Dermatology Practical & Conceptual

Spitz Nevus with HRAS Q61R Arising in a Giant Nevus Spilus of the Leg

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Introduction

Spitz nevi developing within nevus spilus represent a rare clinical entity and pose diagnostic and management challenges [1]. We present a case that adds to the limited literature on this uncommon association, particularly highlighting the molecular findings that support the genetic relationship between these lesions (Table 1).

Case Presentation

We present a 15-year-old female with a giant congenital melanocytic nevus spilus involving her left lower extremity, measuring 60×30 cm and present since birth. On skin examination, numerous melanocytic macules and papules (1 mm–1 cm) were distributed over a light brown macular background (Figure 1). The patient had previously undergone excisions of two dysplastic compound nevi from the same thigh, both reported as low-grade dysplasia.

Dermoscopy showed multiple nevi with junctional, compound, and dermal patterns, some displaying dysplastic features (Figure 2). Notably, a lesion on the posterior leg showed clinical asymmetry. An excision was performed to exclude melanoma. Histopathology revealed classical features of Spitz nevus: large epithelioid and spindle melanocytes within a symmetrical compound proliferation. Next-generation sequencing identified an HRAS mutation (c.182A>G, p.Gln61Arg, variant allele frequency 30.13%), consistent with published pathogenic variants for Spitz and congenital nevi (Figure 3) [3]. The case was thus diagnosed as Spitz nevus arising on a giant nevus spilus.

Conclusion

Although nevus spilus is considered benign, its potential for malignant transformation is recognized, particularly when dysplastic nevi or atypical features are present [2]. This risk increases with large or giant lesions, as seen here, and with

Table 1. Literature review of Spitz nevus arising on nevus spilus.

First Author (Year)	Age/ Sex	Nevus Spilus Type/Size	Number of Spitz Nevi	Location	Molecular Findings	Key Notes/ References
Winkelmann (1961)	6/F	Not specified	Multiple	Not specified	Not available	First report; "juvenile melanoma"
Prose (1983)	4/F	Not specified	Multiple	Not specified	Not available	Multiple benign juvenile melanomas
Akasaka (1993)	17/M	Hyperpigmented macule	Multiple agminated	Thigh	Not available	Agminated juvenile melanoma
Herd (1994)	8/F	Hyperpigmented patch	Multiple agminated	Buttock	Not available	Agminated Spitz nevi
Hofmann-Wellenhof (1994)	10/F	Not specified	Solitary	Not specified	Not available	Spitz nevus on nevus spilus
Aloi (1995)	3/M	Congenital speckled lentiginous nevus	Multiple agminated	Leg	Not available	Agminated Spitz nevi
Betti (1997)	16/M	Unusual speckled lentiginous nevus	Multiple agminated	Thigh	Not available	Intradermal Spitz nevi
Aida (2010)	6/F	Not specified	Multiple agminated	Trunk	Not available	After chemotherapy
Torti (2011)	5/F, 8/F	Not specified	Multiple agminated	Trunk	HRAS mutation (G13R)	Molecular analysis; agminated Spitz nevi
Sarin (2013)	6/F	Not specified	Multiple agminated	Trunk	HRAS mutation (G13R)	HRAS mutation confirmed
Porubsky (2018)	16/F	Extensive nevus spilus	Multiple	Trunk	Not specified	Genomic analysis performed
Goto (2020)	7/F	Giant congenital hyperpigmented macule	Multiple agminated	Trunk	TRPM1-PUM1-LCK fusion	Novel three-way gene rearrangement
Goto (2021)	6/F, 8/F	Not specified	Multiple agminated	Trunk	GOPC-ROS1 mosaicism	Two cases, mosaicism
Kervarrec (2022)	7/F	Not specified	Multiple agminated	Trunk	HRAS Q61R mutation	Agminated Spitz nevus
Current Case (2025)	15/F	Giant congenital nevus spilus (60x30cm)	Solitary	Leg	HRAS Q61R mutation	Confirmed by NGS, giant lesion, history of dysplasia



Figure 1. The giant nevus spilus on the patient's leg.

