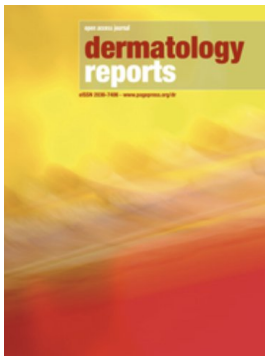

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Melanoma arising in nevus spilus: a systematic review and report of two new cases

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Abstract

Nevus spilus (NS) is a melanocytic lesion characterized by multiple darker macules or papules within a lighter-brown background patch. It is generally considered benign, but rarely melanoma may arise within NS. This association is controversial and poorly quantified. We systematically reviewed the literature on melanoma arising in NS and describe two additional reports. Clinical, histopathologic, molecular, and outcome data were extracted from all eligible cases. The aim of our study was to analyze the clinicopathological patterns, risk factors, and management implications. A total of 39 cases met inclusion criteria, suggesting that melanoma arising in NS is rare but not anecdotal. Most cases occurred in large, congenital, zosteriform lesions; the predominant location was the trunk, followed by the lower and upper limbs; the most common histotype was superficial spreading melanoma (SSM). Favorable outcomes were associated with early detection and thinner lesions, whereas thicker or nodular melanomas and delayed diagnosis correlated with poorer prognosis. Molecular data were limited but suggested possible heterogeneity, with infrequent *BRAF*/*NRAS* mutations. The risk of melanoma arising in NS appears to be subtype-dependent rather than uniform. Routine prophylactic excision of NS lesions is not supported by current evidence. A structured clinical and dermoscopic follow-up – particularly for larger, congenital, and segmental lesions – may represent a balanced management strategy, facilitating earlier identification of malignant transformation and ultimately improving patient outcomes. Further molecular profiling studies are needed to clarify pathogenetic mechanisms and refine risk stratification.

Introduction

Cutaneous melanoma can arise in association with pre-existing melanocytic nevi.[1] Among these, nevus spilus (NS), also referred to as speckled lentiginous nevus, is a rare melanocytic lesion characterized by a light brown patch containing scattered darker macules or papules.[2-5] NS may be present at birth (congenital) or appear later during childhood or adulthood (acquired).[5] It is typically classified into small (<1.5 cm), medium (1.5-19.9 cm), and large (>20 cm). According to its distribution pattern, we recognize a segmental/zosteriform form of NS, also known as zosteriform.[3,6,7]

NS was long regarded as a benign lesion; however, the first case of melanoma arising within NS was described by Perkinson in 1957.[8] Since then, additional cases have been reported, particularly in giant congenital or zosteriform subtypes,[3,7] suggesting a low but non-negligible risk of malignant transformation.[5-7,9]

The aim of this systematic review is to collect and analyze all reported cases of melanoma arising in NS, focusing on relevant clinical and histopathological features to improve the understanding of

malignant transformation in NS and to identify factors that may guide diagnosis, follow-up, and clinical management. In addition, we present two new cases from our own experience.

Case Reports

Case 1

A 35-year-old woman with Fitzpatrick skin phototype II, fewer than 10 melanocytic nevi, and no personal or family history of melanoma presented with a speckled pigmented lesion on her left forearm, measuring 5.0×3.6 cm. The lesion had been present since the age of 10 years. Over the previous year, the patient had noted recent changes, with the appearance of an asymptomatic papule within the pre-existing flat macule, possibly after a traumatic event.

Dermoscopy showed pattern asymmetry, brown globules, irregular in size and shape, dotted vessels, peripheral homogeneous light to dark brown areas and central white reticular depigmentation. An incisional biopsy of the recently developed papule revealed features consistent with a non-ulcerated superficial spreading melanoma (SSM), with a Breslow thickness of 0.2 mm. No mitotic figures were detected, and mild solar elastosis was present (Figure 1).

The tumor was completely excised, followed by a wide local re-excision according to the American Joint Committee on Cancer (AJCC) 8th edition guidelines for pT1a melanoma. The patient has been undergoing follow-up every 6 months for 3 years, with no evidence of local recurrence or distant metastasis.

