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Dermoscopy of nodular/plaque-type primary cutaneous T- and B-cell lymphomas: a retrospective comparative study with pseudolymphomas and tumoral/inflammatory mimickers by the International Dermoscopy Society

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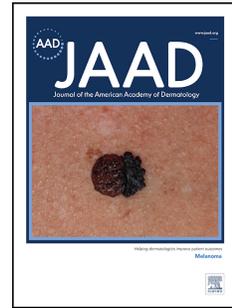
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3 Title: **Dermoscopy of nodular/plaque-type primary cutaneous T- and B-cell lymphomas:**
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6 Short title: **Dermoscopy of nodular/plaque-type PCLs and their mimickers**

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74 **ABSTRACT:**

75 **Background:** Limited data on dermoscopy of nodular/plaque-type T/B-cell primary cutaneous
76 lymphomas (PCLs) is available.

77 **Objective:** To describe dermoscopic features of nodular/plaque-type PCLs, comparing them
78 with those of clinical mimickers (pseudolymphomas, tumors, and inflammatory lesions) and
79 investigating possible differences according to histological subtypes.

80 **Methods:** Participants were invited to join this retrospective multicenter case-control study by
81 submitting histologically/immunohistochemically confirmed instances of nodular/plaque-type
82 PCLs and controls. A standardized assessment of the dermoscopic images and comparative
83 analyses were performed.

84 **Results:** A total of 261 lesions were finally included (121 PCLs/140 controls). Orange
85 structureless areas was the strongest PCLs dermoscopic predictor on multivariate analysis
86 when compared to tumors and non-infiltrative inflammatory dermatoses. On the other hand, a
87 positive association was found between PCLs and either unfocused linear vessels with branches
88 or focal white structureless areas when compared to infiltrative inflammatory dermatoses,
89 whereas white lines were predictive of PCLs over pseudolymphomas. Differences in the
90 vascular pattern were also seen between B- and T-cell PCLs and among B-cell PCLs subtypes.

91 **Limitations:** Retrospective design and the lack of a dermoscopic-pathological correlation
92 analysis.

93 **Conclusion:** Nodular/plaque-type PCLs display dermoscopic clues which may partially vary
94 according to histological subtype and whose diagnostic relevance depends on the considered
95 clinical differential diagnoses.

96

97 **Capsule summary:**

- 98 • Our study increases the knowledge on dermoscopy of nodular/plaque-type cutaneous
99 lymphomas by comparing their dermoscopic features with those of clinical mimickers
100 and investigating possible differences according to histologic background.
- 101 • Significance of dermoscopic findings in nodular/plaque-type cutaneous lymphomas
102 should be interpreted based on the considered differential diagnosis and histologic
103 subtype.

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121 INTRODUCTION

122 Primary cutaneous lymphomas (PCLs) are a heterogeneous group of T- and B-cell lymphomas
123 localized on the skin with no evidence of extracutaneous involvement at the time of
124 diagnosis.^{1,2} Except for mycosis fungoides and lymphomatoid papulosis that display peculiar
125 morphologic patterns, most types of PCLs manifest as nonspecific reddish-purple nodules or
126 plaques, with a consequent wide list of possible differential diagnoses that includes tumoral
127 and inflammatory conditions.¹⁻³ The most common forms of nodular/plaque-type T-cell PCLs
128 are CD30+ anaplastic large cell lymphoma (CD30+ ALCL) and CD4+ small/medium
129 lymphoproliferative disorder (CD4+ SMLD), while marginal zone lymphoma (MZL) and
130 follicle-center cell lymphoma (FCL) represent the most frequent variants of nodular/plaque-
131 type B-cell PCLs.^{1,2}

