of controversy, and multicenter controlled trials may be needed to further investigate and validate the use of sentinel lymph node and the prognostic importance of regional lymph node status in invasive EM.[5]

EM affects men and women almost equally and has a better prognosis than OIHN melanoma. Our study shows that the single most important prognostic factor is regional lymph node metastases, followed by distant metastases (stage IV disease), and Breslow thickness greater than 2 mm.

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Longitudinal brush pigmentation on the hyponychium, a dermoscopic feature observed in pediatric nail matrix nevi

To the Editor: Differentiating nail matrix nevus (NMN) from subungual melanoma on clinical grounds is challenging, especially in children, because their NMNs may mimic clinical features of subungual melanoma.[1-3] We reported a dermoscopically linear and parallel pigmentation in a longitudinal direction on Hutchinson sign of the hyponychium in children with NMN.[3] We named this pattern longitudinal brush pigmentation (LBP) and consider it a distinctive dermoscopic feature observed in pediatric NMN.

To further support this, we present the clinical, dermoscopic, and histologic features of hyponychial LBP associated with longitudinal melanonychia in additional 15 children observed between 2014 and 2019. Biopsy specimens of the hyponychial LBP were performed in 14 patients and nail matrix biopsy specimen in 1 patient.

All patients showed LBP at the hyponychium, brown lines that are perpendicular to the skin groove, like a brush (Fig 1; dermoscopic images of all 15 cases can be seen in Supplemental Fig 1 available via Mendeley at https://data.mendeley.com/datasets/smj68n5xrt/1). Demographic and clinical data are shown in Table I. The mean age of onset was 25 months and mean width of melanonychia was 54.3% of the total nail width. Five of 15 patients had nail dystrophy (33.3%). Six cases developed LBP on hyponychium during follow-up and the remaining 9 cases already presented with hyponychial LBP at the initial visit to our clinic. The average time from onset of melanonychia to development of hyponychial LBP was 27.5 months. Irregular pattern including color variegation and inconsistency in longitudinal melanonychia was observed in all cases and globular pigmentation was observed in 6 children.

Eleven of 14 punch biopsy specimens from hyponychium with LBP showed a nested proliferation of banal melanocytes (Supplemental Fig 2). The remaining 3 biopsy specimens revealed the proliferation of solitary melanocytes predominantly along the dermoepidermal junction without atypia. One case showed some atypical cells but revealed a nested growth pattern of banal melanocytes in subsequent serial sections (Supplemental Fig 2).

Although larger studies correlating histologic findings of hyponychial LBP with those of the nail matrix in pediatric melanonychia cases are needed, the observation of benign histologic growth pattern at the hyponychial LBP supported the clinical impression of NMN in our cases. We suggest that

Fig 1. Dermoscopic images of patient 1. Dermoscopy shows the Hutchinson sign at the hyponychium with longitudinal brush pigmentation aligned parallel to the longitudinal direction.

Table I. Demographic and clinical data of 15 melanonychia cases

Patient no.	Age of onset, mo	Sex	Affected nail*	Width of melanonychia (% of nail width)	Nail dystrophy	Time from onset of melanonychia to development of hyponychial LBP, mo	Length of follow-up, mo
1	4	M	R5F	100	−	14	41
2	<1	M	L1F	33.3	−	LBP present at initial visit	33
3	8	M	L4F	66.7	+	56	30
4	2	M	L1F	39.5	+	LBP present at initial visit	13
5	36	F	L1F	72.7	+	LBP present at initial visit	14
6	<1	F	L3T	52.4	−	LBP present at initial visit	42
7	71	F	R4F	25	−	LBP present at initial visit	24
8	24	M	R1T	100	−	29	24
9	36	M	R2T	48	−	LBP present at initial visit	8
10	60	F	R3F	100	−	LBP present at initial visit	9
11	5	F	L1F	71.2	+	31	27
12	40	M	R2F	29.6	+	LBP present at initial visit	6
13	80	M	L1T	40.3	−	LBP present at initial visit	17
14	11	F	L1F	13.1	−	18	28
15	3	F	L3F	22.8	−	17	30

