Chapter 14

Cancer of the Ovary

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Anatomy of the ovary

There are 2 ovaries and each ovary is small, oval-shaped and attached to each side of the uterus via a thin, fibrous ovarian ligament (see Chapter 1). A layer of cells called the epithelial cells covers the surface of the ovary. Below the surface of the ovary, embedded in the tissues of the ovary called the stroma, are many minute structures called follicles. These follicles develop during ovulation to release oocytes (eggs). The central portion of the ovary is made up of stroma and blood vessels (Please also see chapter 5 benign ovarian cyst and video 5.1).

Types of Cancer of the Ovary

Cancer of the ovary can arise from the 3 tissues of the ovary namely:

1) **The epithelial layer - Epithelial Cancer of the Ovary**
2) **The follicles of the ovary - Ovarian Germ Cell Tumours**
3) **The stromal layer of the ovary - Ovarian Sex Cord Stromal tumours**

1) Epithelial Cancer of the Ovary

Incidence and mortality

This is the most common ovarian cancer. Its peak incidence is from 70 to 74 years of age. It is rare below the age of 40. Due to its location in the abdomen, this cancer is usually diagnosed at a later stage and so death from this cancer (mortality rate) is the highest among all gynaecological cancers.

Risk Factors

a) Nulliparous (women who have not delivered before) have a higher risk than women who have delivered one or more babies (parous women).

b) Breast feeding reduces the risk of this cancer

c) Tubal ligation reduces the risk of this cancer as well.

d) In women who are infertile, medication to induce ovulation such as clomiphene citrate, if taken for more than 12 months, may increase the risk.

e) Taking oral contraceptive pills reduce the risk.

f) Early menarche and late menopause may increase the risk.

g) Hormone replacement treatment may increase the risk slightly.

h) Patients with a history of breast cancer have a higher risk of this cancer.

i) Risk of ovarian cancer is higher in women who have first degree relatives with ovarian cancer.

j) High intake of meat and animal fat increases the risk.

k) High incidence of ovarian cancer has also been attributed to obesity.

Cause

The cause of epithelial ovarian cancer is not known. It is believed to be due to a defect in the repair process of the surface epithelium after frequent ovulation.

Prevention

a) Oral Contraceptives: Taking oral contraceptive pills for a duration of at least 5 years reduces the relative risk of developing epithelial ovarian cancer by 50%.

b) Tubal ligation and hysterectomy reduce the risk as well.

c) Prophylactic oophorectomy (removing the ovaries) reduces the risk by 80%.

d) Genetic testing in patients with high risk of developing ovarian cancer.

Screening for ovarian cancer

There is no effective screening method to detect early ovarian cancer. The following screening tests have been evaluated:

a) Pelvic examination: This has limited value in detecting ovarian cancer.

b) Transvaginal ultrasound: Transvaginal ultrasound is sensitive in detecting lesions in the ovaries but it is not specific enough to say that the lesions are cancer.

c) CA125 (g) is a tumour marker (g) that is raised in many pelvic and abdominal conditions. It is not a specific marker for cancer of the ovary. This means that if it is raised it does not mean that the woman has ovarian cancer. There are many non-cancer diseases (eg endometriosis) that can cause a rise in CA 125. However, if it is done serially, a rise in its level may indicate ovarian cancer.

d) Multimodal screening: Several studies are ongoing in this area, looking at a combination of transvaginal ultrasound and CA125 to screen the population for ovarian cancer.

Types of epithelial ovarian cancer

a) Serous
b) Mucinous
c) Endometroid
d) Clear Cell
e) Transitional cell
f) Undifferentiated

Symptoms

a) abdominal discomfort, pain, distension
b) nausea,dyspepsia,constipation
c) irregular vaginal bleeding

Diagnosis

a) Abdominal examination: The abdomen may feel distended with fluid. Masses may be felt in the abdomen.
b) Pelvis examination: masses may be felt next to the uterus
c) Abdominal and transvaginal ultrasound: Ovaries may be seen to be enlarged with solid and cystic areas. Fluid may also be seen in the abdomen (ascites)
d) CT and MRI scans of the abdomen and pelvis: This may show ovarian masses with or without ascites. Nodules may be seen in other parts of the abdomen including the omentum and/or liver. Pelvic and/or paraaortic lymph nodes may also be enlarged.

