dysgerminoma to the presence of syncytiotrophoblast-like giant cells in their histology [26]. Gynecomastia reported in the case included in study may have resulted to the raised level of B-HCG or to the reversed high estrogen/testosterone ratio present in this patient.

LDH was not performed in the study as it was considered to be non-specific. Haase and Vinocur stated that this substance is widely distributed in human tissues and is therefore of limited value in establishing tumor type, response to treatment or both [1].

Recent studies demonstrated that conservative fertility-sparing surgery is the procedure of choice in young patients with pediatric ovarian tumors confined to one ovary. Advanced stages are not always accompanied by extensive pelvic disease and should not be a contradiction to preservation of the uterus and contralateral ovary [27,28].

In the present study, every effort was made to spare as much reproductive / endocrine tissue as possible. In non-neoplastic ovarian cysts, only those above 5 cm in

diameter or complicated by torsion or hemorrhage were excised. Simple cystectomy was only performed for uncomplicated cases. Those who were conserved (n=4) did not recurrecur. This conservative surgery was also performed for cases of mature teratomas with excision of the tumor and preservation of any remaining ovarian tissue with the fallopian tubes.

Although bivalving of the contralateral ovary for closer internal inspection was recommended by some authors for the incidence of bilaterality (10 %) in these tumors [29], yet this concept was not adopted to avoid ovarian tissue destruction and peritoneal adhesions that may later affect the fertility of the child. This approach was supported by Low et al [27].

Oophorectomy or salpingo-oophorectomy was performed in epithelial and stromal tumors. Haase and Vinocur stated that if such lesions are detected at the time of diagnostic laparoscopy, complete surgical staging and resection by conventional laparotomy is currently recommended due to the lack of sufficient data regarding the safety and efficacy of this approach in treatment of such lesions [1].

In malignant lesions, the uterus was only excised on block with the tumor in the case of dysgerminoma. Omentectomy and lymph nodal sampling were added in certain cases. Gobel et al stated that in general, there is no role for debulking surgery in pediatric germ cell tumors. Usually, surgery of metastases is not indicated unless they show an insufficient response to chemotherapy [26]. In the present study, two cases had liver metastases that partially responded to chemotherapy but unfortunately both have died 6 and 8 months following surgery from recurrence and progression of the disease.

Because germ cell tumors in children are relatively infrequent, studies usually combined germ tumors of all sites. As a result, it is difficult to extract the data for ovarian lesions only.

Forty years ago, no effective therapy for germ cell tumors existed[1]. Their use has clearly a major impact in converting this often-fatal disease into a highly curable one. Before chemotherapy, the risk of recurrence for adults with completely resected ovarian germ cell tumors ranged from 25% to nearly 100% [6]. Depending on their distinct biology, the histological subenteties differ significantly in their response to chemotherapy and radiotherapy. Germinomas are highly sensitive to both radio and chemotherapy.

Historical reports of the 1980s discussed treatment regimen including vincristin, actinomycin D, cyclophosphamide (VAC), and adriamycin combined with irradiation. Twelve of twenty (60%) children with ovarian germ cell tumors were alive and free of recurrence[30].Mann et al achieved a survival rate of 78% in 29 girls with ovarian germ cell tumors treated with cisplatin, vinblastin and bleomycin (PVB) [31].

From the 1980s, etoposide has been introduced as the first drug active in cisplatin resistant germ cell tumors. Nair et al reported their findings in 107 patients with germ cell tumors in children that included 43 girls with ovarian tumors, of these, only 22 received multiagent chemotherapy . A complete response was seen in 6 of 11 patients treated with PVB regimen compared with 10 of 11 patients who completely responded to treatment with PEB; with etoposide replacing vinblastin [32].

Recently some studies have shown the superior efficacy of carboplatinum regimen replacing the cisplatinum (JEB) in an attempt to reduce the cumulative nephro-and ototoxicity of the later [33]. On the other hand, Marina et al in a POG and CCG intergroup study of 73 patients with extracranial immature teratomas that included 44 patients with ovarian lesions, concluded that in children, regardless of the primary tumor location, these lesions could be treated effectively with surgical excision alone because the 3-year event-free survival was 93%. A comprehensive surgical staging procedure does not seem essential in the treatment of such patients. The combination of surgical resection followed by chemotherapy in cases of recurrent disease produced 3-year overall and tumor free survival of 100% and 98.6% respectively illustrating the excellent outcome of this group of patients [25].

