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Letter to Editor

Subungual pigmented squamous cell carcinoma presenting as longitudinal melanonychia: a case report with review of the literature

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Occurrence of squamous cell carcinoma (SCC) in the nail is rare [1], although it is the most common epithelial malignancy of the nail apparatus [1, 2]. Less than 300 cases of subungual SCC (invasive or *in situ*) have been reported in the English-language literature [2]. The clinical diagnosis of this type of tumor may be difficult and is often missed and/or delayed because of the heterogeneity of the clinical signs [1, 2]. Retrospective analyses of subungual SCC revealed that the clinical signs included subungual hyperkeratosis, leukonychia, erythronychia, and onycholysis, and it is often clinically diagnosed as verruca or onychomycosis [1, 2]. Approximately 10% of subungual SCC cases showed longitudinal melanonychia [1, 2], and a few cases of pigmented SCC *in situ* (Bowen's disease) of the nail have been reported, among which some of them resembled malignant melanoma clinically [3-6]. However, the histopathological mechanism by which subungual SCC presents as melanonychia, such as the presence of melanocytes within the lesion, have not been evaluated yet. Herein, we report a case of subungual pigmented SCC presenting as longitudinal melanonychia with concise histopathological analysis and review of the literature.

A 59-year-old Japanese female presented with a brownish streak on her right thumbnail. She had a past history of breast cancer 12 years before, and lung metastasis had been detected 5 years after the breast surgery. Physical examination revealed a relatively well-circumscribed evenly colored longitudinal melanonychia, measuring 2 mm in width, in her right thumbnail. Neither color heterogeneity nor Hutchinson's sign was detected. Biopsy was performed under a clinical diagnosis of melanocytic nevus of the nail, and subsequently, she underwent a longitudinal excision.

Histopathological study of the biopsy specimen revealed proliferation of atypical squamous cells invading into the superficial dermis (**Figure 1A**). Atypical squamous cells had enlarged round to oval nuclei showing disorganization of the nuclear alignment at the periphery of the squamous cell nests (**Figure 1B**, **1C**). Hypergranulosis and hyperkeratosis were also noted (**Figure 1B**, **1C**). The peculiar finding of the present case was the presence of melanin pigment within the cytoplasm of the neoplastic squamous cells and a few dendritic melanocytes without nuclear atypia within the tumor nests (**Figure 1B**, **1C**).

Immunohistochemical studies were performed using an autostainer (Ventana) by the same method as previously reported [7-10]. The dendritic melanocytes were positive for S-100 protein and Melan-A (**Figure 2**), but negative for HMB-45. Human papilloma virus (HPV) was not detected in the neoplastic squamous cells.

Accordingly, an ultimate diagnosis of subungual pigmented SCC was made.

The histopathological and immunohistochemical features of the operative specimen were fundamentally the same as those of the biopsy

