Ovarian Neoplasms in Adolescent Girls

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Ovarian tumors in the adolescent girl pose a special challenge since the need for preservation of genital tissue and reproductive function has to be balanced against the need for complete excision of the tumor. Though most of the ovarian neoplasms in this age group are benign, the possibility of a malignancy must be kept in mind.

Incidence

Functional ovarian cysts are very frequent in adolescents due to the higher incidence of anovulatory cycles in this age group. However, their incidence is not well documented since most are managed conservatively.

Ovarian neoplasms account for approximately 1% of all malignant tumors in girls aged 17 years or below (Young and Miller, 1975). In 26 cases of childhood ovarian tumors, 92% of the girls had a germ cell tumor (Oumachigui et al 1990). Epithelial tumors of the ovary are thus uncommon in childhood. However, in the adolescent age group the incidence of epithelial ovarian tumors increases (Breen and Maxson, 1977). Cyclic stimulation of the ovaries by gonadotrophins seems to be necessary for epithelial tumors and they therefore manifest at a later age. However, serous and mucinous tumors predominate and other tumors such as Brenner's tumor are rarely found. The incidence of epithelial tumors increased from 0.5% below nine years to 16% at the age of 10-14 years and further increased to 28% in the 15-17 year old age group (Breen and Maxson, 1977).

Clinical Presentation

Ovarian neoplasms in adolescent girls may be asymptomatic and may be detected as an incidental finding at a surgery such as appendicectomy or during a sonography done for some other reason. Many girls with an ovarian mass will complain of only vague discomfort such as abdominal fullness or bloating which is invariably treated with antispasmodics and antiflatulents. The vast majority of children with malignant ovarian tumors are detected at an advanced stage (Oumachigui et al, 1990). Though recurrent abdominal pain is a common complaint in young girls and ovarian neoplasia an extremely uncommon cause for the same, the clinician should not overlook ovarian neoplasia. Torsion may occur in as many as 35-40% of ovarian tumors in adolescents (Mahour et al, 1976, Ehren et al, 1984). Rarely, abdominal and/or flank pain may suggest a spinal cord tumor (Neinstein, 1989). Adnexal masses in young girls are more commonly associated with acute complications such as torsion, haemorrhage and rupture than are similar masses in adults. These individuals are frequently wrongly diagnosed to be suffering from appendicitis (Breen and Maxson, 1977; Orr et al, 1976). The use of imaging modalities such as X-ray and ultrasound will increase the diagnostic accuracy to 80 per cent (Orr et al, 1976).

Occasionally a young girl with a hormone producing ovaian tumor will present with, either pecocious puberty, abnormal vaginal bleeding or symptoms and signs of virilisation and hirsuitism. Tumors such as a dysgerminoma which destroy ovarian tissue may present as a case of amenorrhoea which then must be differentiated from tuberulosis which often presents as an abdominopelic mass due to encysted ascites in the Indian subcontinent. Endodermal sinus tumors grow extremely rapidly and classically a young female presents with pain and a lump in the lower abdomen and a history of fever over a period as short as only two weeks.

Other causes of abdominal distention should also be ruled out. An abdomino-pelvic mass with cyclic abdominal pain and amenorrhoea suggests a hematocolpos or hematometra secondary to an imperforate hymen or vaginal septum. An obstructed uterine horn can also result in haematometra and a pelvic mass. Though myomas of the uterus can occur in young girls they are extremely rare and a solid mass on sonography in a young girl is more likely to be a solid ovarian tumor than a fibroid. Pregnancy must be considered as a differential diagnosis of uterine enlargement.

Mesonephric and paramesonephric elements can also frequently give rise to cystic masses such as para-ovarian

and paratubal cysts in young girls. An important cause of an abdominal or pelvic mass in adolescence is pelvic inflammatory disease and especially tuberculosis. In 41 adolescent patients with a palpable mass in the abdomen seen by the author, the final diagnosis was tuberculosis in four cases and adnexal masses due to other infections in three cases (Krishna and Salvi, 1994). Masses arising from other systems such as tumors of the gastro-intestinal tract, urinary tract, musculo skeletal system or lymphatic system can also occur. A pelvic kidney may also be encountered on occasion and it is mandatory to confirm the presence of a normal kidney on pre-operative sonography or by palpation at laparotomy before proceeding to excise a retroperitoneal mass of doubtful origin.