Case 2

A 23-year-old woman with a family history of melanoma and fewer than 50 melanocytic nevi presented during her routine 6-month nevi check-up at our Melanoma Unit. She had a 2.7×1.0 cm flat speckled lesion on her back, light to dark brown in color, containing darker papules with irregular borders, measuring between 0.4 and 0.1 cm. The lesion had been present for over 10 years and was clinically consistent with NS.

Dermoscopy revealed a reticular pattern, light to dark brown in color, with progressive thickening of the network lines, which had become dark brown to black over the preceding three years. Histopathologic examination showed a compound atypical melanocytic proliferation consistent with SSM in the radial growth phase arising within NS. The Breslow thickness was 0.5 mm, with no ulceration, mitotic activity, or solar elastosis. Preferentially expressed antigen in melanoma (PRAME) immunohistochemistry was strongly positive (Figure 2).

The melanoma was completely excised with clear margins and staged as pT1a according to the AJCC 8th edition. A wide local re-excision was subsequently performed according to current guidelines.

The patient started dermatologic follow-up every 6 months, with no evidence of local recurrence or distant metastasis after 1 year.

Both of our cases were wild type for the *BRAF* V600E mutation, as assessed using the monoclonal antibody *BRAF* V600E (Gennova Scientific, S.L., Sevilla, Spain) on the Dako Omnis immunostainer (Agilent).

Materials and Methods

Search strategy

We conducted a Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)-guided search (inception to June 25, 2025) in PubMed/MEDLINE, Embase, and Cochrane Library, combining controlled vocabulary (Medical Subject Headings [MeSH] and Embase Subject Headings [Emtree]) and keywords for "nevus spilus" and "melanoma", as follows:

i) PubMed: ("nevus spilus"[Title/Abstract] OR "nevoid lentigo"[Title/Abstract] OR "speckled lentiginous nevi"[Title/Abstract] OR "speckled lentiginous nevus"[Title/Abstract] OR "zosteriform lentiginous nevus"[Title/Abstract]) AND ("Melanomas"[Title/Abstract] OR "Malignant Melanoma"[Title/Abstract] OR "Melanoma"[Title/Abstract] OR "Malignant Melanomas"[Title/Abstract] OR "melanoma malignant"[Title/Abstract] OR "melanomas malignant"[Title/Abstract] OR "Melanoma"[MeSH]).

ii) Embase: ('melanoma'/exp OR 'fortner melanoma':ab,ti OR 'malignant melanoma':ab,ti OR 'melano-carcinoma':ab,ti OR 'melano-sarcoma':ab,ti OR 'melanoblastoma':ab,ti OR 'melanocarcinoma':ab,ti OR 'melanocytic malignancies':ab,ti OR 'melanocytic malignancy':ab,ti OR 'melanoma (e)':ab,ti OR 'melanomalignoma':ab,ti OR 'melanosarcoma':ab,ti OR 'melanotic carcinoma':ab,ti OR 'pigmentary cancer':ab,ti OR 'melanoma':ab,ti) AND ('nevus spilus'/exp OR 'nevoid lentigo':kw,ti OR 'speckled lentiginous nevi':kw,ti OR 'speckled lentiginous nevus':kw,ti OR 'zosteriform lentiginous nevus':kw,ti OR 'nevus spilus':kw,ti).

iii) Cochrane Library: ("nevus spilus" OR "speckled lentiginous nevus") AND melanoma.

Inclusion and exclusion criteria

We included English-language case reports/series with histopathologically confirmed melanoma arising within clinically recognized NS, without limits on age or sex. We excluded articles not presenting clinical cases, reports of melanoma not associated to NS, NS without melanoma, and records for which full-text access was unavailable.

Study selection and data extraction

References were managed using Zotero 7 to organize records and remove duplicates. Screening was conducted in two steps: titles and abstracts were first assessed for eligibility by B.A., followed by independent full-text review by M.D.P and B.A. The reference lists of the selected articles were also reviewed to identify additional relevant cases, as illustrated in the PRISMA diagram (Figure 3).
Eligibility was independently confirmed by both reviewers (M.D.P. and B.A.) according to PRISMA guidelines; discrepancies were resolved by consensus. Data from each included case was extracted into Microsoft Excel. The collected information included: age, sex, NS clinical subtype, lesion location, NS size, melanoma histotype, Breslow thickness, ulceration, stage according to the 8th edition of AJCC (2017), molecular status, actinic damage, comorbidities, treatment, and follow-up. The resulting table (Table 1) was double-checked for accuracy by the other reviewers (P.P. and C.C.).

