The Clinical Spectrum of Primary Cutaneous CD4+ Small/Medium-Sized Pleomorphic T-Cell Lymphoproliferative Disorder: An Updated Systematic Literature Review and Case Series

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Keywords

Primary cutaneous CD4+ small/medium-sized pleomorphic T-cell lymphoproliferative disorder · Cutaneous T-cell lymphoma · Primary cutaneous lymphoma

Abstract

Background: Primary cutaneous CD4+ small/medium pleomorphic T-cell lymphoproliferative disorder (SMPLPD) is a provisional entity within the 2016 World Health Organization classification of primary cutaneous lymphomas. The condition is currently classified as a lymphoproliferative disorder to emphasize its benign course and discourage aggressive, systemic treatment modalities. **Objective:** To provide a relevant synthesis for the dermatological practitioner on the prevalence, presentation, and treatment of SMPLPD. **Methods:** We conducted an updated systematic literature review and a retrospective chart review of diagnosed cases of SMPLPD from 2 Canadian academic cutaneous lymphoma centers. **Results:** A total of 23 studies with 136 cases were extracted from the systematic review and 24 patients from our retrospective chart review. SMPLPD proved relatively common accounting for 12.5% of all cutaneous T-cell lymphomas encountered in our cutaneous lymphoma clinics,

second in frequency only to mycosis fungoides. The typical clinical presentation was that of an older individual (median age 59 years) with an asymptomatic solitary lesion on their upper extremity. The most common clinical differentials were cutaneous lymphoid hyperplasia, basal cell carcinoma, and lymphoma unspecified. T follicular helper markers were reliably detected. The main treatment modalities were surgical excision, local radiation therapy, and topical or intralesional steroids. Cure was achieved in the vast majority of cases. **Conclusions:** SMPLPD is an underdiagnosed T-cell lymphoma with an overtly benign clinical course. The condition has an excellent prognosis and responds well to skin-directed therapies. Practitioners should be aware of this condition to avoid aggressive systemic treatments.

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Introduction

CD4+ primary cutaneous small/medium pleomorphic T-cell lymphoproliferative disorder (SMPLPD) is a provisional entity within the spectrum of primary cutaneous T-cell lymphomas (CTCLs). Historically, SMPLPD has been considered a rare, poorly defined disease with an

undetermined malignant potential [1]. In 2016, the World Health Organization (WHO) working group reclassified this entity as a lymphoproliferative disorder, rather than a lymphoma, due to accumulating evidence of its benign prognosis [2]. As a provisional entity, SMPLPD remains poorly described and not well understood in dermatology, leading to misdiagnosis and unnecessary staging procedures and aggressive treatments.

The canonical presentation of SMPLPD is that of a solitary violaceous nodule or papule typically on the head, neck, upper extremities, or upper trunk. About a quarter of cases may manifest as multiple lesions [3]. Patients usually present later in life, but lesions have been documented between the ages of 6 months and 91 years [4]. Systemic features, disseminated or generalized multifocal disease, or rapidly progressing lesions are inconsistent with SMPLPD [5]. The histopathological hallmarks are a diffuse nonepidermotropic lymphocytic infiltrate of CD4+ and CD3+ mature lymphocytes with associated, variably abundant B cells. Additional markers PD1, BCL-6, and CXCL13 commonly seen in the T cells suggest that SMPLPD specifically originates from follicular helper T (T_{FH}) cells. The frequently observed admixture of B cells is likely due to malignant T_{FH} cells causing B-cell activation [6]. The prognosis is excellent, with a cited 5-year disease-specific survival rate of 100% [6].

Prior to the WHO 2016 publication on malignant lymphomas, SMPLPD was seldom diagnosed. With a deepening knowledge of SMPLPD in recent years, the frequency of the diagnosis has increased precipitously. Herein, we have reviewed SMPLPD cases from our institutions and performed a literature review to summarize its clinicopathological features.