Investigations

Imaging modalities such as songraphy, CT scan and MRI form the cornerstone for evaluation of these young individuals. The exact size, location, internal consistency, relationship with other structures and the presence of associated factors such as ascites, metastatic lymph nodes and spread to other organs such as the liver can be determined in a non invasive fashion. Plain X-Ray films of the abdomen and pelvis are especially useful in visualising calcification in teratoms (Ehren et al, 1984, Mahour et al, 1976).

Tumor markers are extremely useful in monitoring ovarian neoplasms. CA 125 is elevated in epithelial tumors. Alphafetoproteins (AFP) and human chorionic gonadotrophins (HCG) are elevated in endodermal sinus tumor and nongestational choriocarcinoma respectively. However, in embryonal carcinomas both AFP and HCG are elevated. HCG may also be elevated in polyembryoms or mixed germ cell tumors which consist of a combination of various tissue types.

In gonadal stromal tumors such as granulosa cell tumors or arrhenoblastomas, hormone assays and vaginal cytology are especially useful to monitor the individual. It is extremely important to differentiate tuberculosis as a cause of an abdominopelvic mass in the Indian sub-continent since the treatment in such cases would be essentially conservative. Tumor markers such as CA 125 may be elevated even in tuberculosis and therefore the clinician will have to resort to a combination of investigations such as a strongly positive Mantoux test and a positive blood or tissue fluid Elisa to arrive at a diagnosis.

Pathology of Ovarian Neoplasia in Adolescence

The majority of adnexal masses in adolescence will be functional cysts, which range in size from 3 cm to 10 cms. Of the ovarian neoplasms in female patients under the age of 21 years, germ cell tumors are the most common and about one third of germ cell tumors encountered in those below 21 years are malignant. As the girl approaches adulthood, the incidence of tumors of epithelial origin starts rising. The benign cystic teratoma has the highest incidence in this age group (Ehren et al, 1984; Lucraft 1979; Bennington et al 1968). In the study by Caruso et al, (1971) of 305 teratomas of the ovary, there were no cases among children below 10 years while 8.5 per cent of the tumors occurred in adolescent girls (menarche to 19 years.)

As many as 26 to 35 per cent of ovarian tumors in adolescence are malignant (Chakraborti and Lee, 1990; Ehren et al, 1984; Breen and Maxson, 1977). Solid or solid and cystic adnexal tumors, though rare in adolescence are almost always dysgerminomas or malignant teratomas.

Dysgerminomas are analogous to the seminoma of the testes and are bilateral in about 10% of cases. In 105 dysgerminomas reviewed by Asadourian and Taylor (1969) seven occurred in the age group of 0-9 years while three occurred between 10-19 years. The other germ cell tumors which are encountered in adolescent girls are immature teratomas, endodermal sinus tumors, embryonal carcinomas, polyembryomas, choriocarcinomas and mixed germ cell tumors. Immature teratomas account for upto 20% of the malignant ovarian tumors found in women under the age of 20 years and consist of immature embryonic structures that may be admixed with mature elements. The prognosis depends upon the FIGO stage (Table 1) and grade of the tumor. Grade 3 tumors consist of the most immature tissue and often have a higher proportion of immature neuroepithelium while grade 0 tumors have mature elements.

The histo-pathology of ovarian tumors in 30 adolescent girls managed at the King Edward Memorial Hospital, Mumbai is depicted in Table 2.

Management

Functional ovarian cysts which are less than 6 cms in diameter can be observed for 3 months. Oral contraceptives may be used for three months to promote regression. Surgery is reserved only for those cysts that persist or increase in size and in those where the initial size is over 6 cms. Cystectomy and not oophorectomy is the treatment of choice.