Staging

Stage 1 : Growth limited to the ovary

Stage 1A : Limited to one ovary

Stage 1B : Limited to both ovaries

Stage 1C : Tumour 1A/1B with tumour on the surface or capsule rupture or malignant cell in ascites /peritoneal washout

Stage 2 : Growth involving one or both ovaries with pelvic extension

Stage 2A : Extension and/or metastases to the uterus and/or tube

Stage 2B : Extension to other pelvic tissues

Stage 2C : Tumour stage 2A/2B with tumour on the surface of ovaries or capsule rupture or malignant cell in ascites /peritoneal washout.

Stage 3 : Tumour in one or both ovaries with histologically confirmed extension outside the pelvis

Stage 3A : Tumour grossly limited to true pelvis with microscopical seedling

Stage 3B : Tumour of one or both ovaries with implants not exceeding 2cm in diameter

Stage 3C : Peritoneal metastasis of more than 2 cm

Stage 4 : Growth involving one or both ovaries with distant metastases.

Treatment

Treatment will depend on the stage of the disease, the health of the patient and whether fertility is to be preserved.

a) Surgery

Surgery is the mainstay of treatment in ovarian cancer. Sometimes the stage of the ovarian cancer can only be confirmed during surgery.

In patients with advanced cancer (stage 2 and above) surgery will involve removal of the uterus (hysterectomy), both the ovaries (salpingoophrectomy) and the omentum; a fatty layer of tissue within the abdomen (omentectomy). The lymph nodes in the pelvis and abdomen may also be removed. If the cancer has spread into the abdominal cavity, all visible cancer tissues will be resected.

If the cancer is only in one ovary and is of low malignant potential, than just removal of the ovary may be sufficient (salpingoophrectomy). This will preserve (not affect) fertility.

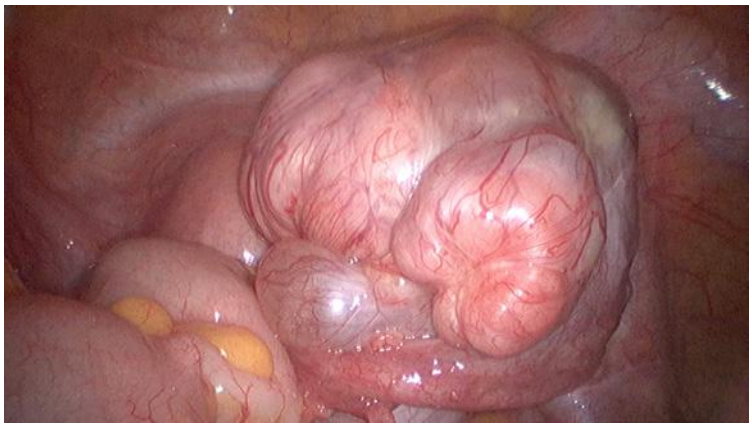

Figure 14.1 Laparoscopy showing a right ovarian cancer

Figure 14.2 large ovarian tumor
at the time of surgery

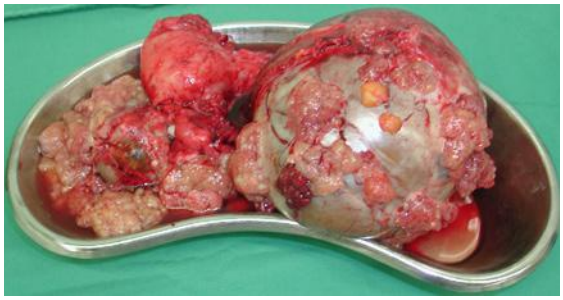

Figure 14.3 Surgery specimen
(Total abdominal hysterectomy and bilateral
salpingoopherectomy and omentectomy)

b) Chemotherapy

Chemotherapy is a procedure using anti-cancer drugs to kill cancer cells. This treatment is often given after surgery. Sometimes, especially in advanced ovarian cancer, chemotherapy may be given before surgery to shrink the tumour so as to make the surgery easier. This is called neoadjuvant chemotherapy.