Material and Methods

Systematic Literature Review

Literature Search Strategy

We conducted an updated systematic search for all cases of SMPLPD reported following the recent 2018 review by Salah [4] that had previously amalgamated the literature until March 24, 2018. We searched PubMed, Scopus, and all Web of Science databases from March 25, 2018, until April 7, 2020, using the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) framework (Fig. 1) [7]. The search keywords used were: CD4 AND (small OR medium) AND (T cell OR T-cell) AND (lymphoma OR lymphoproliferative). Duplicate studies were removed. Two reviewers independently screened texts by title and abstract and, subsequently, full text to evaluate for inclusion. Any differences were resolved by discussion and consensus among reviewers. Final included articles were reference-screened for related works not captured in the initial search.

Eligibility Criteria for Study Selection

Our inclusion criteria consisted of any texts describing primary cases of SMPLPD diagnosis in humans, adhering to the 2018 WHO-European Organization for Research and Treatment of Cancer (EORTC) update, and that were published between March 25, 2018, and March 31, 2020 [6]. We excluded duplicate articles or study populations, studies utilizing the prior distinction of “lymphoma” rather than “lymphoproliferative disorder,” and studies without texts in English. Furthermore, we integrated 6 additional studies published prior to our search date range previously included in Salah’s systematic review that adhered to our inclusion criteria.

Data Extraction

The following data were extracted: authors, dates of publication, study designs, number of cases, age and sex of patients, whether lesions were solitary or multifocal, the anatomic sites of lesion involvement, associated clinical symptoms, immunohistochemistry, T-cell receptor gene (TCR) rearrangement status, treatments, outcomes, and duration of follow-up.

Study Quality and Risk of Bias Assessment

A modified Newcastle-Ottawa Scale was used to evaluate the risk of bias in the included studies. There is a lack of validated measures to evaluate the quality of uncontrolled studies such as case reports and series. Therefore, prior works have foregone the comparability and adjustment items originally described in the Newcastle-Ottawa Scale and focused on items assessing selection, representativeness of cases, and descriptions of response and outcome [4, 8]. The resultant bias assessment is represented in 5 binary (yes/no) questions: (1) Did the presented case(s) represent all cases from the medical center? In the event that the authors did not explicitly state this, we assumed whatever was presented was representative for the entire institution as a result of the condition’s rarity. (2) Was the diagnosis made correctly? (3) Were other important diagnoses excluded? Specifically, we evaluated whether the authors described attempts to exclude a systematic presentation or other common differentials. (4) Were all important data cited in the report? (5) Was the outcome correctly ascertained? The quality of the reports was described based on answers to the above questions. Works were deemed high quality with a low risk of bias if all 5 questions were answered by yes, moderate quality with a moderate risk of bias if 4 questions were answered by yes and 1 by no, and low quality with a high risk of bias if 2 or more questions were answered by no.

Retrospective Chart Review

Data Extraction

We performed a retrospective chart review of patients diagnosed with SMPLPD from 2 academic cutaneous lymphoma clinics (University of Alberta, Edmonton and University of Calgary, Calgary) between January 1, 2016, and January 1, 2020. Ethics approval was obtained from the Health Research Ethics Board of Alberta Cancer Committee, and digital chart access was granted through a provincial electronic medical record via Alberta Health Services. Only patients who fulfilled the clinical and histopathological criteria of SMPLPD as defined by the 2018 WHO-EORTC classification (identical to the 2016 WHO classification) were included [2, 6].

Fig. 1. PRISMA search strategy.

Clinical data such as age at diagnosis, sex, clinical features, histology, treatment, duration of follow-up, and outcome were extracted. The date of diagnosis was determined as the date of the first pathology-confirmed biopsy. Clinical notes from the biopsy record were evaluated to determine presumed clinical diagnosis, presenting features (solitary vs. multiple lesions), site of lesion, and lesion history. In the pathology reports we specifically recorded the following immunohistochemistry data: CD3, CD4, CD7, CD8, CD10, PD-1, and BCL-6. TCR rearrangement data were included if available. Therapies, clinical outcomes, and total duration of follow-up were extracted from consultation notes and remaining clinical records.