Results

We systematically reviewed the literature to identify cases of melanoma arising within NS. A total of 35 publications (37 cases) published since 1957 were included,[4-38] along with two additional cases from our own experience, for a total of 39 cases. Clinical and histopathological details varied across reports, and some articles lacked complete information. Patient age ranged from 21 months to 87 years, with most diagnoses occurring in adults. The mean age at diagnosis was 50 years. Both males (n=18) and females (n=21) were affected, without evident sex predilection.
The most common NS subtype was the congenital speckled form, whereas acquired and segmental/zosteriform forms were less frequently reported. Lesions were found on various body sites, with no cases involving the head. The trunk was the most frequently affected region (n=18), followed by the lower limbs (n=14). Only a few cases involved the upper extremities (n=3). In some patients (n=4), adjacent regions were simultaneously affected, most commonly the trunk together with the upper limbs. NS size ranged from small macules (~1.5 cm) to giant lesions (>20 cm), with segmental/zosteriform types generally exceeding 10 cm. In the reported cases, most melanomas arose within NS larger than 5 cm (n=26).
The histological subtype of melanoma was not always specified. When reported, SSM was the most common (n=26), followed by nodular melanoma (n=6) and melanoma *in situ* (n=5). Breslow thickness ranged widely, from *in situ* (n=5) to thin melanomas (≤1 mm; n=15) and thicker invasive cases measuring up to 8 mm (n=15). Ulceration was absent or not reported in most cases, with only one case of nodular melanoma described as ulcerated. Among cases where staging was available or could be determined (or updated) according to the AJCC 8th edition, most melanomas were diagnosed at an early stage (Tis, T1; n=20), while 15 cases were diagnosed at a more advanced stage (T2, T3, T4). Among the latter, 6 patients developed metastatic disease.

Molecular data were limited. Only two nodular melanomas, among those reported in the literature, were tested for *BRAF*, both resulting wild type. Overall, molecular profiling was rarely performed, and when available, no consistent pattern of *NRAS*, *HRAS*, or other driver mutations emerged. As our cases were thin melanomas, we preferred to assess the mutational status of *BRAF* V600E by immunohistochemistry rather than by more tissue-consuming NGS techniques, and both cases were wild type.

Reported risk factors included history of sunburns (n=3) and high sun exposure (n=4). Most patients had no significant comorbidities or none. Among those with comorbidities, the most common were neurofibromatosis type 1 (NF1) (n=3) and history of previous skin tumors, including both melanoma (n=2) and non-melanoma skin cancers (n=3). Additional comorbidities included cardiovascular diseases (n=3), psoriasis (n=2), and hypothyroidism (n=1).

Treatment of melanoma arising within NS was predominantly surgical (n=38). Most patients underwent excision, ranging from excisional biopsies to wide local excisions with 1 to 3 cm margins. One patient, the youngest in this review (21 months), did not undergo surgical excision but only incisional biopsies of a giant congenital nevus, which did not reveal malignant cells. However, a subsequent bone marrow biopsy showed diffuse melanoma infiltration, interpreted by the original authors as a possible deep melanomatous component not detectable by skin biopsies of the giant nevus. Additional procedures included sentinel lymph node biopsy (n=4) and lymph node dissection (n=4). In selected cases, adjuvant therapies, such as immunotherapy (*e.g.*, pembrolizumab) (n=1), chemotherapy (n=1), radiation (n=2), and tumor vaccination (n=1), were administered.

Follow-up duration varied widely, ranging from short-term postoperative surveillance to over 11 years. Outcomes were generally favorable, with most patients remaining disease-free after treatment (n=19). One patient remained free of recurrence and metastasis for 5 years but died of cardiovascular causes. Among the six patients who developed metastatic disease, five died despite aggressive treatment. These patients had thicker tumors (n=1), nodular tumors (n=2; Breslow 8 and 6.7 mm), or experienced delayed diagnosis (n=2).