There are many different drugs that can be given in chemotherapy for cancer of the ovary. Often, a combination is given. The choice of drug, and how and when it is given, depends on the stage of the cancer and how much it has spread. The most common treatment for ovarian cancer is a platinum-containing drug (carboplatin), which is used alone or in combination with other drugs such as paclitaxel.

Chemotherapy is usually given as a drip into the vein, but it is sometimes given as tablets. Some studies have looked into giving chemotherapy directly into the abdomen. This is called intraperitoneal chemotherapy. Most often, chemotherapy is given as outpatient treatment, but sometimes a short stay in hospital may be necessary. It is usually given in cycles, with a period of treatment followed by a period of rest, to allow the body to recover. Most women are given six cycles of chemotherapy.

Monitoring during chemotherapy

During chemotherapy, several things can be done to see whether the treatment is effective

a) If the CA125 is high before surgery or chemotherapy, but decreases after this indicates that the cancer is responding to chemotherapy.

b) If the tumour is visible on a CT or ultrasound scan when diagnosed, repeated scans may be done to see whether it has shrunk

c) Sometimes another operation, known as 'second-look surgery', can be carried out usually by laparoscopy to see whether the cancer has shrunk

If, after chemotherapy, all tests show that the patient is clear of cancer, then the patient is said to be in remission. This means that the cancer is under control.

Side effects of chemotherapy

Chemotherapy not only destroys cancer cells, it also destroys normal cells especially immune cells. Side effects include:

a) Infections

b) Loss of appetite

c) Nausea and vomiting

d) Tiredness

e) Loss of hair

f) Sore mouth

Many of these side effects can be prevented or controlled with medication

Chemotherapy for cancer that has relapsed (come back)

Ovarian cancer can relapse after treatment. If this happens, another course of chemotherapy may be necessary. The same drugs can be given again or a different combination of chemotherapy drugs may be administered. This is called second-line treatment. The choice of drugs will take into account which drugs were used in previous treatments, and the side effects and benefits of the drugs.

c) Radiotherapy

Radiotherapy is usually not used to treat ovarian cancer except in exceptional circumstances.

Prognosis

5 year survival rates are as follows

Stage	5 year survival rate
1	91.5%
2A	83.5%
2B	66.5%
3A	45%
3B	36%
4	14%

2) Germ Cell tumours of the ovary

Ovarian Germ cell tumours are tumours that arise from the cells that will become eggs (ovum) in the ovary. The majority of ovarian germ cell tumours are benign and are called dermoid cysts or mature teratoma (see chapter 5). Malignant ovarian germ cell tumours are rare accounting for 1-2 % of all ovarian malignancies.

Classification

There are many types of malignant Germ cell tumours of the ovary. The most common are:

a) Dysgerminoma
b) Yolk-sac tumours
c) Immature teratoma
d) Mixed germ cell tumours

Causes of germ cell tumours

The cause of germ cell tumours is unknown. Germ cells are a normal part of the ovary, but sometimes changes in these cells make them divide and grow too quickly to become a tumour.

Signs and Symptoms

a) Abdominal distension with a palpable abdominal mass
b) Acute abdominal pain due to twisted, haemorrhage or ruptured ovarian cyst.
c) Abdominal distension
d) Fever
e) Abnormal vaginal bleeding
f) Increasing need to pass urine

Diagnosis

Several tests can be performed to make a diagnosis of this tumour

a) Blood tests

Elevation of AFP (alpha-fetoprotein) and serum beta HCG (human chorionic gonadotrophin) is suggestive of ovarian germ cell tumours in young women.

b) Ultrasound scan

Ultrasound scans can be done both abdominally and transvaginally to look at pelvic organs. Enlargement of the ovaries can be visualised on ultrasound.

c) CT (computerised tomography) scan

A CT scan may be performed to have a three-dimensional view of the abdomen and pelvis.

Staging

Staging of these tumours is similar to that of epithelial cancer stated earlier in this chapter.

