Ovarian Cancer in Children—
Guide for a Difficult Decision

Hugh R.K. Barber, M.D.

The difficulty of diagnosing ovarian cancer in a child is surpassed only by confusion over treatment. Although the ovary is the most common site of gynecologic tumors in children, fortunately, only one in 10 is malignant.

Ovarian neoplasms may occur at any time in childhood or adolescence, but tend to be more frequent between the ages of 10 and 14 years. This finding suggests that release of a control mechanism or pituitary stimulation of a latent factor may trigger tumor development.

Ovarian cancer poses certain problems in children that are not as significant in adults: it is associated with increased cachexia and ascites; larger tumors cause relatively greater pressure symptoms and dyspnea; evolution is more rapid, due to the limited space for tumor expansion; tumors generally have a higher degree of virulence as a result of the child’s less effective immunologic defenses. Of course, the effects of therapy on a child’s future development must always be considered.

Diagnosis

Ovarian cancer may produce few symptoms in the early stages. The degree of symptomatology and physical signs are in direct relation to the tumor’s rapidity of growth, location, degree of malignancy, potential for hormone production and possible complications such as torsion, rupture, hemorrhage or infection. Since ovarian tumors in children are abdominal and originate embryologically from the level of T10, not surprisingly, pain and mass in the abdomen are commonly seen. Pain may be due to the relatively small pelvic and abdominal cavities, which cause the new growth to stretch the peritoneum and produce pressure on adjacent organs.

General, pelvic and rectal examinations are essential. Rectal examination often indicates that the pelvis is free of tumor; however, a negative finding does not rule out ovarian cancer, which may frequently present as an abdominal mass in the early stages. In most instances it is impossible to palpate normal ovaries in children. Therefore, it can be assumed that if an ovary is enlarged on palpation, it is abnormal.

Baseline blood counts, urinalysis and blood chemistries must be obtained. A flat plate of the abdomen may help determine the presence of a dermoid cyst. If time permits, intravenous pyelograms and X-ray studies of the gastrointestinal tract are indicated. Radiologic studies of the bone age may be useful in a patient with a suspected hormone-producing tumor. A hormone assay profile may also be valuable in diagnosis; the alpha-
fetoprotein titer has been found to be elevated in extra-embryonal endodermal sinus tumors as well as certain embryonal carcinomas. Although rare, a hormone-producing tumor has a clinical picture related to the hormone it produces. Pneumoperitoneum has been used to outline small tumors, and ultrasonic methods have recently been introduced. The role of laparoscopy in assessing abdominal and pelvic masses in children must still be determined.

The clinical picture and physical findings usually point to the diagnosis. However, the differential diagnosis must include: appendiceal abscess, intussusception, obstruction, salpingitis, hematometra, pylonephritis. Wilms' tumor, neuroblastoma and retroperitoneal sarcoma.

**Treatment**

It is difficult to accept a diagnosis of ovarian cancer in a child, and even harder the surgery that deprives her of reproductive potential. Although therapy must be appropriate for the patient and extent of disease, generally the internal reproductive organs should be radically extirpated when a cancer has spread beyond the ovary. If a tumor is encapsulated and freely movable or if there is any doubt about the presence of tumor or its type, then it is usually best to perform a unilateral salpingo-oophorectomy. The pelvis should be aspirated, and the fluid sent for a cell block. If the tumor proves to be highly malignant, the abdomen may be opened and the remaining reproductive organs excised. In certain low grade cancers, unilateral salpingo-oophorectomy is adequate treatment.

**Tumors of Epithelial and Stromal Origin**

Although epithelial tumors comprise 90 percent of ovarian tumors, they are rarely seen in children, particularly before puberty. However, if an encapsulated, unilateral, mucinous or serous cystadenocarcinoma is found in a child in the absence of positive cells in the pelvis, unilateral salpingo-oophorectomy with bisection and biopsy of the opposite ovary is sufficient treatment. If there is any evidence of spread beyond the ovary, a total hysterectomy, bilateral salpingo-oophorectomy, appendectomy and omentectomy (if an omentum has been developed) should be performed. The role of $P^{32}$ has not been determined, but should be used as in the adult, with the dose lowered to 10 millicuries.

