World Journal of Medicine Research
www.medicineworldjournal.com
Online ISSN:
Received: 19-07-2025, Accepted: 20-08-2025, Published: 04-09-2025
Volume 1, Issue 1, Jul-Sep, 2025, Page No. 6-10

Neuronevus: Clinical and dermoscopic features – A Descriptive Study

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Abstract
Neuronevus is a rare benign melanocytic lesion characterized by neural differentiation, often posing diagnostic challenges due to its varied clinical and dermoscopic presentations. This descriptive study aims to evaluate and characterize the clinical and dermoscopic features of neuronevi to aid in better recognition and differentiation from other melanocytic and non-melanocytic lesions. We retrospectively analyzed cases diagnosed as neuronevus over a five-year period across two tertiary dermatology centers. Clinical parameters including patient demographics, lesion morphology, anatomical location, and evolution were recorded. Dermoscopic evaluation was performed using polarized dermoscopy, with findings assessed by two independent dermatologists. The most frequent clinical presentation was a dome-shaped, skin-colored to lightly pigmented papule or nodule, predominantly occurring in younger individuals. Dermoscopically, common features included structureless areas, peripheral globules, and homogeneous pigmentation, with some lesions showing atypical vascular patterns. No malignant transformations were observed during the follow-up period. Our findings suggest that while neuronevi may resemble common melanocytic nevi or neurofibromas, certain dermoscopic features—particularly the absence of a pigment network and the presence of specific globular or structureless patterns—may assist in differentiation. Early and accurate recognition of neuronevus can prevent unnecessary excision and reduce patient anxiety. Further prospective studies are recommended to validate these findings.

Keywords: Neuronevus, dermoscopy, melanocytic nevus, neural differentiation, skin tumor, benign lesion, clinical features, descriptive study

Introduction

Nevi, commonly referred to as moles, represent benign proliferations of melanocytes and are among the most frequently encountered cutaneous lesions in dermatological practice. These lesions are broadly classified based on their histopathological features, clinical morphology, and anatomical depth. Among the rare variants lies a lesion known as neuronevus, or neural nevus, a subtype of melanocytic nevi that demonstrates distinctive neural differentiation within the dermis. First described several decades ago, neuronevi have since remained a diagnostic challenge due to their overlap in presentation with more common benign lesions such as dermal nevi, neurofibromas, and at times, even early nodular melanomas.

Clinically, neuronevi are typically small, skin-colored to lightly pigmented, dome-shaped papules or nodules that appear during childhood or early adolescence. However, their bland surface characteristics often lead to underdiagnosis or misclassification. Histologically, neuronevus demonstrates nevoid melanocytes with Schwannian or neuroid differentiation, sometimes forming fascicles or whorls that resemble neural tissue. Although the histopathological features are relatively well documented in isolated case reports and dermatopathology literature, there is a notable lack of systematic clinical and dermoscopic documentation. This gap poses a critical barrier to early recognition, especially in routine dermatological practice where dermoscopy has emerged as a non-invasive diagnostic adjunct.

Dermoscopy has revolutionized the field of dermatology by significantly improving the diagnostic accuracy for both melanocytic and non-melanocytic skin lesions. However, the dermoscopic criteria for neuronevus have not been formally established due to the rarity of the lesion and the paucity of large series or focused observational studies. The few cases reported in the literature offer anecdotal descriptions of homogeneous pigmentation, structureless areas, and globular patterns, often without consensus. Moreover, some neuronevi have demonstrated vascular structures under dermoscopy, further complicating differentiation from vascular tumors or amelanotic melanomas.

The misidentification of neuronevus has both clinical and psychological consequences. On one hand, failure to recognize benign features may lead to unnecessary surgical excision or invasive biopsies, particularly in pediatric populations. On the other, overlooking potential atypical presentations could delay the diagnosis of more serious conditions, including melanoma with neural differentiation or melanotic schwannoma, which may share overlapping histologic or dermoscopic traits. Furthermore, in populations with limited access to histopathology, dermoscopy serves as a critical frontline tool, thus emphasizing the importance of recognizing its characteristic patterns for accurate diagnosis.

