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Case Report

Pregnancy and Melanoma: Recommendations for Clinical Scenarios

Juliana Berk-Krauss [a,b], Tracey N. Liebman [a], Jennifer A. Stein [a,*]

[a] The Ronald O. Perelman Department of Dermatology, New York University School of Medicine, New York, NY
[b] Yale University School of Medicine, New Haven, CT

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ABSTRACT

Managing pregnant patients with a history of melanoma or with a melanoma diagnosis can be daunting and confusing for dermatologists. We present three clinical scenarios that raise questions about the safety of pregnancy in patients with a history of melanoma, skin biopsies during pregnancy, and excisions and sentinel lymph node biopsies during pregnancy. Our recommendations incorporate the most up-to-date clinical data to help guide clinicians when faced with pigmented lesions and melanoma in a pregnant patient.

Directions: Choose the single best response.

1. A 33-year-old woman comes to you for a total body skin exam and to discuss the safety of pregnancy. She has a past medical history of a 0.3mm-melanoma (stage IA) that was completely excised 4 years prior. She has since been disease free and receives total body skin examinations (TBSE) every 6 months. Her father died of a melanoma at age 50, and she is very concerned about her risk of melanoma. She is Fitzpatrick skin type II and used tanning beds occasionally in college. On physical exam the patient has light brown hair and blue eyes, mild sun damage and fewer than 50 nevi. You note no lesions of concern.

What would you advise?

A. She should wait another year to get pregnant. The hormones from pregnancy are known to increase the patient's risk for recurrence, and her risk of recurrence is still very high in the first five years after her melanoma diagnosis.
B. She can go ahead with pregnancy and increase TBSEs to every month. Pregnancy increases the risk for melanoma recurrence, and monthly TBSE's are a good way to catch melanoma early.
C. She can go ahead with a pregnancy and continue with TBSEs every 6 months.
D. She should be referred to a medical oncologist to assess potental risks.
E. Before becoming pregnant, she should undergo full-body imaging tests to rule out metastatic melanoma.

Explanation:

Pregnancy is not contraindicated in women diagnosed with localized malignant melanoma (MM) (Driscoll et al., 2016). There exists no conclusive evidence that pregnancy increases the risk of MM recurrence. While some studies have shown that MM diagnosed during or immediately after pregnancy worsens prognosis (Byrom et al., 2015; Kyrgidis et al., 2017), the preponderance of data does not consistently indicate an impact on outcome (Daryanani et al., 2003; Driscoll et al., 2016; Johansson et al., 2014; Stensheim et al., 2009).

Patients can be told that the relationship between MM and pregnancy is not fully understood, and the decision to conceive should incorporate one's medical history and personal preferences. This particular patient has a low likelihood of recurrence given the stage of her MM, the length of her disease-free survival, and the absence of other known MM risk factors (Balch et al., 2009). Although melanoma recurrence can occur many years from initial diagnosis (Gamel et al., 2002), the highest risk is in the first 2-3 years (Driscoll et al., 2016; Hohnheiser et al., 2011).

It is recommended that patients with a history of melanoma have at least an annual TBSE, ranging from every 3 to 12 months based on the risk for recurrence and new primary melanoma (Bichakjian et al., 2011). Further increasing the frequency of TBSEs is not known to improve outcomes. This patient's last visit during pregnancy should ideally be a few months before the due date for logistical reasons in case there are any lesions that might need to be biopsied or excised. It is important to always counsel pregnant patients on the importance

* Corresponding author: Jennifer A. Stein, MD, PhD, The Ronald O. Perelman Department of Dermatology, 240 E 38th St., 11th Fl, New York, NY 10016.
E-mail address: Jennifer.Stein@nyumc.org (J.A. Stein).

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of sun protection and monitoring lesions (ABCDE criteria: asymmetry, border irregularity, color variegation, diameter >6mm, and evolution) for identification of potential new melanomas (Abbasi et al., 2004).

2. A 27-year-old woman is 9-weeks pregnant and comes to you with an evolving lesion of concern on the mid-back. She has no personal or family history of skin cancer. She is Fitzpatrick skin type III. On physical examination, she has brown hair and brown eyes and few moles.

What would you advise?

A. Any changing lesion during pregnancy should be immediately biopsied.
B. If the lesion demonstrates any classic features for melanoma, perform a biopsy with a narrow margin.
C. Defer biopsy until after the first trimester when the risk for miscarriage is lower.
D. Refer the patient to a surgical oncologist for an excisional biopsy.

