



Cancer and pregnancy

Recommendations from the society for diagnosis and therapy of haematological and oncological diseases



Publisher

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Date of document: June 2021

Compliance rules:

• Guideline

· Conflict of interests

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1 General information

A cancer during pregnancy is always an exceptional situation for the pregnant woman and her relatives, but also for the attending physicians, and represents a very rare event. Pregnancy-associated cancers are those that occur during pregnancy up to 1 year after delivery. Data regarding tumor type, incidence, and progression are still relatively sparse because of the rarity and heterogeneity of these conditions. For example, some studies only consider pregnancies that end in live birth, while other studies include miscarriages and abortions [1]. The number of cancers diagnosed during pregnancy is approximately 1 per 1000 to 1 per 1500 pregnancies per year [2]. The most common cancers are gynecological tumors (including mainly breast cancer followed by cervical cancer), thyroid carcinomas, diseases of the hematopoietic system (e.g., leukemias, lymphoma), and melanoma (black skin cancer) [3].

Pregnancy is not a risk factor for cancer. In several retrospective analyses, no difference was found between pregnant and non-pregnant women with regard to the frequency, type of tumor, and course of cancer during pregnancy.

There is also no evidence to date that hormonal stimulation in the context of infertility treatment increases the risk of cancer [4].

When cancer occurs during pregnancy, the well-being of the patient and the well-being of the unborn child must be considered. Care must be comprehensive and involve the patient's environment (partner, relatives) and all disciplines involved at an early stage and on an ongoing basis. In Onkopedia, separate recommendations on pregnancy are integrated in some guidelines, e.g. in acute promyelocytic leukemia.

2 Good to know

2.1 Is an abortion necessary?

Treatment recommendations for pregnant cancer patients are based on a limited body of experience. Each of these diagnoses therefore requires a multimodal therapeutic approach in close and early consultation with the disciplines involved, especially between obstetric medicine and the treating oncologists. Clinical uncertainties and ethical dilemmas will always remain part of these decision-making processes [5].

In general, with the diagnosis of cancer in pregnancy, immediate termination of pregnancy is not mandatory. Decisive influencing factors are the type of tumor, localization and spread of the disease, the week of pregnancy and the patient's wishes. It is important that both further diagnostics and a possibly necessary start of therapy are not delayed by the existing pregnancy. According to §218a, an abortion for medical reasons is not illegal even after the 12th

week of pregnancy (SSW), if there is a danger to life or a serious impairment of the physical or mental health of the pregnant woman, which can only be averted by an abortion.

If the cancer diagnosis was made in the first trimester (1st to completion of the 12th week of pregnancy) and the immediate implementation of a drug-based tumor therapy (e.g. chemotherapy) and/or radiation is necessary, there is a general recommendation to terminate the pregnancy. Since in these first weeks the formation of all organs in the embryo takes place and thus there is a special vulnerability to harmful influences, malformations, miscarriages or intrauterine death of the child are not uncommon [6]. In the literature, there are some individual case reports of successfully terminated pregnancies despite diagnosis and therapy of cancer in the 1st trimester. Purely surgical therapeutic approaches, e.g., removal of a malignant skin tumor, are possible relatively independently of the duration of pregnancies, despite diagnosis and therapy of cancer in the 1st trimester. Purely surgical therapy approaches, e.g. removal of a malignant skin tumor, are possible relatively independently of the duration of pregnancy.

2.2 Does ending my pregnancy early affect my chances of surviving my cancer?

To date, no studies have been able to prove that premature termination of pregnancy improves cancer survival (e.g. in breast cancer). In the 2nd and 3rd trimesters, organ formation is largely complete, so that in the case of initial diagnosis from the 2nd trimester onwards, it is usually possible to maintain the pregnancy. For initial diagnosis from the 35th week of gestation, there is a recommendation to aim for delivery before initiating chemotherapy, if possible [7, 8]. There should be a period of approximately 2 weeks between the last chemotherapy and the intended delivery to minimize the side effects of chemotherapy on the hematopoiesis of mother and child [7]. Regardless of the duration of pregnancy, prenatal care and delivery should be planned in a level 1 perinatal center (see also under point 4 Perinatal Centers), i.e., a specialized facility for pregnant women or premature and newborn infants. Depending on the obstetric indication, a spontaneous delivery or a delivery by cesarean section (sectio) may be performed.