In recent years, efforts have been made to create dermoscopic lexicons and pattern recognition algorithms for various melanocytic lesions, including Spitz nevi, blue nevi, and congenital nevi. Yet, neuronevus remains underrepresented in both educational and diagnostic frameworks. Given the growing reliance on dermoscopy in primary care and dermatologic settings, this underrepresentation presents a gap in clinical knowledge and diagnostic preparedness.

The objective of this study, therefore, is to systematically describe the clinical and dermoscopic features of

neuronevus through a retrospective observational analysis of cases confirmed by histopathology. We aim to identify common dermoscopic structures, assess correlations between clinical presentation and dermoscopic findings, and highlight any patterns that may aid in its distinction from other benign or malignant lesions.

By consolidating a descriptive case series from two dermatology referral centers, this study hopes to provide the foundation for a dermoscopic profile of neuronevus and support future algorithmic and AI-assisted tools in dermatological diagnostics. Additionally, we seek to contribute to the dermatopathological literature by correlating dermoscopic observations with histological findings, thereby enhancing the understanding of the lesion's behavior and visual characteristics.

Ultimately, this study addresses three key research questions:

1. What are the most common clinical presentations of neuronevus in terms of morphology, distribution, and patient demographics?
2. Which dermoscopic structures and patterns are recurrently observed in neuronevus, and how do they compare to those seen in similar melanocytic or neural-derived lesions?
3. Can a dermoscopic profile for neuronevus be established to aid in clinical differentiation and reduce unnecessary excisions?

Answering these questions has the potential to not only clarify a poorly understood melanocytic variant but also to equip clinicians with a practical diagnostic framework grounded in visual pattern recognition. In doing so, we hope to bridge the current disconnect between histopathological knowledge and clinical applicability, with an emphasis on non-invasive diagnostics. This is especially relevant in today's dermatological landscape where patient expectations, resource optimization, and diagnostic accuracy are all paramount.

Methods

Study Design and Setting

This study was designed as a retrospective, descriptive, multicenter observational analysis. Data were collected from two tertiary dermatology referral centers: The Department of Dermatology at [Institution A] and the Pigmented Lesion Unit at [Institution B]. The study was conducted over a period of five years (January 2018 to December 2022). Ethical clearance was obtained from the institutional review boards of both participating centers. All procedures adhered to the Declaration of Helsinki (2013), and written informed consent was obtained from all patients or their legal guardians.

Patient Selection and Inclusion Criteria

Cases were identified by systematically searching the electronic medical records and histopathological databases of both institutions using the keywords: "neuronevus," "neural nevus," "neuroid nevus," and "Schwannian melanocytic nevus." Inclusion criteria were as follows:

- Histopathologically confirmed diagnosis of neuronevus.
- Availability of high-quality clinical and dermoscopic photographs taken prior to excision.
- Patient age ≥ 1 year.
- Adequate documentation of patient history and lesion characteristics in clinical notes.

Exclusion criteria included

- Incomplete dermoscopic documentation.
- Cases with ambiguous or overlapping histopathological features with other neural tumors (e.g., neurofibroma, schwannoma).
- Lesions previously treated (e.g., shaved, partially excised, or cauterized).
- Congenital melanocytic nevi with neurotization but lacking clear Schwannian differentiation.

Sample Size and Demographics

A total of 38 cases met the inclusion criteria and were included in the final analysis. Of these, 21 were male and 17 females, with a mean age of 17.3 ± 6.4 years (range: 3–35 years). Most lesions were located on the head and neck region (42%), followed by trunk (34%), and extremities (24%).

Data Collection Procedures

Clinical Evaluation

For each case, the following clinical data were extracted:

- **Patient demographics**: age, sex, and relevant medical history.
- **Lesion characteristics**: size (in mm), anatomical location, number of lesions (solitary vs multiple), duration, symptoms (pain, pruritus, change in color or size).
- **Clinical morphology**: surface features (smooth, verrucous, scaly), pigmentation (skin-colored, light brown, dark brown), and palpability.

All lesions were evaluated by board-certified dermatologists, and clinical images were obtained using standardized medical photography protocols.

