Primary cutaneous CD4+ small/medium-sized pleomorphic T-cell lymphoproliferative disorder in a young woman

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Abstract

Primary cutaneous CD4+ small/medium T-cell lymphoproliferative disorder (CD4+PCSM-LPD) is a low-grade cutaneous T cell disorder. There is no standardized approach to treatment of CD4+ PCSM-LPD due to its rarity. Herein, we discuss a 33-year-old woman with CD4+PCSM-LPD which resolved after a partial biopsy. We highlight that conservative and local treatment modalities should be considered prior to utilizing more aggressive and invasive treatment options.

Keywords: CD4+PCSM-LPD, CD4+, cutaneous lymphoma, lymphoproliferative disorder, medium, small, T cell

Introduction

Primary cutaneous CD4+ small/medium T-cell lymphoproliferative disorder (CD4+PCSM-LPD) is a rare, poorly understood low-grade cutaneous T-cell disorder that is characterized by the major prevalence of small to medium-sized CD4+ pleomorphic T cells [1]. It typically presents as a violaceous or erythematous papule, plaque, nodule, or tumor [2], most commonly located on the face, neck, or upper limbs [3]. Patients with a single lesion have a favorable prognosis, with a 5-year survival rate greater than 60% [3].

We report a case of CD4+PCSM-LPD and discuss this patient's clinical and histopathologic findings in the context of emerging knowledge about this condition. We hope this addition to the literature will help characterize CD4+PCSM-LPD to reduce misdiagnosis and aggressive treatments.

Case Synopsis

A 33-year-old woman was referred for evaluation of a painful cyst on the right antihelix of 6 weeks' duration, which had decreased in size after a 7-day course of antibiotics but did not completely resolve. Physical examination revealed a smooth light purple 2cm nodule on the right scaphoid fossa. The lesion was firm, non-mobile, and tender to palpation; no punctum was appreciated (**Figure 1**).

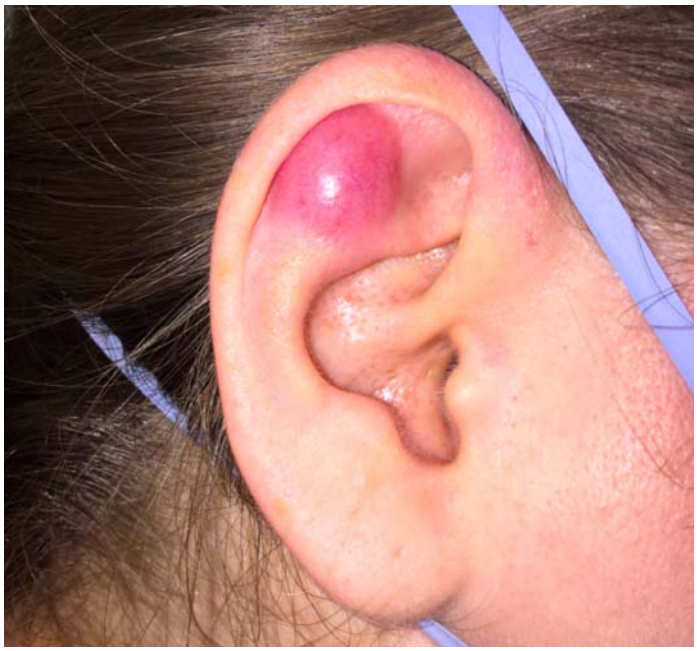

Figure 1. *A solitary firm, non-mobile, smooth light purple 2cm nodule on the right scaphoid fossa.*

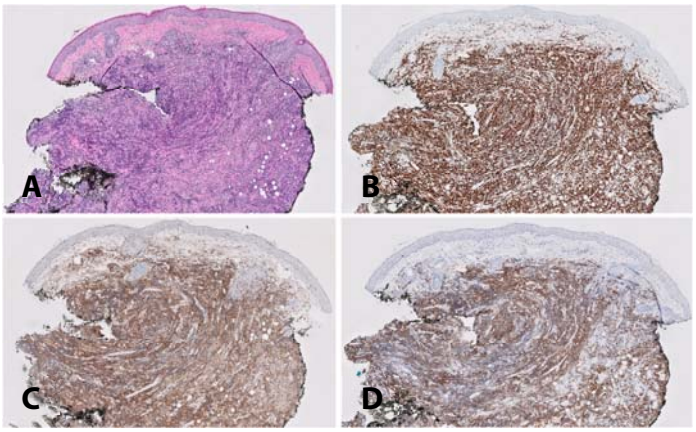

Figure 2. *Primary cutaneous CD4+ small/medium T-cell lymphoproliferative disorder (CD4+PCSM-LPD) H&E and immunohistochemistry (IHC)***. A)** *Histologically, CD4+PCSM-LPD is seen as dense, nodular-to-diffuse pan-dermal infiltrates of small/medium-sized neoplastic lymphoid cells (H&E, 40×.* ***B)*** *CD3 highlights the neoplastic cells. IHC, 40×.* ***C)*** *CD4 is co-expressed by a majority of the neoplastic cells. IHC, 40×.* ***D)*** *CD20 highlights a notable admixture of B cells. IHC, 40×.*

Given the atypical appearance, a 4mm punch biopsy of the nodule was sent for histopathologic examination; this showed a nodular-to-diffuse pan-dermal infiltrate comprised of small-to-medium-sized atypical lymphoid cells exhibiting variable pleomorphism admixed with histiocytes and fewer plasma cells and eosinophils. By immunohistochemistry, a majority of the atypical lymphoid cells showed CD3 and CD4 expression (**Figures 2, 3**). PD1 highlighted a subset of the atypical lymphoid cells, with occasional small clusters and rosette-like arrangements seen. A considerable admixture of B cells was highlighted by CD20; in situ hybridizations for kappa and lambda immunoglobulin light chain RNA showed polytypic light chain expression. High throughput sequencing (HTS) at Adaptive Biotechnologies demonstrated dominant sequences in TCR beta and TCR gamma, supporting a diagnosis of CD4+PCSM-LPD.

