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Plantar Spitz Nevus Resembling Malignant Melanoma: Description of Immunohistochemical Findings

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Abstract

Spitz nevus (SN) is predominantly distributed throughout the lower extremities, while an acral location is rare. Since SN occasionally resembles the clinicopathological presentation of malignant melanoma (MM), it presents a diagnostic challenge, especially on glabrous skin. Past reports suggest that several genetic aberrations are associated with specific clinicopathological subtypes of melanocytic tumors. Immunohistochemistry can provide a clue to the presence or absence of a molecular aberration typical of Spitz tumors. We describe a case of a plantar SN with genetic analysis, including anaplastic lymphoma kinase (ALK), ROS proto-oncogene 1 (ROS1), BRAF (V600E) protein, and BRCA1-associated protein-1 (BAP1). However, we were not able to detect a characteristic gene aberration. To the best of our knowledge, no genetic aberrations in plantar SN cases have been reported. A comprehensive understanding of tumor genomics is expected to play an essential role in the classification of melanocytic tumors. Further genetic research on plantar SN is required to establish new criteria for distinguishing between SN and MM.

Keywords

Spitz Nevus, Plantar, Malignant Melanoma

1. Introduction

Melanocytic neoplasms include several tumor types that are characterized by distinct clinical features, histopathological appearances, genetic aberrations, and clinical behavior [1]. However, there are diagnostically challenging melanocytic neoplasms with conflicting morphological criteria. Spitz tumors represent a distinct subtype of melanocytic lesions with characteristic histopathologic features, some of which overlap with melanoma [2]. Spitz nevus (SN) is predominantly

distributed throughout the lower extremities (143/333, 42.9%), while an acral location is rare (13/333, 3.9%) [3]. SN, especially on glabrous skin, is notoriously difficult to distinguish from malignant melanoma (MM). Nowadays, a comprehensive understanding of tumor genomics is expected to play an essential role in the classification of melanocytic tumors [4]. Advances in the knowledge of the molecular pathways and genomic aberrations associated with these neoplasms have permitted opportunities for a reduction in the number of uncertain diagnoses and a more objective distinction between Spitz tumors and Spitz-like neoplasms [5]. Further genetic research on plantar SN is required to establish new criteria for distinguishing between SN and MM. Hence, we present a case of plantar SN that was evaluated by genetic analysis.

2. Case Summary

A 39-year-old man was referred to our hospital with a 5-year history of a pigmented macule on the sole of his left foot. The lesion enlarged gradually and comprised a symmetrical 7 × 5 mm-sized dark brownish macule at the center of his left sole, with partially indistinct borders, uniform coloring, and no elevation (**Figure 1(a)**). Dermoscopy demonstrated a hyperpigmented structureless center and radially distributed peripheral streaks on the ridges, a so-called starburst pattern (**Figure 1(b)**).

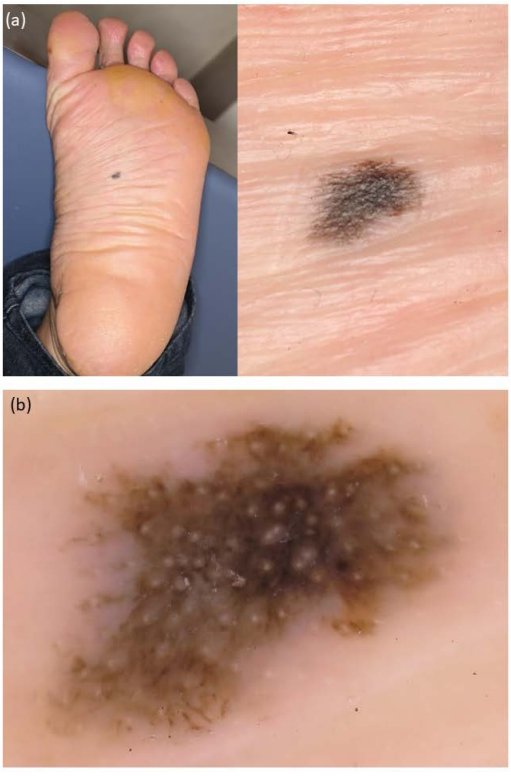

Figure 1. (a) Dark brownish macule on the center of left sole, with partially indistinct borders, uniform coloring, and no elevation. (b) Dermoscopy showed a hyper pigmented structureless center and distributed peripheral streaks on the ridges, so-called starburst pattern.

We performed a complete excision of the lesion. The subsequent histopathological examination revealed that the lesion was symmetrical and well circumscribed at low-power magnification (**Figure 2(a)**). The tumor cells were epithelial or spindle-shaped and hypermelanotic; none exhibited cytological atypia. They were predominantly nested and arranged at the dermal-epidermal interface and papillary dermis. As is characteristic of Spitz nevus (SN), Kamino bodies were present at the epidermal-dermal interface (**Figures 2(b)**, **Figures 2(c)**).

