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Nevus Spilus

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Nevus spilus (NS), also known as speckled lentiginous nevus (SLN), is a relatively common cutaneous lesion that is characterized by multiple pigmented macules or papules within a pigmented patch. It may be congenital or acquired; however, its etiology remains unknown. NS deserves its own place in the spectrum of classification of important melanocytic nevi; as a lentigo and melanocytic nevus, it has the slight potential to develop into melanoma. Accordingly, we recommend consideration of punch excisions of the speckles alone if excision of the entire NS is declined.

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Nevus spilus (NS), also known as speckled lentiginous nevus (SLN), is a relatively common cutaneous lesion that is characterized by multiple pigmented macules or papules within a pigmented patch. Historically, NS referred to a solitary, hairless, pigmented macule that was not associated with neurofibromatosis or McCune-Albright syndrome. The term was redefined in 1952 by Ito and Hamada¹ and reinforced by Cohen et al² in 1970 as a circumscribed tan macule in which more darkly pigmented, raised, and/or flat melanocytic or nevomelanocytic elements are distributed. The exact etiology of NS is unknown, but postulations include a defect in neural crest melanoblasts as well as a possible role for genetic and environmental factors.

There are 3 types of lentigo: lentigo simplex, solar or senile lentigo, and lentigo maligna. Lentigo simplex may appear at any age, though it most

frequently arises in childhood as an evenly pigmented, brown to black patch that is indistinguishable from a junctional melanocytic nevus. Special types of lentigo simplex are lentiginosis profusa (or LEOPARD syndrome)^{3,4} and NS. NS is both a lentigo and a melanocytic nevus.

Clinical Description

NS is a pigmented patch on which multiple darker macules or papules appear at a later stage (Figure). The term *spilus* is derived from the Greek word *spilos* (spot). Three types of NS exist: small or medium sized (<20 cm), giant, and zosteriform. The lesions may be congenital or acquired, appearing as subtle tan macules at birth or in early childhood and progressing to the more noticeable pigmented black, brown, or red-brown macules and papules over months or years.⁵ NS may occur anywhere on the body but is most commonly identified on the torso and extremities. Several morphologic patterns of zosteriform NS may be evident, including blocklike, linear, and extensive, with the latter encompassing large areas of the body. When distributed in a blocklike fashion, a sharp midline demarcation may be discernible. Furthermore, when linear in morphology, NS typically occurs along the lines of Blaschko.⁶ A clinical variant form divided between the upper and lower eyelid also has been described.⁷ The dimension of the background pigmented patch is variable, but it usually ranges from 2 to 10 cm. The maculopapular spots within the nevus also are variable in size. They usually measure from 1 to 3 mm in diameter but may measure up to 9 mm.

Histopathology

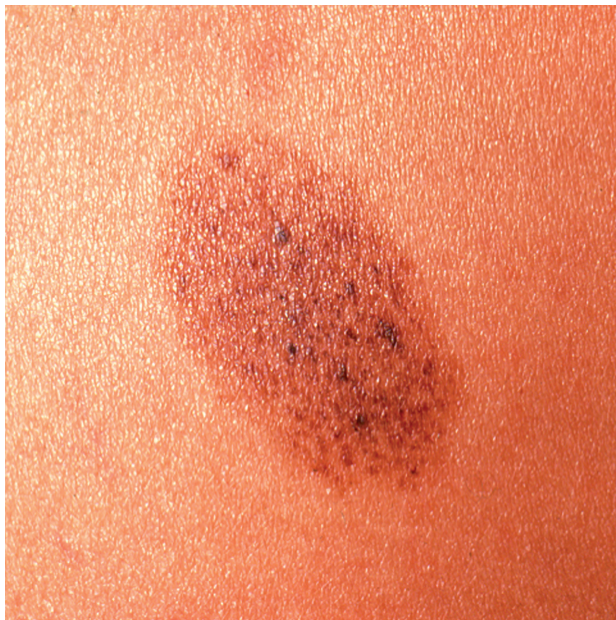
Histologically, the light brown macule or patch usually shows mild melanocytic hyperplasia.⁸ Furthermore, it may show features of lentigo simplex, including small to moderate rete ridge elongation; increased melanocyte concentration in the basal layer, as well as increased melanin in both melanocytes and basal keratinocytes; and dermal melanophages. The speckles show junctional nests