Discussion

NS, also referred to as (mosaic) speckled (lentiginous) nevus, nevus on nevus, or spotty nevus,[26] represents a distinctive melanocytic lesion clinically characterized by multiple darker macules or papules within a lighter pigmented, non-hairy, patch of variable diameter, often along Blaschko's lines. It appears to be slightly more frequent in individuals of Northern European ancestry.[39] NS may be present at birth or appear later in life, and its pathogenesis is still not completely understood, likely involving developmental melanocytic anomalies and environmental factors,[3] although a clear

association with sun exposure has not yet been demonstrated. While generally regarded as a benign entity, our systematic review indicates that NS carries a potential risk of malignant transformation, that, although uncommon, is a clinically meaningful event. Therefore, it deserves structured attention rather than anecdotal consideration, as melanoma arising in NS may occasionally result in fatal outcomes.[9,13,20,24,30] The available evidence suggests that malignant transformation is not randomly distributed across all NS subtypes, but appears to cluster in specific clinical subsets. In fact, most of the 39 cases of melanomas collected in this systematic review arose within congenital NS, particularly in larger and segmental/zosteriform lesions, and were most frequently located on the trunk and extremities. No cases involving the head were reported. Although the absolute number of reported cases is limited, this distribution suggests that lesion size, congenital onset, and segmental pattern may reflect an underlying mosaic susceptibility, potentially conferring localized biological vulnerability rather than a uniform risk across all NS subtypes.

Histopathologically, SSM was the most common subtype,[7,36] followed by nodular melanoma, mirroring patterns seen in other melanocytic lesions. Prognosis was strongly correlated with stage at diagnosis and Breslow thickness: *in situ* or thin melanomas (≤1 mm) showed favorable outcomes, whereas thicker or nodular lesions carried a higher risk of metastasis and mortality. These findings highlight the critical importance of early detection, for which dermoscopy plays a pivotal role in identifying atypical features in new lesions or changes within long-standing NS.

Risk factors analysis suggests that large congenital or segmental/zosteriform NS carry a higher risk of malignant transformation.[3] Additionally, fair skin, history of sunburns, and high sun exposure were frequently reported among several affected patients, although available data remain limited.[7,8,35]

Molecular insights remain limited and partially inconclusive. While common melanoma driving mutations, such as those involving the genes *BRAF* or *NRAS*, appear infrequent in the few NS-associated melanomas analyzed, activating *HRAS* mutations, previously identified in several sporadic NS,[40] suggest the possibility of a distinct molecular pathway. This raises the hypothesis that at least a subset of NS-associated melanomas may follow a pathogenetic pathway different from conventional SSM, potentially sharing features with lesions within the Spitz spectrum. The predominance of SSM morphology, despite the potential for alternative molecular drivers, further supports that clinic-pathological classification alone may not fully reflect the underlying genomic landscape of this disease. Comprehensive molecular profiling through multicenter collaborative efforts will be essential to clarify whether melanoma arising in NS represents a biologically distinct subgroup within the melanoma spectrum, as such distinction may have interesting implications for pathogenesis and targeted therapies.

Particular attention should be given to patients with NF1, in whom NS is relatively common and may be associated with increased melanoma risk.[41,42] Given the known involvement of the *RAS* pathway in NF1 pathogenesis, this association may further support the hypothesis of pathway-specific susceptibility in selected patients. A recent systematic review reported NS as the most frequent nevus type in NF1 patients (44.8%) and suggested that these individuals may have a higher risk of developing melanoma, which tend to be thicker and associated with poorer prognosis compared to the general population.[42] Despite the lack of specific management guidelines, regular clinical and dermoscopic surveillance, ideally on an annual basis, could be justified in NF1 patients, even in the absence of additional risk factors.

Surgical excision remains the cornerstone of treatment, aiming for complete removal of the melanoma and, when appropriate, the entire NS, particularly when clinical monitoring is challenging. Close and continuous follow-up is essential for early detection of eventual recurrence or progression.

Compared with other precursor melanocytic lesions, NS appears to carry a relatively lower overall risk of malignant transformation. Nevertheless, the clustering of the melanomas reported in the literature in larger, congenital, and segmental subgroups supports a risk-adapted surveillance strategy rather than a uniform management. Prophylactic excision of all NS does not seem justified based on current evidence, while a structured clinical and dermoscopic follow-up, particularly of the higher-risk lesions subset, may represent a balanced and evidence-informed approach.