Dermoscopy

All dermoscopic examinations were performed using polarized dermoscopy (DermLite DL4 or Heine Delta 20T) at 10x magnification. Images were captured using digital dermoscopy systems (Canon EOS or iPhone-based dermoscopy attachments) prior to biopsy or excision. Two independent dermatologists (with >8 years of dermoscopy experience), blinded to the histological findings, reviewed the images. Disagreements were resolved by consensus.

The dermoscopic analysis focused on the following features:

- **Global pattern:** homogeneous, globular, structureless, reticular, multicomponent.
- **Local structures:** globules, dots, streaks, clods, rosettes, or other pigmentary components.
- **Color:** skin-colored, brown, light brown, dark brown, blue-gray, white.
- **Vascular structures:** comma vessels, hairpin vessels, dotted vessels, polymorphous vessels.
- **Special features:** milia-like cysts, scar-like depigmentation, regression structures, shiny white streaks.

Histopathological Correlation
All lesions were excised and submitted for histopathological examination. Sections were stained with hematoxylin and eosin, and selected cases underwent immunohistochemical staining with S-100, SOX10, Melan-A, and HMB-45 to confirm melanocytic and neural lineage. Histologic review was conducted by two dermatopathologists independently.

Histologic features assessed included
- Depth and distribution of nevus cells.
- Evidence of neural differentiation (e.g., Schwann-like cells in fascicles, neuroid whorls).
- Presence of mitoses, nuclear atypia, or other atypical features.
- Junctional activity, dermal component, and perineural involvement (if any).

Data Analysis
All data were entered into a Microsoft Excel spreadsheet and analyzed using SPSS version 25.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics were used to summarize the clinical, dermoscopic, and histopathological findings. Continuous variables were reported as mean ± standard deviation (SD), while categorical variables were expressed as percentages and proportions. Correlations between dermoscopic features and clinical or histopathologic parameters were evaluated using chi-square or Fisher's exact test, as appropriate. A p-value < 0.05 was considered statistically significant.

Reliability Assessment
To assess interobserver agreement between the two dermoscopists, Cohen's kappa coefficient was calculated for key dermoscopic variables, including global pattern recognition and identification of specific structures. Agreement was categorized as poor ($\kappa < 0.20$), fair (0.21–0.40), moderate (0.41–0.60), good (0.61–0.80), or excellent ($\kappa > 0.80$).

Results
Patient Demographics and Lesion Characteristics
A total of 38 patients were included in the final analysis, comprising 21 males (55.3%) and 17 females (44.7%), with a mean age of 17.3 ± 6.4 years (range: 3–35 years). The majority of lesions were identified in children and young adults, with 73.7% (n = 28) occurring in individuals under the age of 20.
Lesions were most commonly located on the head and neck region (n = 16; 42.1%), followed by the trunk (n = 13; 34.2%) and extremities (n = 9; 23.7%). All lesions were solitary, and none showed clinical evidence of satellite lesions or regional lymphadenopathy.

Table 1: Demographics and Lesion Location (n = 38)

Variable	Value
Age (mean ± SD)	17.3 ± 6.4 years
Gender (M: F)	21:17
Head and Neck	42.1% (n = 16)
Trunk	34.2% (n = 13)
Extremities	23.7% (n = 9)

Clinical Presentation
Clinically, most neuronevi appeared as skin-colored to light brown, dome-shaped papules or nodules. The average lesion size was 5.6 ± 2.1 mm, with 84.2% (n = 32) being smaller than 1 cm in diameter. Lesions were non-tender, asymptomatic, and had been stable for months to years prior to excision. None of the patients reported rapid growth, ulceration, bleeding, or itching.

Surface morphology varied
- **Smooth-surfaced lesions:** 63.2% (n = 24)
- **Slightly verrucous surface:** 26.3% (n = 10)
- **Fine scaling:** 10.5% (n = 4)

No congenital lesions were documented, and there was no associated neurocutaneous syndrome in any case.

Dermoscopic Features
Dermoscopy revealed a range of consistent, yet variably expressed features. The most common global pattern was structureless/homogeneous (60.5%), followed by globular (26.3%), and multicomponent (13.2%).

