introduction

Cancer complicates pregnancy very rarely (estimated incidence 1:1000 pregnancies), though this co-existence is likely to become more common in view of the prolongation of reproductive age and women’s tendency to delay childbearing. It is estimated that up to 20–30% of malignant tumors occur in women younger than 45 years [1]. The diagnostic and therapeutic management of a pregnant patient with cancer is especially difficult because it involves two persons, the mother and the fetus. Obstetricians and oncologists should strive to offer optimal maternal treatment and safeguard fetal well-being (when the two are compatible!).

Management of gestational cancer implicates medical, ethical, psychological and religious issues. The patient and her family should be actively involved in the decision-making process following counseling and adequate information.

tumors in pregnancy

The most common tumors diagnosed during pregnancy are breast cancer, cervical cancer, melanoma, leukemias/lymphomas. Lung, gastrointestinal, urological and other malignancies are rarely observed [1].

There is evidence that diagnosis is delayed, as symptoms and signs of malignancy are masked by those of pregnancy. Cervical cancer is a notable exception, probably because frequent gynecological examinations lead to early diagnosis. Manifestations and physical history for each malignancy are typical for those that affect non-pregnant patients of the same age.

Older case reports and retrospective series indicated a more aggressive biology of gestational tumors and dismal prognosis in pregnant patients. However, more recent population studies of pregnant patients who were matched to non-pregnant patients of the same age and disease stage showed that response to therapy and prognosis are similar [2].

Ionizing radiation is an integral part of radiodiagnostic and radiotherapeutic procedures. It carries deterministic biological effects that are dependent on the radiation dose administered (safety of threshold dose) and stochastic effects of which only the probability, not the severity, is linearly associated with administered dose (safety threshold dose absent).

Radiation deterministic effects result from fetal cellular damage and are congenital malformations, miscarriage, stillbirth, mental retardation, intrauterine growth retardation (IUGR) and premature delivery. The safety threshold dose for these effects is an absorbed dose of 100 mGy. Stochastic effects result from fetal cellular modification (mutation) and are second tumors, leukemias, myelodysplastic syndromes and late injury of normal tissues [3].

Diagnosis of malignancy in pregnant women should follow oncological principles (adequate biopsy and staging). Chest X-ray is safe and coupled with abdomino-pelvic ultrasound provides crude staging information. When more detail is needed, brain computed tomography (CT), mammography and magnetic resonance imaging (MRI) scans (without gadolinium during the first trimester) are safe.

Abdominal films, radioisotope scans, barium enemas, intravenous urography, positron emission tomography (PET) and abdominal CT scans should be avoided.

treatment

Following diagnosis and staging, the tumor type, stage, gestational period and patient wishes will define the therapeutic strategy [4].

The impact of chemotherapy and radiotherapy depends greatly on the age of gestation (Table 1). During the first 2 weeks, an ‘all or nothing’ effect is seen (spontaneous abortion or normal fetal development). Weeks 3–12 make up the critical period of organogenesis, during which teratogenesis may occur.

Table 1. Effects of anti-neoplastic treatment by gestational age

<table>
<thead>
<tr>
<th>Gestational stage</th>
<th>Embryonal/fetal development</th>
<th>Impact</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weeks 0–2</td>
<td>Undifferentiated multicellular organism</td>
<td>‘All or nothing’: spontaneous abortion or normal development</td>
</tr>
<tr>
<td>Weeks 3–12</td>
<td>Organogenesis</td>
<td>Spontaneous abortion, major congenital anomalies</td>
</tr>
<tr>
<td>Second and third trimesters</td>
<td>Intrauterine growth and maturation, continuing development of CNS, gonads, teeth–palate, eyes, ears</td>
<td>Functional defects and minor anomalies of late-forming tissues, stillbirth, IUGR, premature delivery, myelosuppression</td>
</tr>
</tbody>
</table>

CNS, central nervous system; IUGR, intrauterine growth retardation.
Continuing development of the central nervous system, eyes, palate and genitals up to week 20 results in a marginally elevated risk of malformation of these organs.

Second and third trimester exposure to chemotherapy or low doses of radiotherapy is relatively safe: stillbirth, IUGR, premature delivery, low birth weight and fetal myelosuppression may occur at a frequency of 15–40\% [1, 5, 6].

radiotherapy

Radiation therapy of supradiaphragmatic disease sites (brain, neck, breast, chest, mediastinum, axilla) has been reported in pregnant women without sequels, especially in the first trimester when the uterus is distant from the radiation fields. Absorbed fetal doses have been calculated in the range 30–200 mGy [7]. Still, such radiation therapy requires meticulous planning and shielding, expertise, involves some risk of fetal defects and carries risk of litigation. Most experts do not advocate radiation therapy during pregnancy, since it is seldom absolutely necessary before delivery.

chemotherapy

Chemotherapy should not be administered during the first trimester: if there is an absolute indication for it, termination of pregnancy is advised. Second and third trimester chemotherapy is relatively safe with appropriate monitoring and provided delivery should take place at least 2–3 weeks after the last cycle so as to avoid maternal/fetal myelosuppression. Of course, the pregnant woman should be ready to accept the marginally elevated risks of IUGR, stillbirth and minor malformations. Premature delivery, low birth weight and IUGR are seldom irreversible or fatal.

Vinca alkaloids, anthracyclines, 5-fluorouracil (5FU), cyclophosphamide seem to be the less deleterious, while anti-folates and alkylating agents the most. Taxanes, platinum compounds and targeted agents (trastuzumab, rituximab, imatinib) have been administered in only a handful of pregnant patients and should be avoided [1, 2, 5, 6].

Deferral of therapy (chemotherapy or radiotherapy) until delivery of a viable fetus (after the 32nd week) is also a viable option for certain circumstances, such as early cancer, low-grade tumors and late-stage pregnancy.

Cumulating evidence suggests that at least 60–75\% of pregnancies can be carried to term despite diagnosis of malignancy, though a positive publication bias may be present: successful deliveries are reported, abortions not.

In contrast to radiation (2- to 3-fold increased risk of second tumors), chemotherapy does not seem to be associated with long-term physical, cardiac, neurodevelopmental, reproductive effects or second tumors [8].

maternal/fetal outcome

Pregnancy does not seem to modify the biology and prognosis of cancer, neither do subsequent pregnancies increase the risk for relapse [1, 4, 9]. Still, following cancer treatment a woman is advised to wait anything from 6 months (recovery of oocytes from chemotherapy-induced damage) to 2–5 years (to lower the risk of relapse) before embarking on childbearing.

Placental metastases are extremely rare. When seen, melanoma, breast cancer and leukemias/lymphomas of the mother are the causative tumors [2]. Fetal metastases are rarer, seen in 20\% of cases with placental metastases present. It is prudent to histologically examine the placenta in cases of gestational cancer. Finally, abortion does not affect the behavior or outcome of gestational cancer and should be advised in selected circumstances: (i) first trimester pregnancy with absolute indication for anticancer therapy, (ii) advanced malignancy and poor maternal life expectancy, (iii) advanced stages of gynecological cancers, (iv) inadvertent fetal exposure to radiation doses >100–200 mGy, (v) mother unwilling to accept the small increase in the risk of malformation or growth restriction.

disclosures

No significant relationships.

references