Basal Cell Carcinoma Arising in Nevus Sebaceous During Pregnancy

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PRACTICE **POINTS**

- Benign neoplasms arise more frequently in nevus sebaceous (NS) lesions than do malignant neoplasms.
- The hormonal changes that occur during pregnancy and puberty appear to play a role in the development of neoplasms in NS lesions.
- Monitoring NS lesions more closely during periods of hormonal change may help diagnose malignant transformations in these patients.

To the Editor:

Nevus sebaceous of Jadassohn (or nevus sebaceous [NS]) is a congenital hamartomatous disorder initially described by Jadassohn[1] in 1895. Nevus sebaceous occurs in 0.3% of newborns[2] and is most commonly identified on the face and scalp.[3,4] Mehregan and Pinkus[5] characterized NS as an organoid tumor containing multiple skin components with 3 life stages. The first stage—occurring during infancy—consists of immature hair follicles and sebaceous glands. The second stage—beginning at puberty—shows development of sebaceous glands, epidermal hyperplasia, and maturation of apocrine glands. The final stage involves formation of secondary benign and malignant neoplasms.

Historically, basal cell carcinoma (BCC) was thought to be the most common neoplasm arising in NS.[5-8] In 1993, Ackerman et al[9] introduced a new definition of trichoblastoma (TB), expanding the definition to encompass previously excluded benign follicular neoplasms. Large studies conducted after this new definition was proposed suggested that syringocystadenoma papilliferum and TB develop more frequently than does BCC.[3,4,10-15] Furthermore, Cribier et al[4] and Merrot et al[15] reviewed prior cases of NS using the new definition and asserted that the majority of previously diagnosed cases of BCC were considered to be TB under the new criteria. With the advent of modern diagnostic testing, the rate of secondary benign neoplasm growth is now thought to be between 7% and 19%, with syringocystadenoma papilliferum arising in 2% to 13% of cases and TB in 1.5% to 7%.[3,4,10-14] Malignant neoplasms are observed much less frequently, with BCC arising in 0% to 1% of NS cases.

Nevus sebaceous lesions typically enlarge during puberty, while malignant neoplasms occur almost exclusively in adulthood,[4,10-12] suggesting that hormones contribute to NS stage progression. We present the case of a woman who developed BCC in a previously asymptomatic NS during pregnancy.

A 32-year-old woman who was otherwise healthy presented to our dermatology clinic with a pink-yellow verrucous plaque on the right temporal hairline extending to the preauricular area of the face. The patient had no personal or family history of skin cancer and no history of tanning bed use. She reported that the lesion had been present since birth. A diagnosis of NS was made.

Two years later, she presented with a new bleeding growth atop the previously diagnosed NS that had been present for approximately 4 months (Figure). At this visit she was pregnant (30 weeks' gestation). Physical examination revealed a 4-mm, brown, pearly papule at the inferior margin of the previously noted pink verrucous plaque on the right temporal hairline. A biopsy was performed and histopathology displayed aggregates of basaloid cells with a high nuclear to cytoplasmic ratio, peripheral palisading, and abundant melanin, consistent with pigmented BCC. The patient was referred for Mohs micrographic surgery; the lesion was removed with

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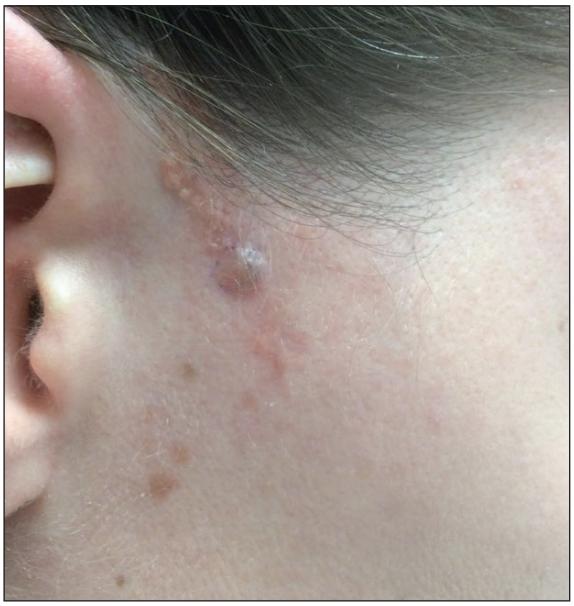

Basal cell carcinoma arising in a previously asymptomatic nevus sebaceous.

clear margins. The patient had no recurrence of BCC at 36-month follow-up.

Few studies have looked at the signal transduction pathways leading to malignant neoplasm formation in NS. Nevus sebaceous lesions are theorized to result from postzygotic genetic mutations in *HRAS* and *KRAS* oncogenes,[16,17] which also are altered in squamous cell carcinoma and BCC.[18] Similarly, Xin et al[19] detected loss of heterozygosity of the human patched gene, *PTCH*, a tumor suppressor in the hedgehog pathway that has been implicated in sporadic BCC formation, suggesting that this loss of heterozygosity may predispose to secondary BCC formation.[20,21] However, loss of *PTCH* heterozygosity could not be replicated by Takata et al[22] and Levinsohn et al.[16]

Increased numbers of androgen receptors have been demonstrated in NS basal keratinocytes and sebaceous glands.[23] Nevus sebaceous lesions enlarge during puberty,[5] and malignant neoplasms arise almost exclusively in adulthood.[3,4,10-13] The androgen surge during puberty and increased androgen levels in adulthood may promote sebaceous gland development and epidermal hyperplasia that result in progression of NS lesions from the first stage to the second stage. Basal cell carcinomas also express androgen receptors and have abnormal androgen hormone metabolism,[24,25] though they do not display a notable number of estrogen or progesterone receptors.[26] Therefore, increased androgen levels in adulthood also may contribute to progression to secondary neoplasm formation in the third stage.

Similarly, cases of rapid growth of NS lesions during pregnancy, a state of increased testosterone production,[27] have been reported.[28] We present a case of a BCC arising in a previously asymptomatic NS during pregnancy. To our knowledge, no large studies have assessed the effect of hormone level changes during pregnancy on NS growth and secondary malignant transformation. Prior to the 1990s, prophylactic excision of NS during childhood was recommended to prevent malignant neoplasm formation.[29,30] More recently, a more conservative approach has been advocated because of a lower rate of malignant transformation than previously thought; some dermatologists recommend close monitoring as an alternative to early removal.[4,13,14,29,31] This case report proposes that pregnancy may be a time of increased risk for malignant transformation and that NS lesions might require close monitoring during pregnancy.

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