

Advanced Granulosa Cell Tumor and Pregnancy: A Case Report, How to Treat and How to Preserve Fertility?

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Abstract

Granulosa cell tumors of the ovary are rare ovarian malignancy developed on stromal ovarian cells and characterized by estrogen secretion. Histologically, there are divided on two types: adult granulosa tumors, which are more frequent and occurring in perimenopausal and post-menopausal women and juvenile granulosa tumors, which are rarer and occurring in teenager and adolescent girls.

The association between GCT and pregnancy is a rare condition with therapeutic challenge consisting on the pregnancy and the fertility outcome in a hand and the oncological results in the other.

We present a case report of an adult granulosa cell tumor discovered fortuitously during caesarian section. We report the management of this tumor and the way to preserve the fertility.

Keywords: Granulosa cell tumor; Ovarian cancer; Pregnancy; Fertility sparing

Introduction

Granulosa cell tumors of the ovary are a rare ovarian malignancy presenting 3-5% of ovarian tumors [1]. The atypical cells are developed from ovarian stroma and those tumors are classified within the sex-cord stromal tumour category. Histologically, there are two distinct types of granulosa cell tumor: the most common type is the adult granulosa cell tumors with a frequency of 95% of all granulosa cell tumors; it occurs usually in perimenopausal and post-menopausal women with a peak incidence at 50-55 yrs. The second types is the juvenile granulosa cell tumors, which are less frequent and rare presenting 5% of granulosa cell tumors and occurring in teenager and young women [1,2]. Those tumors are the most frequent hormone-secreting ovarian tumors and are generally characterized by insidious growth, low malignancy potential and late recurrence [3].

Occurring in patients with an active sexual life and in reproductive age, granulosa cell tumors can be associated with pregnancy. In published papers, 10% of granulosa cell tumors were discovered during pregnancy [4]. The management of this association is a real challenge because it must consider the pregnancy and the fertility outcome.

In this case we report an advanced adult granulosa cell tumor discovered fortuitously in caesarian section in a 30 years old patients. The management of this malignancy was based on surgery and chemotherapy. The patient had a fertility sparing procedure consisting an ovarian tissue cryopreservation.

Case Report

A 30 yrs old patient, gravida one and para one. In her medical history, we note a prolactin adenoma treated by Quinagolide until she

becomes pregnant spontaneously. An intermittent abdominal unspecific pain marked the pregnancy follow up. In 32 week of gestation, the patient underwent a caesarian section for a placental abruption. The newborn weight was 1925 g and his Apgar score was 2-5-10. Intra operatively, a voluminous ruptured tumor depending on the right ovary was discovered. It measures 40 × 30 cm and was wedged behind the uterus (Figures 1 and 2). Inspection of the peritoneal cavity showed a 4 cm localized omental induration. The patient underwent a right adnexectomy with a partial omental removing.



Figure 1: A voluminous ovarian tumour.

Histological examination showed an adult granulosa cell tumor of the right ovary with an omental metastasis and the immuno-histo-

chemistry study showed an intensive and diffuse marking by FOXL2. The tumor was IIIc staged.

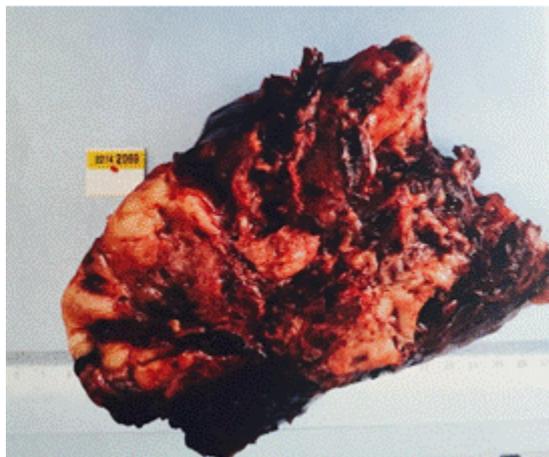


Figure 2: A ruptured ovarian tumour.

Abdomino-pelvic MRI and cerebral CT were normal. CA 125 blood level was 23 UI/l.

A multidisciplinary consultation decided to complete surgery with a total hysterectomy, a left adnexectomy, a total omentectomy, an appendicectomy and a multiple peritoneal biopsies. All the samples were free from malignant involvement in the histological study.

The patient had a fertility sparing procedure consisting on cryopreservation of ovarian tissue from the cortical region of the left ovary.

After surgery, the patient had a systemic chemotherapy based on BEP protocol (Bleomycine, Etoposide and Cisplatin). Totally, she had four chemotherapy cycles. Actually, the patient had 18 month of follow-up with no recurrence or metastasis disease.