132 Although the definitive diagnosis relies on histological and immunohistochemical
133 analyses, growing evidence supports a possible role of dermoscopy in increasing the index of
134 suspicion for PCLs besides clinical/anamnestic data.⁴⁻¹² However, while dermoscopic features
135 of mycosis fungoides have been investigated by several case-control studies, data on cutaneous
136 lymphomas manifesting as nodules and/or plaques are scarce, with few case reports/series and
137 only one small case-control study published in the literature.¹² Additionally, little information
138 is available on possible dermoscopic differences among PCLs and on the usefulness of
139 dermoscopy for the differential diagnosis between nodular/plaque-type PCLs and either
140 pseudolymphomas or clinically similar inflammatory lesions.¹²

141 The aim of this study was to investigate the dermoscopic morphology of different PCL
142 subtypes manifesting as nodules or plaques and to assess the value of dermoscopic criteria for
143 the discrimination of PCLs from clinical mimickers (including pseudolymphomas, tumors, and
144 inflammatory lesions). The study was conducted in accordance with ethical guidelines and IRB

145 approval was obtained.

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147 **MATERIALS AND METHODS**

148 This was a retrospective case-control study which was part of a larger project on PCLs launched
149 by the *International Dermoscopy Society* (IDS) via an online call published on the IDS website
150 (www.dermoscopy-ids.org).

151 **PCLs diagnosed by histological and immunohistochemical analyses, clinically**
152 **manifesting as single/multiple nodules or plaques were eligible for the current analysis**
153 **(in case of multiple lesions in a single patient, we considered only the target lesion that**
154 **was biopsied). Lymphomatous conditions presenting with either different clinical**
155 **morphologies (i.e., lymphomatoid papulosis and mycosis fungoides, typically**
156 **characterized by papules and scaly patches/plaques, respectively) or extra-cutaneous**
157 **manifestations (i.e., leukemia cutis and systemic lymphomas with secondary cutaneous**
158 **involvement) were therefore excluded from the study.** Additionally, patients currently or
159 previously treated were also not included to avoid biases resulting from possible modifications
160 of dermoscopic patterns by therapies.

161 The control group consisted of nodular/plaque-type skin lesions for which PCL was
162 included into the clinical differential diagnosis at the time of initial presentation; only untreated
163 and histologically confirmed lesions were considered eligible (immunohistochemistry and
164 molecular analyses were also required for pseudolymphomas diagnosis).

165 High quality clinical and dermoscopic pictures (captured at x10 magnification) as well
166 as information on patients' age and gender, target lesion localization, and histological subtype
167 (for PCLs group) were mandatory.

168 Two independent investigators (EE, AL), blinded to clinical presentation and final
169 diagnosis, evaluated the images for the presence of predefined dermoscopic criteria.
170 Interobserver agreement was evaluated through Cohen's kappa coefficient. Dermoscopic
171 variables were selected according to the recent consensus document by the IDS on dermoscopy
172 of infiltrative, infectious and inflammatory dermatoses, which includes five standardized basic
173 parameters with several possible sub-items for each of them:¹³ (I) vessels (morphology and
174 distribution); (II) scales (color and distribution); (III) appendages findings; (IV) “other
175 structures” (features other than vessels, scales and follicular findings) (including color and
176 morphology); and (V) “specific clues” (features strongly suggestive of a dermatosis due to a
177 strict correlation with highly specific/sensitive histological findings).

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179 **Statistical analysis:**

180 All separate clinical and dermoscopic variables were included in the analysis. Categorical data
181 are presented as numbers and frequencies and were compared using Pearson's chi-square test.
182 Relative risks were calculated for all dichotomous variables. Crude and adjusted odds ratios
183 and corresponding 95% confidence intervals (95% CI) were calculated by univariate and
184 conditional multivariate logistic regression, respectively. Forward inclusion and backward
185 elimination were used. Alpha level was set at 0.05 and an alpha level of 0.20 was used as cut-
186 off for variable removal in the automated model selection for multivariate logistic regression.