Benign ovarian neoplasms too should be managed by conservative surgery either by laparoscopy or laparotomy. Cystectomy with preservation of ovarian tissue is the treatment of choice and every attempt must be made to preserve any residual ovarian tissue. Salpingo ophrectomy is reserved for those cases with associated torsion and infarction. However, derotation of a twistted ovarian cyst with subsequent restoration of ovarian circulation followed by cystectomy has also been described. Mahour et al (1976) recommend bisecting the opposite normal ovary in ovarian teratomas since the incidence of bilaterality is 10-15 per cent. However, preoperative ultrasound imaging along with careful intraoprative inspection should be sufficient to exclude a cyst in the contralateral ovary. Bisecting the ovary may not be able to identify small tumors in the other ovary and has the added risk of periovarian adhesion formation resulting in infertility.

Generally malignant germ cell ovarian tumors that occur in women less than 20 years old are unilateral and if they are stage IA, only the involved ovary is removed. In more advanced cases, in which there are metastases, cytoreduction should be attempted. Since the chemotherapy is quite effective, tumor reductive resection may be less important for a cure, in non-epithelial varieties. Today with advanced imaging technology in young patients with an ovarian neoplasm the opposite normal appearing ovary need not be bisected or biopsied. However, the abdomen should be thoroughly explored to determine the presence of intraperitoneal and retroperitoneal spread. Suspicious areas should be biopsied and enlarged pelvic or paraaortic nodes excised.

Table 1:

FIGO Staging for Carcinoma of the Ovary

Staging of ovarian carcinoma is based on findings at clinical examination and by surgical exploration. The histologic findings are to be considered in the staging, as are the cytologic findings so far as effusions are concerned. It is desirable that a biopsy be taken from suspicious areas outside of the pelvis.

Stage 1	Growth limited to the ovaries.
Stage IA	Growth limited to one ovary; no ascites present containing malignant cells. No tumor on the external surface; capsule intact
State IB	Growth limited to both ovaries; no ascites present containing malignant cells. No tumor on the external surfaces; capsules intact
Stage IC*	Tumor classified as either Stage IA or IB but with tumor on the surface of one or both ovaries, or with ruptued capsule(s); or with ascites containing malignant cells present or with positive peritoneal washing.
Stage II	Growth involving one or both ovaries with pelvic extension
Stage IIA	Extension and/or metastasis to the uterus or tubes or both
Stage IIB	Extension to other pelvic tissues
Stage IIC*	Tumor either Stage IIA or IIB but with tumor on the surface of one or both ovaries; or with capsule(s) ruptured; or with ascites containing malignant cells present or with positive peritoneal washings.
Stage III	Tumor involving one or both ovaries with peritoneal implants outside the pelvis and/ or positive retro-peritoneal or inguinal nodes. Superficial liver metastasis equals stage III. Tumor is limited to the true pelvis but with histologically proven malignant extension to small bowel or omentum.
Stage IIIA	Tumor grossly limited to the true pelvis with negative nodes but with histologically confirmed microscopic seeding of abdominal cavity.
Stage IIIB	Tumor of one or both ovaries with histologically confirmed implants of abdominal peritoneal surfaces, none exceeding 2 cm in diameter; nodes are negative

Stage IIIC Abdominal implants greater than 2 cm in diameter and/or positive retroperitoneal or inguinal nodes.

Stage IV Growth involving one or both ovaries with distant metastases. If pleural effusion is present, there must be positive cytologic findings to allot a case to Stage IV. Parenchymal liver metastasis equals Stage IV.

Notes

1. This staging system reflects the clinical need to document whether the cancer is limited to the ovary or spread beyond the ovary. As such, extended surgical staging is a prerequisite to proper documentation. This would usually include peritoneal cytology, multiple peritoneal biopsies and omentectomy together with a sampling of the retroperitoneal nodes in those patients in whom the cancer is clinically limited to the ovary.
2. This system requires that ascites, if present, must contain malignant cells in order to advance the stage.
3. Diagnostic imaging techniques may be helpful in determining the need for primary referral but do not affect the staging except in the unusual event of intrahepatic metastases being present.

