Cancer and Pregnancy: From biology to Treatment Choices

Fedro A Peccatori[1], MD, Hatem A Azim Jr.[2], MD.

(1) Department of Medicine, Division of Haematology-Oncology, European Institute of Oncology, Milan, Italy
(2) Department of Medical Oncology, National Cancer Institute, Cairo University, Cairo, Egypt.

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Although the incidence of cancer in pregnancy is not fully known, it is estimated that 1:1000 pregnancies are complicated by a malignant neoplasm [1]. The most frequent tumors which complicate pregnancy are those that have a higher incidence during the childbearing age. Specifically, cancers of the breast, cervix, melanoma, lymphomas and acute leukemia are the most common gestational cancers [2]. Since there is a clear trend to postpone pregnancy to later in life, the co-association between cancer and pregnancy is becoming more frequent [3]

Accumulating evidence suggests that pregnancy per se is not a dismal prognostic variable. Survival appears to be similar between pregnant and non-pregnant cancer patients.

Staging work up of cancer during pregnancy should be limited to diagnostic tests that do not damage the fetus. In particular, examinations with ionizing radiation should be performed only in the second and third trimester; during the first trimester of pregnancy, only absolutely necessary radiologic investigations are justified. Other diagnostic procedures such as excisional or incisional biopsies, endoscopies, lumbar puncture or bone marrow biopsies can be safely performed with the appropriate caution.

The treatment of malignant neoplasms during pregnancy should benefit the mother, especially in the case of curable malignancies, without damaging the fetus, whenever possible. Special care should be taken to retain mother's reproductive system intact when possible, for future gestations. Surgery under general anesthesia is safe at all gestational ages, even if abdominal surgery can be associated with a higher incidence of fetal loss, particularly during the first trimester [4]. Care in maintaining adequate maternal pressure and blood volume should be taken, to avoid the risks of maternal and fetal hypotension.

Systemic chemotherapy can be safely administered during the second and third trimester [5]. Data in more than 100 patients with different neoplasms report that anthracyclines and alkylating agents are safe after the first trimester, with an incidence of fetal malformation similar to that of the untreated population [6]. Specific schedules to minimize fetal drug exposure and systemic maternal toxicity, while maintaining high antitumor activity, are warranted. Recent data about weekly Epirubicin administration in breast cancer patient are a good example of the above mentioned strategy [7]. Vinca alkaloyds can be administered also in the first trimester [8], while anti-metabolites like methotrexate are associated with a high proportion of fetal wastage and should be avoided [9]. Few data are available about the administration of monoclonal antibodies during pregnancy. Prolonged trastuzumab treatment during pregnancy has been associated with oligo-anhydramnios and should be avoided, whenever possible [10]. Rituximab has a more favourable toxicity profile, but fetal lymphopenia has been described, so caution is mandatory [11, 12]. Hormonal treatment should be avoided during pregnancy. Data about Tamoxifen administration during pregnancy are scanty, but the occurrence of genital and systemic malformation after selective estrogen receptors modulators administration suggests caution [13]. Moreover the higher incidence of vaginal clear cell carcinoma in offsprings of mother treated with synthetic estrogens during the first trimester should be always kept in mind. Whenever an anti neoplastic systemic treatment is administered during pregnancy, the mother and her fetus should be strictly followed in a tertiary care obstetrical structure. Fetal well being and growth should be frequently monitored, due to the higher risk of intra uterine growth restriction and premature delivery associated with chemotherapy administration. A thorough follow up of the newborns, including cardiological, neuropsychological and reproductive assessment should be always planned, to acquire more information about the effects of in utero exposure to antineoplastic agents.

Radiotherapy should be avoided during gestation, particularly if it involves the subdiaphragmatic region [14]. Data about fetal risks of ionizing radiations during pregnancy are mainly derived from animal models or from the Japanese nuclear bombing cohort. Even if some controversy still remains, a threshold below 100 mGy (100 mSv) is usually considered safe for the onset of unwanted deterministic fetal damages, which include fetal death, fetal malformation or mental retardation. On the other hand the linear no-threshold hypothesis postulates that any exposure to ionizing radiations, even at low dosage could be harmful. These unwanted stochastic effects include the risk of fatal pediatric cancer before the age of 15 and can be estimated around 0.006%/mGy received during the intra uterine life.
When treatment cannot be delayed, or the risk of fetal malformation of unwanted side effects is considered too high, termination of pregnancy is advisable although the prognosis does not appear to be different between patients who underwent pregnancy termination or elected to continue the pregnancy.
Malignancies during pregnancy are a dramatic event with a profound impact on the life of the patient, the unborn child, the family and the treating caregivers. A multidisciplinary approach that includes an appropriate psychological support is essential for proper treatment of this difficult situation.

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