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Primary Cutaneous Lymphomas in Pediatric Age Group: Experience of a Single Dermatology Center

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There are more than 15 types of primary cutaneous lymphomas (PCLs) having different biologic behaviors that constitute a relatively common problem in dermatological practice.[1] As they usually affect adults, data about PCLs arising in childhood are limited.[1–9]

We retrospectively analyzed the data of PCLs in our tertiary dermatology department from 1997 to February 2022 focusing on the frequency of patients diagnosed in the pediatric age range (defined as ≤18 years old). The number of pediatric lymphoma patients and the ratio of pediatric patients among each PCL type were determined. Patients diagnosed with pityriasis lichenoides, idiopathic follicular mucinosis, pseudolymphomas, and secondary skin involvement of systemic hematologic neoplasia were not included. The study was approved by the institutional ethical committee of İstanbul University İstanbul Faculty of Medicine and conducted in accordance with the Declaration of Helsinki (approval number: E-29624016-050.99-801731).

Over the 25-year period, 73 cases of pediatric PCL were diagnosed in total. We encountered a majority of mycosis fungoides (MF) (n = 54, 74%) (mean age: 9.7 ± 4 [2–18] years) followed by lymphomatoid papulosis (LyP) (n = 16, 21.9%) (mean age: 9.4 ± 3.9 [2–17]). In 1 pediatric patient, an association between MF and LyP was observed. Primary cutaneous marginal zone lymphoma (PCMZL) (n = 2) (mean age: 16 [14–18] years), extranodal natural killer (NK)/T-cell lymphoma, nasal type (n = 1), and primary cutaneous CD4+ small/medium T-cell lymphoproliferative disorder (n = 1) were other PCLs in our series. While pediatric MF cases constituted 7.9% of all MF cases in our cohort, children account for 22.5% and 5% of our LyP and PCMZL patients, respectively.

The distribution of PCLs seems to show some differences between adults and children, especially on the spectrum of cutaneous B-cell lymphomas.[3,8,9] Furthermore, the frequency of different types of PCLs in childhood varies in reported large series; 4 of which were from European countries,[2,3,5,6] 1 from Asia,[4] and 1 from Canada[7] (Table 1). However, these series have some differences such as being reported from different disciplines, variability in the threshold of the patients' age, and the inclusion of systemic lymphomas with secondary skin lesions in all of them, unlike our study (Table 1).

Mycosis fungoides is the most common cutaneous lymphoma in children and adolescents in 3 of these series (39.4%, 38.7%, and 34.8%) like our study (74%).[2,3,6] Even if the ratio of secondary lymphomas was excluded from the above mentioned studies, the ratio of MF would range between 39% and 44%,[2,3,6] and the ratio of MF patients in our pediatric PCL series represents the highest result already reported (Table 1). Mycosis fungoides, which almost always has an excellent prognosis in childhood, shows a significant difference in prevalence according to geographic location.[8,10–12] There are many studies about pediatric MF in the literature with a reported prevalence of 5% to 17% of all MF cases in different cohorts.[8] Pediatric MF patients constituted 7.9% of all our MF cases. Remarkably, in a previous study from our clinic evaluating the period between 1997 and 2011, this rate was 5.4% and a striking increase in ten years has been observed.[13] Similar to our series, an increased incidence of pediatric MF has been highlighted in many reports.[8–12,14] The reasons for the increase in the frequency of pediatric MF are open to debate. Better recognition of the clinical features of the disease and increased awareness among physicians that it can be diagnosed in childhood leading

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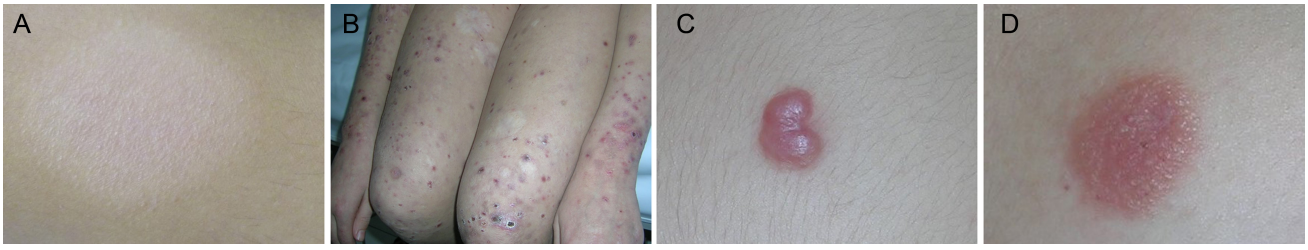

Figure 1. Pediatric primary cutaneous lymphomas representing as (A) a fine scaly and atrophic hypopigmented lesion on arm compatible with mycosis fungoides; (B) multiple papules with hemorrhagic crusts on some of them associated with atrophic scars of former lesions compatible with lymphomatoid papulosis; (C) a large erythematous papulonodule with smooth surface on the back of an adolescent male compatible with primary cutaneous marginal zone lymphoma; (D) an erythematous, infiltrated plaque on the trunk of a child compatible with primary cutaneous CD4+ small/medium T-cell lymphoproliferative disorder.

