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OPINION ARTICLE

Melanoma and Pregnancy☆

Melanoma y embarazo

S. Serrano-Ortega,* A. Buendía-Eisman

Professor of Dermatology, Universidad de Granada, Granada, Spain

We have often heard and still hear statements like ''If you have had melanoma you should not get pregnant'' or ''If you are pregnant and you develop melanoma, your pregnancy has to be terminated''. We have even made such statements ourselves, whether to prevent the recurrence of hypothetically residual disease or to avoid a poor prognosis.

There has been a great deal of controversy over the years regarding the links between cutaneous melanoma and pregnancy. Given the existence of studies that argue for and against a worse prognosis, it is essential to draw on sufficient data to be able to decide the most suitable approach to melanoma in pregnant women.

The incidence of melanoma is increasing steadily in most developed countries, whereas the birth rate is falling. In Spain the highest incidence of cutaneous melanoma is 11.9 cases per 100 000 population for males in Zaragoza, and 8.7 cases per 100 000 population for women in Tarragona; the lowest incidence, for both men and women, is in Cuenca, with 3.3 and 2 cases per 100 000 population, respectively.[1] In 2009 in Spain, the average number of births per 1000 inhabitants was 10.75, ranging from 18.07 in Melilla to 7.76 in Asturias.[2]

The incidence of melanoma during pregnancy ranges from 2.8 to 8.5 cases per 100 000 pregnant women.[3,4] The estimated incidence of cancer during pregnancy is 1 case per 1000 pregnancies—the most frequent being cervical cancer, breast cancer, melanoma, lymphoma, and acute leukemia.[5] Pregnancy may affect prognosis and treatment, and there may be fetal involvement, due both to the disease and the treatment.

The debate over the possible negative link between pregnancy and cutaneous melanoma began in 1951 with the publication of an article in *Cancer* by Pack and Scharnagel,[6] who described a series of 10 pregnant women with melanoma, half of whom died within 2 to 30 months. Subsequent studies seemed to confirm this poor prognosis, giving possible hormonal influences as the explanation. However, these studies lacked scientific rigor, as they failed to take into account other prognostic factors or to draw comparisons with control groups. The first case-control studies, dating from the mid-1980 s, demonstrated that survival was comparable for similarly aged pregnant and nonpregnant women with melanoma.[7–10] Today we can say, with a certain margin of certainty, that pregnancy does not alter melanoma prognosis.Published in this issue of *Actas Dermosifiliográficas* is an excellent review by Borges et al,[11] which depicts the various scenarios that arise regarding a pregnant woman with pigmented lesions: changes in nevi; melanomas diagnosed during, before, and after pregnancy; and the use of oral contraceptives or hormone replacement therapy. This excellent review has inspired our commentary below.

- *Changes in nevi*. Skin pigmentation may change or darken, and nevi may change or grow during pregnancy. As a broadly applied generalization, however, this statement is potentially dangerous. This is because a changing or new nevus during pregnancy may be interpreted as a 'normal' aspect of pregnancy, when, in fact, it could mark the onset of cutaneous melanoma that is actually diagnosed when it is thicker, and therefore indicative of a poorer prognosis.[8] We are of the opinion that pregnant women—like those who are not pregnant—with numerous moles or dysplastic nevi should be monitored, and

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* Corresponding author.
E-mail address: consultadermatologia@gmail.com (S. Serrano-Ortega).

biopsies should be performed if there are any suspicious changes.

- *Influence of pregnancy on skin melanoma*. There is no difference in the prognosis for women diagnosed with skin melanoma—irrespective of whether or not they are pregnant—once the diagnosis is adjusted to take into account tumor thickness and development stage.[5]

The repercussions of pregnancy on the natural history of cutaneous melanoma can be explained in 2 ways: the overall increase in melanoma incidence and the influence exerted by hormones.

A recent study demonstrated an annual 2.7% increase in the incidence of cutaneous melanoma in women aged between 15 and 39 years, with exposure to UV radiation identified as the main cause.[12,13] The incidence of melanoma in women doubles with every 10 additional years of life; thus, for women of childbearing age, women aged 20-30 years account for 5% of all women diagnosed with melanoma, those aged 30-39 years for 11%, and those aged 40-49 years for 19%.[14] A frequent practice nowadays is for women to postpone motherhood for career reasons, or, as often happens, for women to start a new family after the age of 35-40 years. According to the National Institute of Statistics,[15] there were 486 127 births in Spain in 2009. These births showed an increasing distribution up to age 31-35 years: 4.1% for women in the 15-20 age bracket, 11% for the 21-25 age bracket, 25.85% for the 26-30 age bracket, and 37.8% for the peak 31-35 age bracket. There was then a drop to 24% for those in the 36-40 age bracket.

A prospective cohort study examined the possible links between gynecological history and cutaneous melanoma.[16] No differences in risk were found between nulliparous women and women who had given birth 1 or more times, and no association was found between age during the first or last pregnancy and the risk of skin melanoma. In contrast, a lower risk was reported for women whose menarche commenced after 15 years (RR = 0.67, 95% CI: 0.46-0.49), and for women with irregular menstrual cycles. There were no differences in risk associated with age at menopause.

There is sufficient evidence available to indicate that pregnancy does not alter the melanoma prognosis, irrespective of whether the cutaneous melanoma develops before, during, or after pregnancy.[17] However, since melanoma recurrence is more frequent in the first 3 years post-intervention, high-risk patients should be advised to wait 3 years before becoming pregnant.

- *Melanoma treatment during pregnancy*. The main goal is to avoid complications for the mother and fetus. Surgical treatment is theoretically not contraindicated. Once a diagnosis is established, the tumor along with a surgical margin is removed, and the wound is closed applying the general principles of surgical dermatology. In our hospital we proceed as follows. We first check that the fetus is alive, if possible by means of a gynecological examination on the same day as surgery. We always use local anesthesia (lidocaine or mepivacaine without adrenaline). General anesthesia is usually not necessary if the tumor is small and reconstruction is possible by drawing the wound edges together or use of a small local flap. For more serious surgery, we use general anesthesia, but also locally infiltrate the surgery site with lidocaine or mepivacaine without adrenaline, as this means we can reduce post-operative analgesia. Anesthetic drugs can be safely used after the first trimester.

When indicated, a sentinel node biopsy can be performed. The International Committee on Radiological Protection considers risk to be negligible for a dose of less than 1 mSv for the radiotracer, and for a dose of about 0.4 mSv during the sentinel node biopsy.[18] The time elapsing between radiocolloid injection and surgery should be kept to a minimum. In our hospital we inject the radiocolloid, perform the lymphoscintigraphy, and immediately dispatch the patient to surgery, all within an hour.

When lymphadenectomy is necessary, modern anesthesia techniques are such that surgery can be performed without any problems for the mother or the fetus.

In conclusion, current knowledge indicates that melanoma does not contraindicate pregnancy, and that pregnancy should not alter the therapeutic approach to skin melanoma.

Conflicts of interest

The authors declare that they have no conflicts of interest.

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