187 **Variables that were statistical significantly associated with diagnoses, were also**
188 **controlled via multivariate logistic regression. Because a large number of predictors were**
189 **to be included in the univariate analyses we employed the Bonferonni correction for**
190 **multiple hypothesis testing (setting $P < 0.001$ for 10-30 variables). The Type I error**
191 **probability associated with all tests in this study was set to 0.05. Statistical analyses were**

192 performed using the statistical package for social sciences statistical software (version 24.0,
193 IBM SPSS Statistics for Windows, Armonk, NY, USA: IBM Corp).

194

195 **RESULTS**

196 A total of 261 lesions provided by 16 different centers were finally recruited for the analysis,
197 including 95 B-cell PCLs (44 MZL, 37 FCL, and 14 diffuse large cell B-lymphomas) and 26
198 T-cell PCLs (17 CD30+ ALCL and 9 CD4+ SMLD) in the lymphomas group (total cases: 121)
199 and 33 pseudolymphomas, 56 tumors (17 basal cell carcinomas, 9 squamous cell carcinomas,
200 8 adnexal tumors, 4 Merkel cell carcinomas, 3 dermatofibrosarcoma protuberans, 3 seborrheic
201 keratoses, 3 metastases, 2 amelanotic melanomas, 2 cellular dermatofibromas, 2 leiomyomas,
202 1 dermal nevus, 1 atypical Spitz tumor, and 1 Kaposi sarcoma), 29 infiltrative inflammatory
203 dermatoses (21 granulomatous dermatoses and 8 histiocytoses), and 22 non-infiltrative
204 inflammatory dermatoses (8 discoid lupus erythematosus, 6 granuloma faciale, 2 lupus
205 tumidus, 2 persistent insect bites, 2 epidermoid cysts, 1 molluscum contagiosum, and 1
206 hypertrophic lichen planus) in the control group (total cases: 140).

207 Details on analytic results and comparative analysis of dermoscopic findings for cases
208 and controls (as a whole and divided into clinical subtypes) are shown in Tables S1 and 1. The
209 interobserver agreement for dermoscopic variables was high with Cohen's kappa ranging from
210 0.67 to 0.91.

211 The main vascular findings of nodular/plaque-type PCLs turned out to be unfocused
212 linear vessels with branches (39.7%) followed by unfocused dotted (28.9%) and linear-curved
213 (28.1%) vessels, while focal white and orange structureless areas (54.5% for both of them)
214 along with white lines (total: 42.1%; unspecifically arranged: 25.6%) were the most common
215 non-vascular features. Of note, all the aforementioned dermoscopic findings, along with orange

216 globules, resulted to be significantly more common in PCLs group compared to the control
217 group. On the other hand, well-focused vessels (linear, linear with branches, and linear-curved),
218 dotted vessels with white halos, diffuse white structureless areas, brown and blue globules, and
219 brown, purple and yellow structureless areas were significantly more common in the controls.
220 Nevertheless, only a few of the aforementioned criteria were found to represent robust
221 diagnostic predictors in the univariate (Table S2) and multivariate analysis (Table 2). In detail,
222 the latter revealed a positive association between nodular/plaque-type PCLs and the following
223 findings: focal white (OR 2.35; 95%CI 1.29-4.28) and orange (OR: 3.96; 95%CI 2.13-7.34)
224 structureless areas, orange globules (OR: 6.62; 95%CI 1.17-37.44), and white lines (total) (OR:
225 1.94; 95%CI 1.02-3.69) (Figure 1). Conversely, linear vessels with branches (well-focused)
226 and purple structureless areas showed an inverse correlation (OR: 0.30; 95%CI 0.12-0.74 and
227 OR: 0.18; 95%CI 0.04-0.85, respectively).