Explanation:

Dermatologists should generally use standard clinical and dermoscopic guidelines when approaching a concerning lesion on a pregnant patient. It is important to keep in mind that during pregnancy, nevi on the breasts and abdomen commonly grow with normal skin expansion. Sometimes corresponding transient dermoscopic changes in melanocytic nevi on expanding skin can be seen, however, these changes do not necessarily imply malignancy (Bieber et al., 2016). Patients with atypical nevi may undergo more changes in their moles during pregnancy (Ellis, 1991), though recent evidence suggests that normal nevi should not experience significant change, including darkening (Bieber et al., 2016). Pregnant patients should take seriously changes in nevi not attributed to skin stretching.

Biopsies performed during any trimester of pregnancy are safe. Specimens should be obtained promptly from lesions that raise concern of malignancy, at any point in pregnancy. Due to high dose epinephrine-induced uterine artery spasm rarely observed in animal and *in vitro* studies (Bieber et al., 2016; Ralston and Shnider, 1978), physicians can opt to use lidocaine without epinephrine as a local anesthetic (Driscoll and Grant-Kels, 2009). However, the low doses of lidocaine with epinephrine used in dermatologic surgery are not teratogenic and are generally considered safe (Richards and Stasko, 2002). As with non-pregnant patients, it is recommended that 1- to 2-mm biopsy margins are used to increase the likelihood of completely clearing atypical melanocytic lesions (Bichakjian et al., 2011).

The majority of studies indicate that women diagnosed with MM during pregnancy do not have thicker tumors or other features that would worsen survival (Driscoll et al., 2016). However, a relationship between pregnancy and MM cannot be ruled out. Additionally, delay in diagnosis during pregnancy is a real concern. Pregnant patients, especially those with known melanoma risk factors, should be monitored closely and educated about the malignant (ABCDE) features of melanoma (Abbasi et al., 2004).

3. You diagnose a 36-year-old woman with a 1.1 mm melanoma who is 18-weeks pregnant. It is not ulcerated and there are no mitoses.

What would you advise?

A. She should wait until after delivery to undergo any treatment.
B. She should have an excision under local anesthesia, but defer sentinel lymph node biopsy until after pregancy.
C. She should have an excision and a sentinel lymph node biopsy.
D. She should terminate the pregnancy as soon as possible because the high levels of estrogen will activate her melanoma.

Explanation:

Melanoma excisions during pregnancy are safe and necessary. Tumors 1.01-2mm should be excised using a 1-2cm margin (National Comprehensive Cancer Network). If the procedure is to be performed under local anesthetic, the same considerations should be made as with skin biopsies (see question #2). Wide local excisions performed under general anesthesia may require fetal monitoring by an obstetrician.

Sentinel lymph node status is the most important prognostic factor in patients with >1.0mm melanomas (Bichakjian et al., 2011). According to national guidelines, it is recommended that this patient receive a SLNB. When tumors are 0.8 - 1.0mm in thickness, SLNB can be discussed and pursued in appropriate clinical scenarios.[17]

While SLNBs raise concerns regarding the fetal effects of exposure to radioactive colloid and blue dye, used separately or in combination to identify the sentinel lymph node(s) draining the primary tumor, the procedure is generally considered safe for pregnant patients (Andtbacka et al., 2013). Radiation doses in this scenario are notably much less than the National Council on Radiation Protection and Measurement limits for a pregnant woman (Pandit-Taskar et al., 2006); and the standard dose can be lowered without sacrificing radiographic information (Adelstein, 1999). Lymphazurin (isosulfan blue) is often avoided because of the rare risk of severe allergic reactions and anaphylaxis (Cordeiro and Gemignani, 2017), while methylene blue is contraindicated because of its known association with fetal abnormalities (atresia of the ileum and jejunum) when administered during the first trimester (Toesca et al., 2014). Ultimately, the specific SLNB techniques employed are surgeon and institution-specific.

If the SLNB is positive, imaging to identify the extent of disease is the next appropriate workup step (National Comprehensive Cancer Network). In pregnant patients, imaging modalities involving ionizing radiation and radionuclides should be limited. According to the American College of Obstetrics and Gynecologists' Committee on Obstetric practice, the techniques of choice during pregnancy include: chest radiograph with appropriate shielding, ultrasonography, and magnetic resonance imaging (MRI; preferably without gadolinium) (Anonymous, 2016). Computed tomography (CT) scan (without contrast), and nuclear medicine studies can be performed if necessary, since they are typically administered at doses that have not demonstrated fetal harm (Anonymous, 2016).

If after disease-staging therapeutic agents are warranted, it is important to be aware that newer melanoma agents, such as targeted drugs (BRAF inhibitors) and checkpoint inhibitors (anti-PD1 and anti- CTLA4), may be teratogenic. Pregnancy and breast-feeding are discouraged up to 2 weeks after the last dose of BRAF inhibitors (i.e. vemurafenib), 3 months after anti-CTLA4 treatment (i.e. ipilimumab), and 5 months after anti-PD1 treatment (i.e. nivolumab).