Charts were independently reviewed at each academic institutional site (Edmonton and Calgary) by at least 2 separate reviewers and were aggregated for final analysis.

Results

Systematic Literature Review

Study Characteristics and Demographics

A total of 23 studies with 136 cases of SMPLPD were included in the final systematic review (Fig. 1). We identified 10 (43.5%) case reports, 7 (30.4%) case series, 5

(21.8%) retrospective cohort studies, and 1 (4.3%) prospective cohort study (shown in online suppl. Table S1; for all online suppl. material, see www.karger.com/doi/10.1159/000511473). The evaluated risk of bias in the included studies was low in 14 (60.9%), moderate in 8 (34.8%), and high in 1 (4.3%; shown in online suppl. Table S2).

Clinical Presentation

Clinically, the majority of the reviewed cases manifested classically as singular asymptomatic lesions with an anatomic predilection for the head, neck, and upper extremities (Table 1). Of the 114 patients whose lesion number was described, 106 (93.0%) presented with solitary disease and 8 (7.0%) with multifocal lesions. The most common anatomic locations were the head and neck ($n = 69$, 58.0%), followed by the trunk ($n = 31$, 26.1%), the upper extremities ($n = 12$, 10.1%), and the lower extremities ($n = 7$, 5.9%). Most lesions were asymptomatic, although 4 cases described accompanying pruritus. The most common initial clinical diagnoses reported prior to biopsy were reactive lymphoid hyperplasia ($n =$

Table 1. Patient, disease, immunohistochemical, and clinical data of patients diagnosed with primary cutaneous CD4+ small/medium pleomorphic T-cell lymphoproliferative disorder

	Literature review (<i>n</i> = 136)	Retrospective chart review (<i>n</i> = 24)
Mean age (range), years	58.1 (13–95)	54.4 (30–73)
Sex F/M, <i>n</i> (%)	71/65 (52.2)	11/13 (45.8)
Frequency of all T-cell cutaneous lymphomas, %	NA	12.5
Clinical differential diagnoses raised, <i>n</i>		
Lymphoid hyperplasia	24	4
Basal cell carcinoma	12	7
Lymphoma unspecified	8	0
Mycosis fungoides	0	4
Insect bite reaction	6	0
Cyst	0	3
Mean duration to diagnosis (range), months	NA	8.0 (1–36)
Lesion presentation, <i>n</i> (%)		
Single	106 (93.0/93.9)	19 (79.2)
Multiple, localized	8 (7.0)	5 (20.8)
Anatomic localization, <i>n</i> (%)		
Head and neck	69 (58.0)	15 (45.5)
Trunk	31 (26.1)	10 (30.3)
Arms and shoulders	12 (10.1)	6 (18.2)
Lower extremities	7 (5.9)	2 (6.1)
Immunohistochemistry ¹ , <i>n</i> (%)		
CD4 ⁺	122 (100)	24 (100)
CD3 ⁺	45 (100)	24 (100)
CD8 [−]	11 (100)	1 (100)
CD7 [−]	28 (68.3)	7 (46.7)
CD10 [−]	9 (90.0)	14 (100)
PD-1 ⁺	117 (99.2)	18 (94.7)
BCL-6 ⁺	25 (89.3)	10 (71.4)
CXCL13 ⁺	60 (100)	NA
TCR clonality, <i>n</i> (%)		
Monoclonal	95 (100)	18 (90.0)
Polyclonal	0 (0)	2 (10.0)
Treatment, <i>n</i> (%)		
Biopsy ²	18 (13.4)	7 (19.4)
Excision	57 (42.5)	13 (36.1)
Radiation therapy	27 (20.1)	2 (5.6)
Photodynamic therapy	0 (0)	1 (2.8)
Topical steroid	18 (13.4)	4 (11.1)
Intralesional steroid	2 (1.5)	4 (11.1)
Systemic steroid	3 (2.2)	0 (0)
Topical antibiotic	0 (0)	3 (8.3)
Oral antibiotic	2 (0.9)	1 (2.8)
Cyclophosphamide	1 (0.7)	0 (0)
Methotrexate	1 (0.7)	0 (0)
Cyclin-dependent kinase inhibitor	3 (2.2)	0 (0)
Hydroxychloroquine	2 (1.5)	0 (0)
Imiquimod	0 (0)	1 (2.8)
Final outcome, <i>n</i> (%)		
Complete resolution, no recurrence	107 (95.5)	22 (95.7)
Partial improvement	5 (4.5)	1 (4.3)
Mean duration of total follow-up (range), months	18.2 (1–48)	14.0 (2–95)

