Ovarian Cancer: A Case Report

Abstract

Ovarian cancer is a very common cancer among women. It is an extremely diverse disease requiring several treatment options. Occasionally ovarian cancer is diagnosed during pregnancy. An unusual case study is presented showing in-vitro fertilization affecting the growth of an ovarian tumor.

Introduction

Ovarian cancer is extremely hard to diagnose in its early stages.\(^1\) Patients who are eventually diagnosed with ovarian cancer are typically asymptomatic and in the late stages where the cancer has metastasized to other organs.\(^1\) Approximately 15\% of all ovarian cancer are diagnosed at an early stage.\(^1\) The five year survival rate for stage I ovarian cancer is approximately 92\% but the survival rate decreases dramatically as the stage of the cancer increases, approximately 18\% for stage IV ovarian cancer.\(^1\) Early stage ovarian cancer at times is diagnosed during pregnancy. Due to the early stage of the cancer, survival rates are better but the questions arise of how to treat the cancer. Surgery can be performed in some cases but chemotherapy must wait until after the patient has delivered the baby.

Treatments are dependent on the histologic diagnosis of the tumors. There have been over 100 types of ovarian tumors characterized, each with a very different treatment and management plan.\(^3\) Ovarian tumors are classified into three very broad categories, epithelial ovarian tumors, germ cell ovarian tumors, and sex cord stromal ovarian tumors.\(^1\) Each category is subdivided several times depending upon the attributes of the tumor. Correct diagnosis of the tumor will lead to better treatment options for each patient.

Causes, incidence and risk factors

The exact cause of ovarian cancer is unknown. According to the American Cancer Society in the year 2013 in the United States approximately 22,240 women will be diagnosed with ovarian cancer and about 14,230 women will die from ovarian cancer.\(^1\) Ovarian cancer ranks ninth in the most common cancers among women and fifth in cancer deaths among
women. It is the cause of more deaths than any other cancer of the female reproductive system. Many risk factors have been attributed to ovarian cancer and include the following:

- Age of the women; older women are at the highest risk of developing ovarian cancer.
- Reproductive history; women who have fewer children and the later in life she gives birth are at a higher risk of developing ovarian cancer.
- Estrogen only replacement taken for more than five years will increase the risk but birth control pills will decrease the risk.
- Fertility drugs may or may not increase the risk of developing ovarian cancer.
- Family history of ovarian cancer; breast cancer or colorectal cancer can also increase the risk of developing ovarian cancer.
- Personal history of breast cancer will also increase the risk especially if there is a mutation in the BRCA1 or BRCA2 genes.\(^1\-^4\)

**Symptoms**

The symptoms of ovarian cancer are often vague or attributed to or blamed on other more common conditions. The following are the more common symptoms that can be caused by ovarian cancer:

- bloating or swelling of the abdomen
- difficulty eating or feeling full quickly
- lower abdominal or pelvic pressure and pain and/or the need to urinate more often than normal

Other possible symptoms may include the following:

- abnormal menstrual cycles
- digestive problems
- vaginal bleeding that occurs between periods
- sudden weight gain or loss
- back pain with an unknown reason that worsens over time
- excessive hair growth that is coarse and dark

If any of these symptoms occur on an almost daily basis for more than a couple of weeks an appointment with a gynecologist is recommended.\(^1\-^3\)
Diagnosis

Once an appointment is made with a gynecologist a patient will undergo several tests to help determine whether or not they have ovarian cancer. A patient's history is taken and a physical exam is performed looking for signs of ovarian cancer. The physician will be looking for masses on the ovaries, abdominal masses or signs of fluid in the abdomen. Further testing will be ordered if the physician believes there are signs of ovarian cancer. Imaging studies will be performed to confirm whether or not a mass is present. Ultrasound is the preferred imaging modality of physicians when a patient's ovaries or abdomen are suspected of having a mass. Ultrasound will also be able to distinguish if a mass is solid, typically a tumor, or if it is a fluid filled cyst.