2.3 Can cancer therapy be performed during pregnancy?

Many of the recommended chemotherapies can also be performed during pregnancy. Most experience in this regard is available for treatments during the 2nd and 3rd trimesters. The blood-placenta barrier, through a variety of different filtering and passage mechanisms, ensures that many chemotherapeutic agents arrive in the amniotic fluid and presumably also in the unborn child (fetus) at a much lower concentration [9]. The problem of administering maximally effective therapy to treat the cancer as successfully as possible while giving as little chemotherapy as possible to protect the unborn child drives every treatment decision. Sometimes treatment protocols can be modified such that certain agents are replaced with other, less toxic therapeutic agents or that monotherapy is given until delivery instead of combination therapy. In most cases, continuation of therapy is necessary after delivery, so breastfeeding is not possible in these cases [10, 11]. Aspects related to "fertility and fertility preservation" in the context of cancer treatment are listed in a separate AYApedia chapter. Surgical procedures for the treatment of cancer should, if possible, be performed during the 2nd trimester, as the uterus itself then still allows abdominal surgery [12]. In principle, however, surgical intervention can be performed at any time during pregnancy, as mentioned above. Radiation, in turn, should be postponed until after delivery whenever possible. If this is not possible, it is important to make sure that the radiation is performed by a highly experienced team of radiation therapists in collaboration with experienced oncologists. It is also advisable to plan the irradiation carefully, to shield the uterus and the unborn child as well as possible, and to divide the irradiation into small individual doses over a longer period of time [13, 14].

2.4 What influence does pregnancy have on the diagnosis/therapy of my cancer?

The diagnosis of cancer during pregnancy can sometimes be delayed (denser breast tissue, general non-specific symptoms such as fatigue or nausea) [12]; on the other hand, pregnant women are generally under close medical care, which is why tumors can also be detected at an early stage without symptoms (especially cervical cancer). Many examination methods, including invasive ones, such as fine needle and punch biopsies, endoscopies or bone marrow punctures, can also be performed during pregnancy without any problems. Surgical procedures are also usually possible at any time during pregnancy, depending on the type and location of the procedure. In the case of general anesthesia during the 1st trimester, there is a slightly increased risk of miscarriage [12]. In principle, pregnancy has no influence on the prognosis of cancer. No statistically significant difference in long-term, as well as disease-free survival between pregnant and non-pregnant women has been found so far [15].

2.5 Which imaging examination methods can be used?

The imaging method of first choice during pregnancy is ultrasound, as it does not use X-rays. MR tomography also does not require X-rays, but due to the strong magnetic field, its use in the 1st trimester (time of organ development) is not recommended [16]. Some contrast agents, e.g., gadolinium-based contrast agents, are contraindicated during pregnancy. CT and X-ray examinations should be avoided throughout pregnancy. In exceptional cases, X-ray examinations, such as a mammogram, are nevertheless possible, as only a very low dose of radiation is used. However, any exposure to X-rays should always be done in close consultation between the treating disciplines and is always a case-by-case decision.

Nuclear medicine studies (e.g., FDG-PET, bone scintigraphy) should be postponed until after delivery [12].

2.6 What effects can chemotherapy have on my child?

If therapy becomes necessary, it should begin promptly so as not to jeopardize the success of the therapy and thus the desired cure.

