

EVERYONE'S GUIDE FOR CANCER THERAPY
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OVARIAN GERM CELL TUMORS

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Germ cell tumors account for approximately 5 percent of all ovarian malignancies. They almost always occur in women of reproductive age and are most frequently found in women in their teens or twenties. Many types of germ cell tumors are extremely aggressive, fast-growing malignancies. In the past they were often fatal within two years even though frequently confined to one ovary at the time of diagnosis. With surgery and modern multi-agent chemotherapy, the cure rate is excellent.

Types There are six main cell types: dysgerminoma, endodermal sinus tumor, embryonal carcinoma, choriocarcinoma, immature teratoma and mixed germ cell tumors.

There are also rare cell types such as struma ovarii, carcinoid and malignant transformation of a benign dermoid.

How It Spreads Ovarian germ cell tumors can spread directly to the adjacent pelvic organs and through the lymph system to the pelvic, aortic, chest (mediastinal), groin and neck lymph nodes. They may also spread to the surfaces of the abdominal cavity and to distant organs such as the liver, lungs and brain.

What Causes It The cause is not clear.

RISK FACTORS

At Significantly Higher Risk

- Premenopausal women.
- Women with abnormal (dysgenetic) ovaries usually containing male chromosomes.

SCREENING

No definitive screening method is available, except for a routine annual pelvic, abdominal and rectal examination.

COMMON SIGNS AND SYMPTOMS

These tumors often do not cause any symptoms. Some women, however, will have a rapidly enlarging pelvic or abdominal mass and vague pain in the lower abdomen. Other women can experience abnormal vaginal bleeding or acute abdominal symptoms, including pain and shock.

DIAGNOSIS

Physical Examination

- In addition to careful pelvic exam, a general physical examination should pay particular attention to the lymph nodes in the neck above the collarbone, the axillae and the groin.
- An abdominal examination may find an enlarged liver, a mass or masses or excessive fluid (ascites).

Blood and Other Tests

- Serum beta human chorionic gonadotropin (hCG) is elevated in choriocarcinoma.
- Serum alpha-fetoprotein (AFP) is elevated in endodermal sinus tumors.
- Serum lactate dehydrogenase (LDH) is elevated in dysgerminoma.
- One or more of the tumor markers-serum hCG, AFP and LDH-may be elevated in mixed germ cell tumors.
- Serum CA-125 may also be elevated.

Imaging

- Abdominal and pelvic CT scan (on occasion).
- Chest x-ray.

Endoscopy and Biopsy

- The definitive diagnosis is made on histologic evaluation of the removed ovary.

STAGING

The International Federation of Gynecology and Obstetricians (FIGO) staging classification for malignant epithelial carcinomas of the ovaries is also used for staging malignant germ cell tumors of the ovary. Germ cell tumors of the ovary are surgically staged.

Stage I

Cancer is confined to one or both ovaries.

- **Ia** Cancer is limited to one ovary. There is no tumor on the surface of the ovary, the surface of the tumor is unruptured and there is no ascites.
- **Ib** Growth is limited to both ovaries. There is no tumor on the surface of either ovary, the surface of the tumors is unruptured and there is no ascites.
- **Ic** The tumor is either Stage Ia or Ib, but there is tumor on the surface of one or both ovaries, at least one of the tumors has ruptured, ascites is present or the abdominal washings contain malignant cells.

Stage II

The cancer involves one or both ovaries with extension to other pelvic structures.

- **IIa** There is extension of the tumor or metastases to the uterus and/or the fallopian tubes.
- **IIb** There is extension to other pelvic organs such as bladder or rectum.
- **IIc** The cancer is either stage IIa or IIb, but there is tumor on the surface of one or both ovaries, at least one of the tumors has ruptured, there is ascites with malignant cells or the washings from the abdominal cavity contain malignant cells.

Stage III

The tumor involves one or both ovaries with tumor present outside the pelvis or there is cancer in the abdominal or groin lymph nodes.