The main limitations of our review include the small number of cases due to the rarity of malignant transformation in NS, the retrospective and descriptive nature of available studies, variability in clinical and histopathological data (collected over several decades, reflecting differences in reporting and staging the lesions), and limited molecular information. Moreover, the absence of denominator data and population-based cohorts prevents precise risk estimation, underscoring the need for prospective registries to better define the true incidence of melanoma arising in NS. All these factors may introduce publication bias and limit the generalizability of our conclusions.

Conclusions

Although NS is generally regarded as a benign lesion, malignant transformation is a clinically meaningful event, albeit rare. The available evidence suggests that melanomas arising in NS are not uniformly distributed across all the clinical variants of NS, but are more frequent in patients with larger, congenital, and segmental/zosteriform lesions. Our synthesis highlights that the molecular characterization and the collection of prospective data remain unmet clinical needs to improve the understanding and management of this condition. Current data do not support routine prophylactic

excision of NS, but rather a risk-adapted strategy based on structured clinical and dermoscopic surveillance of high-risk lesions.

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Figure 1. Case 1. **A**) Clinical aspect. Pigmented speckled lesion of the forearm, measuring 5.0×3.6 cm, with a newly developed asymptomatic papule. **B**) Dermoscopic aspect. Pattern asymmetry with brown globules, irregular in size and shape, dotted vessels, peripheral homogeneous light to dark brown areas and central white reticular depigmentation. **C**) Histopathological aspect. Atypical compound melanocytic proliferation characterized by an asymmetric growth pattern, consistent with non-ulcerated SSM (Haematoxylin-eosin. Original magnification: 40x). **D**) Lentiginous growth pattern (Haematoxylin-eosin. Original magnification: 100x). **E**) Pagetoid spread (Haematoxylin-eosin. Original magnification: 200x).

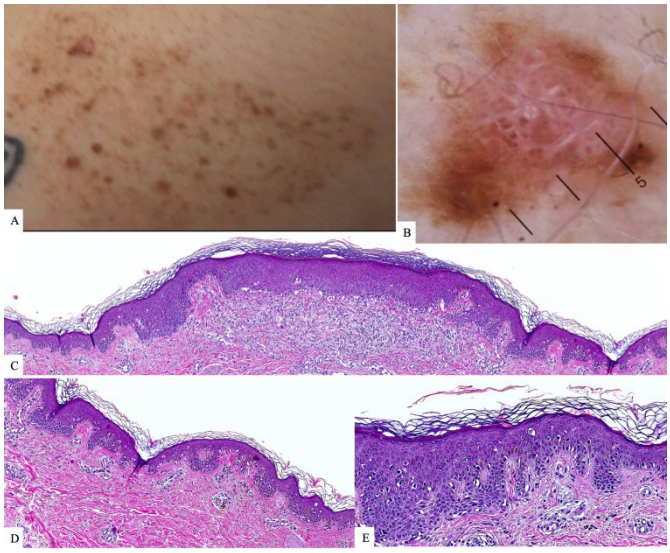

Figure 2. Case 2. **A**) Clinical aspect. A 2.7×1.0 cm flat speckled lesion of the back, with small darker papules with irregular borders. **B**) Dermoscopic aspect. Reticular pattern, light to dark brown in color, with progressive thickening of the network lines. **C**) Histopathological aspect. Atypical compound melanocytic proliferation, consistent with non-ulcerated SSM (Haematoxylin-eosin. Original magnification: 40x). **D)** Lentiginous growth pattern of markedly atypical melanocytes, with pagetoid spread (Haematoxylin-eosin. Original magnification: 200x). **E**) PRAME immunohistochemistry. Strongly positive (Original magnification: 200x).