228 When it comes to the comparative sub-analysis between PCLs and each subtype of
229 controls, several significant differences were observed (Table 1), with a variable correlation on
230 univariate (Table S3) and multivariate (Table 2) analyses. In particular, multivariate positive
231 predictors for nodular/plaque-type PCLs included orange structureless areas (when compared
232 to tumors [OR: 65.01; 95%CI 6.86-616.10] and non-infiltrative inflammatory dermatoses [OR:
233 10.46; 95%CI 2.23-49.01]), focal white structureless areas (when compared to infiltrative [OR
234 9.47; 95%CI 2.03-44.12] and non-infiltrative inflammatory dermatoses [OR: 10.10; 95%CI
235 2.16-47.34]), unfocused linear vessels with branches (when compared to infiltrative
236 inflammatory dermatoses [OR: 4.25; 95%CI 1.09-16.59]), and white lines (when compared to
237 pseudolymphomas [OR: 2.50; 95%CI 0.99-6.24]) (Table 2; Figures S1-S2). On the other hand,
238 diffuse white structureless areas, brown structureless areas, and purple structureless areas
239 turned out to be negatively associated with PCLs (all of them when compared to tumors [OR:

240 0.05, 0.08, and 0.12, respectively] and only the last one when compared to infiltrative
241 inflammatory dermatoses [OR: 0.02]) (Table 2; Figure S1).

242 The dermoscopic analysis according to histological PCLs subtypes revealed only one
243 potent predictor for the differential diagnosis between B-cell and T-cell PCLs: the presence of
244 unfocused dotted vessels (Table S4), which were significantly more common in T-cell PCLs
245 (OR for B-cell PCLs: 0.31 (95%CI 0.12-0.79) in the multivariate analysis (Figure S2). Several
246 differences were observed among the B-cell PCLs subtypes (Table S5), yet only the presence
247 of unfocused linear vessels with branches resulted to be relevant on multivariate analysis, with
248 an OR of 2.79 (95%CI 1.07-7.28) for MZL (Figure S2). Finally, no significant dermoscopic
249 difference was found among T-cell histological subtypes (Table S6).

250

251 **DISCUSSION**

252 In line with available literature data, the present analysis confirms that orange and white focal
253 structureless areas are the most common non-vascular dermoscopic findings of nodular/plaque-
254 type PCLs (either B-cell or T-cell).⁴⁻¹² These features are supposed to correlate to the dense
255 dermal cellular infiltrate (“mass effect”) and either dermal reactive fibrosis or focally reduced
256 “grenz zone” due to patchy, nodular, more superficial infiltrate in the papillary dermis,
257 respectively.^{8,11} Of note, the presence of orange color (either as globules or focal structureless
258 areas) displayed the strongest positive association with nodular/plaque-type PCLs when
259 compared to the entire control group, consistently with previous data.⁴⁻¹² Additionally, white
260 lines and focal white structureless areas were also positively linked to nodular/plaque-type
261 PCLs, whereas purple structureless areas and well-focused linear vessels with branches showed
262 a negative association. Indeed, vascular structures in nodular/plaque-type PCLs were mainly
263 blurred likely due to their location in deeper dermis with consequent scattering of light by

264 dermal collagen fibers,¹⁴ which may be increased in such lesions.^{8,11} Interestingly, dermal
265 fibrosis might also be responsible for the presence of white lines, that turned out to be a relevant
266 finding in our study.

267 **Notably, compared to previous analyses,^{4,5,8} we observed a lower prevalence of**
268 **follicular plugs and a different predominant vascular pattern, with linear vessels with**
269 **branches being the most frequent.** It is possible that such differences are due to different
270 sample size, different types of included lymphomas and variability of the lesions' duration,
271 since the histological background may vary according to the lesion's evolution stage.¹¹
272 However, the latter hypothesis has never been investigated so far due to the difficulty to assess
273 the precise onset of each nodule/plaque in multilesional instances.