If a mass is found further testing is conducted. Blood work and other imaging modalities, computed tomography (CT), magnetic resonance imaging (MRI) and positron emission tomography (PET) scans, may be used to diagnose the type and stage of the ovarian cancer that has been discovered. Blood work will look for a patient's red blood cell count, white blood cell count and platelet count along with looking at liver and kidney functions and a patient's CA-125 count and many more levels of substances found in the blood that may indicate which type of ovarian cancer is present. Patients with a high CA-125 score are more likely to have some type of cancer. CT, MRI and PET scans will be conducted to find out whether or not tumors are present and to detect if the cancer has metastasized to other parts of the body. A patient diagnosed with ovarian cancer will undergo further tests to determine the type and stage of the ovarian cancer present. These tests include laparoscopy of the abdomen and pelvic region, colonoscopy and biopsy of the tumors to help stage and type the cancer so that a treatment plan can be built around the patient's ovarian cancer.

Stages and types of ovarian cancer

Ovarian cancer is staged according to the AJCC/TNM System. The letter T describes the extent of the primary tumor, N is the absence or presence of metastasis to nearby lymph nodes and M is the absence or presence of distant metastasis. Each category is then subdivided depending on several different factors, location, metastasis, lymph node involvement and size of tumor are just a few (see Figure 1). Each TNM category can then be used to describe the tumor in each of the four stages that describe how advanced the cancer is. Stage I cancer is still
contained within the ovary or ovaries. Stage II cancer has spread from the ovary or ovaries to nearby tissues in the pelvis but has not spread to lymph nodes, the lining of the abdomen or distant sites. Stage III cancer has spread beyond the pelvis to the lining of the abdomen or to the lymph nodes. Stage IV cancer is the most advanced, it has spread to the liver, the lungs or other organs located outside the peritoneal cavity. Ovarian cancer that has went away with treatment and then recurred is classified as recurrent ovarian cancer (see Figure 2).  

**Broad Classifications of Ovarian Cancer**

Ovarian cancer is broadly classified into three classes. Each class of ovarian cancer is distinguished from one another by the tissue in which it is found in the female reproductive system (see Figure 3). The following discusses each broad classification and their respective subdivisions.

**Class I: Epithelial Ovarian Tumors**

These tumors are derived from the epithelium cells on the surface of the ovary and are referred to as surface epithelial tumors. Epithelial ovarian tumors are the most common form of ovarian cancer, accounting for approximately 80% of ovarian tumors. These surface epithelial tumors can be further subdivided into three categories.

- **Benign surface epithelial ovarian tumors** are not cancerous. Tumors are simple, non-stratified epithelium with no cytologic atypia. Treatment is surgical removal of the tumor with preservation of the ovarian tissue.

- **Borderline (low-malignant potential [LMP] or atypical proliferative) tumors** are the most commonly misdiagnosed subtype of ovarian tumors. They are a borderline form of cancer that may eventually spread and invade other tissues. This type of tumor tends to occur in younger women and can be treated conservatively if the correct histologic diagnosis is found. Borderline tumors will have epithelial proliferation with stratification and tufting, variable mitotic activity and nuclear atypia and no stromal invasion.

- **Invasive carcinoma** have typically spread beyond the ovary metastasizing to other organs. They are classified by stromal invasion and cytologic atypia.

**Class II: Germ Cell Ovarian Tumors**
Germ cell tumors account for approximately 10-15% of ovarian tumors and are derived from the oocyte or eggs that are in the ovaries.\textsuperscript{1-3} Germ cell tumors are divided into two categories.

- Benign germ cell tumors are nearly always mature cystic teratomas, they are not cancer. They are successfully treated by the surgical removal of the tumor with preservation of the uninvolved ovarian tissue. Chemotherapy treatment is not necessary.
- Malignant germ cell tumors also require surgical removal but of the whole ovary. Intensive multiagent chemotherapy is required after removal. The chemotherapy administered for malignant germ cell tumors is completely different from the chemotherapy received after surgical treatment of surface epithelial tumors.\textsuperscript{1-3}

**Class III: Sex Cord Stromal Ovarian Tumors**

Sex cord stromal ovarian tumors are the least common type of ovarian tumors, accounting for approximately 5-10% of diagnosed ovarian tumors.\textsuperscript{1-3} Sex cord stromal tumors are derived from the stromal component of the ovary, the hormone production site of the ovary. Tumors derived from the stroma can be associated with abnormal production of sex steroid hormones. Some symptoms include abnormal vaginal bleeding during reproductive age and postmenopausal women exceptionally early puberty in children. Ovarian tumors that produce male sex hormones can cause a female to take on male characteristics such as increased growth of hair on various parts of the body, balding, deepening of the voice, increase in muscle mass and enlargement of the clitoris.\textsuperscript{1-3}