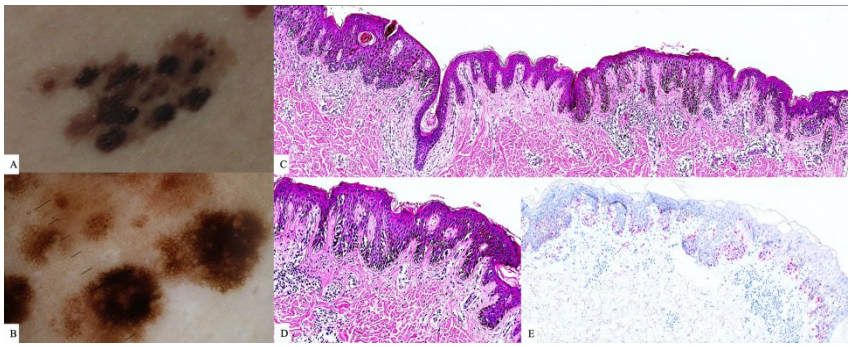

Figure 3. PRISMA diagram of included studies. A total of 170 records were identified through database searches: PubMed (n=67), Embase (n=102), and the Cochrane Library (n=1). After removing duplicates, 89 records remained for title and abstract screening. Of these, 57 were excluded, and 32 full-text articles were assessed for eligibility. An additional 11 records were identified through the reference lists of these 32 articles. In total, 43 articles were retrieved, and their full texts were screened according to our criteria. Thirty-five articles describing 37 cases of melanoma arising in NS met the eligibility criteria and were included in the study.

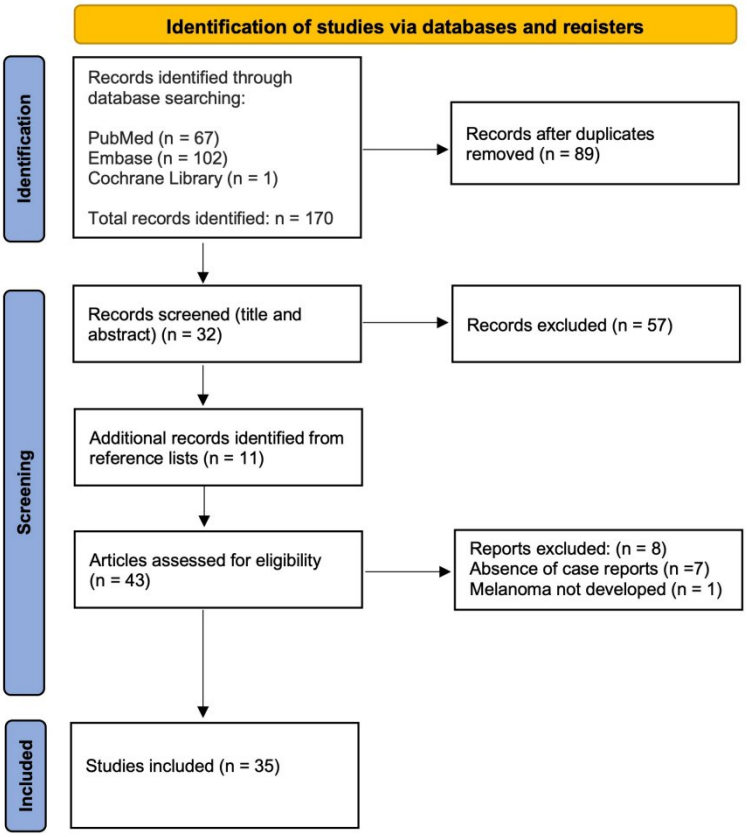

Table 1. Overview of reported cases of melanoma arising in NS (n=39). Data include patient demographics, nevus characteristics, melanoma subtype, Breslow thickness, staging according to AJCC 8th edition, treatment, and follow-up outcomes. Missing information is indicated as not reported (NR).