274 We also compared dermoscopic features of nodular/plaque-type PCLs to those of each
275 clinical category of mimickers, highlighting several relevant differences. Indeed, whereas
276 orange structureless areas turned out to be strongly associated with PCLs when compared to
277 tumors and non-infiltrative dermatoses, they were of no aid in distinguishing PCLs from
278 infiltrative dermatoses and pseudolymphomas. This is because the latter entities are also
279 histologically characterized by a dense cellular infiltrate giving rise to orange color on
280 dermoscopy.^{15,16} However, according to our findings, unfocused linear vessels with branches
281 and focal white structureless areas predicted the diagnosis of nodular/plaque-type PCLs when
282 compared to infiltrative dermatoses, whereas the presence of white lines is predictive of
283 nodular/plaque-type PCLs over pseudolymphomas. These differences are related to the
284 histological background, since infiltrative dermatoses, especially granulomatous dermatoses,
285 are often typified by a dense cellular infiltrate that displaces the dermal vessels upwards, so
286 that they appear sharper on dermoscopy (as they are closer to the skin surface).¹⁵ On the other
287 hand, the association between nodular/plaque type PCLs and both focal white areas and white

288 lines might be due to the higher prevalence of reactive fibrosis compared to infiltrative
289 dermatoses and pseudolymphomas.^{11,13,17} Of note, this is the first study highlighting a possible
290 dermoscopic variability between PCLs and pseudolymphomas as previous analyses assessed
291 such conditions together, without comparing their dermoscopic features.^{8,12} The subgroup
292 analysis between PCLs and other tumors also revealed three negative PCL predictors: white
293 structureless areas (diffuse), purple structureless areas and brown structureless areas, with the
294 first two usually encountered in keratinizing tumors and the last one typical of pigment-
295 producing lesions (of either melanocytic or non-melanocytic derivation).

296 Finally, our analysis revealed a variability in the dermoscopic vascular pattern of PCLs
297 according to their histological subtype. Specifically, unfocused dotted vessels predicted T-cell
298 over B-cell PCLs, while unfocused linear vessels with branches predicted marginal zone
299 lymphoma over other B-cell PCLs variants. No significant difference was found among T-cell
300 PCLs subtypes. It is possible that the observed variability in vascular morphology might be due
301 to different patterns of angiogenesis as it has been demonstrated that vessels growth in PCLs
302 is influenced by tumor cell type, as well as different microenvironments.^{18,19}

303 The main limitation of the present study is the retrospective design, which is prone to
304 recall and observation biases, that were addressed by involving evaluators who did not
305 contribute to sample collection. A large number of predictors have been included in the
306 univariate analyses without correction for multiple hypothesis testing. In fact, we chose to
307 analyze each predictor separately as several features are very likely to be statistically significant
308 just by spurious association or chance given the amount of independent tests that were
309 performed. Additionally, the p-value of each significantly flagged predictor is indicative of its
310 value (with values $P < 0.001$ demonstrating those of importance) and those predictors that
311 remain statistically significant in the multivariate analyses are already adjusted for the effect

312 of other predictors and therefore **can be deemed statistically significant**. Finally, all
313 mentioned dermoscopic-pathological correlations were based on previous studies or common
314 reasoning and the possible influence of lesion duration on dermoscopic appearance was not
315 considered. Consequently, our results should be interpreted with caution and future research
316 including dermoscopic-histological analyses and analysis according to lesion stage are needed
317 to confirm our findings.

318 In conclusion, our findings emphasize that nodular/plaque-type PCLs may display
319 several vascular and non-vascular clues on dermoscopy and the diagnostic significance of
320 dermoscopic criteria remarkably varies according to the clinical differential diagnosis.
321 Additionally, some differences in terms of vascular dermoscopic pattern may be observed
322 among PCLs subtypes. However, the decision to biopsy a specific lesion cannot rely only on
323 dermoscopic features, but should be based on integrating anamnestic, clinical and dermoscopic
324 findings, according to the “two-step” rule (clinical differential diagnosis followed by
325 dermoscopic examination).¹⁶ On the other hand, dermoscopy may guide clinicians in sampling
326 the most informative lesion/area, as some dermoscopic features are likely to be related to more
327 relevant histological findings (e.g., orange areas and compact lymphomatous cellular
328 infiltrate).

