REVIEW ARTICLE
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Pregnancy and melanoma

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ABSTRACT

Numerous malignant diseases reach their incidence peak in female fertile years. That is the reason why these diseases are the second most common cause of death of women in their generative age. However, neoplastic processes are rarely diagnosed in pregnancy and there are no clear-cut guidelines on whether the pregnancy should be terminated in order that a proper treatment could be applied. We have not enough knowledge jet about the consequences for both the mother and her child if the pregnancy is allowed to continue despite the diagnosis of malignancy. Melanoma is one of the most common tumours diagnosed in pregnancy (8% of all diagnosed neoplasms). Some studies present the data on successfully terminated pregnancies in these women but also point out the risks the fetus is exposed to due to possible application of cytotoxic therapy, as well as the danger of transplacental spread of this process to the placenta and fetus.

KEY WORDS: *Pregnancy; Melanoma; Pregnancy Outcome*

INTRODUCTION

Many malignant diseases in women reach their incidence peak in the female generative period and therefore it is not surprising that tumours are cited as the second most common cause of death in that period (1). Some authors state that in the USA 19% of women aged 15 to 34 years die of cancer (2). The incidence of all malignant tumours in pregnancy is 0.07% to 0.1%, and the shift of the childbirth age towards older age groups means that the coincidence of tumours and pregnancy is to be expected in an even higher percentage (1,2). The most frequent tumours in pregnancy are breast cancer, gynecologic tumours (carcinoma of the uterine cervix and ovarian tumours), melanoma and lymphomas (1-3).

Any malignant disease in pregnancy is a diagnostic as well as a therapeutic problem. In addition to medical issues, there are also numerous ethical, psychic and social dilemmas (4). The fact is that at present we do not know enough about the influence of pregnancy on tumor and the influence of tumor and therapeutic proceedings on pregnancy. Due to low incidence of some tumours in pregnancy it is not possible to conduct relevant large-scale studies. The experiences published so far relate most often to individual cases or small groups of patients, which does not allow any standardization. Each case, therefore, has to be considered separately and the decisions are to be made by oncologist, gynecologist and the affected woman herself (5). All the benefits should be considered, as well as the harmful effects in case of the decision to terminate pregnancy in order to immediately start with appropriate therapy. On the other hand, in case of the decision to continue pregnancy, all potential harmful effects on fetus of diagnostic and treatment procedures have to be considered. In both cases the patient has to be extensively informed and the doctor's role is to help the patient in decision making with his/her knowledge and experience (3).

In the past, the diagnosis of malignant tumor in pregnancy meant inevitable pregnancy termination (5). Attitudes regarding such situations have somewhat changed, since the fact is that some therapeutic interventions as the consequence have permanent infertility. In numerous studies, investigations on the influence of treatment on the fetus are under way, or their goal is to improve the methodologies, which may help in preserving fertility after anticancer treatment. These investigations are the imperative if we consider the facts that new therapeutic procedures may induce cure or long-lasting disease-free interval (DFI) and that the incidence peak of many malignant tumours shifts towards younger age groups (6).

FREQUENCY OF MELANOMA IN PREGNANCY

Melanoma is a major health care problem due to its growing incidence especially in younger populations. In some countries 30% to 35% of female melanoma patients are in their reproductive period (2). Out of 1000 deliveries there are 0.14% to 2.8% cases of melanoma; 8% of all malignancies in pregnancy are melanomas (7).

SYMPTOMS

Melanoma symptoms in pregnancy are identical to those in non-pregnant women. Every change of color, size, configuration, pigmentation, bleeding or ulceration requires further examinations and confirmation of melanoma diagnosis. About 2/3 of all melanomas occur in preexistent pigmented changes. Hyperpigmentation, which may be one of the pregnancy symptoms, can mask the underlying malignancy and delay the right diagnosis (1,2).