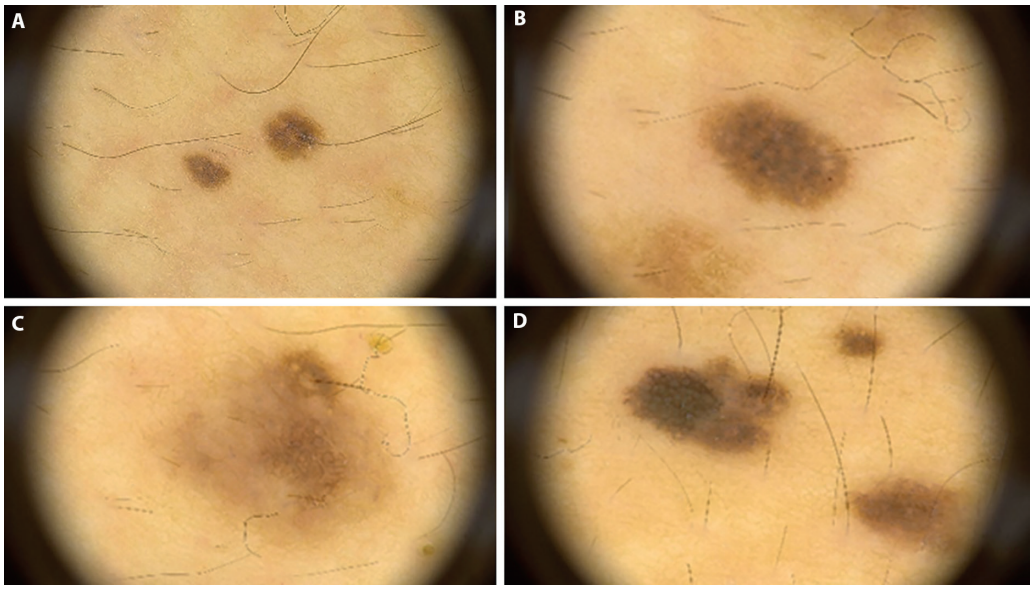


Figure 2. A-C) Dermoscopic magnification of the lesions; D) the excised lesion (Spitz nevus)

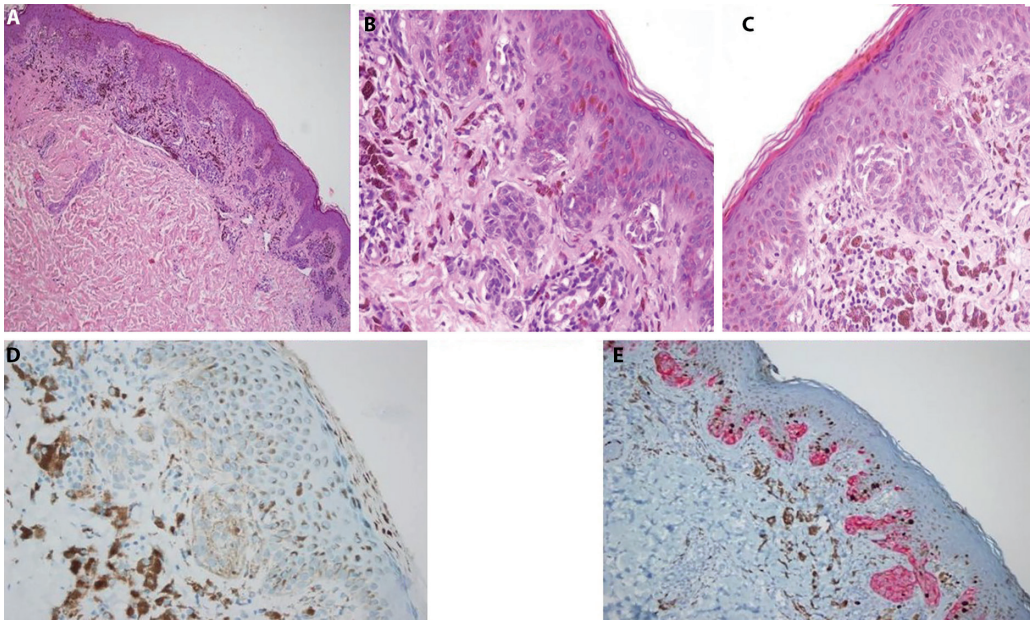


Figure 3. Microscopically, the lesion is a compound melanocytic proliferation composed of large cells with eosinophilic cytoplasm. Nuclei are equal to the size of basal keratinocytes and nucleolus is prominent in some of the cells. Coarse melanin pigment is observed in their cytoplasm. Retraction artifact is seen around some epidermal nests. A) Compound melanocytic lesion with prominent melanophages in the dermis (H&E x100); B-C) Large cells with retraction artifact and prominent nucleoli (H&E x400); D) BRAF (IHC x400); E) Mart1-Ki67 dual staining (IHC x200)..

a prior history of dysplasia. A total of 24 cases of Spitz nevus arising on nevus spilus, both solitary and agminated, have been reported in the literature [3-5]. Management approaches include complete excision for atypical or changing lesions and close monitoring for others.

The presence of a somatic HRAS mutation supports a genetic link reported in prior cases of Spitz nevi on nevus spilus backgrounds [3,5]. Regular follow-up every six months and selective biopsy of morphologically suspicious lesions remain crucial to early detection of malignant change.

In conclusion, Spitz nevus can arise within a giant congenital nevus spilus, complicating clinical management due to overlapping features with melanoma and underlying genetic alterations. Close clinical surveillance and molecular analysis are essential to optimizing outcomes in these complex melanocytic lesions.

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