**Germ Cell Tumors**

Germ cell tumors are almost always found in children and adolescents, rather than adults. A knowledge of their natural history guides the surgeon in treatment. Dysgerminomas are highly radiosensitive and have a bilateral rate of five to 10 percent. Although controversial, therapy for an encapsulated, unilateral dysgerminoma in a young girl is unilat-
eral salpingo-oophorectomy. This is based on the assumption that there are no tumors in the opposite ovary, no positive para-aortic nodes and no positive cells in the pelvis, although some investigators dispute the value of cytology in these tumors. Patients should be followed every two months for the first two years with chest X-rays every six months. If there is any evidence of spread, total hysterectomy and bilateral salpingo-oophorectomy is advised. The role of postoperative X-ray therapy is best determined individually.

Embryonal teratoma, choriocarcinoma, endodermal sinus tumor and polyvesicular vitelline tumor are highly malignant. When unilateral and encapsulated, treatment by unilateral oophorectomy is as effective as total hysterectomy and bilateral salpingo-oophorectomy. Few survive surgery and radiation therapy has little to offer, since these tumors are relatively radioresistant. The role of combination chemotherapy must be established; however, reports indicate that increased survival rates may follow total hysterectomy, bilateral salpingo-oophorectomy and triple chemotherapy (vincristine, actinomycin D and cyclophosphamide).

More than 50 percent of ovarian tumors in children are benign cystic teratomas, which can be excised simply with preservation of the ovaries in most cases. In the occasional cancer arising in a cystic teratoma, unilateral oophorectomy is indicated, if there is no evidence of spread.

**Gonadoblastoma**

Gonadoblastomas are composed of both germ cells and gonadal stromal cells. Most patients are intersexual and have primary amenorrhea. Approximately 90 percent of the cases are chromatin negative. The most frequently encountered karyotypes are 46 XY and 45 XO/46 XY. Hyaline bodies, simulating Call-Exner bodies, are typical and foci of calcification are common. Calcifications may be demonstrated on X-ray studies of the pelvis and abdomen. Malignant potential is determined by the germ cell present. Approximately half of the gonadoblastomas are associated with dysgerminoma and are therefore relatively benign. Occasionally, endodermal sinus tumor, choriocarcinoma and embryonal carcinoma may represent the germ cell type present in the tumor and the malignancy rate is then increased. Since these tumors are commonly found in the intersexual patient, bilateral oophorectomy is indicated.

**Gonadal Stromal Tumors**

Some gonadal stromal tumors have the potential to produce either an estrogenizing or masculinizing effect. The only important malignant tumor of the female cell type is the granulosa cell cancer, which is usually unilateral and has a late recurrence rate beyond five years. Me-
tastasis or recurrence is typically confined to the pelvis. Since the tumor has a low grade of malignancy, conservative surgery in the form of unilateral oophorectomy is indicated when the tumor is unilateral and encapsulated.

Among the male cell types, the Sertoli-Leydig cell tumors (arrhenoblastoma) are the most significant and generally occur in women of childbearing age. When functioning endocrinologically, they feminize and then masculinize the patient. If malignant, such tumors usually spread within the pelvis and, rarely, to distant organs. Indications for conservative surgery are the same as for granulosa cell tumors. Since there is no correlation between the histologic findings and the clinical course, as well as the natural history of late recurrence, it is sound judgment to perform total hysterectomy and bilateral salpingo-oophorectomy after the patient has completed her family.

Gynandroblastomas comprise about 10 percent of gonadal stromal tumors and are composed of cells from both male and female cell types in about equal proportions. Management is the same as for granulosa tumors.

**Sarcoma of the Ovary**

Sarcomas of the ovary are relatively rare, but when present are generally found in children. Usually primary, they may be the result of secondary malignant change in a fibroma or teratoma. The tumor is highly malignant, and patients rarely survive five years. If encapsulated and unilateral, there is no advantage to radical over conservative surgery. However, with evidence of spread, total hysterectomy and bilateral salpingo-oophorectomy are indicated. Triple chemotherapy is given although its value has not been determined.

**Other Ovarian Tumors**

These tumors are not specific for the ovary, such as Burkitt’s lymphoma. Cytoxan treatment may be adequate to control Burkitt’s lymphoma, unless the ovary is greatly enlarged or complicated by torsion or hemorrhage. If the lymphoma is unilateral, oophorectomy is indicated; removal of a lymphoma should be followed by chemotherapy.

**Metastatic Ovarian Cancer**

Metastases to the ovaries do occur in children. For example, there are reports of Krukenberg tumors with a primary lesion in the upper gastrointestinal tract. As much of the tumor, primary and metastatic, should be removed surgically.

**Summary**

Ovarian cancer in children, beyond the localized stage, is one of the most frustrating of all gynecologic diseases. Total surgical extirpation of localized disease is the only hope for cure. As yet, early diagnosis is more a matter of chance than scientific method.