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381 **Figures legend:**

382 **Figure 1.** Marginal zone B-cell primary cutaneous lymphoma (PCL): dermoscopy reveals the
383 main clues, i.e., white (black arrow) and orange (white arrow) structureless areas, unfocused
384 vessels with branches (white arrowhead), and white lines (black arrowhead) (A). Follicle-
385 center B-cell PCL: dermoscopy shows orange globules, along linear (arrowheads) and linear-
386 curved (arrows) unfocused vessels (B).

387 **Figure S1.** Marginal zone B-cell primary cutaneous lymphoma (PCL): dermoscopic
388 assessment shows focal orange structureless areas, unfocused linear vessels with branches, and
389 follicular plugs (A); dermoscopy of basal cell carcinoma also reveals linear vessels with
390 branches, but they are sharper than those seen in PCL (B). CD30+ anaplastic large cell PCL:
391 dermoscopic examination displays white lines and polymorphous vascular pattern (dotted,
392 linear-curved and linear with branches vessels) along with both orange and white focal
393 structureless areas (C); squamous cell carcinoma: diffuse white structureless area, purpuric
394 structureless areas, and linear-irregular vessels are seen on dermoscopy (D). Follicle-center B-
395 cell PCL: dermoscopy reveals both white and orange structureless areas as well as unfocused
396 linear vessels with branches (E) (*reused with permission from J Eur Acad Dermatol Venereol*
397 *2021. doi: 10.1111/jdv.17219*); dermoscopic assessment of sarcoidosis also shows orange
398 structureless areas and linear vessels with branches, yet they are more focused than those seen
399 in PCL (F). Follicle-center B-cell PCL: dermoscopic examination displays both orange (arrow)
400 and white (arrowhead) focal structureless areas along with unfocused linear/linear-curved
401 vessels (G); dermoscopy of lupus tumidus reveals linear/linear-curved vessels with no orange
402 area (H).

403 **Figure S2.** Dermoscopy of both marginal zone B-cell primary cutaneous lymphoma (PCL) (A)
404 and B-cell pseudolymphoma (B) shows unfocused linear/linear-curved vessels and follicular

405 plugs, yet only the former also displays white lines. The main dermoscopic differences between
406 B-cell (follicle-center variant – C) and T-cell (CD 30+ anaplastic large cell lymphoma – D)
407 PCL regards the vascular pattern, with the latter being positively associated with dotted vessels.
408 Considering the group of B-cell PCLs, marginal zone lymphoma (E) is more commonly
409 associated with unfocused linear vessels with branches than other variants, as shown in figure
410 F, in which follicle-center cell lymphoma mainly shows linear/linear-irregular vessels.

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Table 1. Dermoscopic comparative analysis between nodular/plaque-type T and B primary cutaneous lymphomas and control subgroups (neoplastic lesions, infiltrative inflammatory dermatoses, non-infiltrative dermatoses, and pseudolymphomas), with prevalence data and statistical differences