Reference	Age	Sex	NS type	Lesion location	NS size (cm)	Melanoma histotype	Breslow (mm)	Ulceration	Stage according AJCC 8th ed	Molecular mutation	Actinic damage	Comorbidities	Treatment	Follow-up
Perkinson, 1957	44	F	Café au lait spot	Right anteromedial thigh	7×4	SSM	NR	NR	NR	NR	Sunburn	NF1	Surgical excision, groin dissection	NR
Wagner et al., 1989	61	M	Acquired, Speckled	Abdomen (left periphery)	2×3	Melanoma in situ	0	NR	Tis	NR	NR	NR	Surgical excision	NR
Rhodes et al., 1990	79	F	Congenital, Speckled	Right leg (medial calf)	8×7.5	Nodular melanoma	NR	No	NR	NR	NR	Cardiovascular diseases, colitis, electrolyte deficiencies, mild metabolic acidemia	Surgical excision	No recurrence/metastasis over 5 yrs, death due to heart disease or stroke
Rütten et al., 1990	50	F	Congenital, Speckled	Left lower leg	NR	SSM	0.5	NR	T1a	NR	NR	NF1	Surgical excision	No metastasis after clinical staging
Stern et al., 1990	53	F	Congenital, Speckled Zosteriform	Right upper extremity, neck, thorax, abdomen	NR	Nodular melanoma	6.7	NR	T4	NR	NR	NR	Surgical excision	Died of metastatic disease
Bolognia et al., 1991	43	M	Zosteriform Speckled	Upper back, left neck ,left shoulder	NR	NR	1.6	NR	T2	NR	NR	Psoriasis	Incisional biopsies 4 atypical lesions	Died of metastatic disease
Guillot et al., 1991	59	F	Congenital, Speckled	Left groin	Giant	SSM with a nodule	1.1	NR	T2	NR	NR	NR	Surgical excision	NR
Kurban et al., 1992	60	M	Acquired, Speckled	Back	10×12	SSM	1.5	NR	T2	NR	NR	NR	Surgical excision	No recurrence/metastasis over 2 yrs
Borrego et al., 1994	55	F	Congenital, Speckled Segmental	Left shoulder	4.4×3.5	SSM	1.3	No	T2a	NR	NR	NR	Surgical excision	NR
Cox et al., 1994 (Case 1)	42	F	Congenital	Ankle	NR	SSM	0.5	NR	T1a	NR	NR	NR	Surgical excision	No local or at distance recurrences during 3 yrs
Vázquez-Doval et al., 1995	53	M	Congenital, Speckled	Left thigh	4×3	SSM	NR	No	NR	NR	NR	Hypothyroidism	Surgical excision	NR
Grinspan et al., 1997	44	F	Congenital, Speckled	Left lumbar region (back area)	6×4	SSM	1.2	NR	T2	NR	NR	None	Surgical excision	No recurrence/metastasis over 5 yrs
Weinberg et al., 1998	53	F	Congenital, Speckled	Left flank	NR	SSM	1.3	No	T2a	NR	NR	NR	Surgical excision, lymph node dissection, tumor vaccine, Interferon, chemotherapy, radiotherapy	Died of metastatic disease
Yoneyama et al., 2005	85	F	Congenital, Speckled	Right lower leg	10×20	SSM	1.8	No	T2a	NR	NR	NR	Surgical excision	No recurrence/metastasis during 3 yrs
Piana et al., 2006	28	M	Congenital, Speckled	Left arm	5	SSM (3biopsy)	1.0(A), 0.7(B), 0.3(C)	No	T1b(m)	NR	NR	None	Surgical excision, sentinel lymph node biopsy	NR
Zeren-Bilgin et al., 2006	45	M	Congenital, Speckled, hairy	Right lower back	10×18	Nodular melanoma	8	Present	T4b	NR	NR	None	Surgical excision	No recurrence/metastatic during of 15 months
Bin Amer et al., 2007	21 mo	M	Congenital, Giant Speckled	Lower trunk and bilateral thighs	Giant	NR	NR	No	NR	NR	NR	NF 1	Planned palliative chemotherapy (refused)	Died of metastatic disease
Haenssle et al., 2009 (Case 1)	42	M	Congenital, Segmental	Left abdomen and lower back	Extensive	SSM	0.6	NR	T1a	NR	NR	NR	Surgical excision	No relapse/metastasis during 11.5 yrs
Meguerditchian et al., 2009	60	M	Congenital, Speckled	Medial left calf	15×10	SSM	0.8, 1	No	T1b(m)	NR	Sun exposure, Sunburns	NR	Surgical excision, sentinel lymph node biopsy	No recurrence/metastasis over 2 yrs
Angit et al., 2011	65	F	Congenital, Speckled	Mid-lower lumbar back	9×3	SSM	1.1	No	T2a	NR	NR	Chronic obstructive airway disease, osteoarthritis, hypertension, psoriasis	Surgical excision	NR
Cecchi et al., 2012	47	M	Congenital, Zosteriform	Upper right back near midline	Giant	SSM	0.4	No	T1a	NR	Sun exposure	None	Surgical excision	No recurrence/metastasis during 2 yrs
Karam et al., 2012	68	M	Acquired, Speckled	Left axilla / lateral lesion of nevus spilus	4.5×1.2	SSM	1.1	No	T2a	NR	NR	NR	Surgical excision, sentinel lymph node biopsy	No recurrence /metastatic disease
Spagnolo et al., 2012	42	F	Acquired, Speckled	Inferior part of leg	8	Melanoma in situ	0	No	Tis	NR	NR	NR	Surgical excision	NR
Corradin et al., 2014	80	M	Congenital, Speckled	Right thigh	~7	Melanoma in situ	0	NR	Tis	NR	NR	BCC, melanoma (10 yrs prior)	Surgical excision	NR