Decisions around tests and treatments in pregnancy should be made based on patient and family preferences, and in collaboration with a multidisciplinary medical team (Driscoll and Grant-Kels, 2007).

References

Abbasi NR, Shaw HM, Rigel DS, et al. Early diagnosis of cutaneous melanoma: revisiting the ABCD criteria. JAMA 2004;292(22):2771–6.
Adelstein SJ. Administered radionuclides in pregnancy. Teratology 1999;59(4):236–9.
Andtbacka RH, Donaldson MR, Bowles TL, et al. Sentinel lymph node biopsy for melanoma in pregnant women. Ann Surg Oncol 2013;20(2):689–96.
Balch CM, Gershenwald JE, Soong S-J, et al. Final Version of 2009 AJCC Melanoma Staging and Classification. J Clin Oncol 2009;27(36):6199–206.
Bichakjian CK, Halpern AC, Johnson TM, et al. Guidelines of care for the management of primary cutaneous melanoma. American Academy of Dermatology. J Am Acad Dermatol 2011;65(5):1032–47.

Bieber AK, Martires KJ, Driscoll MS, Grant-Kels JM, Pomeranz MK, Stein JA. Nevi and pregnancy. J Am Acad Dermatol 2016;75(4):661–6.
Byrom L, Olsen C, Knight L, Khosrotehrani K, Green AC. Increased mortality for pregnancy-associated melanoma: systematic review and meta-analysis. J Eur Acad Dermatol Venereol 2015;29(8):1457–66.
Cordeiro CN, Gemignani ML. Breast Cancer in Pregnancy: Avoiding Fetal Harm When Maternal Treatment Is Necessary. Breast J 2017;23(2):200–5.
Daryanani D, Plukker JT, De Hullu JA, Kuiper H, Nap RE, Hoekstra HJ. Pregnancy and early-stage melanoma. Cancer 2003;97(9):2248–53.
Driscoll MS, Grant-Kels JM. Hormones, nevi, and melanoma: an approach to the patient. J Am Acad Dermatol 2007;57(6):919–31 [quiz 932-916].
Driscoll MS, Grant-Kels JM. Nevi and melanoma in the pregnant woman. Clin Dermatol 2009;27(1):116–21.
Driscoll MS, Martires K, Bieber AK, Pomeranz MK, Grant-Kels JM, Stein JA. Pregnancy and melanoma. J Am Acad Dermatol 2016;75(4):669–78.
Ellis DL. Pregnancy and sex steroid hormone effects on nevi of patients with the dysplastic nevus syndrome. J Am Acad Dermatol 1991;25(3):467–82.
Gamel JW, George SL, Edwards MJ, Seigler HF. The long-term clinical course of patients with cutaneous melanoma. Cancer 2002;95(6):1286–93.
Hohnheiser AM, Gefeller O, Gohl J, Schuler G, Hohenberger W, Merkel S. Malignant melanoma of the skin: long-term follow-up and time to first recurrence. World J Surg 2011;35(3):580–9.
Johansson AL, Andersson TM, Plym A, Ullenhag GJ, Moller H, Lambe M. Mortality in women with pregnancy-associated malignant melanoma. J Am Acad Dermatol 2014;71(6):1093–101.
Kyrgidis A, Lallas A, Moscarella E, Longo C, Alfano R, Argenziano G. Does pregnancy influence melanoma prognosis? A meta-analysis. Melanoma Res 2017;27(4):289–99.
National Comprehensive Cancer Network. Melanoma (Version 1.2017). https://www.nccn.org/professionals/physician_gls/pdf/melanoma.pdf, Accessed date: 24 August 2018.
Anonymous. Committee Opinion No. 656: Guidelines for Diagnostic Imaging During Pregnancy and Lactation. Obstet Gynecol 2016;127(2):e75-0.
Pandit-Taskar N, Dauer LT, Montgomery L, St Germain J, Zanzonico PB, Divgi CR. Organ and fetal absorbed dose estimates from 99mTc-sulfur colloid lymphoscintigraphy and sentinel node localization in breast cancer patients. J Nucl Med 2006;47(7):1202–8.
Ralston DH, Shnider SM. The fetal and neonatal effects of regional anesthesia in obstetrics. Anesthesiology 1978;48(1):34–64.
Richards KA, Stasko T. Dermatologic surgery and the pregnant patient. Dermatol Surg 2002;28(3):248–56.
Stensheim H, Moller B, van Dijk T, Fossa SD. Cause-specific survival for women diagnosed with cancer during pregnancy or lactation: a registry-based cohort study. J Clin Oncol 2009;27(1):45–51.
Toesca A, Gentilini O, Peccatori F, Azim Jr HA, Amant F. Locoregional treatment of breast cancer during pregnancy. Gynecol Surg 2014;11(4):279–84.