Discussion

Granulosa cell tumors (GCT) are a rare malignant ovarian tumor with a frequency of 3-5% of all ovarian malignancies [1]. It is the most common hormonal secreting ovarian tumor and is classified within sex-cord ovarian malignancy [3]. Histologically, this entity is divided in two subtypes: the most common is adult granulosa cell tumor with a frequency of 95% of all GCT, occurring usually in perimenopausal and post-menopausal patient. The second type is the juvenile GCT characterized by occurring in teenager patient and young women, the frequency of Juvenile GCT is about 5% of all GCT [1,2]. Granulosa cell tumors are the most common hormonal secreting tumor of the ovary. They secrete estrogen [5]. This hormonal production is responsible of early clinical presentation of these tumors such us vaginal bleeding, hypo fertility or amenorrhea. GCTs are detected 80-90% of the time in stage I [6]. 10% of granulosa cell tumors were discovered during pregnancy [4].

In the reported case, the patient has a medical history of a prolactin adenoma treated until she begins her pregnancy. There are many publications demonstrating the relation between estrogen secretion and the stimulation of lactotrop cells in the pituitary gland [7]. After the surgery, it was not necessary to treat the prolactin adenoma

because of the normal cerebral CT and the suppression of estrogen production.

Adnexal masses are detected in 1-2% of all pregnancies. Most of these are asymptomatic [8]. Usually there are discovered during the first trimester because of obstetrics ultrasound examination and the small size of the uterus. The majority of these tumors disappear in the second trimester: there are functional ovarian tumors. The clinical management of adnexal masses during pregnancy is based on ultrasonographic aspect and tumor size. Tumor markers are not useful in the prediction of the malignancy or the origin of adnexal masses during pregnancy because if the unspecific elevation of tumor markers during the first trimester of pregnancy [8]. MRI is an important tool to predict malignant ovarian tumor and to manage adnexal masses during pregnancy [9]. In a recent retrospective study, it was found that adnexal masses occurred in 0.15% of pregnancies. Fifty percent of these ovarian tumors were mature cystic teratomas, 20% were cystadenomas, and 13% were functional ovarian cysts. Malignancy occurred in 13% of them [8]. In another review on ovarian carcinoma during pregnancy, 35% were borderline carcinomas, 30% epithelial invasive tumors, 17% dysgerminomas, 13% granulosa cell tumors, 5% undifferentiated carcinomas. Most of the patients (74%) were diagnosed as stage I [10]. Usually, ovarian tumors during pregnancy are discovered in the first trimester during the routine ultrasonographic examination. Tumors detected in the third trimester present 8.7% of all cases [10]. The difficulties to detect an ovarian tumor during the second and the third trimester are related to the uterine size and the concentration of the operator to examine only the uterine cavity. In our case and despite a regular follow up of the pregnancy, the ovarian tumor was not detected because of the rupture of the tumor. The challenge in the management of adnexal masses during pregnancy is the pregnancy outcome and the oncologic risk. In our case, the ovarian GCT was discovered fortuitously during caesarian section so the most important challenge is the fertility sparing management.

The prognosis of GCT is better than epithelial ovarian carcinoma. Those tumors are characterized by a slow evolution, low malignancy potential and late recurrence. The management is based on surgery specially fertility sparing surgery such unilateral adnexectomy in the case of localized and unilateral tumor. Actually, there are controversies in the surgical procedures to treat GCT. Radical surgery does not necessarily allow having a low rate of relapse and an important survival rate comparing with conservative surgical procedures. Norris et al. [11] and Novak et al. [12] reported no differences in relapse rates between conservative and radical surgeries for stage IA patients. In the same time Evans et al. [13] also found a high relapse rate and a low survival rate associated with conservative surgery.

Based on the study of Zhang et al. [14], Mancari [15] suggested in an important study that there is a place for conservative surgery without hysterectomy in younger women. The Zhang paper reported on 132 patients 50 years of age or younger and who had stage I disease, of which 61 (46%) underwent standard surgical treatment (including hysterectomy) and 71 (54%) had a uterine-sparing procedure. The five-year survival rates of these respective women were 97% and 98%. In our case, a conservative surgery was not indicated because of the stage IIIc of the tumor. The patient underwent a radical surgery. Fertility sparing procedures (cryopreservation of ovarian tissue) was indicated.

For patients presenting GCT a close follow up is to carry on. It is based on clinical examination, imaging and tumour markers, including CA125 and inhibin. In the study of Mom et al. [16] serum inhibin A

and B concentrations were elevated in 58% and 85% of patients, respectively, at recurrence, with elevations in inhibin B concentrations predating recurrences by a median of 11 months (range 8-19 months).

The impact of adjuvant chemotherapy for high-risk patients has not been proven by prospective randomized studies. Platinum-based chemotherapy is currently used for patients with advanced stages or recurrent disease, with an overall response rate of 63% to 80% [17]. In this case, the patient has an adjuvant chemotherapy based on platinum (BEP).

The management of GCT tumor is based on surgery. Conservative procedures are possible on early stage tumors. Multidisciplinary coordination is required between gynecologic oncologist, oncologist, obstetrician, biologist and endocrinologist.

A special mention is required for the psychological and sexual counseling to complete the management and to guarantee a good quality of life.

To improve surgical management of GCT especially fertility-sparing procedures, more multi-centric studies are required to fix indication and modalities of conservative surgery, and to predict fertility and oncologic results and outcome.

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