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Early stage ovarian cancer in pregnancy. Diagnostic, therapeutic strategies

Mihaela Vilcu[1,2], Nicolae Bacalbasa[1,2,3], Irina Balescu[4], Diana Gheorghiu[5]

1. "Ion Cantacuzino" Clinical Hospital, Bucharest, Romania

2. "Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania

3. Center of Excellence in Translational Institute, Fundeni Clinical Institute, Bucharest, Romania

4. "Ponderas" Academic Hospital, Bucharest, Romania

5. Obstetrics and Gynecology Clinic, "Sf. Pantelimon" Urgency Hospital, Romania

Correspondence:
Dr. Irina Balescu
E-mail address: irina.balescu@ponderas-ah.ro

Abstract

Although the appearance of adnexal masses during pregnancy is a common event, most often these masses prove to be functional, a spontaneous resolution being expected. Unfortunately, in certain cases malignancy is suspected; in these cases the most appropriate therapeutic strategy should be established based on the stage of the neoplasia, gestational age and patients' wish. The present paper present a literature review of the main therapeutic options.

Keywords: *ovarian cancer, pregnancy, therapeutic options*

Introduction

Up to 2% of women will develop adnexal masses during pregnancy, this event being most often encountered during the first trimester of pregnancy; in the meantime, it will usually resolve spontaneously before the 16th weeks of pregnancy; unfortunately, up to 6% of all cases will prove to have a malignant origin, ovarian cancer being the fifth most common tumor encountered in pregnancy[1,2]. More frequently encountered malignancies during pregnancy include breast and cervical cancer, melanoma and lymphoma[3]. However, in the last decades a slightly increased incidence has been reported, especially due to the increasing use of ultrasound and due to postponing childbearing to an older age[4].

Adnexal masses found in pregnancy might be pregnancy related and non-pregnancy related, with ovarian and non-ovarian origin; when it comes to the non-ovarian masses, they usually consist of uterine fibroids, para-ovarian cysts and hydrosalpinx while the most commonly encountered ovarian masses are functional cysts, mainly induced by the hormonal changes; however, functional cysts will disappear at a certain moment. Contrarily to functional cysts, non-functional ovarian masses do not disappear during pregnancy and are usually represented by endometriomas, dermoid cysts and epithelial ovarian tumors[5]. In cases presenting adnexal masses in very early stages of pregnancy (i.e. when intrauterine gestational sac is not visible yet) the differential diagnostic of extrauterine pregnancy should be taken in consideration. In cases presenting both intrauterine gestational sac and an ovarian mass, the differential diagnostic of the ovarian mass should include corpus luteum or theca lutein cysts, both of them disappearing most often during the 16th week of pregnancy and endometriomas; unfortunately, the differential diagnostic between endometriomas and ovarian cancer can be sometimes difficult to be established, due to the fact that the high levels of circulant progesterone could induce the modification of the cystic walls[5-7]. However, it is widely recommended that any adnexal mass larger than 5 cm which persists after the 16th week of gestation and which presents an atypical sonographic aspect should be removed[4]. As for the cases diagnosed with ovarian malignancies, the most commonly encountered histopathological subtypes include epithelial ovarian cancer, germ-cell or sex-cord tumors[8].

Whenever the ultrasound aspect is suspect, other imagistic studies such as magnetic resonance imaging or positron emission computed tomography should be taken in consideration[9]. As for the utility of tumoral markers tests in pregnancy, the specificity of CA125, beta-human chorionic gonadotropin or alpha-fetoprotein remains low due to the fact that increased values might be encountered even during normal pregnancies. For example, during a normal pregnancy course, CA 125 values are increased until 30-40 days of gestation, reporting a peak during 35-60 days of gestation and decreasing by the end of the first trimester[10]. However, once the diagnostic of concomitant ovarian cancer is established, these markers might be used in dynamics in order to monitor the response to treatment and the evolution of the disease. Other tumor markers such as inhibin B, anti- mullerian hormone or human epididymis 4 might be useful due to the fact that their values are not increased during normal pregnancies[11].

The Influence of Pregnancy on Cancer and the Inverse Correlation

It was showed that pregnancy per se does not influence ovarian cancer progression due to the fact that most ovarian malignancies diagnosed during

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pregnancy are not hormone dependent; in the meantime ovarian cancer progression can occur if oncological treatment is delayed[12]. Therefore, cancer per se does not influence the pregnancy course, the neonatal outcomes or infant death[13]; however, cancer's management can influence the pregnancy's outcomes.

The Role of Surgery in Early Stage Ovarian Cancer Associated with Pregnancy

Unlike in other cancers diagnosed during pregnancy, in which oncological treatment can be delayed until foetal maturity, in ovarian cancer the treatment should be performed as fast as possible in order to prevent the progression of the disease[4]. Unfortunately so far there are no standardized therapeutic guidelines regarding the most appropriate therapeutic strategy, individualized therapy being needed[14].

