SKIN

BRIEF ARTICLE

A Case of Primary Cutaneous CD4+ Small/Medium T-cell Lymphoproliferative Disorder

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ABSTRACT

Primary cutaneous CD4+ small/medium T-cell lymphoproliferative disorder (PCSM-TCLPD) is a rare lymphoproliferative condition that typically manifests as a solitary, asymptomatic cutaneous nodule. Systemic involvement is uncommon, and diagnosis is confirmed via biopsy, which reveals a predominant population of CD4-positive T-cells with a follicular helper T-cell phenotype. Treatment generally involves conservative local approaches, including biopsy, topical steroids, or excision, with many cases demonstrating spontaneous regression after biopsy. This report presents the case of a 68-year-old woman with a 6.0 x 6.0 mm subcutaneous nodule on the left preauricular cheek. The lesion appeared over 4–5 weeks and was asymptomatic. Biopsy revealed a dense lymphohistiocytic infiltrate of predominantly CD4-positive T-cells, with clonality confirmed through molecular studies. Additional workup, including complete blood count, metabolic panel, and imaging, revealed no systemic involvement. Oncology recommended observation without further excision. At three months post-biopsy, the lesion had not recurred.

PCSM-TCLPD, which accounts for 5% of primary cutaneous lymphomas, was reclassified as a lymphoproliferative disorder by the World Health Organization in 2016 due to its indolent nature. While its prognosis is excellent, with a five-year survival rate near 100%, careful diagnostic and therapeutic strategies are critical. Spontaneous remission post-biopsy supports the role of conservative management, minimizing invasive interventions. This case underscores the importance of recognizing PCSM-TCLPD's clinical and histopathological features to ensure accurate diagnosis and optimize patient outcomes while avoiding unnecessary procedures. Further research is needed to refine treatment and follow-up strategies for this rare condition.

INTRODUCTION

Primary cutaneous CD4+ small/medium T-cell lymphoproliferative disorder (PCSM-TCLPD) is an uncommon lymphoproliferative disorder that typically presents as an asymptomatic nodule. Systemic involvement is uncommon. The diagnosis is confirmed by biopsy, which demonstrates lymphocytic infiltrate including a predominant T-cell population with a follicular T-helper phenotype. Treatment generally is focused on conservative local treatments including biopsy, topical steroids, and excision. Despite its rare nature, understanding this disorder is crucial for accurate diagnosis and appropriate management. We report a

patient with PCSM-TCLPD who had spontaneous remission after biopsy.

CASE REPORT

A 68-year-old female presented to a dermatology clinic with a 6.0 x 6.0 millimeter pink subcutaneous nodule affecting the left preauricular cheek of 4-5 week duration (**Figure 1**). The patient denied bleeding, pain, pruritus, drainage, or associated symptoms with the lesion. The patient's past medical history included a 25-pound weight loss over the past year which stabilized after undergoing a cholecystectomy. Family medical history was only notable for a non-melanoma skin cancer in a sister. There were no palpable lymph nodes or systemic symptoms. The patient had no history of trauma or new medications. A 6-millimeter punch biopsy was performed. Initial histopathology revealed atypical lymphoid infiltrate and was sent for further immunophenotyping and characterization.

Further analysis showed dense lymphohistiocytic infiltrate extending from the superficial dermis to the subcutaneous adipose tissue which involved the edges and deep margin of the biopsy specimen. The infiltrate consisted of CD4-positive T-cells (90%), CD8-positive T-cells (10%) with few plasma cells present. The abnormal lymphocytes spared the epithelium, and no follicular mucinosis was present (**Figures 2 and 3**). The lymphocytes were characterized as small and medium-sized CD4-positive T-cells with irregular nuclei as well as increased expression of T-follicular helper markers such as PD1, BCL6, and CXCL13. The T-cells demonstrated evidence of clonality with molecular studies of the T-cell receptor gamma and T-cell receptor beta genes.

