PRIMARY CUTANEOUS CD4+ SMALL/MEDIUM T-CELL LYMPHOPROLIFERATIVE DISORDER PRESENTING WITH LOCALIZED FOREARM LESIONS
ARM LESIONS IN CUTANEOUS CD4+ T-CELL LPD

LOKALİZE ÖNKOL LEZYONLARIYLA SEYREDEN PRİMER KUTANÖZ CD4+ KÜÇÜK/ORTA T HÜCRELİ LENFOPROLİFERATİF BOZUKLUK

KOLDA CD4+ T HÜCRELİ LENFOPROLİFERATİF BOZUKLUK

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ABSTRACT

Primary cutaneous CD4+ small/medium T-cell lymphoproliferative disorder (CD4+PCSM-LPD) is a rare and indolent lymphoproliferative condition characterized by atypical CD4+ T-cell infiltrates confined to the skin. We report the case of a 46-year-old male who presented with multiple asymptomatic red-to-violaceous papules and nodules localized on the left forearm, persisting for two years. Histopathological examination of a skin biopsy revealed a dermal infiltrate composed predominantly of small-to-medium atypical T lymphocytes with focal epidermotropism. Immunohistochemical staining confirmed CD4 positivity and excluded B-cell lineage markers. Further systemic evaluation showed no evidence of extracutaneous involvement. The patient was treated with topical corticosteroids and oral doxycycline, and marked clinical improvement was observed within one month. No recurrence or new lesions were observed during the 1-year follow-up period. This case highlights the importance of considering CD4+PCSM-LPD in the differential diagnosis of cutaneous lymphoid infiltrates and suggests that conservative therapeutic approaches may be considered in the management of localized disease.

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ÖZET

Primer kutanöz CD4+ küçük/orta T hücreli lenfoproliferatif bozukluk (CD4+PCSM-LPD), deriye sınırlı atipik CD4+ T hücre infiltratlarıyla karakterize nadir ve yavaş seyirli bir lenfoproliferatif hastalıktır. Bu yazıda, iki yıldır sol önkolda lokalize, asemptomatik, kırmızı-mor renkli çok sayıda papül ve nodülle başvuran 46 yaşında bir erkek olgu sunulmaktadır. Deri biyopsisinin histopatolojik incelemesinde, odaklanmış epidermotropizm gösteren, küçük-orta boyutlu atipik T lenfositlerden oluşan dermal infiltrasyon izlendi. İmmünohistokimyasal boyama CD4 pozitifliğini doğrularken B hücre soyuna ait belirteçler negatif bulundu. Sistemik değerlendirmede ekstrakutanöz tutulum saptanmadı. Hastaya topikal kortikosteroid ve oral doksisiklin tedavisi uygulanarak bir ay içinde belirgin klinik iyileşme izlendi. Bir yıllık izlem süresince nüks veya yeni lezyon gelişimi gözlenmedi. Bu olgu, kutanöz lenfoid infiltratların ayırıcı tanısında CD4+PCSM-LPD'nin dikkate alınması gerektiğini ve lokalize hastalıklarda konservatif tedavi yaklaşımlarının değerlendirilebileceğini vurgulamaktadır.

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A preliminary version of this case was previously presented as a poster presentation by Aslı Aldemir at the 32nd National Dermatology Congress on November 22, 2024.

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Introduction

Primary cutaneous CD4+ small/medium T-cell lymphoproliferative disorder (CD4+PCSM-LPD) is a rare subtype of cutaneous T-cell proliferations with an indolent course and incompletely defined pathogenesis (1). Although part of the cutaneous lymphoid proliferation spectrum, its biological behavior and optimal management remain uncertain due to the lack of large-scale studies.

Clinically, CD4+PCSM-LPD usually presents as a solitary, slow-growing red-to-violaceous papule or nodule on the head, neck, or upper extremities (2). Histopathology typically shows a dermal infiltrate of small-to-medium pleomorphic CD4+ T cells (3). Epidermotropism may be focal but is not dominant, complicating distinction from other proliferations (4).

Because of its rarity and overlap with aggressive lymphomas, it may be misdiagnosed or overtreated. Awareness of its unique clinicopathological features is crucial to avoid unnecessary interventions.