NA, not available; TCR, T-cell receptor. ¹ Percentages were calculated based on the available data reported.

² Spontaneous regression following biopsy.

Fig. 2. Clinical spectrum of primary cutaneous CD4+ small/medium T-cell lymphoproliferative disorder. **a** Erythematous indurated plaque on the extensor elbow. **b** Violaceous tumor with a peripherally erythematous patch and adjacent erythematous papule distributed over the extensor elbow. Appreciable follicular

prominence. **c** Erythematous scaling plaque on the right glabella. **d** Indurated erythematous plaque with crusting of the infranasal area. **e** Poorly demarcated brown-pink patch with elevated slightly erythematous peripheral borders. **f** Indurated light pin nodule on the posterior forearm.

24), basal cell carcinoma (BCC; $n = 12$), lymphoma unspecified ($n = 8$), and insect bite reaction ($n = 6$) [9].

Histopathological Features

As per the definition of SMPLPD, the neoplastic T cells were CD4+ in all reviewed cases. CD3 was reported and found positive in 45 patients with no cases of negative expression described. Among the cases stained, there were no CD8+ cases, and CD7 expression was decreased or lost in 68.3% of patients. Regarding the T_{FH} markers, PD-1 was evaluated in 117 patients with all but 1 demonstrating positive expression; CXCL13 was positively expressed in all 60 stained, and BCL-6 was positive in 25 of the 28 stained. A total of 67 patients were stained for PD-1, CXCL13, and BCL-6 concurrently with 50.7% demon-

strating expression of all 3 markers. All 95 cases where TCR clonality was stated were monoclonal for β - and/or γ -chain gene rearrangements.

Treatment and Outcomes

A total of 112 cases had treatment and outcome data with the mean duration of follow-up being 18.2 months (range 1–48). In all cases, the disease course was benign with no systemic dissemination or disease-related mortality observed. Surgical excision was the most common treatment employed either alone (44.6%) or in combination with radiation therapy (4.5%) and resulted in complete remission in all cases except for a recurrence in 1 patient [10]. There were 17 cases of described spontaneous remission following biopsy. The majority of treated

Fig. 3. Anatomical distribution of primary cutaneous CD4+ small/medium T-cell lymphoproliferative disorder lesions in the chart review. Red, lesions that presented solitary; blue, lesions that presented in multiples; outline of the circles corresponds to whether the lesion was on the anterior (solid) or posterior (dashed) surfaces. Excluded from the figure were 2 lesions, one on the right buttock and the other on the left posterior calf. Localizations were approximated based on descriptions from clinical notes.

cases (95.5%) experienced complete resolution with no recurrence while the remaining 4 cases experienced clinical improvement following therapy.