<i>Dermoscopic variable</i>	<i>Lymphomas (n= 121) N (%)</i>	<i>Neoplastic lesions (n=56) N (%)</i>	<i>Infiltrative dermatoses (n=29) N (%)</i>	<i>Non-infiltrative dermatoses (n=22) N (%)</i>	<i>Pseudolymphomas (n=33) N (%)</i>	<i>p-value*</i>
Dotted vessels (unfocused)	34 (28.1)	8 (14.3)	4 (13.8)	5 (22.7)	9 (27.3)	-
Dotted vessels (with white halo)	0 (0.0)	5 (8.9)	0 (0.0)	0 (0.0)	0 (0.0)	0.003 [§]
Dotted vessels (unspecific distribution)	24 (19.8)	6 (10.7)	1 (3.4)	1 (4.5)	7 (21.2)	0.048 ^{§§}
Linear vessels (well-focused)	0 (0.0)	2 (3.6)	3 (10.3)	0 (0.0)	0 (0.0)	0.007 ^{§§}
Linear vessels (peripheral distribution)	3 (2.5)	4 (7.1)	1 (3.4)	3 (13.6)	4 (12.1)	0.047 [†] 0.038 ^{††}
Linear vessels with branches (well-focused)	11 (9.1)	18 (32.1)	12 (41.4)	0 (0.0)	1 (3.0)	<0.001 [§] <0.001 ^{§§}
Linear vessels with branches (unfocused)	48 (39.7)	10 (17.9)	3 (10.3)	9 (40.9)	15 (45.5)	0.006 [§] 0.002 ^{§§}
Linear curved vessels (well-focused)	0 (0.0)	3 (5.4)	3 (10.3)	0 (0.0)	2 (6.1)	0.031 [§] 0.007 ^{§§} 0.045 ^{††}
Linear curved vessels (unfocused)	35 (28.9)	14 (25.0)	2 (6.9)	6 (27.3)	4 (12.2)	0.015 ^{§§}
White structureless areas (total)	69 (57.0)	34 (60.7)	7 (24.1)	4 (18.2)	17 (51.5)	0.002 ^{§§} 0.001 [†]
White structureless areas (diffuse)	3 (2.5)	9 (16.1)	0 (0.0)	2 (9.1)	0 (0.0)	0.002 [§]
White structureless areas (focal)	66 (54.5)	25 (44.6)	7 (24.1)	2 (9.1)	17 (51.5)	0.004 ^{§§} <0.001 [†]
Brown structureless areas (total)	1 (0.8)	6 (10.7)	0 (0.0)	1 (4.5)	1 (3.0)	0.004 [§]
Orange structureless areas (total)	73 (60.3)	1 (1.8)	22 (75.9)	4 (18.2)	16 (48.5)	<0.001 [§] <0.001 [†]
Orange structureless areas (focal)	66 (54.5)	1 (1.8)	15 (51.7)	2 (9.1)	12 (36.4)	<0.001 [§] <0.001 [†]
Yellow structureless areas (total)	0 (0.0)	3 (5.4)	3 (10.3)	0 (0.0)	0 (0.0)	0.031 [§] 0.007 ^{§§}
Purple structureless areas (total)	3 (2.5)	7 (12.5)	4 (13.8)	0 (0.0)	0 (0.0)	0.012 [§] 0.026 ^{§§}
Brown globules	0 (0.0)	4 (7.1)	0 (0.0)	0 (0.0)	1 (3.0)	0.009 [§]
Blue globules	0 (0.0)	6 (10.7)	0 (0.0)	0 (0.0)	0 (0.0)	0.001 [§]
Orange globules	8 (6.6)	0 (0.0)	1 (3.4)	0 (0.0)	1 (3.0)	-
White lines (total)	51 (42.1)	14 (25.0)	12 (41.4)	3 (13.6)	7 (21.2)	0.030 [§] 0.015 [†] 0.042 ^{††}
White lines (unspecifically arranged)	31 (25.6)	8 (14.3)	6 (20.7)	3 (13.6)	4 (12.1)	-