Tavoloni Braga et al., 2014	31	M	Not reported	Middle left back	NR	Melanoma in situ	0	NR	Tis	NR	NR	Dysplastic nevus syndrome	Surgical excision	NR
Gescheidt-Shoshany et al., 2015	63	M	Large Segmental Speckled	Left thorax, upper limb, shoulder, axilla	>20	Nodular melanoma	8	NR	T4M1	BRAF negative	NR	None	Surgical excision, lymph node dissection, radiation, IV immunoglobulins	Died of metastatic disease
Tagliavanti et al.,2016	42	F	Congenital	Right inguinal region	NR	SSM, spitzoid features	0.7	No	T1a	NR	NR	NR	Surgical excision	No local/distance recurrences during 3 yrs
Boot-Bloemen et al., 2017	64	F	Acquired (Infancy),Speckled	Back	20–40	Melanoma in situ	0	No	Tis	NR	NR	NR	Surgical excision	No recurrences/metastases
Boot-Bloemen et al., 2017	49	F	Congenital (birth), Speckled	Leg	>40	SSM	0.7	No	T1a	NR	NR	NR	Surgical excision	No recurrences/metastases
Boot-Bloemen et al., 2017	41	M	Acquired (Infancy), Speckled	Back, arms	>40	SSM	0.6,0.7	No	T1a(m)	NR	NR	Melanoma	Surgical excision	No recurrences/metastases
Brito et al., 2017	83	M	Congenital, Speckled	Right arm and forearm (A,B,C), upper back (D)	27×10	2 SSM (A,B), 2 in situ (C,D)	2.5 (A), 1.2 (B), 0 (C,D)	No	T3a(m)	NR	Sun exposure	NR	Surgical excision, sentinel lymph node biopsy	No metastasis
Miura et al., 2018	49	F	Congenital, Speckled	Left thigh	6.5×2.5	Nodular melanoma	3.5	NR	T3a	NR	NR	NR	Surgical excision, resection of an in-transit metastasis, left inguinal lymph node dissection	No recurrence/metastasis during 3 yrs
Kordeva et al., 2023	36	F	Congenital, Speckled	Right lower lateral hip	Medium	SSM	0.8	NR	T1b	NR	NR	None	Surgical excision	NR
Racanelli et al., 2023	47	F	Congenital, Speckled	Left lateral arm	9.5×5.3	SSM	0.2	NR	T1a	NR	NR	BCC (3 years prior)	Surgical excision	NR
Sheridan et al., 2023	87	M	Speckled	Left mid back	>20	SSM	0.3	No	T1a	NR	Extensive photodamage	Multiple NMSC	Surgical excision	No recurrence reported
Tchernev, 2023	51	F	Congenital	Right lateral thoracic	10×15	Nodular melanoma	2.3	No	T3a (M1b)	BRAF negative	Sunburns	Hypertension (10-15 years)	Surgical excision, pembrolizumab	Distant metastasis to lung
Sansoni et al., 2024	72	M	Speckled	Right upper quadrant of abdomen	5.5×1.8	SSM, in situ	0.3	No	T1a	NR	NR	NR	Surgical excision	No relapse/metastases
Di Prete et al., 2026	35	F	Acquired, Speckled	left forearm	5×3.6	SSM	0.2	No	T1a	BRAF negative	Mild solar elastosis	None	Surgical excision	No recurrences/metastases during 3 yrs
Di Prete et al., 2026	23	F	Acquired, Speckled	Back	2.7×1	SSM	0.5	No	T1a	BRAF negative	No	None	Surgical excision	No recurrences/metastases during 1 yrs

NS, nevus spilus; AJCC, American Joint Committee on Cancer; SSM, superficial spreading melanoma; NF1, neurofibromatosis type 1; BCC, basal cell carcinoma; NMSC, non-melanoma skin cancer.