Patients diagnosed with PCSM-TCLPD receive laboratory testing including a complete blood count and blood chemistry in addition to human T-cell lymphotropic virus testing, *TCR* gene rearrangement analysis and, sometimes, computed tomography and PET scans to monitor for systemic disease.[1] The patient was referred to oncology for evaluation of potential systemic disease. The patient underwent lab work-up including complete blood count with differential, complete metabolic panel, HTLV serology, flow cytometry, and peripheral blood TCR gene rearrangement. A splenic ultrasound was negative. Oncology recommended conservative observation and did not recommend excision despite the positive margins to the base and peripheral edges of the biopsy specimen. The patient was advised to monitor for recurrence and follow up with oncology in one year to repeat labs. The patient was also advised to follow up with dermatology annually for skin cancer screenings. At our patient's three month follow up visit, there were no signs of recurrence at the site of the biopsy and no new suspicious lesions were present elsewhere.

DISCUSSION

PCSM-TCLPD is a rare disease that exists within the spectrum of cutaneous T-cell lymphomas.[2] PCSM-TCLPD was reclassified as a lymphoproliferative disorder, rather than a lymphoma, by the World Health Organization (WHO) in 2016.[3] PCSM-TCLPD classically presents as a single, asymptomatic erythematous or violaceous nodule, tumor or plaque confined to the skin of the head, neck and trunk and accounts for approximately 5% of all primary cutaneous lymphomas.[2,4] It commonly presents in patients aged 50-60 years old.[4] However, clinical presentation is diverse with reported

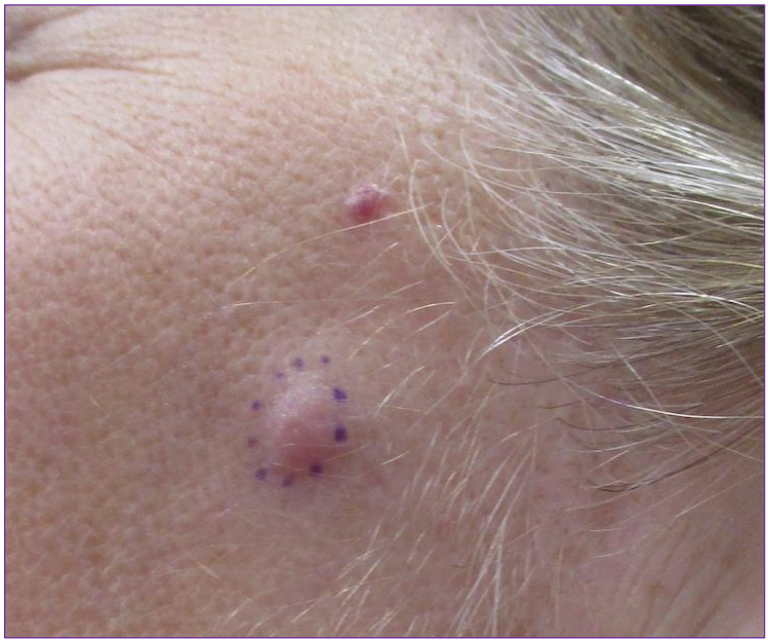

Figure 1. This clinical photograph shows the 6.0 x 6.0 millimeter pink subcutaneous nodule affecting the patient's left preauricular cheek.