**Treatment**

After diagnosis of ovarian cancer several treatment options are available. The main treatments for ovarian cancer are surgery, chemotherapy, hormone therapy, targeted therapy and radiation therapy.\textsuperscript{1-3} Quite often 2 or more different types of treatments are used.\textsuperscript{1} Surgery is used to treat all stages and types of ovarian cancer. Surgery may be the only treatment needed for some early stage ovarian cancers. Surgery may include any one or all of the following:

- Total hysterectomy, removal of the uterus
Bilateral salpingo-oophorectomy, removal of both ovaries and fallopian tubes, however if the cancer is only in one ovary and the patient wishes to try and get pregnant the unaffected ovary and fallopian tube will not be removed.

Complete or partial removal of the omentum, the fatty layer that covers and pads organs in the abdomen.

Lymph nodes and other tissues in the pelvis and abdomen will be examined, biopsied and/or removed.

Debulking, removing as much of the tumor and/or tumors as possible.

Chemotherapy is the use of drugs to treat any cancer that may remain after surgery or if cancer comes back. Chemotherapy for ovarian cancer is typically a combination of 2 or more drugs given intravenously (IV), into the veins, or intraperitoneal (IP), directly into the abdominal cavity. The drugs used will depend on the stage and classification of the ovarian cancer. Epithelial and germ cell tumors are treated with chemotherapy while stromal tumors are more often treated with hormone therapy. Hormone therapy is the use of hormone-blocking drugs or hormones to fight cancer.

Prognosis

Survival rates of patients with ovarian cancer are determined by looking at the 5-year survival rate of other patients diagnosed with ovarian cancer. Combined together the 5-year survival rate for all ovarian cancers is 44%. Patients diagnosed younger than 65 do better and have better survival rates than women diagnosed after 65. For all stage I ovarian cancers diagnosed and treated the patients survival rate is 92%, however, only about 15% of all ovarian cancers are found at this early stage. Each type of ovarian cancer will have its own very different 5-year survival rating but all show that early diagnosis dramatically increases a patients chance of surviving ovarian cancer.

Follow-up care

Careful follow-up care is highly recommended for patients whose ovarian cancer has gone into remission. A physical exam every 2-4 months for the first 2 years followed by every 6 months for 3 years and then every year is recommended. Blood tests to monitor CA-125 levels will also be ordered if the patients levels started out high when diagnosed with ovarian cancer.
CT scans of the chest, abdomen and pelvis may also be ordered periodically.\textsuperscript{1-3} Any changes or concerns a patient might have should be discussed with their doctor. Side effects of treatments may last several weeks to months while others may not go away at all. Lifestyle changes may also be recommended, such as eating better and getting plenty of rest and exercise.

**Prevention**

Since the cause of ovarian cancer is unknown there really is not any defined screening for ovarian cancer. Blood tests, such as the CA-125 level, and pelvic ultrasounds are a possibility but some patients have a naturally high CA-125 level and pelvic ultrasounds can be costly to the patient. A female with a high risk of ovarian cancer can have the BRCA gene testing but this test only shows that there is a mutation that may or may not cause cancer. Females with a BRCA-1 or BRCA-2 gene mutation may elect to have her ovaries and fallopian tubes removed but the possibility of developing ovarian cancer in other parts of the pelvis still exists.

**Case Study 1**

A 40-year-old female patient who was unable to have children made the choice to undergo in-vitro fertilization (IVF). The patient's ovaries were super stimulated by chemicals to help ovulation occur. After each cycle an ultrasound was performed to see if ovulation had occurred. During the ultrasound the ovaries were carefully evaluated and measured. After the third cycle of IVF the patient developed a right complex ovarian cyst, approximate size was 5.4 mL(see Figure 4). The diagnosis was a benign complex cyst and no further investigations were performed. The cyst grew larger after the fourth IVF cycle and increased significantly after the fifth IVF cycle, approximate size was 39.5 mL(see Figure 5). Ultrasound of the right ovary showed that “It contained homogeneous internal echoes in the cystic component, with irregular mural projections and internal vascularity.”\textsuperscript{9} Since the patient wished to continue with IVF treatments a conservative surgery was chosen, a right ovarian cystectomy. Findings during surgery warranted a right salpingo-oophorectomy and omentectomy. Further testing showed the cyst to be invasive endometrioid adenocarcinoma. The patient opted for a total hysterectomy after extensive counseling.