Here we report an unusual case of CD4+PCSM-LPD presenting with multiple asymptomatic lesions on the left forearm. By detailing the diagnostic process and therapeutic response, this case adds to the literature and underscores the importance of clinicopathological correlation to prevent overtreatment.

Case Presentation

A 46-year-old male patient presented to our dermatology outpatient clinic with asymptomatic erythematous lesions localized to the left forearm. The lesions had gradually developed and persisted for about two years without pain, pruritus, or systemic symptoms. His personal medical history was unremarkable; however, his brother had been diagnosed with an abdominal desmoplastic small round cell tumor.

On dermatological examination, multiple well-demarcated red-to-violaceous papules and nodules, measuring 3 to 10 mm in diameter, were observed on the extensor surface of the left forearm (Figure 1A). There was no ulceration, crusting, or evidence of secondary infection.

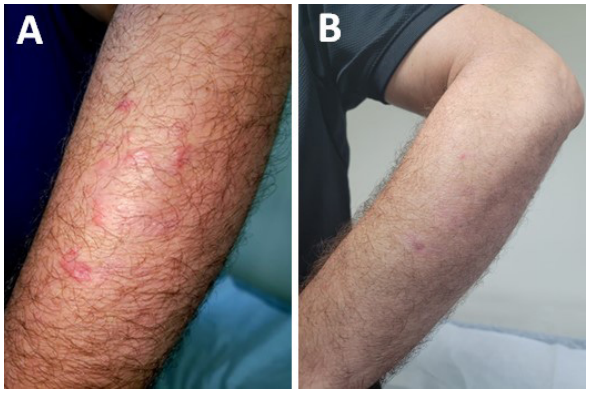

Figure 1. (A) Multiple red-to-violaceous papules and nodules measuring 3–10 mm in diameter on the left forearm at initial presentation and (B) marked regression of the papular and nodular lesions at the patient's one-month follow-up examination after treatment with topical corticosteroids and oral doxycycline.

A 4-mm punch biopsy was obtained from a representative lesion. Histopathological evaluation demonstrated a dense perivascular, periadnexal, and interstitial dermal infiltrate composed predominantly of small-to-medium-sized atypical lymphocytes with focal epidermotropism (Figure 2A). Immunohistochemical staining revealed diffuse positivity for CD3 and CD4, with focal positivity for CD8 (Figure 2B). The neoplastic infiltrate was negative for B-cell markers including CD10, CD20, CD21, PAX5, and MEM1, as well as for CD30, CD117, and ALK1. Bcl-2 was positive. Based on the clinical presentation, histopathological features, and immunophenotypic profile, a diagnosis of CD4+PCSM-LPD was established.

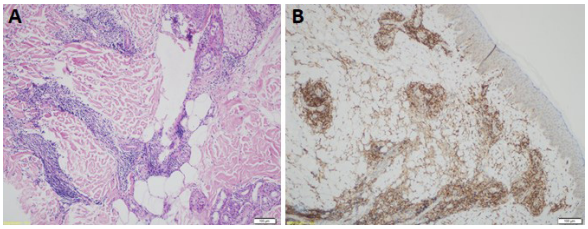

Figure 2. (A) Atypical lymphoid cells infiltrating the deep dermis and interstitial areas, Hematoxylin and Eosin, 100× and (B) Atypical cells showing CD4 positivity in perivascular, periadnexal, and interstitial areas, CD4 immunohistochemical staining, 100×.

Following histopathological diagnosis, the patient was referred to the hematology department for further evaluation. A comprehensive diagnostic workup was recommended, including complete blood count, biochemical panel, peripheral blood smear, superficial ultrasonography for lymph node assessment, and thoracic computed tomography. All laboratory investigations—including hematological and biochemical parameters and the peripheral blood smear—were within normal limits. Thoracic computed tomography and superficial ultrasonography of the cervical, axillary, and inguinal regions revealed no evidence of pathological lymphadenopathy. Although extensive imaging is not always mandatory in localized and clinically indolent cases of CD4+PCSM-LPD, positron emission tomography (PET) imaging was recommended in this patient as part of the hematological evaluation. The patient declined PET imaging.