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Hyperpigmented background patch containing multiple darker pigmented macules and papules.

of nevus cells typically at the lowest points in the rete ridges, diffuse junctional activity, and dermal nevus cell aggregates. Nevus cells also have been histologically detected within both the speckles and the nonspeckled hyperpigmented background.² The maculopapular speckles within a nevus may be variable histologically, ranging from lentiginos to junctional, compound, or intradermal nevi, to Spitz, blue, or neural nevi.⁹ Speckles occasionally may represent a melanoma.⁵ At various times during the progression of a nevus, different types of maculopapular spots also may appear within the nevus.¹⁰ Occasional giant melanin granules also may be evident, as has been described in lentigo simplex and café au lait spots.¹¹

Epidemiology

In one study, NS was shown to have a prevalence in the general population similar to that of congenital melanocytic nevi, with an age-dependent prevalence of 0.2% to 2.3%.¹² In a survey of newborns with NS, low prevalence rates of 0.2% have been reported, with subsequent speculation that NS is acquired rather than congenital.¹³ In contrast, another study has reported that approximately 80% of NS are present at birth or during early infancy as subtle tan café au lait spots early in their course.⁵ Prevalence rates range between 1.3% to 2.1% in school-aged children and adolescents. In adults, the frequency of nevi more than 1.5 cm in diameter is 2.3%. No racial or gender predominance has been demonstrated.¹²

Clinical Significance

The number of patients described with melanoma occurring within NS, including some fatal cases, has been increasing.⁵ Although NS is considered a benign nevus, this report has raised concern regarding the malignant potential of NS and therefore has affected its management. The risk of developing melanoma in NS is substantially heightened if NS has been present since birth, is more than 4 cm in diameter, and is giant or zosteriform in morphology.¹⁴ Recently, a multifocal melanoma was diagnosed on an NS and subsequently was excised with the nevus without recurrence.⁸ In another case, a melanoma developed within an NS, which itself exhibited melanocytic dysplasia histologically.¹⁵ Further characterization by flow cytometry showed DNA aneuploidy within the melanoma as well as in one of the darker pigmented papules within the NS. Nevertheless, melanoma arising within NS is rare. The overall morbidity and mortality associated with malignant transformation of NS are reflective of the melanoma itself with regard to the usual features, including histologic depth.

In addition to malignant potential, NS has been associated with a specific entity that is characterized by facial features (unique), anorexia, cachexia, and eye and skin anomalies (known as FACES syndrome). More recently, it has been proposed as part of the SLN syndrome, which is characterized by NS of the papular type and ipsilateral neurologic abnormalities such as dysesthesia, muscular weakness, or hyperhidrosis.^{16,17}

Until recently, it has been accepted that NS (or SLN) is a single clinical entity. However, it has been proposed that more than one type of SLN exists. SLN occasionally is associated with complex birth defects such as phacomatosis pigmentovascularis, phacomatosis pigmentokeratocica, or SLN syndrome, and different types of SLN have been associated with each one. Macular SLN is a hallmark of a particular type of phacomatosis pigmentovascularis, whereas papular SLN typically is present in phacomatosis pigmentokeratocica as well as SLN syndrome,¹⁸ which is an important clinical distinction.

Diagnosis

NS should be distinguished from café au lait spots, agminated lentiginos, Becker pigmented hairy nevus, or other simple melanocytic macules. Many times, NS may be difficult to diagnose clinically, and histologic analysis may be helpful. Solitary café au lait spots are coffee-colored macules that lack intralesional hyperpigmented macules or papules and may be seen in up to 20% of healthy individuals with no systemic associations.¹⁹⁻²¹ However, multiple café au lait spots are linked with neurofibromatosis and