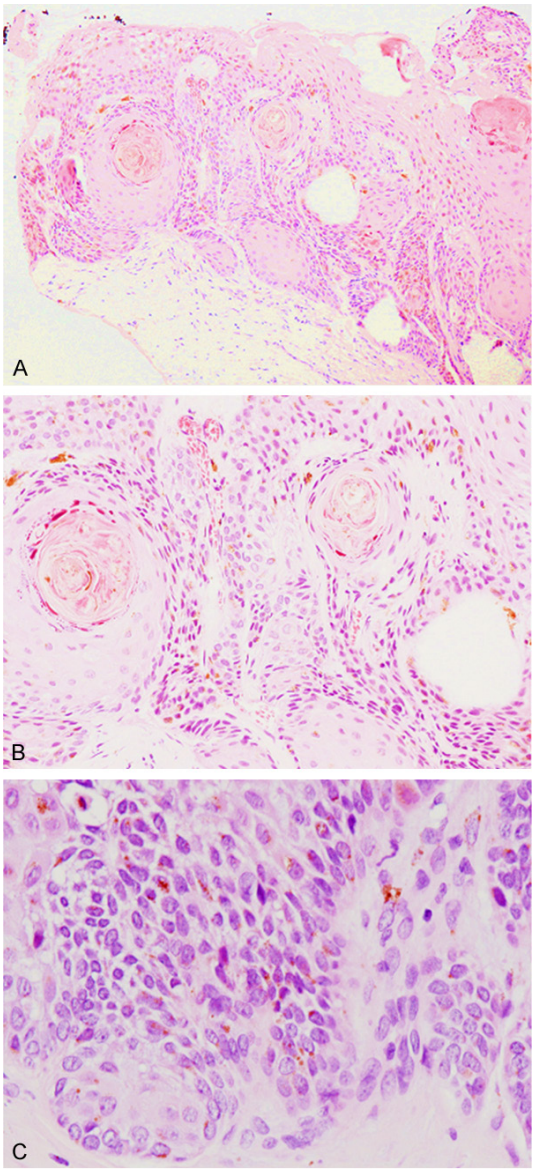

Figure 1. Histopathological features of the biopsy specimen of the thumbnail showing longitudinal melanonychia clinically. A: Proliferation of atypical squamous cells invading into the superficial dermis. HE, x 40. B: Atypical squamous cell proliferation accompanying hypergranulosis and hyperkeratosis. HE, x 200. C: Neoplastic squamous cells have large round to oval nuclei and melanin pigment within the cytoplasm of the tumor cells. A few dendritic melanocytes are also present. HE, x 400.

specimen. The tumor was located in the nail bed and had invaded into the superficial dermis. The tumor was completely resected.

In this report, we describe a case of subungual pigmented SCC presenting clinically as longitudinal melanonychia. Baran and Simon first

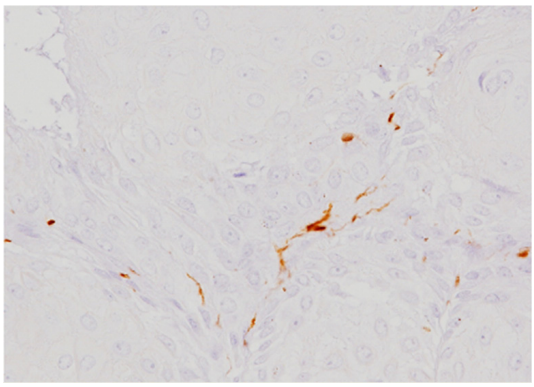

Figure 2. Immunohistochemical finding of the biopsy specimen of the thumbnail. S-100 protein is expressed in the dendritic melanocytes, x 400.

described that longitudinal melanonychia is one of the clinical features of Bowen's disease of the nail [11]. Since then, it has been recognized that approximately 10% of subungual SCC cases clinically presented as longitudinal melanonychia, and some of these cases may have been misdiagnosed as malignant melanoma [1-6]. However, elucidation of the histopathological mechanism of subungual SCC cases exhibiting longitudinal melanonychia has not been performed. In the present case, the tumor showed longitudinal melanonychia and was clinically diagnosed as melanocytic nevus. Histopathological and immunohistochemical analyses of the present tumor clearly demonstrated the presence of melanocytes and melanin pigment within the cytoplasm of the neoplastic squamous cells, which resulted in the clinical appearance of melanonychia.

Only a few reports of subungual pigmented Bowen's disease have been reported [3-6]. Data on the presence of melanocytes or melanin pigment within the cytoplasm of the tumor cells is not available in these cases [3-6]. However, this report is the first to demonstrate the presence of melanocytes and melanin pigment within the tumor cells of the neoplastic squamous cells, which resulted in the clinical manifestation of melanonychia.

It has been well recognized that various non-melanocytic neoplasms sometimes accompany non-neoplastic melanocytes within the tumor, and this phenomenon has been described as "melanocytic colonization" [12-19]. These pigmented lesions, especially pigmented skin appendage tumors, may be misdiagnosed clini-

cally as malignant melanoma, as well as subungual pigmented SCC [19]. The concise mechanism by which melanocytes and/or melanin pigment appear remains unclear. However, a few hypotheses regarding melanocytic colonization in non-melanocytic lesions have been proposed. For example, it has been hypothesized that the epithelial cells may produce factors which simulate the proliferation and differentiation of melanocytes, such as stem cell factor and endothelin-1 [20]. However, pigmented non-melanocytic lesion not associated with production of these factors has been reported [15]. Therefore, additional studies are needed to clarify the mechanism of melanocytic colonization in non-melanocytic lesions.

HPV infection has been clearly associated with pathogenesis of SCC of the nail [6, 21, 22]. In the present case, HPV was not detected in the lesion by immunohistochemical analysis, and in some of the previous reports of this type of tumor, HPV was not observed either [4].

In conclusion, we describe an additional case of subungual pigmented SCC presenting clinically as longitudinal melanonychia. This is the first report to demonstrate presence of melanin pigment within the cytoplasm of the tumor cells and melanocytes within the SCC which resulted in melanonychia. Approximately 10% of subungual SCC cases present clinically as longitudinal melanonychia, therefore, additional clinicopathological studies are needed to clarify the cause and mechanism of melanonychia in subungual SCC.

Disclosure of conflict of interest

None.

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