to keeping the biopsy threshold low for histopathological diagnosis may be among the reasons for this increase. In addition, since our clinic is a reference center for cutaneous lymphomas, patients referred from other clinics might partially explain the increased frequency. However, a genuine increase in the incidence can not be overlooked. In addition, it may be suggested that the true incidence of pediatric MF may be higher because symptoms often present in childhood, but patients with mild findings may not be diagnosed as MF until adulthood.[8,11]

Lymphomatoid papulosis was the most common PCL type in childhood in the other 3 large series (24.4%, 27.8%, and 47%) which is unusual for PCL distribution in adulthood.[4,5,7] Lymphomatoid papulosis represented the second most common (21.9%) PCL type among our pediatric patients. The rate of association with other lymphomas in our pediatric LyP patients[15] was lower than the adult cases, and in our series only in 1 pediatric LyP patient showed association with MF. Interestingly, primary cutaneous anaplastic large cell lymphoma (PCALCL) which was commonly seen (11.1%-19.5%) in some series was not diagnosed among our pediatric patients.[4,6,7] In 1 of our patients presenting with a rapidly enlarged solitary nodule which was excised completely, PCALCL was the initial diagnosis. However, recurrent papules and nodules with a tendency for

Table 1. Review of the Literature Data Regarding the Distribution of Primary Cutaneous Lymphomas in Pediatric Patients

Variables	Cerroni[2]	Boccara et al[5]	Kempf et al[3]	Moon et al[4]	Fink-Puches et al[6]	Colmant et al[7]	Present study
Year	2020	2012	2015	2014	2004	2022	2022
Country	Austria	France	Switzerland	Korea	Austria	Canada	Turkey
Specialty	Dermatology	Pathology	Dermatology	Dermatology	Dermatology	Pediatrics	Dermatology
Patient number	178†	51	31	41	69	36	73
Age cut-off value	18	15	18	20	20	18	18
Primary cutaneous lymphoma subtypes (%)							
Mycosis fungoides	39.4	9.8	38.7	22	34.8	16.7	74
Lymphomatoid papulosis	16.1	47.1	32.6	24.4	15.9	27.8	21.9
Primary cutaneous anaplastic large cell lymphoma	4.4	-	9.7	19.5	18.8	11.1	-
Subcutaneous panniculitis-like T-cell lymphoma	3.9	2	-	2.4	1.4	-	-
Extranodal natural killer/T cell lymphoma, nasal type	1.1	2	-	4.9	1.4	2.8	1.3
Primary cutaneous γ/δ T cell lymphoma	1.7	2	-	-	-	-	-
Primary cutaneous CD4+ small/medium T-cell lymphoproliferative disorder	8.3	-	3.2	2.4	2.8	2.8	1.3
Hydroa vacciniforme-like lymphoproliferative disorder	4.4	-	-	-	-	-	-
Primary cutaneous marginal zone lymphoma	8.3	-	9.7	2.4	10.1	11.1	2.7
Primary cutaneous follicle center lymphoma	2.2	-	-	-	1.4	-	-
Secondary cutaneous lymphomas	10	37.2	6.5	21.9	10.1	33.6	-

†A total of 57 cases were previously published by Fink-Puches et al.[6]

rapid spontaneous regression occurring in the following years changed the diagnosis of the patient to LyP.

Primary cutaneous marginal zone lymphoma was a relatively common type of B-cell cutaneous lymphoma in large pediatric PCL series with the highest rates up to 11.1%.[6,7] In our series, PCMZL seen in 2 adolescent patients represented the B-cell PCLs. On the other hand, PCMZL is also the most common B-cell lymphoma in our practice, and pediatric cases constituted 5% of them. Extranodal NK/T-cell lymphoma, nasal type, and primary cutaneous CD4+ small/medium T-cell lymphoproliferative disorder seen in our pediatric series in 1 patient each were also reported in most large series with low rates.[2,4,7,9]

Our results include only patients seen in the dermatology department and this may cause a selection bias for PCLs usually without systemic involvement. However, PCL types causing early systemic involvement such as primary cutaneous aggressive epidermotropic CD8+ T-cell lymphoma, primary cutaneous diffuse large B-cell lymphoma, leg type, and Sezary syndrome are also very rare and have never been reported in large series about pediatric lymphomas, like our study (Table 1).[3,8]

In conclusion, the results of our large series support the information that MF and LyP are the most common types of PCLs in childhood but MF shows the highest rate.

Ethics Committee Approval: The study was approved by the institutional ethical committee of İstanbul University İstanbul Faculty of Medicine(approval number: E-29624016-050.99-801731).

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