syndromes such as McCune-Albright syndrome.²² Histologically, café au lait spots also show an increase in melanin, with macromelanosomes sometimes seen in the melanocytes and basal keratinocytes.²³ Macromelanosomes, which are most closely associated with café au lait spots of neurofibromatosis, also are seen in café au lait spots without neurofibromatosis and occasionally in NS, lentigo simplex, Becker nevus, melanocytic nevus, dysplastic nevus, and healthy skin.²⁴ Café au lait spots may require distinction from early NS that is still in its nonspeckled, tan, hyperpigmented form. Histologic analysis of NS shows variability between speckles within the same NS, but NS consistently has been shown to contain nevus cells. Although café au lait spots containing nevus cells have been described,²⁵ the presence of speckles within these spots was not recorded. A melanoma arising within a café au lait spot has been described, but histologic evaluation of other spots from the same patient showed nevus cells.²⁶ It is possible that this patient had multiple NS instead of simple café au lait spots. These findings suggest that the café au lait spot and NS are 2 seemingly similar but separate entities clinically and histologically.

Agminated lentiginosities are defined as numerous lentiginosities (small pigmented macules with sharp circumscribed borders) that are geographically arranged in a dermatomal distribution, a midline clustered pattern, or a checkerboard pattern, either unilaterally or bilaterally.²⁷ Agminated lentiginosities usually present in early childhood but also may be detected at birth.²⁸ NS also may present at birth or early childhood as an unspeckled immature nevus. This clinical and epidemiologic similarity to NS can make distinction difficult. As agminated lentiginosities progress, however, they appear on healthy background skin rather than the hyperpigmented tan background of NS.²⁷

Becker nevus is another commonly confused entity, but its distinction from NS may not be evident until the Becker nevus progresses. When it first surfaces, it may resemble a café au lait spot and remain that way for many years before the classic hypertrichosis of the nevus becomes evident.^{29,30} Other nonclassified pigmented macules can be described as melanotic macules.

Management

NS has prompted a variety of approaches to its management. Both aggressive and conservative treatment measures have been used. Cases of transformation into melanoma mandate excision.³¹ In such cases, the entire NS must be excised to prevent recurrence and eliminate the field defect; therefore, a large scar can result. Because of the prevalence of NS in the pediatric population and the slight

chance of malignant transformation, this aggressive treatment option only should be undertaken when there is clear evidence of melanoma. We recommend consideration of punch excisions of the speckles alone if excision of the NS is declined. Less aggressive treatment options include baseline assessment with long-term follow-up in association with education of the patient and family about the signs of melanoma.⁵ Studies have demonstrated that with adequate training and experience, physicians can successfully diagnose melanoma 60% to 70% of the time; with dermatoscopy, the accuracy rises into the 90% range. Using pattern analysis and the ABCD rule of dermatoscopy, high-risk lesions that warrant biopsy and subsequent excision can be identified.³² In 2000, Johr and Binder³³ discussed the use of MoleMax II™, a computer system with an epiluminescence microscopy camera, in NS management. High-resolution images can be taken and stored in the patient's file and visualized at future visits for comparison. This system allows precise detection mechanisms and pinpoints precise areas to recheck, which provides confidence to both the physician and patient that suspicious areas are being assessed to be potentially excised for histologic diagnosis; additionally, it enables patients (and their families) to follow their condition with physicians.³³

Two other relatively newer treatment modalities include laser therapy and intense pulsed light. Superficial and deep melanocytic lesions have been treated by an intense pulsed light source with certain parameters; NS showed good clinical clearance.³⁴ In another study, NS on the face of a 23-year-old woman was treated with 4 sessions of intense pulsed light using a 590-nm filter; she remained clear at 6-month follow-up.³⁵ Laser therapy for NS is easy to use and shows an enhanced cosmetic effect.³⁶ We are reticent to recommend either treatment because neither one has been shown to protect against the development of melanoma.

Conclusion

NS is a benign cutaneous anomaly that has malignant potential with the ability to develop fatal consequences. Prevalence rates of NS are similar in both pediatric and adult populations, but management of NS varies in the 2 groups. Although surgical excision may be favored in adults, especially in patients with a history of skin cancer and sun exposure, more conservative management may be warranted and acceptable in children because of the risk of melanoma transformation. It is important to distinguish NS from café au lait spots, congenital melanocytic nevi, and Becker nevi, and to advise patients about the risk for and warning signs of melanoma.

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