F, Female; *LBP*, longitudinal brush pigmentation; *M*, male.
*The first letter specifies right (R) or left (L), and the last specifies finger (F) or toe (T). A number between them indicates which finger or toe is affected.

the presence of LBP on the hyponychium may be a feature consistent with a benign process in pediatric patients with melanonychia who otherwise present with clinical findings consistent with NMN and who lack more concerning clinicodermoscopic findings or worrisome history. Conservative management through long-term clinical follow-up may still be an option for such patients, and all patients presented in this study are being closely followed over the long term. However, obtaining nail matrix biopsy specimens may be warranted in clinically worrisome pediatric melanonychia cases despite the observation of hyponychial LBP. Any Hutchinson sign (including hyponychial LBP) in adult melanonychia patients should prompt consideration for obtaining a biopsy specimen of the nail matrix.

In conclusion, we underscore the importance of clinical and dermoscopic examination of the entire

nail unit, including the hyponychium, in pediatric patients with longitudinal melanonychia. We propose that hyponychial LBP is a distinctive dermoscopic feature observed in pediatric longitudinal melanonychia and that its presence supports the clinical impression of NMN in pediatric patients.

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Anti–tumor necrosis factor therapy is associated with increased in situ squamous cell carcinoma of the skin: A population-based case-control study

To the Editor: Tumor necrosis factor inhibitors (TNFis) have been associated with an increased risk of keratinocyte carcinoma in patients with rheumatoid arthritis and psoriasis, but population-wide data are lacking.[1-3] A population-based case-control study was performed to analyze the association between TNFis and keratinocyte carcinoma using the Icelandic Cancer Registry and the Icelandic Prescription Medicine Register.[4,5] All patients with an initial, histologically confirmed diagnosis of invasive squamous cell carcinoma (SCC), SCC in situ (SCCis), or basal cell carcinoma (BCC) were included as cases and were identified using an *International Classification of Diseases, 10th revision* code between 2003 and 2017. Patients taking cyclosporine, azathioprine, or mycophenolate mofetil were excluded. Risk-set sampling was used to pair each case with 10 age- and sex-matched control subjects. Patients were considered exposed to TNFi if they filled ≥1 prescription for adalimumab, etanercept, infliximab, or golimumab before their first diagnosis of keratinocyte carcinoma. Multivariable conditional logistic regression was performed and adjusted for age, sex, and the use of photosensitizing medications (tetracyclines or oral and topical retinoids) and hydrochlorothiazide. Adjusted odds ratio (aORs) and 95% confidence intervals (CIs) were estimated.

Four thousand seven hundred patients with BCC, 1013 with invasive SCC, and 1167 with SCCis and 47,293, 10,367, and 11,961 control subjects, respectively, were identified (Table I). TNFi exposure was associated with an increased risk of SCCis (aOR 3.13 [95% CI 1.15-8.55]; Table II) but not invasive SCC. Overall TNFi exposure was not associated with risk of BCC (aOR 1.68 [95% CI 0.91-3.11]).

This population-based study shows a significantly increased risk of SCCis, but not invasive SCC, among TNFi users compared with the general Icelandic population. While other studies found an association between TNFi and SCC,[2,3] they did not separate invasive SCC and SCCis in their analyses. It is possible that our study was not powered to detect differences in invasive SCC and BCC risk. Iceland has a low level of background ultraviolet light exposure in a population that is almost exclusively white. The SCCis risk increase with TNFi exposure could be even greater in regions with higher exposure to ultraviolet light. This study differs from the Swedish population-based study of TNFi and keratinocyte carcinoma in that it includes all patients taking TNFis, whereas the Swedish study only studied patients with rheumatoid arthritis.[2] Previous studies have not shown an increased risk of BCC with TNFi use.[2,3]

Study limitations include the inability to adjust for sun exposure, patient comorbidities, and indication for TNFi use. Similarly, we were unable to adjust for exposure to phototherapy, which may have been