Surgical Management of Ovarian Germ Cell Tumors at National Cancer Institute, Cairo University

Thesis research

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Introduction

ovarian germ cell tumors are classified according to the site of origin to:

gonal germ cell tumors which get raised from gonads (testicular and ovarian germ cell tumors).

Extra-gonal germ cell tumors which present in extra gonadal sites, such as the retro-peritoneum, mediastinum or central nervous system, without an evident gonadal primary. At least some of these cases represent metastases from occult and/or regressed gonadal primaries. However, germ cell tumors can arise in these extra gonadal sites independent of gonadal involvements (Wenstien and Hirsch, 2011).

In National Cancer Institute (NCI), Cairo University, tumors of the female genital system represented 4.70% of total malignancy. A total of 135 cases of ovarian malignant tumors accounting for 29.22% of female genital tract malignancies and 1.37% of total malignancy are represented during the years 2003-2004 (Mokhtar et al 2007).

Malignant ovarian tumors include epithelial ovarian cancer, germ cell tumors in addition to other less common tumors of low malignant potential. (Garcia et al., 2007).

Although it may arise from all cell types composing the ovaries as primary tumors of epithelial, sex cord-stromal, or germ cell origin and metastatic tumors that frequently originate in the gastrointestinal tract, the epithelial carcinomas are by far the most common (85-90% of all ovarian cancer) (Kurman et al., 2010).
In young females, germ cell tumors account for 30% of ovarian tumors, but only 1 to 3% of ovarian cancers in North America. In younger women germ cell tumors are more common, thus in patients under the age of 21, 60% of ovarian tumors are of the germ cell type, and up to one-third are malignant (Siegel et al., 2012).

Ovarian germ cell tumors can be difficult to diagnose (find) early. Often there are no symptoms in the early stages, but tumors may be found during regular gynecologic examinations (checkups). A woman who has swelling of the abdomen without weight gain in other places should see a doctor. A woman who no longer has menstrual periods (who has gone through menopause) should also see a doctor if she has bleeding from the vagina (Goff et al., 2012).

Serum tumor marker test Certain substances are linked to specific types of cancer when found in increased levels in the blood. These are called tumor markers. An increased level of alpha fetoprotein (AFP), human chorionic gonadotropin (HCG) or lactate dehydrogenase (LDH) in the blood may be a sign of ovarian germ cell tumor (Stankovic et al., 2006).

The prognosis (chance of recovery) and treatment options depend on the following: (Hunn et al., 2012).

The histopathological type of cancer.

The size of the tumor.

The stage of cancer (whether it affects part of the ovary, involves the whole ovary, or has spread to other places in the body).

The patient’s general health.
Treatment options and recommendations depend on several factors, including the type and stage of cancer, possible side effects, the patient’s preferences and personal considerations, such as the woman's age, planning to have children and the sexual function (Van Nagell et al., 2011).

In young women with early disease removing the only affected ovary is the standard type of care for fertility preservation (Safra et al., 2011).

Unilateral salpingo-oophorectomy with preservation of the contralateral ovary and the uterus (fertility sparing surgery) is now considered the adequate surgical treatment for patent with ovarian germ cell tumors this surgical approach should be considered, even in the case of advanced disease, because of the sensitivity of the tumor to chemotherapy (Colombo et al., 2012).

The surgeon should also remove the omentum to determine whether the cancer has spread. Also doing lymph node sampling pelvic and para-aortic, tissue samples, and fluid from the abdomen (Safra et al., 2011).

Numerous combination chemotherapy regimens have been shown to produce responses in patients with ovarian germ cell cancer. Since the mid-1990, a chemotherapy combination consisting of the combination of paclitaxel and a platinum compound has been accepted as the standard of care. Most researches has focused on further optimization of these regimens to maximize clinical benefit while minimizing toxicity, and investigation into alternative taxanes (e.g. docetaxel), other novel agents
and other treatment schedules are on going (McGuire and Markman, 2003).

Radiation treatment for ovarian germ cell tumor is not usually used to treat ovarian cancer, but it may be used to relieve side effects. Which depend on the dose and the area of the body being treated, but may include fatigue, mild skin reactions, upset stomach, and loose bowel movements. Side effects of internal radiation therapy may include abdominal pain and bowel obstruction. Most side effects usually go away soon after treatment is finished (Vencken et al., 2011).

Recurrence of ovarian germ cell tumor is associated with incurable diseases in most cases. Thus, the main obstacle to an effective treatment is the failure of the initial chemotherapy to eradicate a sufficient number of tumor cells to prevent disease recurrence. In this context, deficiency in the apoptotic cascade among tumor cells is the key hallmark (Vergote et al., 2010).
Aim of the Work

To evaluate the surgical role in the management of ovarian germ cell tumors at National Cancer Institute (NCI), Cairo University. This study focused on confirming diagnosis, histo-pathological typing and staging of the disease. Studying the plan of treatment either surgical or chemotherapy and factors affecting the surgical management. Detecting what is the incidence of ovarian germ cell tumors in relation to other types of ovarian tumors.
Patients and methods

This is a retrospective study to review the NCI experience in management of ovarian germ cell tumors. The study includes 75 patients with ovarian germ cell tumors at NCI, Cairo University between January 2010 till December 2013.

Medical record and data:

1- Medical records:

Data pertinent to NCI hospital based registry were used to generate a list of all patients diagnosed with ovarian germ cell tumors in the previously mentioned period of time. Records were scrutinized at archives of biostatistics, epidemiology and pathology department, from 75 cases only 54 were available.