Treatment

Most women with malignant germ cell tumour of the ovary can be cured. Treatment will depend on the site and type of germ cell tumour. Treatment is usually a combination of surgery and chemotherapy.

a) Surgery

In most women, the tumour only involves 1 ovary and so surgery is performed to remove just that ovary and the fallopian tube (unilateral salpingoophrectomy). If this is the surgery performed, then fertility is preserved. However, if both the ovaries are involved then both the ovaries and the uterus may need to be removed (total abdominal hysterectomy and bilateral salpingoopherectomy).

b) Chemotherapy

Malignant Germ cell tumours are very sensitive to chemotherapy. Except for stage 1 disease, chemotherapy is essential to destroy these tumours.

c) Radiotherapy

Occasionally, certain types of germ cell tumours may require radiotherapy.

Fertility

These tumours are often found in young women. If only one ovary is removed, then there is a chance of future pregnancy. If chemotherapy is given, sometimes the remaining ovary may fail to produce eggs but generally, ovulation will resume after completion of the chemotherapy.

If both the ovaries are removed, then the patent will be in menopause. In some women who still have one ovary but have undergone chemotherapy, menopause may occur. Patients who are in menopause will require hormone replacement therapy.

3) Ovarian Sex Cord-Stromal tumours

Ovarian sex cord-stromal tumours originate from the cells in the ovarian matrix (which comprises granulosa, theca, sertoli and leydig cells as well as fibroblasts of stroma origin). The ovarian matrix supports these germ cells. Many of these tumours are steroid producing tumours. Unlike epithelial ovarian cancer, these cancers usually present at stage 1 at diagnosis,

Classification

The most common types of ovarian sex cord-stromal tumours are as follows

a) Fibroma
b) Granulosa cell tumours
c) Sertoli-Leydig cell tumour
d) Thecoma
e) Sertoli cell tumour
f) Leydig cell tumour
g) Fibrosarcoma
h) Sclerosing stromal tumour
i) Mixed or unclassified cell type

Signs and symptoms

Signs and symptoms will depend on the type of tumours

a) Abdominal swelling and/or distension: Fibromas can present with fluid in the abdomen (ascitis) and/or lungs (hydrothorax) and this is called Meig's syndrome
b) Abdominal pain
c) Female hormone (oestrogen) producing tumours may cause: early puberty (precocious puberty), irregular and heavy menses as well as postmenopausal bleeding.
d) Male hormone producing tumours may cause virilization symptoms (eg hoarseness of voice, excessive body hair, acne)

Diagnosis

a) Examination

Physical examination may reveal a pelvic and abdominal mass. Fluid in the abdomen (ascites) may be detected

b) Ultrasound

Ultrasound will show a tumour in one or both ovaries. These tumours are usually solid with some cystic areas.

c) CT scan

CT scan can be done to confirm the ultrasound findings. CT scan may show enlarged lymph nodes.

Treatment

a) Surgery

Surgery is the mainstay of treatment for this type of tumours. Surgery will depend on the age of the patient and her desire for future pregnancy. The surgery of choice is usually removal of the affected ovary and tubes (salpingoophrectomy) with conservation of the uterus and the other tube.

b) Chemotherapy

When the possibility of cancer spread is high (eg large tumours, ruptured during surgery or lymph nodes positive) chemotherapy may be indicated.

c) Radiotherapy

Radiotherpay may be necessary in inoperable or recurrent cases.

d) Hormonal treatment

Tamoxifen (antioestrogen), gonadal releasing hormone agonist and high dose progesterone have been tried for advanced and recurrent tumours.

Prognosis

The five year survival rates for the most common malignant ovarian sex-cord tumour, the granulosa cell tumour is a follows:

Stage	5 year survival rate
1	100-90%
2	75-55%
3	50-22%

Summary

Cancer of the ovary can originate from the 3 layers of the ovary namely the epithelium, the stroma and the germ cells. Epithelial ovarian cancer is the most common type. As the ovary is an Intra-abdominal structure, many cases of cancer of the ovary are diagnosed late. Surgery is the mainstay of management for cancer of the ovary. The type of surgery will depend on the stage of the cancer. Very early cancer of the ovary may be managed by simply removing the involved ovary. In more advanced cancer, removal of the uterus and both ovaries with removal of the omentum and pelvic lymph nodes may be necessary. The patient will also need to under chemotherapy after surgery.