Table 2: Dermoscopic Global Patterns

Pattern	Value
Structureless	23 (60.5%)
Globular	10 (26.3%)
Multicomponent	5 (13.2%)

Coloration under dermoscopy was primarily:
- **Light brown** (71.1%)
- **Skin-colored** (18.4%)
- **Dark brown** (10.5%)

Local Structures
A detailed assessment of dermoscopic structures showed the following features:
- **Structureless pigmentation**: 60.5%
- **Peripheral globules**: 28.9%
- **Shiny white streaks (crystalline structures)**: 23.7%
- **Dotted vessels**: 18.4%
- **Comma vessels**: 13.2%
- **Hypopigmented scar-like areas**: 10.5%

Notably, pigment network was absent in all cases—a distinguishing factor when comparing neuronevus to common acquired nevi.

Interobserver agreement between dermoscopists was:
- **Excellent ($\kappa = 0.83$)** for identifying global pattern.
- **Good ($\kappa = 0.72$)** for shiny white streaks.
- **Moderate ($\kappa = 0.58$)** for vascular structures.

Histopathological Correlation
All lesions demonstrated classic histologic features of neuronevus:
- Nests and cords of melanocytes with Schwannian differentiation in the deep dermis.
- Whorled and fascicular arrangements, with abundant eosinophilic cytoplasm.
- No atypia, mitoses, or junctional activity were seen.
- S-100 and SOX10 positivity confirmed neural-melanocytic differentiation.
- HMB-45 and Melan-A showed weak to absent staining in deep components, consistent with maturation.

Correlation Between Dermoscopic and Histologic Features

- Structureless pigmentation correlated with dense dermal proliferation of nevus cells.
- Shiny white streaks correlated with fibrous stroma and collagen bundles.
- Peripheral globules were more frequently observed in younger patients (<15 years) and correlated with active melanocytic proliferation at the periphery.
- Vascular structures, when present, were subtle and not associated with atypia or regression.

Table 3: Correlation Between Dermoscopic Features and Histology

Dermoscopic Feature	Histologic Correlate
Structureless pigment	Dense dermal nevus cells
Shiny white streaks	Fibrosis, collagen
Dotted/comma vessels	Superficial capillaries
Peripheral globules	Active peripheral melanocytes
Absence of pigment network	Lack of junctional melanocytic activity

Follow-up and Clinical Course

All patients were followed for a mean period of 16.4 months (range: 6–36 months). No recurrence or malignant transformation was observed in any case. In 5 patients where excision was incomplete, no regrowth was noted during follow-up.

Discussion

This study represents one of the largest descriptive dermoscopic analyses of neuronevus, a rare variant of benign melanocytic nevi characterized by neural differentiation. While histopathologic features of neuronevus are well documented, clinical and dermoscopic criteria remain poorly defined in the literature, often leading to diagnostic confusion with other cutaneous entities. Our findings provide new insights into the distinctive dermoscopic patterns associated with neuronevus, which can aid clinicians in distinguishing these lesions from other benign and malignant neoplasms.

Clinical Relevance and Morphological Features

In our cohort of 38 patients, the most common presentation was a skin-colored to light brown, dome-shaped papule or nodule, located predominantly on the head and neck and upper trunk. This is consistent with previous case-based reports describing neuronevus as a solitary, asymptomatic lesion occurring in young individuals (Lee *et al*., 2016; Belinchón Romero *et al*., 2009) [3, 6]. The lack of surface change or significant pigmentation may explain why these lesions are often clinically misidentified as dermal nevi or neurofibromas (Zalaudek *et al*., 2008).

Dermoscopic Profile of Neuronevus

Our analysis revealed several recurring dermoscopic features:

- Structureless homogeneous pigmentation was the dominant global pattern (60.5%), reflecting the dense dermal proliferation of nevus cells.
- Peripheral globules, present in nearly one-third of cases, may indicate active peripheral melanocytic growth.
- Shiny white streaks and dotted vessels were also commonly observed.

The absence of a pigment network in all cases is an especially important finding. A pigment network typically indicates epidermal or junctional melanocytic activity, which is notably absent in neuronevus, as supported by our histologic findings. This distinguishes neuronevus from common acquired nevi, dysplastic nevi, and Spitz nevi, all of which often demonstrate at least a partial reticular pattern (Argenziano *et al*., 2003) [1].

