Pregnancy and Melanoma Risk

Based on the most recent findings, here are important points to consider in patient counseling and evaluation.

Speculation regarding the influence of pregnancy on a woman’s melanoma risk has existed for years. Concern focuses on the possibility that a woman’s decreased relative immunity during pregnancy may permit progression of an existing lesion as well as assertions that estrogen may actually promote tumorigenesis and growth. Current evidence suggests that a woman with a history of melanoma that has been successfully treated need not avoid pregnancy. However, as a general guideline, postponing pregnancy for a period of two years from the time of initial melanoma diagnosis has been proposed, since the majority of patients with metastatic disease will present with new symptoms within two years. Recent research suggests that among women with no history of melanoma, pregnancy has only slight if any influence on the individual’s risk for developing melanoma.1,2

Historical Perspectives
Anecdotal reports dating back 30 years or more have suggested that women who are diagnosed with melanoma during pregnancy may have poorer prognosis, thicker tumors, and more advanced progression of disease than non-pregnant women. While pregnancy is associated with relative decreased immunity, no data to date have confirmed that this immune status contributes to thicker or more rapidly progressing melanomas in pregnant women.

The other commonly identified culprit associated with the alleged poor prognosis for pregnant women is estrogen, based on early findings that some pigmented lesions possess sex-binding hormones. Estrogen has been associated with certain other types of cancer, including breast and ovarian cancer. However, in 1990, researchers cast doubt on the influence of estrogen on melanoma.4 They found no true estrogen receptor in any benign nevi, dysplastic nevi, primary melanomas, or metastatic melanomas.

More recently, researchers studied a possible role for the more recently discovered estrogen receptor-beta (ERbeta) in the progression of melanoma.5 They showed that ERbeta was identified in both benign and malignant melanocytic lesions; melanocytes in dysplastic nevi with severe cytological atypia and lentigo maligna showed the most intense ERbeta immunostaining. ERbeta expression varied in relation to the tumor microenvironment and increasing depth of invasion.

In recent years, several studies have failed to demonstrate that exogenous or endogenous female hormones contribute significantly to increased risk of melanoma or that pregnancy affects melanoma prognosis.6 Among them, a 2004 study compared outcomes for 135 women diagnosed with melanoma during pregnancy and 5,348 women of the same child-bearing age diagnosed with melanoma while not pregnant.6 There was no statistically significant difference in survival between the two groups.

Another study compared outcomes between 412 women diagnosed with melanoma during or within one year of pregnancy (four diagnosed at delivery; 263 diagnosed postpartum) and a group of age-matched, non-pregnant controls from the California Cancer Registry.7 There was no difference in distribution of disease stage or tumor thickness between the two groups. Pregnancy had no impact on survival when controlling for age, race, stage, and tumor thickness. There were no differences in lymph node assessments or lymph node positivity between the two groups.

Pregnancy and Melanoma Risk
Taken together, the most recent findings suggest that pregnancy has no effect on melanoma prognosis; termination of pregnancy in a woman diagnosed with primary melanoma is not recommended, nor is avoidance of future pregnancy for women who have been diagnosed with primary melanoma.1 A two-year waiting period prior to pregnancy may permit a more accurate assessment of the patient’s long-term prognosis.

Questions have lingered, however, regarding the effects of pregnancy history on a woman’s risk of developing melanoma in the future. In a study of 318 Caucasian women newly diagnosed with melanoma, trained interviewers questioned patients about oral contraceptive use, hormone replacement therapy, reproductive history, sun exposure, occupation, and medical history.8 Their responses were compared to those from 395 frequency-matched controls. Clinicians conducted skin exams to assess number and type of nevi, extent of freckling, solar damage, and skin type. Analysis revealed a slightly higher risk for melanoma among women under the age of 55 who had a live birth in the previous five years (odds ratio: 2.6) and among women who had a history of three or more live births (odds ratio: 3.3). Based on a small subset of patients,
Another Reproductive Health Risk

Some evidence has suggested a link between endometriosis and cutaneous melanoma. Now a prospective study confirms the risk. Data for 98,995 French women insured by a national health program were examined for history of endometriosis and other benign gynecological diseases. Women were age 40 to 65 at inclusion. During 12 years of follow-up, 363 melanoma cases were reported among 91,965 subjects. History of endometriosis was significantly associated with a higher risk of melanoma (relative risk: 1.62), as was history of fibroma, compared to patients with no such history. Neither history of ovarian cyst, uterine polyp, breast adenoma/fibroadenoma, nor breast fibrocystic disease was significantly associated with risk.

Researchers concluded that changes in nevi during recent pregnancies are a risk factor for melanoma (odds ratio: 2.9), but neither oral contraceptive use nor hormone replacement therapy were associated with increased risks.

A later study, a pooled analysis of data from 10 case-control studies, found no overall association with ever giving birth and melanoma risk (pooled odds ratio: 0.95). But this study actually found a decreased melanoma risk among women with five or more live births compared to women with none. Women with both earlier age at first birth and higher parity had a lower risk than women with later age at first birth and fewer than five live births. While the researchers conclude these findings could demonstrate an effect of reproductive history on melanoma risk, they note that other differences, such as sun exposure history, could be implicated.

Danish researchers identified similar risks associated with female reproductive history (lowest risk associated lower age at first live birth and multiparity), noting that a woman’s risk for cutaneous malignant melanoma increased 15 percent 10 or more years after the birth of her youngest child compared to the first 10 years after that birth. Importantly, they confirmed similar risk trends among men. Their population-based cohort included more than 3,500,000 individuals. Given the similarity in findings between men and women, researchers concluded that lifestyle factors, rather than exposure to pregnancy hormones, accounted for the identified trends in melanoma risk.

What to Expect

While receiving a diagnosis of primary cutaneous melanoma during pregnancy is likely to induce significant stress for a patient, the data show that pregnancy does not negatively influence survival. Women of child-bearing potential who are not pregnant but have been diagnosed with primary melanoma can be reassured that future pregnancy will not increase the risk for recurrence.

There is a widely-held misconception that change in nevi is common during pregnancy. While lesions may expand as skin stretches in certain body areas (particularly on the front of the body) throughout pregnancy, strictly speaking change in nevi is not “normal” during gestation. Dermatologists should emphasize to their patients the need for regular self-examinations and the importance of follow-up with the dermatologist for any new or changing lesions. Dermoscopic assessment is confirmed valuable when clinicians are prepared to recognize changes that may be associated with skin stretching in pregnancy.

Data suggest a slight if any negative influence of pregnancy on a woman’s risk for developing melanoma in the future. Questioning female patients about their reproductive history, including age at first live birth and number of live births, may help the dermatologist to better assess the patient’s melanoma risk in light of other known risk factors (such as sun exposure, family history, etc.). Future study may identify lifestyle factors that account for any apparent associations between reproductive history and melanoma risk.

1. Lens M, Bastille V. Melanoma in relation to reproductive and hormonal factors in women: current review on controversial issues. Cancer Causes Control. 2008 Jan 16

Survivor Privilege? Low socioeconomic status is a strong predictor of poor survival among patients from different ethnic groups with melanoma, according to a new study (J Clin Oncol Jan 1, 2008). By contrast, people of higher social and economic status were much more likely to be diagnosed with skin cancer at an early stage and to have surgery to excise tumors. Researchers claim poor overall survival seen in black melanoma patients is not explained by low economic status or differences in treatment.