The patient was initiated on a regimen consisting of topical 0.05% diflorasone diacetate ointment (once daily for two weeks), followed by 0.1% mometasone furoate ointment (once daily for two weeks), in conjunction with oral doxycycline 100 mg/day for 14 days. At one-month follow-up, marked clinical regression of the papular and nodular lesions was observed (Figure 1B). Over a 1-year follow-up period, no new lesions or recurrence was noted. Clinical surveillance of the patient is ongoing, with no evidence of systemic progression or cutaneous relapse to date.

Discussion

CD4+PCSM-LPD represents a distinct entity among cutaneous lymphoproliferative diseases. Classified as lymphoma in WHO 2008, it was redefined in 2016 as a lymphoproliferative disorder due to its indolent course, favorable prognosis, uncertain malignant potential, and absence of systemic progression (1). This reclassification highlights the need for a careful diagnostic and therapeutic approach, as CD4+PCSM-LPD's clinical behavior diverges significantly from more aggressive cutaneous lymphomas.

Epidemiologically, CD4+PCSM-LPD is rare, comprising about 3% of primary cutaneous lymphomas, usually affecting middle-aged to elderly adults, though pediatric cases are reported (1). Most patients are asymptomatic, with solitary, slowly evolving red-to-violaceous papules or nodules on the face, neck, or trunk (1). Histopathology shows a dermal infiltrate of small-to-medium pleomorphic CD4+ T lymphocytes with histiocytes and plasma cells, often extending subcutaneously (3). Immunohistochemically, tumor cells express CD3 and CD4, with variable PD1 aiding distinction from other T-cell proliferations (2).

Differential diagnosis is crucial, particularly against localized mycosis fungoides, where epidermotropism is a characteristic feature. In CD4+PCSM-LPD, epidermotropism is minimal or absent, and when present, it is typically focal (4). In our case, localized mycosis fungoides was considered due to the presence of focal epidermotropism; however, the predominance of a dermal small-to-medium-sized CD4+ T-cell infiltrate, the limited and non-dominant epidermotropism, and the absence of typical clinicopathological features of mycosis fungoides favored CD4+PCSM-LPD. Reactive cutaneous lymphoid infiltrate was also included in the differential diagnosis; however, the presence of atypical lymphoid morphology and the

immunophenotypic profile supported a lymphoproliferative disorder rather than a reactive process. Accurate identification is vital, as therapeutic approaches and prognostic implications differ markedly between these entities.

Several clinicopathological factors have been linked to adverse outcomes in cutaneous T-cell lymphoproliferative disorders. These include the presence of disseminated lesions, rapid tumor proliferation, and an elevated percentage (exceeding 30%) of large pleomorphic CD30+ T lymphocytes or increased cellular proliferation indices, features more commonly associated with aggressive lymphomas and warranting heightened clinical vigilance (5).

CD4+PCSM-LPD has an excellent prognosis, with a 5-year survival of 100% and no progression to systemic lymphoma reported (6). Extensive imaging or bone marrow biopsies add little value in staging (7). Localized disease responds well to excision, radiotherapy, or topical/intralesional corticosteroids, which provide rapid regression with good safety (6). Intriguingly, spontaneous remission following diagnostic biopsy has been reported, suggesting an inherent potential for disease quiescence (8). Moreover, case reports have documented complete remission achieved with oral doxycycline, highlighting an intriguing therapeutic avenue that warrants further exploration (9).

Our patient showed marked lesion regression with oral doxycycline and a potent topical corticosteroid, consistent with prior reports of complete or partial remission using doxycycline (9). This supports doxycycline as a non-invasive, immunomodulatory option and reinforces the role of conservative management in cutaneous pseudolymphomas.

Conclusion

CD4+PCSM-LPD follows an indolent course with an excellent prognosis. Management should focus on close monitoring and conservative therapies, reserving systemic treatment for exceptional progressive cases. Our case demonstrated marked clinical regression following topical corticosteroids and oral doxycycline treatment, suggesting that conservative therapeutic approaches may be a reasonable option in selected localized cases. However, the individual contribution of doxycycline, topical corticosteroid therapy, biopsy-related regression, and the natural course of the disease cannot be clearly distinguished.

Limitations

This is a single-case report, limiting generalizability. PET imaging was not performed and might have provided additional information on subclinical systemic involvement. Larger case series are needed to refine optimal diagnostic and therapeutic strategies for CD4+PCSM-LPD.

Ethics Statement: Written informed consent was obtained from the patient for publication of this case report and accompanying images.

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