DEVELOPMENT OF MELANOMA AND POSSIBLE HORMONAL IMPACT

Measurements of melanocyte-stimulating hormone in pregnancy demonstrated its elevation in the 2nd and 3rd trimester, which suggests that hormonal changes in pregnancy stimulate the growth of melanocytes and influence disease development (7). In pregnancy, numerous endogenous hormones are elevated (estrogen, androgen, MSH, FSH, LH) (8,9). However, none of the investigations so far demonstrated any direct link between hormonal changes in pregnancy and disease course and pregnancy termination did not have impact

on improvement nor pregnancy continuation had any impact on poor disease outcome (7). The current belief is that the pregnancy termination is necessary only in stage IV melanomas when aggressive treatment approaches are required and any treatment delay can directly be life threatening.

There is no convincing evidence that exogenous hormones can have impact on melanoma occurrence. With oral contraceptives, hyperpigmentation was observed in the form of chloasma, but there is no direct evidence that melanoma is more common in women who were using oral contraception (10-12). Significant influences were not observed either with antiestrogen therapy (Tamoxifen) or an antiandrogen - cyproteronacetate (13).

THERAPY

In cases of suspect melanoma, excision biopsy is immediately required, followed by histopathologic verification. The disease is staged in the same way in pregnant as well as in non-pregnant women; stages are defined according to the tumour size, process depth, involvement of regional lymph nodes or diagnosis of distant metastases. Disease stage is the most significant prognostic factor in these patients (1,2,7). Travers et al. (14) have found thicker melanin layer in pregnant women and concluded that it was probably the consequence of delayed diagnosis. Many dermatologists believe that melanocytic naevi are prone to alteration in pregnancy (enlargement, dark coloration, etc.), but objective investigations disproved this hypothesis (15).

Melanoma treatment in pregnancy is primarily surgical. Regional lymph node dissection has not demonstrated any significant impact on survival. The use of radiolabeled tracers in order to define sentinel lymph node has been a very useful technique, but it is contraindicated in pregnancy (1). In melanoma treatment in pregnancy cytostatic treatment can be applied after the first trimester (after organogenesis), while immunotherapy is not applied since it significantly increases the percentage of spontaneous abortions (16).

SURVIVAL

The experiences so far have not demonstrated significant survival differences in patients with melanoma diagnosed in pregnancy compared to nonpregnant patients. In several studies it was observed that the DFI was shorter if the malignancy was diagnosed in pregnancy. Nodal metastases are the most common phenomenon (71%), in contrast to satellite cutaneous metastases (13%). As far as distant metastases are concerned, there is no statistically significant difference between pregnant and nonpregnant melanoma patients. The opinion that pregnancy itself is an independent prognostic factor related to DFI has not been confirmed by larger controlled studies (1,2,17).

IMPACT OF MELANOMA ON PREGNANCY

In patients with melanoma in pregnancy it is necessary that the doctor inform the patient on all possible toxic effects of treatment on fetus, but also on the possibility of transplacental dissemination of malignancy. Fetal metastatic deposits are rare, but 30% of all metastatic placental changes were diagnosed in melanoma. It is therefore necessary to perform meticulous and precise histopathologic examination of the placenta after delivery (2).

CONCLUSION

Melanoma is one of the most common tumors in pregnancy (0,14-2,8% of the cases per 1000 deliveries). The symptoms are identical to those in non-pregnant women: change of color, size, and configuration of the pigmented lesion, bleeding or ulceration. Physiologic hyperpigmentation in pregnancy can sometimes deceive physicians and delay proper diagnosis. Up to the present it has not been confirmed that endogenous elevation of hormones in pregnancy or their exogenous application can have any significant impact on the occurrence of melanoma. Melanoma diagnosis is made by excision biopsy with histopathologic verification; a disease stage is the most important prognostic factor. First line therapy for melanoma is surgical, with adjuvant chemotherapy as an option after the first trimester. Immunotherapy cannot be recommended during pregnancy. Investigations so far demonstrated survival of pregnant melanoma cases similar to controls. DFI, as demonstrated, has been shorter in view of nodal metastases but not when distant metastases are concerned. In cases of diagnosed melanoma in pregnancy, the patient has to be informed about fetal toxic effects of possible chemotherapy, but also with transplacental dissemination of malignancy and the possibility of fetal and placental metastases.

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