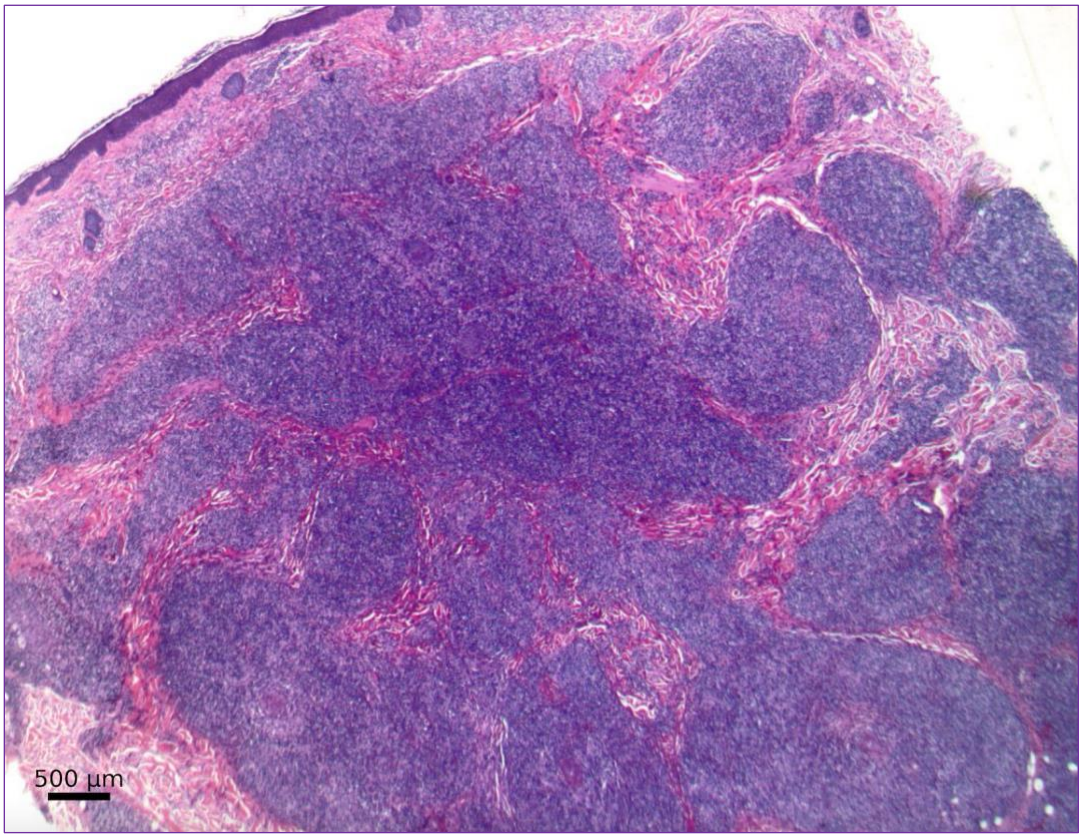

Figure 2. Histopathology slide of the specimen shown at 2x magnification demonstrating the lymphohistiocytic infiltrate extending from the superficial dermis to the subcutaneous adipose tissue.

