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Cutaneous tumors in pregnancy

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Abstract Pregnancy alters the frequency and natural course of certain skin tumors. Pregnancy-associated changes in melanocytic nevi are transient, and there is no substantiated evidence of increased risk of malignant transformation of melanocytic nevi in gestation. Characteristic vascular and pigment-related dermatoscopic features are helpful in evaluating pigmented lesions, but a biopsy should be performed for significant change or other worrisome features in a lesion. Outcomes for pregnancy-associated melanoma do not appear to be poorer compared with nonpregnancy melanoma; however, data are limited for advanced (stage III/IV) melanoma. Some studies suggest increased propensity for lymphovascular spread, but more data are needed for definitive conclusions and guidelines on prognostication, workup, and treatment of pregnancy-associated melanoma. Vascular tumors, particularly pyogenic granuloma *(granuloma gravidarum)*, occur with increased frequency and are associated with pro-angiogenic hormonal influences. Dermatofibrosarcoma protuberans has a more aggressive course during pregnancy with both prompt surgical treatment and close monitoring for recurrence being indicated.

Introduction

The prevalence and behavior of certain skin tumors are affected by pregnancy, whereas others may incidentally occur during pregnancy but warrant special consideration in management. Tumors may be divided into benign hamartomas and malignant cutaneous growths. We discuss benign and malignant skin tumors that occur during pregnancy (Table 1) and place special attention on current evidence, perspectives, and management of melanocytic nevi and melanoma in pregnancy. The classification of tumors in pregnancy is shown in Figure 1.

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Melanocytic tumors

Melanocytic nevi

Melanocytic nevus enlargement and darkening can occur during pregnancy (Table 2; Figure 2), but recent studies do not corroborate early case reports suggesting increased malignant transformation of nevi during pregnancy.[1] Although the biologic behavior of normal melanocytic nevi is not altered by pregnancy according to histologic and clinical studies, it is unclear whether dysplastic nevi in patients with dysplastic nevus syndrome have increased risk for malignant change.[2]

A 1991 study prospectively followed 17 pregnant patients with dysplastic nevus syndrome and documented clinical changes in 76% of nevi, with a 3.9 times higher rate of change in dysplastic nevi during pregnancy.[2] One patient in the study

Table 1 The effect of pregnancy on cutaneous tumors

Increased incidence in pregnancy	More aggressive behavior during pregnancy	Unaffected by pregnancy	Effect of pregnancy uncertain
Pyogenic granuloma	DFSP	Melanoma *	Kaposi sarcoma
ALHE		Keratinocyte carcinoma †	Merkel cell carcinoma
Acrochordon			Mycosis fungoides
Dermatofibroma			
Seborrheic keratosis			
Hyperkeratosis of the nipple			

ALHE, angiolymphoid hyperplasia with eosinophilia; DFSP, dermatofibrosarcoma protuberans.

* Controversial; some studies indicate worse prognosis in pregnancy but most show no difference in stage or outcomes.

† Authors' opinion; limited reports available.

developed melanoma during pregnancy.[2] Hormonal influence on malignant transformation of dysplastic nevi in dysplastic nevus syndrome has been hypothesized. Altered estrogen receptor β (ERβ) expression in changing dysplastic nevi is a plausible mechanism based on limited data. A group has measured the expression of estrogen receptors in normal and dysplastic nevi in pregnant participants and nonpregnant matched controls. They found greater immunoreactivity in dysplastic nevi in both pregnant and nonpregnant women, and the ERβ expression increased with increasing grade of atypia.[1] There was no upregulation in ERβ expression in dysplastic nevi during pregnancy, and the clinical effects of estrogen on ERβ in dysplastic nevi are unknown. ERβ in other tissues has antigrowth effects.[1] In contrast to dysplastic nevi, normal melanocytic nevi increase expression of ERβ during pregnancy,[1] but further studies are needed to clarify the significance of ERβ expression in melanocytic lesions and the natural course of dysplastic nevi in pregnancy.

Mild histologic changes in melanocytic nevi may occur in pregnancy, but they do not appear to correlate with a more aggressive or malignant behavior. A histopathologic review reported a mild increase in atypical histologic features in nevi of pregnant patients compared with those of nonpregnant controls, where the atypical findings were not of sufficient degree to result in diagnostic confusion.[3] Interestingly, the histologic features were no different compared with male controls.[3] A smaller histologic study documented more mitotic figures and higher mitotic rates in nevi from pregnant patients compared with nonpregnant controls, supporting a theory of higher "activation" of cells during pregnancy.[4]

Recent studies evaluating clinical and dermatoscopic changes in nevi during pregnancy report either no change[5] or changes in size, pigment network, or vascular alterations that return to normal within approximately 12 months postpartum.[6–8] Physical stretching of the skin, intrinsic changes such as elevated hormone levels and increased vascularity, and behavioral modifications, including reduced exposure to sunlight, are postulated to contribute to pregnancy-associated changes in nevi.[8] Documented pregnancy-associated dermatoscopic changes include lightening or darkening of pigment,

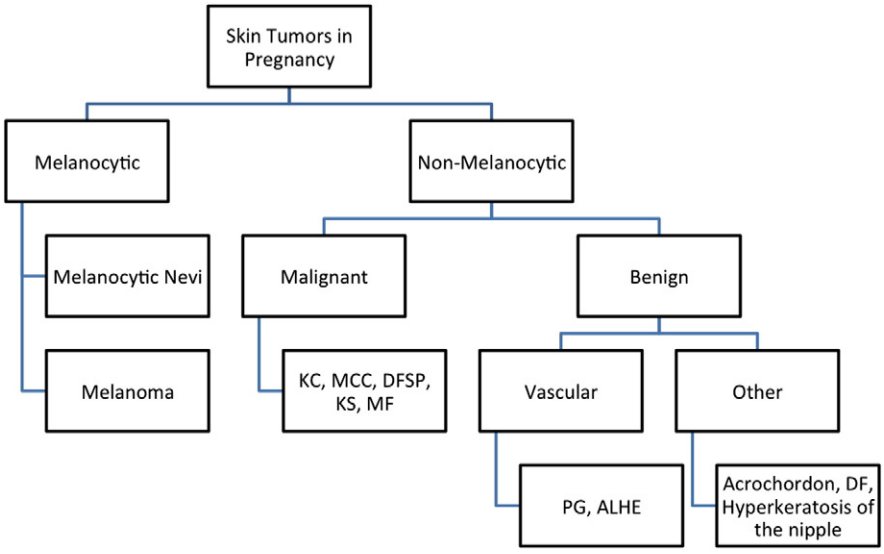

Fig. 1 Classification of tumors in pregnancy. ALHE, angiolymphoid hyperplasia with eosinophilia; DF, dermatofibroma; DFSP: dermatofibrosarcoma protuberans; KC, keratinocyte carcinoma (basal cell carcinoma, squamous cell carcinoma); KS, Kaposi sarcoma; MCC, Merkel cell carcinoma; MF, mycosis fungoides; PG, pyogenic granuloma.