Chemotherapy in the 1st trimester is often associated with an increased rate of miscarriage, fetal malformations, and intrauterine death of the child later in pregnancy [17]. However, there are also case reports in which healthy infants were born in the 1st trimester despite chemotherapy exposure. Nonetheless, chemotherapy in the 1st trimester is considered contraindicated. In contrast, no increased rates of fetal malformations or other disorders have been demonstrated to date when chemotherapy is administered in the 2nd and/or 3rd trimesters, so it is considered relatively safe [18, 20]. At the same time, an increased risk of preterm labor, prematurity, intrauterine growth retardation, or low birth weight (so-called SGA infants, small for gestational age) must be considered [6, 7, 21]. However, most of the disorders were shown by the children due to their prematurity (early preterm birth up to 32nd SSW, late preterm birth 32nd - 36th SSW) and not due to the chemotherapy administered. Therefore, when chemotherapy is administered during pregnancy, it is recommended to aim for delivery after SSW 35 if possible [22]. The risks associated with chemotherapy, even in the 2nd and 3rd trimesters, generally remain less than the potential benefits of treating the cancer for the mother [12].

If possible, chemotherapy should be stopped or paused approximately 2-3 weeks before delivery to allow maternal and fetal bone marrow recovery and thus reduce the risk of infection and/ or sepsis during delivery for both mother and child [23, 24]. Precisely because of the increased

risk of preterm delivery, chemotherapy should be administered only up to 33 weeks gestation [25].

The general recommendation is to plan the next pregnancy, if possible, only after a disease-free interval of two years [10].

2.7 Can I breastfeed my child with breast milk?

Since in most cases therapy is continued postpartum and most substances pass into breast milk and would thus be absorbed by infants in sometimes relevant high concentrations, breast-feeding is usually not recommended [10, 11].

2.8 Is there anything to consider when vaccinating the newborn or infant if I received drug tumor therapy during pregnancy?

Drug therapy during pregnancy can also affect the blood count of the newborn. For example, a reduction in white blood cells (leukocytes) was detectable in approximately one third of newborns who were exposed to chemotherapy in the womb 4 weeks before delivery [26]. These chemotherapy-induced blood count changes in the newborn usually normalize spontaneously within 2-10 weeks after birth. Nevertheless, before vaccinating the infant with a live vaccine (e.g., against rotavirus), a differential blood count should be ordered and vaccination should be performed only when lymphocytes are normal [27].

If the infant was exposed to therapy with a so-called anti-CD20 antibody (e.g., rituximab) during the mother's pregnancy, this should also be taken into account. Anti-CD20 antibodies can cause a persistent reduction in B cells (B lymphocytes) for a period of approximately 6 to 9 months (occasionally longer). Vaccination of the infant with inactivated vaccines (inactivated vaccines) is possible in principle in this situation, but the success of the vaccination is questionable with reduced B-cell counts. Therefore, B-cell counts should be determined prior to vaccination [27].

3 Tips and tricks

Although cancer is very rare in pregnancy, appropriate diagnostics must be initiated immediately in the event of a suspicion. The possibility of psychological support should be taken advantage of or requested as early as possible. Furthermore, information and support services for the care of the child and mother after delivery must be organized in good time. You can find numerous tips and background information about this on the knowledge pages of the German Foundation for Young Adults with Cancer.

In many cases, treatment of the cancer is required beyond birth. This often means separation of mother and child. All treatment decisions should be made in close consultation with an interprofessional team of, for example, gynecologists, pediatricians, hematologists and oncologists, surgeons, psychooncologists, radiologists and radiation therapists.

Tip: Actively approach the health insurance company for assistance (e.g., household help) and keep in close contact with the health insurance company, social services, and also the parental allowance office, since important bureaucratic decisions must be made (e.g., parental leave, sick leave).

4 Further information

Family & Cancer

On the knowledge pages of the German Foundation for Young Adults with Cancer you will

find many more helpful tips and background information: https://junge-erwachsene-mit-krebs.de/wissensbegriffe/category/familie-und-krebs/

Young & Cancer - First Aid

General tips from affected persons for affected persons are offered by the German Foundation for Young Adults with Cancer: https://junge-erwachsene-mit-krebs.de/youth-cancer/first-aid/?lang=en

Perinatal centers

An overview of perinatal centers in Germany and further information can be found at: https://perinatalzentren.org

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7 Disclosure of Potential Conflicts of Interest

according to the rules of the supporting professional societies.