- **IIIa** The tumor is grossly limited to the pelvis, but there is microscopic cancer involving the abdominal cavity (peritoneal) surfaces. The lymph nodes are negative.
- **IIIb** The tumor involves one or both ovaries, there are tumor implants on the peritoneal surfaces less than 3/4 in. (2 cm) in diameter. The lymph nodes are negative.
- **IIIc** The tumor involves one or both ovaries, there are tumor implants on the surface of the abdominal cavity greater than 3/4 in. (2 cm) in diameter or there is cancer in the pelvic, para-aortic or groin lymph nodes.

Stage IV

There are distant metastases to the liver or lungs or there are malignant cells present in the fluid accumulated in the chest cavity.

TREATMENT OVERVIEW

Surgery Surgical removal of the involved ovary or ovaries and removal of as much of the grossly visible tumor as possible is performed in all cases. If there is no spread beyond the ovaries, treatment will involve meticulous surgical staging, including removal of the pelvic and para-aortic lymph nodes, washings of the abdominal cavity to look for malignant cells and careful inspection of the abdominal surfaces with multiple, random

biopsies from the diaphragms and surfaces of the abdominal cavity. An omentectomy (removal of fatty tissue attached to the stomach and large intestine) will also be performed. Recently, laparoscopic minimally invasive surgery has been performed in selected cases with similar results.

The cell type of the tumor is an extremely important factor in determining the prognosis and the appropriate therapy after surgery.

Chemotherapy Women with a tumor confined to one ovary (Stage I) or with a well-differentiated (Grade 1) immature teratoma or dysgerminoma do not require postoperative chemotherapy. All others are usually treated with multi-drug chemotherapy.

Until recently, external radiation therapy to the abdomen and pelvis with a boost to the para-aortic node region was standard therapy for dysgerminomas, but chemotherapy is now used more often to preserve fertility.

Women with other malignant germ cell tumors are treated with chemotherapy after surgery because radiation therapy is ineffective. The most commonly used chemotherapeutic drug regimen includes cisplatin and etoposide with or without bleomycin given monthly for three or four courses.

Second-Look Surgery Occasionally, in women with Stage II, III or occasionally IV disease who have no evidence of persistent cancer after chemotherapy, "second-look" exploratory abdominal surgery is performed to see if they are truly disease-free.

Second-look surgery is not usually performed on correctly staged women with well-differentiated immature teratomas, Stage Ia and Ib dysgerminomas or other Stage I germ cell tumors who had elevated alpha-fetoprotein, hCG or LDH levels before treatment that returned to normal with chemotherapy. Women who have bulky disease after chemotherapy may occasionally benefit from a tumor debulking at a second surgery.

TREATMENT BY STAGE AND CELL TYPES

DYSGERMINOMAS

STAGE Ia

Standard Treatment The involved ovary and fallopian tube and a wedge biopsy of the opposite, normal-appearing ovary and meticulous surgical staging is performed in women who want to preserve their fertility. Women with Stage Ia disease require no further treatment.

About 20 percent of women will have microscopic disease in the opposite, apparently normal ovary (Stage Ib). For women who do not desire more children or who are approaching menopause, a hysterectomy and removal of both tubes and both ovaries is performed.

Investigational None.

STAGE Ib

Standard Treatment Women with this stage of disease are usually treated with three courses of cisplatin, etoposide with or without bleomycin or whole-abdominal radiation therapy after hysterectomy, removal of both fallopian tubes and ovaries and meticulous staging.

Investigational

- Combinations of chemotherapy including varying doses and combinations of carboplatin, cisplatin, ifosfamide, etoposide, vinblastin, and Taxol.
- High dose chemotherapy and autologous bone marrow rescue.

STAGE Ic

Standard Treatment After surgery most gynecologic oncologists recommend three courses of cisplatin, etoposide with or without bleomycin or less commonly whole-abdomen radiation therapy.

STAGES II, III, and IV

Standard Treatment Depending on the extent and location of disease, standard therapy includes a hysterectomy, removal of both tubes and both ovaries, aggressive tumor debulking and at least three courses of cisplatin, etoposide with or without bleomycin.