2- Data:

A predetermined sheet was used to fulfill the objectives of the study.

The following information was collected:

- Patient name, hospital number.
- Age.
- Presentation symptoms, signs.
- Laboratory investigations (Alfa fetoprotein (AFP), human chorionic gonadotropins (BHCG), lactate dehydrogenase (LDH)).
- Imaging investigations (abdomen-pelvic ultrasound, computerized tomography).
- Date and basis of diagnosis.
• Treatment:
  1- Operative type (fertility sparing, radical).
  2- Chemotherapy administration and number of cycles.
  3- Outcome.
• Response rates.
  Response was assessed according to the Response Evaluation Criteria In Solid Tumors (RECIST).
• Overall survival.
• Event free survival.
• Date and state at last visit.

Definitions:
Overall survival (OS): the time in months between the date of diagnosis and death or loss follow up.
Progression free survival (PFS): the time in months between the date of documented response and death, progression or recurrence.
Event free survival (EFS): the time in months between the start of therapy and occurrence of recurrence, progression or death.
Response of therapy (RECIST), (Therasse et al., 2000).
Complete response (CR): complete regression no residual tumor.
Partial response (PR): reduction in longest tumor dimension by more than 30% but still present.
Stable disease (SD): no change or no response to therapy but no progression.
Progressive disease (PD): failure of therapy by 20% increase of disease or new lesion.
Ethical issues:
The present study is a retrospective, based on review of medical records. Hence, approval of NCI ethical committee was secured through the expedited pathway. All measures were taken to protect security and confidentiality of the individual patient information.

**Sample Size Estimation:**

All cases of ovarian germ cell tumors attended and treated at National Cancer Institute, Cairo University during a period of time (from 2010 till 2013).
Statistical Methods

Data will be analyzed using SPSS statistical package version 20, relationship between qualitative data will be done using Chi-square test or Fisher’s exact test as appropriate. Comparison between two subgroups regarding numerical data will be done using either parametric or nonparametric T-test. Comparison between more than two groups regarding numerical data will be done using either parametric or nonparametric ANOVA test as appropriate. A p-value less than 0.05 will be considered significant.
Summary

Germ cell tumors may be gonadal (testicular or ovarian) or extra gonadal.

Ovarian germ cell tumors are rare tumors that affect young women, with early detection and very good prognosis.

Surgery is the primary line of treatment with fertility sparing operation as a standard for patients were indicated.

The only way to diagnose the ovarian cancer is with an exploratory operation. Biopsies can be taken from ovaries or from the omentum, guided by CT or by ultrasound scan.

Chemotherapy after surgery using platinum-based regimen is the standard first-line chemotherapy used for all patients with ovarian cancer.

Radiation therapy is rarely used as the main treatment for this cancer, but it may be used to relieve side effects.

Many strategies such as adjuvant, neoadjuvant, combination, and sequential therapy are under clinical trials to determine the best treatment plans to ovarian cancer patients.
Abstract

**Background:** Ovarian germ cell tumors (GCTS) are rare tumors that affect mainly young females and carry good prognosis.

**Aim:** To repost the experience of the Egyptian National cancer Institute (NCI) in managing ovarian GCTs.

**Methods:** this retrospective study that includes all cases (75 case) with ovarian GCTs presented and treated at the NCI from 2010 to the end of 2013 taking into account the age, symptoms, stage, type of surgery and the outcome. The medical files were accessible only 54 cases (72%).

**Result:** the median age for ovarian (GCTs) were 23 years. Dysgerminoma and teratoma are the most common types. Unilateral ovariectomy and ovarian tumorectomy were the classic surgical procedures. Adjuvant chemotherapy administrated in most cases was BEP with good response rates.

**Key words:** Egyptian National Cancer Institute, Ovaries, Germ-cell tumors, Treatment, Survival.
ملخص الرسالة باللغة العربية:
خلفية عامه: أورام الخلايا الجنينية بالمبيض هي أورام نادرة تحدث بشكل رئيسي في الأعمار الصغرى والمتوسطة وتحمل نسبة علاج جيدة.

الهدف من البحث: دراسة تجربة معهد الأورام القومي المصري في علاج أورام الخلايا الجنينية بالمبيض.

المرضى وطريقة البحث: هذه دراسة رجعية وتشمل جميع الحالات (57 حالة) المصابين بأورام الخلايا الجنينية بالمبيض التي تم علاجها بالمعهد القومي للأورام من عام 2002 وحتى نهاية عام 2013 مع الأخذ بعين الاعتبار العمر، والأعراض، ومرحلة الورم، ونوع الجراحة و النتيجة النهائية. حيث أن الملفات الطبية التي تمكن الوصول إليها 75 حالة فقط (72%).

النتائج: كانت متوسط أعمار المصابين 23 عاما. و أكثر الأنواع شيوعا هي dysgerminoma و teratoma. وكان استئصال المبيض من جانب واحد واستئصال ورم من المبيض من أكثر الإجراءات الجراحية الكلاسيكية. وكان العلاج الكيميائي المساعد في معظم الحالات يعطي أفضل النتائج مع معدلات استجابة جيدة.

الكلمات الرئيسية: المعهد الأورام القومي المصري، أورام الخلايا الجنينية بالمبيض، العلاج، البقاء على قيد الحياة.
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العلاج الجراحي للأورام الجنينية بالمبيض
في المعهد القومي للأورام جامعة القاهرة

دراسة بحثية
للحصول على درجة الماجستير في جراحة الأورام

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