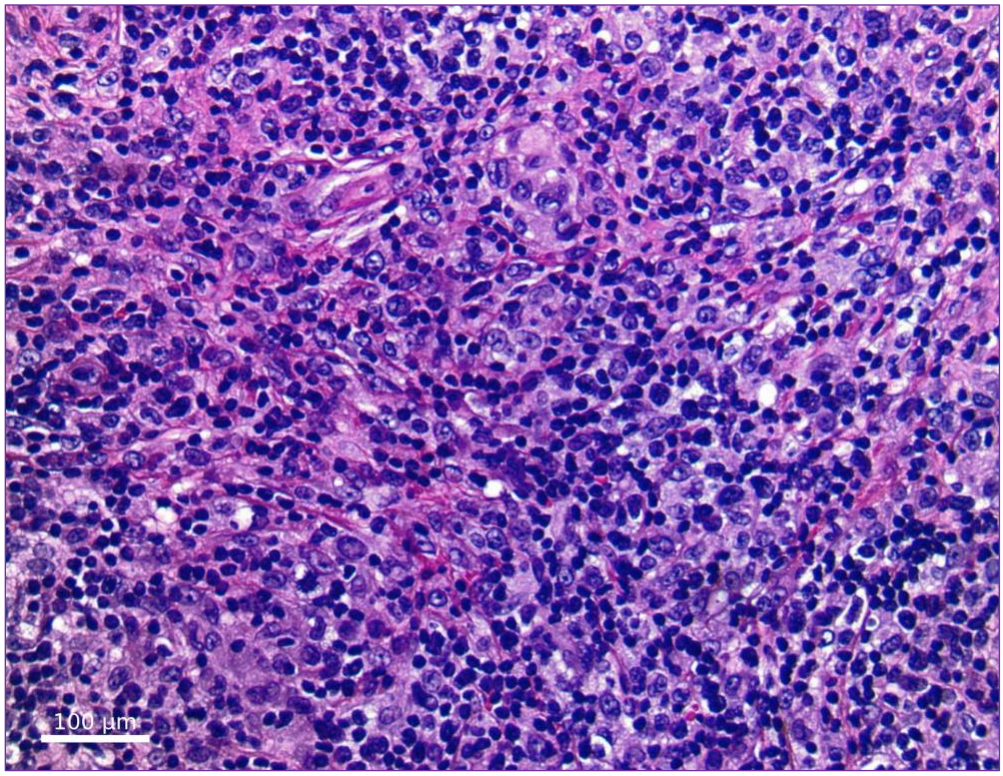

Figure 3. Histopathology slide of the specimen shown at 20x magnification demonstrating the abnormal infiltrate of lymphocytes consisting of CD4-positive T cells (90%), CD8-positive T cells (10%) with a few plasma cells present.

cases of multiple lesions, atypical lesion locations, symptoms including pain and pruritus as well as reports in children.[4-9] It should be noted that in many reported cases of PCSM-TCLPD, the lesions tend to have a relatively quick onset, growing rapidly over the course of a few weeks.[1,6,8] Presentation with or progression to systemic disease is rare and likely not consistent with a diagnosis of PCSM-TCLPD.[4]

Histopathologic examination remains the cornerstone for diagnosing PCSM-TCLPD. Histopathological features characteristically include a dense nodular or diffuse lymphocytic infiltrate including a predominant T-cell population with a follicular T-helper phenotype (CD3+, CD4+, CD8-) and expression of PD-1, BCL-6 and CXCL13 with admixed B-cells, plasma cells and eosinophils. Proliferation as measured by Ki-67 expression is usually less than 10-20% and monoclonal T-cell receptor beta or gamma-chain gene rearrangements are common.[2,4,10,11] Prognosis is exceptional with a reported 5-year survival of nearly 100% and a large proportion of cases spontaneous resolving after initial biopsy.[2,11]

There is no specific consensus regarding management of PCSM-TCLPD, but typically conservative local treatment is recommended. Treatment options include observation, surgical excision, topical, oral, or intralesional corticosteroids, doxycycline, and, in rare cases, radiotherapy or chemotherapy.[9,10] However, due to the potential for spontaneous regression after biopsy, conservative treatments are preferred initially. Unlike many lymphoproliferative disorders, PCSM-TCLPD has been observed to spontaneously regress following biopsy in a significant portion of cases.[2] One possible reason for this could be that the act of performing a biopsy typically causes local inflammation and may provoke

an immune response against any remaining irregular cells. While biopsy remains essential for confirming the diagnosis, unnecessary procedures may be avoided in patients with PCSM-TCLPD, particularly if the lesion does not recur after biopsy. Clinicians should weigh the risks and benefits of invasive procedures considering factors such as lesion size, location, and patient preference. No standardized guidelines exist regarding follow up for patients with PCSM-TCLPD.[2] A review of follow-up periods in published cases of PCSM-TCLPD have means ranging from 9-36 months.[1] Given the benign nature of PCSM-TCLPD in many cases, the need for frequent and intensive surveillance may be questioned. However, the potential for recurrence or progression necessitates follow-up and an individualized approach should be taken based on patient characteristics and disease features.

CONCLUSION

In conclusion, PCSM-TCLPD is a rare lymphoproliferative disorder characterized by an indolent course and favorable prognosis. Given its rare nature and variable clinical presentation, accurate diagnosis relies on histopathological analysis and immunophenotyping. Management is primarily focused on conservative local treatments. Clinicians should be aware of PCSM-TCLPD and consider it in the differential diagnosis of solitary cutaneous nodules. Continued research is necessary to enhance our understanding of this condition and optimize patient outcomes.

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