In the present study, the PEB regimen was adopted in tumors of stage T2 (n=2), T3 (n=6) and T4 (n=2). Only one case of germ cell tumor - an immature teratoma was stage I disease. It remained disease free two years after surgery with no chemotherapy. A similar strategy has been used by Dark et al in a small number of women and children with completely resected stage I germ cell tumors with good results [34]. Since Dysgerminoma is reported to be highly sensitive to radiotherapy, 3000 rads has been given to the single case reported in the study. Although some authors omitted irradiation in pediatric ovarian dysgerminoma to preserve fertility [26], yet in the case included in the study, the other gonad was previously excised so that fertility was not an issue in its protocol of management.

The overall 1.5-year disease-free survival was 82%, but these results are preliminary due to the limited number of patients included in the study that also needs a longer follow-up period.

From this study it was concluded that the most important percept in the management of ovarian masses in children is the development of unique orientation

toward this problem. The dominant attitude should be unwillingness to accept the risk of overtreatment. In an adult, whose reproductive function may have been fulfilled, it is often permissible to chance a total aggressive surgical therapy in merely suspicious or tumors of potential malignancy, but this approach is not tolerable in the child. The surgeon must be cognizant of the peculiar behavior of the premenarchal ovary and familiar with gross appearance of the tumors seen in this age group and if the question of malignancy is raised, he should perform the most conservative surgery and not hesitate to accept the second look attitude.

REFERENCES

1. Haase GM, Vinocur CD : Ovarian tumors . In O'Neill J A, Rowe M I, Grosfeld J L, et al (Eds): Pediatric Surgery (ed 5) Mosby- Year book, pp 513-540, 1998.

2. La Vecchia C, Morris HB, Draper GJ: Malignant ovarian tumors in childhood in Britain, 1962-1978; Br J Cancer 48: 363-374, 1983.

3. Adkins J C : Malignant ovarian and other germ cell tumors. In Hays' DM Pediatric Surgical Oncology. Harcourt Brace Jovanovich (Pub), pp 123-137, 1986.

4. Nussbaum AR, Saunders RC, Hartman DS, et al: Neonatal ovarian cysts: Sonographic- pathologic correlation. Radiology 168: 817-821, 1988.

5. Serov SF, Scully RE, Sobin LH: Histologic typing of ovarian tumors. In International histologic classification of tumors, No 9, Geneva, World Health Organization, 1973, cited by Haase and Vinacur, 1998.

6. Norris HJ, Zirkin HJ, Benson WL: Immature (malignant) teratoma of the ovary. A clinical and pathologic study of 58 cases. Cancer 37: 2359-2372, 1976.

7. Joshi VV: Classification and grading of teratomas in children. In Common Problems in Pediatric Pathology. Joshi VV (ed), Igakushoin (Pub), pp 335-357, 1994.

8. Blohm ME, Vesterling-Horner D, Calaminus G, et al: Alfa 1- fetoprotein (AFP) reference values in infants up to two years of age. Pediatr Hematol Oncol 15: 135-142, 1998.

9. Ehren IM, Mahour GH, Isaacs Jr H : Benign and malignant ovarian tumors in children and adolescents. A review of 63 cases. Am J Surg 147: 339-344,1984.

10. Brown MF, Hebra A, Mc Geehim K and Ross III AJ: Ovarian masses in children: A review of 91 cases of malignant and benign masses. J Pediatr Surg 28: 930-933, 1993.

11. Norris HJ, Jensen RD: Relative frequency of ovarian neoplasms in children and adolescents. Cancer 30: 713-716, 1972.

12. Gribbon M, Ein SH, Mancer K: Pediatric malignant ovarian tumor: a 43-year review. J Pediatr Surg 27: 480-488, 1992.

13. Adelman S, Benson CD, Hertzler JH: Surgical lesions of the ovary in infancy and childhood. Surg Gynecol Obstet 141: 219-225, 1975.