While in patients diagnosed with early stage ovarian cancer during the last weeks of pregnancy the oncological treatment can be delayed until postpartum, in cases in which the diagnostic is established during the first weeks of pregnancy, surgery should be performed as early as possible; the operative moment should be established after a close analysis from both obstetrical and oncological point of view; therefore, if the decision of surgery is taken to early (before the fourth month of pregnancy), a higher risk of miscarriage or luteal function loss exists while if surgery is planned for too late the risk of malignancy progression as well as the one of adnexal torsion or premature labour should be taken in consideration[5]. For patients diagnosed in early stages of pregnancy the most facile option seems to be medically induced abortion followed by standard treatment for ovarian cancer[4].

Fertility and Pregnancy Sparing versus Radical Surgery

If pregnancy sparing therapy is the option for choice, the timing of therapy plays a crucial role, both surgery and adjuvant chemotherapy being recommended only after the end of the first semester of pregnancy. However, the decision should be a multidisciplinary one, involving the obstetrician, the gynaecologic oncologist, the oncologist, the paediatrician, the anaesthetist as well as the patient and her family[4].

According to the International Federation of Obstetrics and Gynaecology (FIGO) for early stage ovarian cancer standard surgery consisting of total hysterectomy with bilateral adnexectomy, peritoneal cytology, peritoneal biopsies and lymphadenectomy should be performed[15]. In cases in which pregnancy sparing surgery is tempted, initial approach should consist of adnexectomy, peritoneal cytology, peritoneal biopsy and omentectomy while in mucinous tumors appendectomy should be added[9]. Another therapeutic option for FIGO stage IA grade 1 epithelial ovarian cancer and germ-cell tumors consists of performing an adnexectomy at the initial moment followed of restaging surgery after delivery; however, this is the option of choice in patients in whom an adequate evaluation of the extra-adnexal lesions cannot be performed at the time of initial surgery[8]. Other options are to perform completion staging surgery during caesarean section or at six-eight months after delivery[4].

In cases in which pregnancy sparing surgery is performed, adjuvant chemotherapy should be associated during the second and third trimester of pregnancy, followed by planned delivery and surgical completion treatment[4]. It has been widely demonstrated that administration of carboplatin and paclitaxel can be safely performed during the second and third trimester of pregnancy, with similar risks to non-pregnant women while bevacizumab should be avoided in pregnant patients[16].

As for the type of surgical approach, both laparotomy and laparoscopy can be taken in consideration. While if open surgery is tempted, minimal uterine manipulation is required in cases in which laparoscopy is desired surgery should be planned during 16 and 20 weeks of gestation[9]; whenever an excessive uterine manipulation is performed, increased doses of tocolytic agents are needed. In the study conducted by Mathevet and contributors, they included 48 pregnant women submitted to laparoscopic surgery during the first (17 cases), second (27 cases) and third trimester of pregnancy (4 cases) and demonstrated that laparoscopy has minimal risks at any moment of the pregnancy for both mother and foetal safety[17]; although no prospective studies are available to compare laparoscopic and open approach, multiple observational studies demonstrate the superiority of laparoscopy during pregnancy[17,18]. However special care in terms of adequate oxygenation and pre-oxygenation as well as of the patients' positioning in Trendelenburg should be taken irrespective of the type of surgical approach. A special care should be taken in order to prevent thrombosis; such cases are predisposed at developing extensive thromboses due to the association between pregnancy, prolonged immobilization and malignancy[19].

Conclusions

Ovarian masses measuring more than 5 cm, with suspect ultrasonographic aspect which persist after the 16th week of pregnancy are considered as suspect and should be removed via laparoscopy or open approach. Whenever the diagnostic of ovarian cancer is established, the further management should be decided by a multidisciplinary team consisting of obstetrician, oncologist, surgeon, anaesthetist, paediatrician and according to the patients' and her family wishes. If medical abortion is decided, completion surgery consisting of total hysterectomy, contralateral adnexectomy, omentectomy, pelvic and para-aortic lymph node dissection will be performed. If pregnancy preservation is desired, surgery might be

completed by peritoneal cytology, peritoneal biopsy and omentectomy while in mucinous tumors appendectomy should be added. Once the staging process is completed, adjuvant platinum based chemotherapy can be administrated during the second and third trimester of pregnancy. In certain cases, depending on the tumoral stage and patient's wish, at the time of caesarean section performing, completion surgery including total hysterectomy and contralateral adnexectomy, pelvic and para-aortic lymph node dissection might be performed. ■

Conflict of interests: The authors declare no conflict of interests.

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