The described cases with systemic therapies were oftentimes those where complete resolution was not achieved. One case described the usage of oral cyclophosphamide and methylprednisolone resulting in the patient developing hemorrhagic cystitis and requiring discontinuation with subsequent lesion recurrence [10]. It should be noted that this was the most serious disease-related morbidity encountered among all reviewed cases and was the consequence of aggressive treatment rather than the condition itself. This regimen was followed by a 10-month course of methotrexate that was ultimately ineffective. Fi-

nally, the same patient achieved lasting complete resolution after just 3 weeks of local low-dose radiotherapy. Two other patients were treated with systemic corticosteroids and achieved only clinical improvement [11], compared to the 15 described cases managed with topical corticosteroids who completely resolved [9]. One case was treated with oral doxycycline without resolution [12].

Retrospective Chart Review

Demographics

A total of 24 patients met our retrospective chart review inclusion criteria and were evaluated between Edmonton ($n = 12$) and Calgary ($n = 12$; shown in online suppl. Table S3). SMPLPD represented the second most common cutaneous lymphoma after mycosis fungoides (11.4 and 13.8% of all CTCLs encountered in cutaneous lymphoma clinics in Calgary and Edmonton, respectively).

Clinical Presentation

Our cohort was clinically very similar to that of the systematic review (Table 1). The mean duration between onset of symptoms and histopathological diagnosis was 8.0 months (range 1–36). Patients typically presented with solitary slow-growing lesions, generally described as “nodules” and “tumors,” and less commonly as “flat plaques” or “papules” ($n = 20$, 83.3%; Fig. 2). Rare patients had multiple lesions ($n = 4$, 16.7%). None of our patients demonstrated disease-related extracutaneous manifestations. Of a total 33 lesions observed, the anatomic sites involved were the head and neck ($n = 15$, 45.5%), the arms and shoulders ($n = 6$, 18.2%), the back and flanks ($n = 6$, 18.2%), the chest and abdomen ($n = 4$, 12.1%), and the lower extremities ($n = 2$, 6.1%). As is typically described, our cohort’s lesions were distributed preferentially on the upper body (Fig. 3). The most common clinical differential diagnoses raised prior to biopsy were BCC ($n = 7$), reactive lymphoid hyperplasia ($n = 4$), mycosis fungoides ($n = 4$), lymphoma ($n = 4$), and cyst ($n = 3$).

Histopathological Features

By the WHO-EORTC definition, all of our cases demonstrated diffuse or nodular nonepidermotropic dermal lymphoid infiltrates of small/medium-sized cells, with mild to moderate cytological atypia, characterized by CD4+ and CD3+ expression. Occasionally, there was an admixture of histiocytes, plasma cells, and eosinophils (Fig. 4, 5). The observed Ki-67 proliferation indices were low, never exceeding 15%. Among the cases stained, varying degrees of CD7 loss were observed in 46.7% of the atypical lymphocyte populations. CD10 was negative in

Fig. 4. Histopathology of primary cutaneous CD4+ small/medium T-cell lymphoproliferative disorder. **a** Dense superficial and deep dermal lymphoid infiltrate separated from the epidermis by a grenz zone. **b** Lymphoid cells are small to medium in size with nuclear pleomorphism. Original magnification $\times 20$ (**a**) or $\times 400$ (**b**).

Fig. 5. The infiltrative population is positive for CD3 (**a**) and CD4 (**b**). Intermixed CD8+ T cells are present in the background in smaller numbers (**c**). Original magnification $\times 40$ (**a-c**).

all 14 cases stained. In approximately half of the cases, B-cell infiltration was prominent leading to the histological differential diagnosis of marginal zone B-cell lymphoma. A T_{FH} phenotype was observed in the atypical lymphocyte population with PD-1 and BCL-6 expression noted in 94.7 and 71.4% of stained samples, respectively. PD-1 was expressed in typical clusters forming rosettes surrounding larger cells (Fig. 6). A total of 20 biopsies commented on TCR- β and/or TCR- γ gene rearrangements with the majority being monoclonal (90.0%).