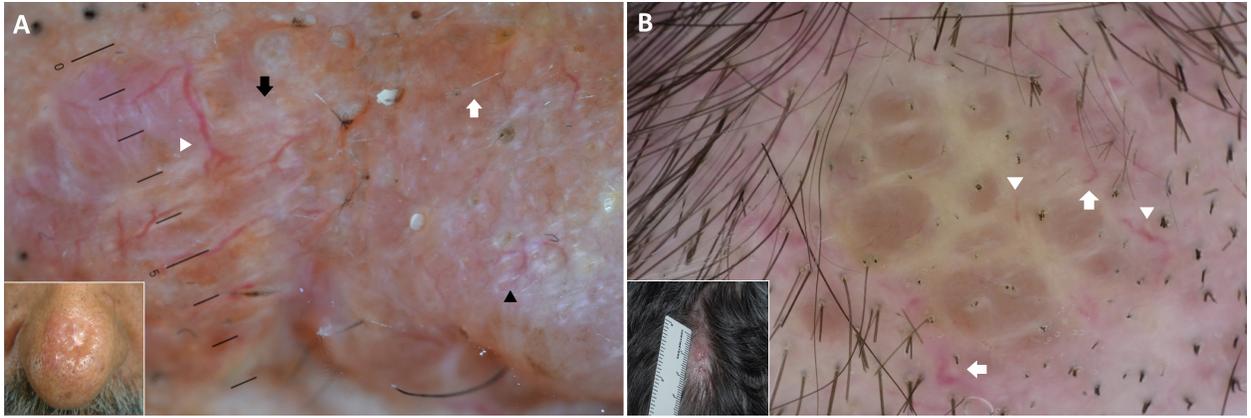
*Pearson's Chi Square test (statistical significance set at p<0.05); [§]Lymphomas vs Neoplastic lesions; ^{§§}Lymphomas vs Infiltrative dermatoses;

[†]Lymphomas vs Non-infiltrative dermatoses; ^{††}Lymphomas vs Pseudolymphomas

Table 2. Multivariate (adjusted) dermoscopic predictors for nodular, plaque-type T and B primary cutaneous lymphomas when compared to the whole control group and different clinical subgroups (neoplastic lesions, infiltrative inflammatory dermatoses, non-infiltrative inflammatory dermatoses, and pseudolymphomas)

<i>Dermoscopic variable</i>	<i>p-value*</i>	<i>OR**</i>	<i>Low 95% CI</i>	<i>High 95% CI</i>
Lymphomas vs all controls				
Linear vessels with branches (well-focused)	0.008	0.300	0.123	0.735
White structureless areas (focal)	0.005	2.350	1.291	4.277
Orange structureless areas (focal)	0.000	3.957	2.132	7.342
Purple structureless areas (total)	0.030	0.180	0.038	0.850
Orange globules	0.033	6.618	1.170	37.437
White lines (total)	0.044	1.935	1.017	3.682
Lymphomas vs neoplastic lesions				
Linear vessels with branches (well-focused)	0.018	0.256	0.082	0.795
White structureless areas (diffuse)	0.025	0.047	0.003	0.681
Brown structureless areas (total)	0.028	0.083	0.009	0.760
Orange structureless areas (total)	<0.001	65.011	6.860	616.101
Purple structureless areas (total)	0.045	0.119	0.015	0.954
Lymphomas vs infiltrative inflammatory dermatoses				
Linear vessels with branches (unfocused)	0.038	4.245	1.086	16.589
White structureless areas (total)	0.004	9.473	2.034	44.118
Purple structureless areas (total)	0.002	0.021	0.002	0.229
Lymphomas vs non-infiltrative inflammatory dermatoses				
White structureless areas (focal)	0.003	10.103	2.156	47.339
Orange structureless areas (total)	0.003	10.464	2.234	49.011
Lymphomas vs pseudolymphomas				
White lines (total)	0.049	2.498	0.999	6.243

*p<0.05 deemed as statistically significant; **Odds ratios approximated via multivariate logistic regression.



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Capsule summary:

- Our study increases the knowledge on dermoscopy of nodular/plaque-type cutaneous lymphomas by comparing their dermoscopic features with those of clinical mimickers and investigating possible differences according to histologic background.
- Significance of dermoscopic findings in nodular/plaque-type cutaneous lymphomas should be interpreted based on the considered differential diagnosis and histologic subtype.

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