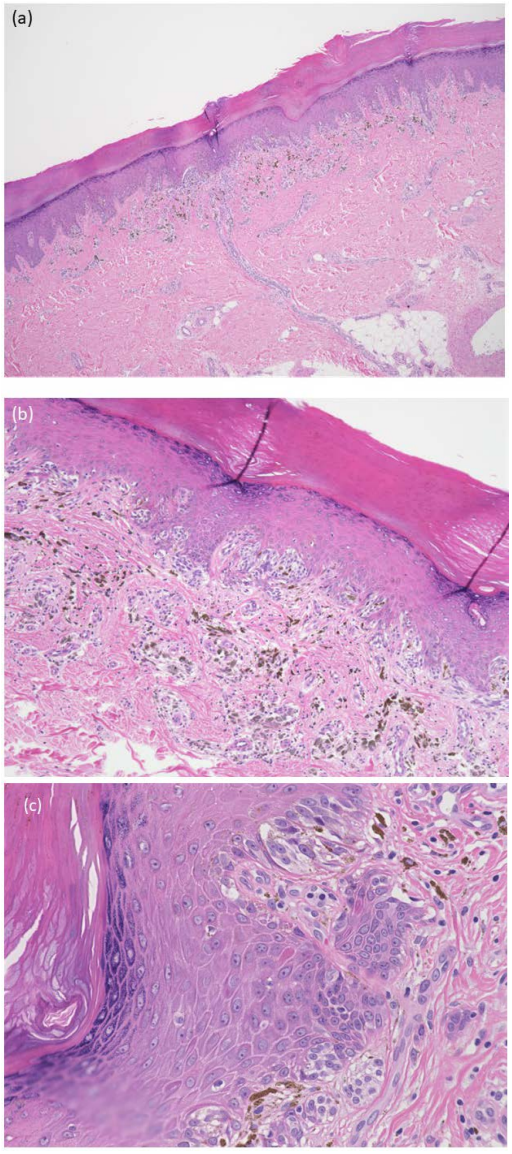

Figure 2. (a) Hematoxylin-eosin (HE) staining showed the lesion was symmetrical and well-circumscribed (original magnification ×40). (b) The tumor cells predominantly nested, arranged at the dermal-epidermal interface and papillary dermis (HE, ×100). (c) The tumor cells were epithelial or spindle-shaped, and hypomelanotic. None of them showed cytologic atypia. Kamino body was presented at the epidermal-dermal interface (HE, ×400).

On immunohistochemical staining using Giemsa staining, tumor cells were negative for anaplastic lymphoma kinase (ALK), ROS proto-oncogene 1 (ROS1), and BRAF (V600E) protein. In addition, the nuclei of the epidermal and tumor cells were negative for BRCA1-associated protein 1 (BAP1). However, since the expected positive controls (epidermal cells) were negative, these results could be due to technical issues. Furthermore, the patient did not undergo genetic testing such as fluorescence in situ hybridization and next-generation sequencing. Based on pathological findings, the patient was diagnosed with SN. Twelve months have passed since excision with no evidence of recurrence. The patient provided informed consent for the publication of this case.

3. Discussion

Dermoscopy is useful for differentiating MM from benign melanocytic nevi. Most acral nevi show pigmentation along the sulci of the skin markings (a "parallel furrow" pattern). Furthermore, nevi located in areas receiving direct pressure from body weight show a "fibrillar" pattern because the cornified layer has a slanting arrangement. However, dermoscopy reveals dominant pigmentation on the ridges of plantar SN [6] [7]. Therefore, plantar SN cannot be distinguished clearly from MM by dermoscopy, making diagnosis difficult. Advances in the knowledge of the molecular pathways and genomic aberrations associated with these neoplasms have permitted opportunities for a reduction in the number of uncertain diagnoses and a more objective distinction between SN and MM. Spitz tumors are biologically distinct from MM, as exemplified by their distinct patterns of genetic aberrations. Up to 50% of SNs show genomic rearrangements involving kinases, such as ALK and ROS1, that are rarely observed in MM [4]. Although rare, sporadic BAP1 inactivation (frequently with activating BRAFV600K mutation) occurs in less than 5% of Spitz tumors [4]. Furthermore, several genetic aberrations are associated with specific clinicopathological subtypes of melanocytic tumors [4]. For example, SN with ALK fusions tend to present as polypoid, amelanotic lesions, forming a plexiform growth of intersecting fascicles of fusiform melanocytes [8]. BAP1-inactivated SN is associated with the epithelioid phenotype, while BRAF-mutated SN is associated with decreased Kamino bodies and hyperpigmented cytoplasm [9]. Although some SN harboring fusion genes, such as ROS1 and neurotrophic tyrosine kinase receptor type 1 (NTRK1), show no specific histological features [4], it is sometimes difficult to identify which gene alterations are associated with SN. Genetic analysis can provide useful information in the differential diagnosis between SN and MM, when certain genetic aberrations are suspected based on clinical findings. The immunostaining for ALK, ROS1, and BAP1 performed in our study revealed no significant findings. Since these genetic aberrations are not typically detected in SN, they may yet harbor undiscovered mutations. Another possible reason for the absence of genetic mutations in our case was the long delay in immunostaining after resection. To the best of our knowledge, there have been no reports of genetic aberrations in plantar SN cases. Further genetic research on plantar SN is required to

establish new criteria for distinguishing between SN and MM.

4. Conclusion

In conclusion, SN occasionally resembles the clinicopathological presentation of MM. A comprehensive understanding of tumor genomics is expected to play an essential role in the classification of melanocytic tumors. Further genetic research on plantar SN is required to establish new criteria for distinguishing between SN and MM. Our case emphasizes the role of genetic research, especially for glabrous SN.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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