Treatment and Outcomes

Surgical excision was the primary treatment modality employed, performed in 13 patients (54.2%), and demon-

strated recurrence-free removal in all cases. Biopsies with subsequent spontaneous regression occurred in 6 patients (25.0%). Radiation therapy was performed in 2 patients (8.3%), both of whom experienced complete recurrence-free resolution. Intralesional steroids were administered in 3 patients (12.5%), with resulting complete regression in 1 and cosmetic improvements in 1. Topical steroids were administered in 4 (16.7%) patients and were ineffective with no improvements noted. Oral minocycline, topical imiquimod, topical mupirocin, topical fucidin, and photodynamic therapy were each attempted once and were ineffective in 3 cases and effective with subsequent recurrence in 2, respectively. The patients who received mupirocin, fucidin, or photodynamic ther-

Fig. 6. PD-1 highlights scattered strongly positive cells across the lesion (**a**) with focal evidence of clustering and rosette formation around larger cells (**b**, arrows). Original magnification $\times 200$ (**a**) or $\times 400$ (**b**).

apy were subsequently completely cured following treatment with excision, radiation therapy, or intralesional Kenalog, respectively. The mean duration of follow-up was 14.0 months (range 2–95).

Discussion

SMPLPD has historically undergone a number of reclassifications, most recently in 2016, and continues to be described as a provisional entity. In the 2005 WHO and European Organization for Research and Treatment of Cancer cutaneous lymphoma classification, SMPLPD was estimated to account for only 2% of all CTCLs [1]. In the 2018 update, this value had tripled to 6% [6]. Our own data suggest even this revised value to be an underestimate. In both the Edmonton and Calgary cutaneous lymphoma clinics, SMPLPD represented 12.5% of all CTCLs and was the second most common CTCL encountered following mycosis fungoides. As the understanding of SMPLPD continues to develop, we believe we will begin observing greater rates of occurrence as cases are increasingly correctly diagnosed.

SMPLPD is demonstrably benign and responds well to conservative treatment measures. There was no disease-related mortality observed in any of our reviewed cases and the greatest example of disease-morbidity resulted from overly aggressive systemic therapy. Prior to being reclassified as a lymphoproliferative disorder, the utiliza-

tion of aggressive treatment measures such as chemotherapies were not uncommon [13–17]. Currently, such systemic treatments are not recommended as their risks outweigh potential benefits.

SMPLPD has previously been a diagnosis of exclusion; however, we found the WHO diagnostic criteria to be precise, unequivocal, and clinically applicable. All of our retrospective cases were unambiguously classified as SMPLPD by clinicopathological correlation. The typical clinical presentation for SMPLPD was that of an asymptomatic solitary nodule or papule on the upper body (usually head or neck) in middle-aged or elderly individuals. Figure 6 illustrates 6 SMPLPD clinical presentations from our own patients. Rarely, locally multifocal presentations, involvement of the lower extremities, accompanying symptoms such as pruritus or pain, and occurrences in younger patients are also possible. Generalized disease, rapid progression, or refractory lesions should prompt investigations into alternative diagnoses [5].

Histopathology classically demonstrates a nonepidermotropic, diffuse, or nodular dermal infiltrate of CD4+ and CD3+ mildly atypical lymphocytes with at least one T_{FH} marker such as PD-1+ in clusters or rosettes, CXCL13, or BCL-6. All 3 markers were found positive in half of the systematically reviewed cases underscoring the fact that their concomitant presence should no longer be considered a requirement for diagnosis [3]. A Ki-67 index of <20% has been suggested as a diagnostic criterion and is supported by the results of our own cohort. TCR analysis

Table 2. Differential diagnoses and diagnostic features [6, 19–24]