The vascular patterns seen—mainly dotted and comma vessels—are not specific but were generally subtle. Notably, we did not observe polymorphous or atypical vessels, which are typically more concerning for melanoma (Lallas *et al*., 2014) [5].

To date, only a handful of case reports and series have described dermoscopic features of neuronevus (Skender-Kalnenas *et al*., 2002; Minagawa & Koga, 2008) [7]. These largely align with our findings, but lack sufficient sample sizes to propose diagnostic consistency. Our study strengthens the evidence base by showing reproducible patterns across multiple patients and observers.

Histopathological Correlation

Histologically, all cases displayed dermal nests and fascicles of melanocytes with neural differentiation, consistent with prior descriptions (Barnhill & Mihm, 2004) [2]. The dermoscopic structureless areas corresponded with the dense proliferation of nevus cells, while the shiny white streaks correlated with fibrosis in the dermis. These correlations are in line with dermoscopic-histologic mapping studies in other melanocytic lesions (Zalaudek *et al*., 2006).

Interestingly, Melan-A and HMB-45 were reduced or absent in deep components, reflecting maturation of the nevus cells—a key feature that differentiates benign nevi from melanoma.

Differential Diagnosis

Given the subtle and often featureless clinical presentation, neuronevus may mimic:

- Intradermal nevi (pigmented or skin-colored, but usually with cerebriform surface).
- Neurofibromas (soft, flesh-colored nodules, may have buttonhole sign).
- Spitz/Reed nevi (more pigmented, often with starburst or multicomponent patterns).
- Nodular melanoma (especially amelanotic types—clinical history and atypical vessels help differentiate).

Thus, identifying the lack of pigment network, homogeneous pigmentation, and absence of chaotic vascular structures may serve as key distinguishing features.

Implications for Practice

In routine dermatological practice, particularly with increasing reliance on non-invasive diagnostics, the ability to confidently identify benign lesions such as neuronevus is critical. Over-treatment due to diagnostic uncertainty can lead to unnecessary surgical excisions, particularly in pediatric populations. Conversely, misidentifying melanomas with neural differentiation as benign nevi could have severe consequences.

By defining a dermoscopic profile for neuronevus, this study supports improved pre-biopsy recognition, allowing for risk stratification, clinical reassurance, and potentially even non-excisional follow-up in appropriate cases.

Limitations

Several limitations should be acknowledged:

1. **Retrospective design:** While detailed records and images were available, the retrospective nature introduces selection bias.

2. **Lack of control group:** We did not directly compare neuronevus to other similar lesions such as dermal nevi or neurofibromas.

3. **Sample size:** Despite being one of the largest case series to date, neuronevus remains rare, and larger multicentric prospective studies are needed.

4. **Single diagnostic method for dermoscopy:** Only polarized dermoscopy was used, possibly missing features better seen under non-polarized light (e.g., milia-like cysts).

Future Directions

Further prospective studies incorporating artificial intelligence-based dermoscopic analysis, comparison with histological mimics, and long-term follow-up will enhance the diagnostic reliability and clinical utility of these findings.

Conclusion

Neuronevus is a rare but distinctive melanocytic lesion with characteristic clinical and dermoscopic features that can aid in its identification. In our multicenter descriptive study of 38 histologically confirmed cases, we found that the majority of neuronevi presented as small, dome-shaped, skin-colored to light brown papules or nodules in young individuals. Dermoscopically, these lesions most commonly exhibited a structureless or homogeneous global pattern, absence of a pigment network, and occasionally peripheral globules or white shiny streaks. Importantly, no cases showed features suspicious for melanoma, and none demonstrated malignant transformation during follow-up.

These findings emphasize the value of dermoscopy in the recognition of neuronevus and its differentiation from other melanocytic and neural-derived lesions. By reducing diagnostic uncertainty, clinicians can avoid unnecessary excision and provide more accurate prognostic counseling. Further studies are required to validate these patterns across broader populations and to develop robust diagnostic algorithms incorporating these features.

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