**Conclusion**
It is unknown how much superovulation drugs will increase a patient's chance of developing ovarian cancer.\textsuperscript{5-9} The use of fertility medications and long-term cancer risks have caused many studies to be performed. There are an extremely limited number of cases of patients developing ovarian cancer occurring during the IVF process. Several long-term studies show only a slightly higher chance of developing ovarian cancer with use of fertility medications when compared to the general population.\textsuperscript{5-9} Other studies show an increased incidence of ovarian cancers but appear skewed with borderline tumors.\textsuperscript{7,8} More studies are warranted due to the small amount of information currently available.

Female patients diagnosed with ovarian cancer will face many trials when it comes to fighting this disease. Females should not ignore symptoms that may point to ovarian cancer, early diagnosis increases their survival rate dramatically. If ovarian cancer is diagnosed all avenues of treatment should be explored and a doctor specializing in ovarian cancer should be counseled with. Ovarian cancer is deadly, but a well-educated woman fighting ovarian, in my opinion, stands a better chance of survival if she knows exactly what she is facing.
References


Figures and Captions


Stage I
The cancer is still contained within the ovary (or ovaries). It has not spread outside the ovary.

Stage I A (T1a, N0, M0): Cancer has developed in one ovary, and the tumor is confined to the inside of the ovary. There is no cancer on the outer surface of the ovary. Laboratory examination of washings from the abdomen and pelvis did not find any cancer cells.

Stage I B (T1b, N0, M0): Cancer has developed in both ovaries but not on their outer surfaces. Laboratory examination of washings from the abdomen and pelvis did not find any cancer cells.

Stage I C (T1c, N0, M0): The cancer is present in one or both ovaries and one or more of the following are present:
- Cancer is on the outer surface of at least one of the ovaries.
- In the case of cystic tumors (fluid-filled tumors), the capsule (outer wall of the tumor) has ruptured (burst)
- Laboratory examination found cancer cells in fluid or washings from the abdomen.

Stage II
The cancer is in one or both ovaries and has spread to other organs (such as the uterus, fallopian tubes, bladder, the sigmoid colon, or the rectum) within the pelvis. It has not spread to lymph nodes, the lining of the abdomen (called the peritoneum), or distant sites.

Stage II A (T2a, N0, M0): The cancer has spread to or has invaded (grown into) the uterus or the fallopian tubes, or both. Laboratory examination of washings from the abdomen did not find any cancer cells.

Stage II B (T2b, N0, M0): The cancer has spread to other nearby pelvic organs such as the bladder, the sigmoid colon, or the rectum. Laboratory examination of fluid from the abdomen did not find any cancer cells.

Stage II C (T2c, N0, M0): The cancer has spread to pelvic organs as in stages II A or II B and cancer cells were found when the fluid from the washings from the abdomen were examined under a microscope.

Stage III
The cancer is in one or both ovaries, and one or both of the following are present: (1) cancer has spread beyond the pelvis to the lining of the abdomen. (2) cancer has spread to lymph nodes.

Stage III A (T3a, N0, M0): During the staging operation, the surgeon may be able to see cancer in the ovary or ovaries, but no cancer is visible to the naked eye in the abdomen and the cancer has not spread to lymph nodes. However, when biopsies are checked under a microscope, tiny deposits of cancer are found in the lining of the upper abdomen.

Stage III B (T3b, N0, M0): There is cancer in one or both ovaries, and deposits of cancer large enough for the surgeon to see, but smaller than 2 cm (about 3/4 inch) across, are in the abdomen. Cancer has not spread to the lymph nodes.

Stage III C: The cancer is in one or both ovaries, and one or both of the following are present:
- Cancer has spread to lymph nodes (any T, N1, M0)
- Deposits of cancer larger than 2 cm (about 3/4 inch) across are seen in the abdomen (T3c, N1, M0).

Stage IV (any T, any N, M1)
This is the most advanced stage of ovarian cancer. In this stage the cancer has spread to the inside of the liver, the lungs, or other organs located outside the peritoneal cavity. (The peritoneal cavity, or abdominal cavity is the area enclosed by the peritoneum, a membrane that lines the inner abdomen and covers most of its organs.) Finding ovarian cancer cells in the fluid around the lungs (called pleural fluid) is also evidence of stage IV disease.

Recurrent ovarian cancer: This means that the disease went away with treatment but then came back (recurred).