Differential diagnosis	SMPLPD	Primary cutaneous marginal zone B-cell lymphoma	Lymphocytoma cutis ¹	Jessner lymphocytic infiltrate ²	Mycosis fungoides (tumor stage)
Typical morphology	Violaceous, sometimes pigmented nodule	Plum-colored papules, nodules, or plaques	Erythematous papules, plaques, or nodules	Erythematous papules and/or plaques	Erythematous or violaceous tumors and scaly plaques with a preceding history of patches or plaques
Distribution	Solitary or locally multifocal Head and neck, upper body and extremities	Usually multifocal	Solitary or locally multifocal	Multiple (rarely solitary)	Multiple lesions Sun-protected areas, later dissemination to the entire skin
Infiltrate	Diffuse or nodular of small or medium-sized CD4 ⁺ T cells; many admixed B cells, low proliferation rate	Nodular with dominant B cells and monotypic plasma cells at the periphery of infiltrates	Nodular or diffuse, mixed, T cells (CD4 ⁺ , CD8 ⁺) and B cells, Plasmacytoid dendritic cells (CD123 ⁺) in small clusters	Diffuse predominantly CD8 ⁺ T cells	Predominantly CD4 ⁺ T cells. High proliferation rate in tumors
Epidermotropism	–				+ (may be absent in tumors)
PD-1 stain	++ Clusters or rosettes	+/- (single, scattered cells)			
BCL-6	+	–	+	–	–
T-cell receptor monoclonality	+	–			+
Kappa/lambda light chain restriction	–	+	–		
Course			Indolent		Malignant
SMPLPD, small/medium pleomorphic T-cell lymphoproliferative disorder. ¹ Synonyms: cutaneous lymphoid hyperplasia, lymphadenosis benigna cutis, cutaneous lymphoplasia, pseudolymphoma of Spiegler-Fendt. Includes <i>Borrelia burgdorferi</i> -induced lymphocytoma. ² Also comprises tumid lupus erythematosus.					

for monoclonal rearrangements in β - and γ -chains may be useful in supporting a diagnosis; however, polyclonal patterns are rarely observed.

BCCs, adnexal tumors and cysts, and Jessner lymphocytic infiltration may often be mistaken for SMPLPD due to their small size and predilection for the head and neck. It is relevant to mention a few histopathological mimickers one should be aware of (Table 2). A few more aggressive lymphomas derive from T_{FH} cells, such as angioimmunoblastic T-cell lymphoma or the rare cutaneous follicular helper T-cell lymphomas [18]. However, these diseases involve lymph nodes or large areas of the skin and are accompanied by systemic symptoms. Cutaneous metastases of angioimmunoblastic T-cell lymphoma are rare but can be distinguished by their association with Epstein-Barr virus (usually identified within the lesion), a waxing and waning course, and maculopapular morphology [18]. SMPLPD may also easily be misdiagnosed as a marginal zone B-cell lymphoma due to a prominent accompanying B-cell component, and it may enter the differential diagnosis of some B-cell predominant cutaneous infiltrates where a significant subset of T cells is noted.

In conclusion, SMPLPD is a common, indolent cutaneous lymphoma presenting as a solitary nodule or tumor on the upper body, head, and neck. Surgical excision is often curative, and no staging procedures are required.

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Key Message

Primary cutaneous CD4+ small/medium-sized pleomorphic T-cell lymphoproliferative disorder is a common, benign cutaneous lymphoma that responds well to conservative treatment measures and does not necessitate aggressive staging or systemic measures.

Statement of Ethics

This study meets the requirements of the law on human research and has been authorized by the Health Research Board of Alberta Cancer Committee under the ID HREBA.CC-19-0303. Verbal consent was acquired from patients for the usage and publication of anonymized images.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

P.S., S.D., A.S., J.H., and R.G.: study design. P.S., S.D., and A.S.: data collection. N.P., J.D., and M.S.: histopathological interpretation. P.S., S.D., A.S., J.D., J.H., and R.G.: writing of the paper.

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