14. Breen JL, Maxson WS: Ovarian tumors in children and adolescents. Clin Obstet Gynecol 20: 607-612, 1977.

15. Towne BH, Mahour GH,Wooley MM, Isaacs Jr H: Ovarian cysts and tumors in infancy and childhood. J Pediatr Surg 10: 311-320, 1975.

16. Imai A, Frurui T, Tamaya T: Gynecologic tumors and symptoms in childhood and adolescence: 10-years experience. Int J Gynecol Obstet 45: 227-230, 1994.

17. Gangir A, Smith J, Eys JV: Improved prognosis in children with ovarian cancers following modified VAC (Vincristin sulfate, Dactinomycin and Cyclophosphamide) chemotherapy. Cancer 42: 1234-1238, 1978.

18. Widdowson DJ, Pilling DW, Coock RCM: Neonatal ovarian cysts: Therapeutic dilemma. Arch. Dis Child 63: 737-742, 1988.

19. Griffith DM: Ovarian cysts and tumors. In Surgery of the Newborn. Freeman NV Burge DM, Griffith M, Malone PSJ. Churchill Livingston, pp 529-531, 1994.

20. Mizumo M, Kato T, Hebiguchi T and Yoshino H: Surgical indications for neonatal ovarian cysts (Abstract). Tohoku J Exp Med 186: 27-32, 1998.

21. Brandt ML, Lucks FT, Filitrault D, et al: Surgical indications in antenatally diagnosed ovarian cysts. J Pediatr Surg 26: 276-282, 1991.

22. Croitoru DP, Aaron LE, Laperge J, et al: Management of complex ovarian cysts presenting in the first year of life. J Pediatr Surg 26: 1366-1368, 1991.

23. Brower R, Dehner LP, Ternber J L: Bilateral ovarian cysts in the neonatal abdominal masses, polyhydramnios and maternal diabetes. Am J Dis Child 128: 731-733, 1974.

24. Van der Zee DC, Van Seumeren IGS, Bax KMA, et al: Laparoscopic approach to surgical management of ovarian cysts in the newborn. J Pediatr Surg 30: 42-43, 1995.

25. Marina NM, Cushing B, Giller R, et al: Complete surgical excision is effective treatment for children with immature teratomas with or without malignant elements: A Pediatric Oncology Group / Children's Cancer Group Intergroup study. Clin Oncol 17: 2137-2143,1999.

26. Gobel U, Sneider DT, Galaminus G, et al: Germ cell tumors in childhood and adolescence Ann Oncology 11: 263 –271, 2000.

27. Low JJH, Perrin LC, Gradon AJ, Hacker NF: Conservative surgery to preserve ovarian function in patients with malignant ovarian germ cell tumors. Cancer 89: 391-398, 2000.

28. Cushing B, Giller R, Ablin A, et al: Surgical resection alone is effective treatment of ovarian immature teratoma in children and adolescents: a report of the Pediatric Oncology Group and the Children's Cancer Group. J Obstet Gynecol 181: 353-358, 1999.

29. Comerci JT: Mature cystic teratoma: a clinicopathologic evaluation of 517 cases and a review of literature. Obstet Gynecol 84:22,1994.

30. Brodeur GM, Howarth CB, Pratt CB, et al: Malignant germ cell tumors in 57 children and adolescents. Cancer 48: 1890-1898,1981.

31. Mann JR : Results of the United Kingdom Children's Cancer Study Group's germ cell tumor studies. Cancer 63: 1657-1666, 1989.

32. Nair R Malignant germ cell tumors in childhood. J Surg Oncol 56: 186-193, 1994.

33. Baranzelli MC, Kramar A, Bouffet E, et al: Prognostic factors in children with localized malignant nonseminomatous germ cell tumors. J Clin Oncol 17: 1212-1218, 1999.

34. Dark GG, Bower M, Newlands E, et al: Surveillance policy for stage I ovarian germ cell tumors. J Clin Oncol 15: 620-624, 1997.