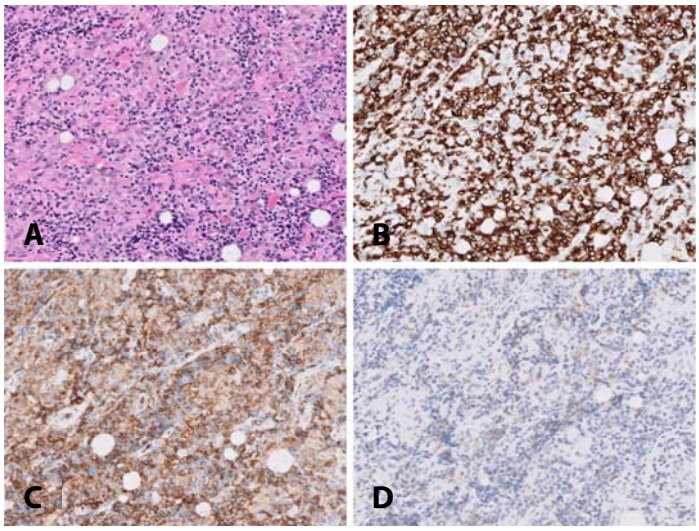

Figure 3. *Primary cutaneous CD4+ small/medium T-cell lymphoproliferative disorder (CD4+PCSM-LPD), higher power H&E and immunohistochemistry (IHC).* ***A)*** *On higher power, CD4+PCSM-LPD is comprised of small/medium-sized neoplastic lymphoid cells exhibiting variable pleomorphism. The background inflammatory cell infiltrate contains abundant histiocytes. H&E, 200×.* ***B)*** *CD3 highlights the neoplastic cells. IHC, 200×.* ***C)*** *CD4 is co-expressed by a majority of the neoplastic cells with a subset of background histiocytes showing dimmer staining. IHC, 200×.* ***D)*** *PD1 highlights a subset of the atypical cells with occasional small clusters and rosette-like arrangements seen. IHC, 200×.*

Complete blood count, comprehensive metabolic panel, lactate dehydrogenase, serum protein electrophoresis, and urine protein electrophoresis were within normal limits. Peripheral blood flow cytometry immunophenotyping showed heterogeneous lymphocytes without aberrant antigen expression. Computed tomography of the neck, abdomen, and pelvis confirmed no pathologic adenopathy. Findings demonstrated no evidence of a hematolymphoid neoplasm.

Approximately one month after the biopsy, the nodule had resolved without intervention, consistent with CD4+PCSM-LPD. The patient was counseled to self-monitor for development of any unusual adenopathy or regression of the lesion and to follow-up with her primary care physician.

Case Discussion

CD4+PCSM-LPD is a rare disease, formerly classified as a primary cutaneous lymphoma, that usually presents as a solitary lesion on the head or neck [4]. Because it exhibits indolent behavior, uncertain malignant potential, and lack of long-term risk of secondary lymphomas or serious sequelae, the World Health Organization to recently updated the disease classification to a "lymphoproliferative disorder" rather than a lymphoma [6,7].

Though there is a paucity of data, $CD4^{+}$ PCSM-LPD generally presents in adults, with an average diagnosis at 50-60 years of age and equal

distribution in males and females [1]. Although fewer young people are affected, our 33-year-old patient highlights that this entity should be included in the differential diagnosis of a solitary lesion on the head or neck.

On pathological evaluation, CD4+PCSM-LPD is typified by dense, nodular-to-diffuse dermal infiltrates comprised of small-to-medium-sized T cells with a minor subset demonstrating pleomorphism admixed with histiocytes and plasma cells [3]. Epidermotropism is inconspicuous in most cases. By immunohistochemistry, the atypical T cells characteristically express CD3, CD4, and variable PD1, as was seen in our case [3]. The major differential diagnosis considerations include mycosis fungoides which characteristically shows a notable intraepidermal component and angioimmunoblastic T-cell lymphoma given the overlapping expression of T follicular helper markers (i.e., PD1, BCL6, CXCL13). However, the diagnosis of CD4+PCSM-LPD depends heavily on clinicopathologic correlation and should be considered only if there is a solitary lesion exhibiting the aforementioned immunomorphologic findings with large cells representing only a minority of the infiltrate and virtual absence of significant epidermotropism.

There is no standardized approach to treatment of CD4+ PCSM-LPD due to its rarity and many lesions undergo spontaneous remission after partial biopsy. Hence, clinical observation may be considered [1]. If treatment is needed, CD4+ PCSM-LPD generally has an excellent response to less invasive and local skin-directed therapies such as corticosteroids (topical or intralesional) and local radiotherapy [1,8]. When needed, CD4+PCSM-LPD may be managed with local excision as well, which has been shown to achieve complete remission [8]. In a recent review of 112 cases, 15% resolved spontaneously following biopsy and 95.5% of treated cases experienced complete resolution with no recurrence (with excision being the most common treatment), [9].

Conclusion

CD4+PCSM-LPD is a poorly understood disorder with a favorable prognosis with no reported long-term risk of secondary lymphomas [5]. As CD4+PCSM-LPD is so rare, case reports are the primary means of expanding collective knowledge about its presentation and prognosis. We report this case of CD4+PCSM-LPD which resolved after a partial biopsy and have summarized the recent literature to highlight that conservative and local treatment modalities should be considered prior to utilizing more aggressive and invasive treatment options.

Potential conflicts of interest

The authors declare no conflicts of interest.

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