The opposite ovary and uterus can be preserved, if normal, in women who want to maintain their reproductive capacity. Whole-abdomen radiation may be given to those women who fail to respond to chemotherapy or who are not interested in preserving their reproductive function.

Investigational Same as Stage Ib.

NON-DYSGERMINOMATOUS GERM CELL TUMORS

These include endodermal sinus tumors, embryonal carcinoma, immature teratoma, choriocarcinoma and mixed germ cell tumors.

STAGE I

Standard Treatment Removal of the affected tube and ovary and surgical staging are generally all that is required since these tumors rarely occur in both ovaries.

Postoperative chemotherapy including cisplatin, etoposide with or without bleomycin is given to all patients with the exception of Grade 1 (well-differentiated) immature teratomas, for three or four courses.

Investigational

- Other chemotherapy, including varying doses and combinations of carboplatin, cisplatin, ifosfamide, Taxol, or etoposide, are currently under investigation.

STAGES II, III, and IV

Standard Treatment Depending on the extent and location of disease, a hysterectomy, bilateral removal of the tubes and ovaries, and aggressive tumor debulking is usually performed. If the opposite ovary and uterus are normal, they can be preserved in women who want to maintain their reproductive function. Four courses of chemotherapy including cisplatin, bleomycin and etoposide are given after surgery.

Investigational

- Experimental therapy for advanced non-dysgerminomatous germ cell tumors includes combinations of other chemotherapeutic drugs such as carboplatin, bleomycin, Taxol, ifosfamide or etoposide.
- High dose chemotherapy and autologous bone marrow rescue.

FIVE-YEAR SURVIVAL RATES

The five-year survival rate for Stages Ia and Ib dysgerminomas and Grade 1 immature teratomas is over 95 percent. Even women with Stage III dysgerminomas have approximately an 80 percent survival rate. Survival rates for women with Stages I and II non-dysgerminomatous germ cell tumors are greater than 90 percent. Women with Stage III and IV disease have survival rates estimated to be greater than 75 percent.

TREATMENT FOLLOW-UP

All women with germ cell tumors need careful follow-up every three months for the first two years after treatment.

- Follow-up should include a careful physical examination and serum hCG, alpha-fetoprotein and LDH and CA-125 levels (depending on which was elevated before therapy).
- Occasionally, radiologic studies such as an abdominal and pelvic CT or MRI scan are performed as required.

RECURRENT CANCER

Germ cell tumors may recur in the pelvis, the abdominal cavity, liver, lungs and lymph nodes. Symptoms may include pelvic or abdominal pain, bleeding, nausea, vomiting, abdominal swelling, weight loss and chronic cough.

- Women with recurrent cancer usually undergo an exploratory laparotomy with aggressive surgical debulking of the tumor.
- Women with recurrent dysgerminoma who did not receive chemotherapy or radiation therapy previously can be treated with combination chemotherapy or pelvic radiation up to a dose of 3,000 to 5,000 cGy over four to five weeks and whole-abdomen radiation therapy, up to 1,500 cGy, with a boost of up to 1,500 cGy to the para-aortic area over several weeks.
- Women with recurrent dysgerminoma who were initially treated with radiation therapy are treated with combination chemotherapy using drugs such as: cisplatin, carboplatin, etoposide, bleomycin, ifosfamide, vincristine, Taxol, or Cytosin.
- Women with recurrent non-dysgerminomatous tumors are generally treated with chemotherapy after surgery, as radiation is not effective on for these tumors. The chemotherapeutic drugs of choice are cisplatin + ifosfamide + bleomycin,

cisplatin + ifosfamide + etoposide or ifosfamide, vinblastine or vincristine + actinomycin-D + Cytosan, or carboplatin + ifosfamide.

THE MOST IMPORTANT QUESTIONS YOU CAN ASK

- What qualifications do you have for treating cancer? will a specialist in gynecologic oncology be involved in my care?
- What kind of germ cell tumor do I have?
- What stage is it?
- Will I still be able to have children?
- Will I need chemotherapy?
- Do I need a second-look operation?