Methods

Patients

After obtaining approval from the Ethics Research Committee of the National Taiwan University Hospital, we retrospectively searched the pathological database of the National Taiwan University Hospital between January 1, 1996, and February 28, 2017, using keywords including nail, basal hyperpigmentation, pigment incontinence, lentigo, lentigines, melanotic macule, nevus, atypical melanocytic hyperplasia, and melanoma. As the diagnosis was based on pathological examination of a representative nail matrix specimen, only cases undergoing biopsy or excision of nail tissues encompassing the nail matrix were included. The cases enrolled were categorized into adult (18 years of age or older) and pediatric (younger than 18 years) groups.

Data Collection and Classification

We examined the medical records and photographic documentation to obtain demographic data and clinical presentations. Clinical features evaluated included age, sex, the involved digit, color, duration of the lesion, percentage of the nail involved, width of the pigmented band, Hutchinson sign (pigmentation of the proximal, distal, or lateral nail fold), pseudo-Hutchinson sign (pigmentation of the nail bed and matrix

seen in the proximal nail fold due to cuticle transparency), nail dystrophy and history of evolution.

We assessed the histopathological features, using hematoxylin and eosin-stained sections in conjunction with Fontana-Masson stain and additional immunohistochemical stains, including melan-A (MART-1), HMB-45, S100, and Ki-67. Pathological features in cases of melanoma specifically assessed included Breslow thickness, mitosis more than 5 every 1 mm^2, and ulceration. In the pediatric cases, we assessed the presence of nuclear atypia, suprabasal melanocytic spread and mean melanocytic counts per stretch of 1 mm. The histopathological features of all cases were independently examined by 2 pathologists and 1 dermatologist.

The causes of LM were categorized into: (1) melanocytic activation, including basal hyperpigmentation, pigment incontinence, and melanotic macule; (2) melanocytic proliferation, including nevocellular nevus, lentigo, atypical melanocytic hyperplasia, and in situ or invasive melanoma.

Statistical Analysis

Statistical differences in the causes of LM between adults and children were analyzed by the χ^2 or Fisher exact test (while $n \leq 5$). The comparison of age between nevus and other disease categories of LM was assessed by the Wilcoxon rank sum test.

Multivariate logistic regression was used to analyze the relative risk of age to diagnoses. Statistics were performed with the SPSS 9.4 software (SPSS Inc., Chicago, IL, USA), and $p < 0.05$ was considered statistically significant.