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Pregnancy after treatment for adult granulose cell tumor: a case report

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Summary

Granulosa cell tumors are sex-cord stromal tumors, and since their incidence is very low, it is difficult to design treatment and evaluate its efficacy. In these cases it is very difficult and challenging to give any advice regarding future pregnancies. In the present case, since treatment of granulosa cell tumor was affected by decision to have another pregnancy, one is inevitably concerned whether the pregnancy and hormonal status regarding pregnancy could change prognostic factors regarding the tumor itself. After the pregnancy the patient declined hysterectomy and her reasons were mainly that she felt safe because the second look during cesarean section showed no evidence of the disease. There are no sufficient data in the literature regarding planned pregnancies during the course of follow up for granulosa cell tumors.

Key words: Adult granulosa cell; Pregnancy; Sex-cord stromal tumors.

Introduction

Being treated for malignant disease often causes numerous dilemmas, fear, and questions that are difficult to answer. Patients are concerned not only regarding prognostic factors and treatment modalities, but as well as future reproduction. Psychological problems are usual after any diagnosis of malignancy and special care and attention are needed. Multidisciplinary approach helps the patient to feel safe and it provides the best treatment options that are based on individual approach. It is vital to give all information needed especially when it comes to pregnancy planning. Another problem arises if the malignancy is rare and there are no sufficient data about nature of the tumor and efficacy of different therapies. In these cases it is very difficult and challenging to give any advice regarding future pregnancies. The patient's decision becomes essential based on available data.

Granulosa cell tumors are sex-cord stromal tumors and since their incidence is very low, it is difficult to design treatment and evaluate its efficacy. In most recommendations after surgery for low risk early stage tumor, only clinical follow up is recommended. Adjuvant chemotherapy has not shown overall survival benefit [1]. Advanced initial stage and early recurrences are poor prognostic factors, though early stage at initial presentation is reported to be favorable overall five-year survival rate of more than 90%. [2]. Granulosa cell tumors are found in association with endometrial cancer in 5% of patients [3]. In cases when conservative operation is performed and uterus sparing, it is necessary to perform curettage to rule out concurrent endometrial cancer [4] Two types of granulosa cell tumors are dominant: adult and juvenile. They express aromatase activity and the result is promoting estrogen synthesis that seems to promote progression of the disease [5]. This is a very important fact that gives rise to aromatase inhibitors therapy especially with relapses [6]. Granulosa cell tumor is not aggressive in nature but tend to relapse many years after initial treatment.

Case Report

In 2014 a young patient 32 years of age was submitted to ultrasound examination due to mild pain of short duration. There was no significant chronic or malignant disease in the family history. The patient had irregular menstrual cycles from time to time, she had one delivery, and one missed abortion. Ultrasound exam revealed a multi-cystic tumor of the right ovary, and diameters were 3 cm, with capsule of 5 mm, uterus with no pathologic changes, endometrium that correlated with the phase of menstrual cycle, left ovary normal, and no fluid in the abdominal cavity. MRI described tumor of the right ovary 40 mm in diameter, with no contrast uptake. Tumor markers were normal.

In June 2014. after thorough conversation with the patient and with appropriate consent, laparoscopic operation was performed and total cystectomy of the right ovary was done (endobag provided no rupture of the tumor in the abdominal cavity) with peritoneal washing and multiple biopsies. Histopathology report revealed granulosa cell tumor adult type, of the right ovary, with no malignant changes in other specimen. Immunochemical stains

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were performed: EMA (-), panCK (-), melanA (-), Inhibin (+++), and Calretinin (+++). Since it was not possible to stage the disease, the patient was submitted to another fertility sparing laparoscopic operation. In July 2014, laparoscopic right adnexectomy was performed as well as multiple biopsies, excision of the specimen from left ovary for cryopreservation, and curettage of the uterine cavity. Histopathology report concluded no residual disease, normal endometrium, and Stage IC .The patient was presented to multidisciplinary gynecologic cancer team. The patient was informed about prognostic factors related to the disease itself as well as treatment modalities. The main concern was whether the patient should receive adjuvant chemotherapy or not. Knowing the fact that most recommendations do not advise chemotherapy in the early stage of granulosa cell tumors, the patient was also informed about protocols that include adjuvant chemotherapy even in early stages of the disease. The patient understood the limitations of efficacy data of chemotherapy due to rare presentations of granulosa cell tumors. She wished to conceive as soon as possible and decided not to receive adjuvant chemotherapy. Follow up after the operation was performed by MRI of the pelvis and abdomen, as well as tumor markers alpha fetoprotein and inhibin B. Imaging and markers were constantly normal.

In October 2014 the patient presented with intrauterine pregnancy of eight weeks gestation. Ultrasound of the left ovary was normal. The pregnancy was uncomplicated. Cesarean section was performed at term on May 20th, 2015 for healthy baby of 3,600 grams. During the cesarean section second look was performed and macroscopically there was no evidence of relapse. Histopathology report on placenta showed excentric insertion of the umbilical cord and normal histology of placental tissue.

Two months after caesarean section, the MRI and tumor markers were normal. A multidisciplinary team suggested that hysterectomy with salpingo-oophorectomy should be performed but the patient declined the operation. All subsequent exams were normal. One year after delivery, all examinations were normal.

Discussion

Rare presentations of granulosa cell tumors allow different approaches regarding therapies due to inconsistent efficacy data. Adult type of granulosa cell tumors seems to be less aggressive but still therapeutic possibilities remain unclear due to small numbers of such patients. There is no firm evidence about therapeutic efficacy of chemotherapy, and the situation becomes even more complicated when desire for pregnancy is involved. Targeted therapies are developing especially after the discovery of FOXL2 mutation that is present in 97% of adult granulosa cell tumors and this important discovery could change the approach to treatment [7]. Still for early stage at the initial presentation, several reports suggest that no adjuvant therapy is needed after primary surgery and long term follow up is needed [8].

In the present case, since treatment of granulosa cell tumor was affected by decision to have another pregnancy, one is inevitably concerned whether the pregnancy and hormonal status regarding pregnancy could change prognostic factors regarding the tumor itself. Is the follow up of the same value when performing with or without pregnancy? Is the tumor still indolent or could the biological behavior change because of the influence of pregnancy? Does Stage IC remain early stage in this case or does it represent a high risk that could trigger relapse of the disease? In the study of Lavazzo *et al*. patients with fertility sparing surgeries were evaluated and recurrences were notices in up to 27.4% [9]. Although the radicalization of the previous operation is recommended, an individual approach remains crucial. The patient declined hysterectomy and her reasons were mainly that she felt safe because the second look during cesarean section showed no evidence of the disease.

There are several studies reporting pregnancies concomitant with granulosa cell tumors, usually diagnosed accidentally [10, 11], but there are no sufficient data regarding planned pregnancies during the course of follow up for granulosa cell tumors. The present patient planned to have another pregnancy most probably with an IVF procedure with frozen ovarian tissue from the previous operation. Apart from normal follow up, we should definitely consider the risks regarding relapse in cases like the present and find a more precise model for treatment recommendations.

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