Pure dysgerminomas treated with unilateral salpingo-oophorectomy can recur in 20% of cases, primarily in tumors over 15 cms, but most of them can be effectively treated with additional surgery, irradiation or chemotherapy. Patients should be closely followed up postoperatively with periodic CT scans done to monitor the abdominal cavity and retroperitoneal lymph nodes. Lymphangiography may also be employed to observe the retroperitoneal lymph nodes. Since these tumors grow rapidly they may rupture spontaneously to cause intraabdominal haemorrhage. The vascular pedicle may twist resulting in necrosis and rupture. An emergency laparotomy is then required. Stromal cell tunors too, in young patients are most often unilateral and germ cell tumor even more so (Rutledge 1992).

Germ cell tumors of the ovary which were once thought to be uniformly fatal are now considered curable (Advani and Nair, 1995). The combinattion of vincristine, actinomycin and cyclophosphamide (VAC) in non-dysgerminomatous tumors administtered for 12 cycles

Table 2.

Histo-pathology of ovarian tumors in 30 adolescent girls at the King Edward Memorial Hospital, Mumbai

	No	%
Epithelial Tumors		
Cystadenoma-Serous	8	26.6
-Mucinous	5	16.6
Serous Cystadenofibroma	1	3.3
Stromal Sex Cord Tumours		
Thecoma	1	3.3
Germ Cell Tumours		
Dysgerminoma	4	13.3
Tetatoma -Mature	6	20
-Immature	1	3.3
Carcinoid	1	3.3
Gonadoblastoma	1	3.3
Mixed (Endodermal Sinus Tumour + Immature Teratoma)	2	6.6

produces a cure rate of 86% in stage 1 disease and sustained remission rate of 50% in patients with metastatic disease (Gershenson et al, 1985). Formey (1978) utilised a program of Actinomycin D, 5 fluorouracil and cyclophosphamide for endodermal sinus tumor. A combination of vinblastin, bleomycin and cisplatin (VBP) is also significantly effecttive (William et al 1989). Subsequently a combination of bleomycin, etoposide and cisplatin (BEP) was found to be equally effective and less toxic (Gershenson et al, 1990). Completely resected stage 1 – 111 tumors can be disease free after 3 cycles of BEP. In immature teratomas, chemotherapy is indicated for metastatic tumors (other than grade 0) and for stage IA tumors that are composed of grade 2 or 3 elements (Herbst, 1987). Chemotherapy may convert grade 2 or 3 metastases to mature elements (grade 0) which require no further therapy (Herbst, 1987).

Dysgerminomas are exquisitely radiosensitive and survival rates are excellent with doses less than 3000 rads required to cure extraovarian residual tumor after primary surgery or for recurrence. However, fertility is destroyed. In an attempt to preserve fertility, BEP has been used to replace radiation therapy in dysgerminomas (Nair et al, 1994). Though the BEP combination has been found to be the most effective regime in germ cell tumors with a complete response of 90%, the exact number of cycles

required is still unclear. Three to four cycles appear to be adequate in stage I or completely resected metastatic tumors while 5 to 6 cycles may be indicated for patients with bulky residual tumor (Advani and Nair, 1995). Tumor marker levels may help in monitoring the therapy.

Conclusion

The extent of the operative procedure in genital neoplasms in adolescent females presents a delicate problem since there is concern about the endocrine function of the ovary, somatic development, menstrual and reproductive function, potential malignancy and possible relapse. Thus, when faced with doubt a reexploration may be a better option than being unnecessarily radical at the initial surgery itself.

Very few studies have addressed the issue of educational achievement (Kelaghan et al 1988) and marriage and divorce (Byrne et al, 1989) in long term survivors of childhood and adolescent malignant neoplasms. Thogh it is obvious that these patients and their families require tremendous coping skills and psychological support both from medical workers and society at large, this aspect is often neglected.

The goal of any treatment strategy for neoplasms is to improve not only patient survival but the quality of that survival and this is even more relevant for adolescents. The quality of life is best achieved by optimal therapy and avoiding unnecessary or over treatment.

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