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Acral angiokeratoma-like pseudolymphoma in a middle-aged woman

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Abstract

Acral angiokeratoma-like pseudolymphoma is a rare type of pseudolymphoma presenting as dark-red papules on the hand or foot. We describe a 59 year old woman who presented with an unusual unilateral, clustered aggregate of scaly violaceous papules on the toe with an indolent course. Skin biopsy showed a prominent vascular proliferation associated with a dermal infiltrate of monoclonally rearranged T-follicular helper phenotype T-cells, in keeping with CD4+ small/medium T-cell lymphoproliferative disorder (SMPTC-LPD). Based on the unique clinical morphology, distribution of the lesions and dermoscopic appearance, a clinicopathologic diagnosis of acral angiokeratoma-like pseudolymphoma was favored. This case demonstrates the importance of clinicopathological correlation in such diagnostically challenging patients who present with overlapping features on the spectrum of pseudolymphoma and cutaneous T-cell lymphoma.

Keywords

cutaneous T-cell lymphoma; pseudolymphoma; skin cancer

Introduction

Primary cutaneous CD4+ small/medium T-cell lymphoproliferative disorder (SMPTC-LPD) and so-called cutaneous pseudolymphoma of the T-cell variety are, in many cases, different descriptors for the same indolent T-lymphocytic proliferation disorder¹. Differentiating between the two entities has been attempted in the past, but may be neither possible nor useful, due to the overlap of clinical appearances and histopathological findings². We describe a case of a middle-aged woman presenting with unusual clinical and histopathological findings that are compatible with a rare pseudolymphoma type known as acral angiokeratoma-like pseudolymphoma, with characteristic histopathologic and molecular features of SMPTC-LPD. Cautious evaluation and follow up were recommended to ensure the ongoing low-grade behavior in this challenging case.

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Case report

A 59-year-old female presented with a two year history of asymptomatic scaly red papules on her left first toe. The patient did not recall any prior insect bite or trauma to the toe. She denied fevers, chills or weight loss. She did not have a significant past medical history nor a family history of skin cancers or hematologic malignancies. On physical examination, two non-tender erythematous-violaceous papules with surrounding scale were seen on the lateral volar aspect of her left first toe (Fig. 1A). The rest of the patient's skin was of normal appearance without lymphadenopathy. Under dermoscopy, the papules exhibited structureless violaceous areas with multicolored areas (rainbow pattern); central and peripheral scaling were noted (Fig. 1B). The clinical differential diagnosis included a vascular or adnexal tumor such as Kaposi's sarcoma, hemangioma/angiokeratoma, pyogenic granuloma or poroma. Outside our institution, a biopsy of the proximal papule was performed. This specimen and a subsequent in-house biopsy specimen were reviewed. Both biopsies showed a mildly dome-shaped, dense, diffuse lymphohistiocytic infiltrate in the dermis with plasma cells. Lymphocytes were small to medium in size with slight nuclear pleomorphism and minor anisocytosis (Fig 2A). Thin to thick walled mid-sized irregularly shaped blood vessels were dispersed evenly throughout the lymphoid infiltrate and a small superficial capillary proliferation was apposed along the dermoepidermal junction (Fig 2A, 2B). The epidermis above the infiltrate was attenuated to atrophic, with transition to the expected hyperkeratotic epidermis at the periphery of the dome shape, where a minor epithelial collarette extended into dermis (Fig 2B). Immunohistochemical studies showed that the predominant population was of CD3, CD2, CD5, CD7, CD4, CD43, and PD-1 positive T-cells (Fig 3A, B) with an elevated CD4:CD8 ratio. CD20, CD79a, and PAX5 highlighted aggregates of B-cells in the mid-aspect of the infiltrate (Fig 3B). CD163 showed scattered histiocytes throughout the lesion (Fig 3C), while a Ki-67 immunostain demonstrated a proliferation index of 5-10%. Polymerase chain reaction (PCR) studies for T-cell receptor (TCR) genes showed T-cell monoclonality while immunoglobulin heavy chain rearrangements were polyclonal (negative). The histological and immunohistochemical findings were consistent with a low grade lymphoproliferative disorder, and based on the immunophenotype and molecular findings, fit best for a primary cutaneous CD4+ small/medium T-cell lymphoproliferative disorder. However, with clinicopathologic correlation, given the vascular proliferation and in consideration of the characteristic typical low-grade behavior of SMPTC-LPD, a diagnosis of pseudolymphoma of the acral angiokeratoma-like type was favored. The patient was reassured about the benign behavior of this uncommon skin condition. In light of the unusual overlapping features of rare pseudolymphoma type and SMPTC-LPD, positron emission tomography computed tomography (PET-CT) was ordered and showed no evidence of extracutaneous disease. The patient was referred for local radiation therapy of the digital lesions.

Discussion

Acral angiokeratoma-like pseudolymphoma is a rare benign condition characterized by clustered unilateral erythematous-violaceous scaly papules on the hand or foot³. The etiology of this unique condition is unknown and no preceding events are identified. Histologically, the lesions show a dense polyclonal lymphocytic infiltrate populating the

superficial dermis and accompanied by a proliferation of thick-walled blood vessels^{3,4}. The indolent chronic course of this condition as well as a lack of systemic involvement, malignant progression or recurrences in previously published cases (that were either observed or excised) further support its non-lymphomatous nature^{3,4}. Topical or intralesional corticosteroid therapies achieve no improvement at all or result in temporary partial response³⁻⁵. This entity was first described in children and was named acral pseudolymphomatous angiokeratoma of children (APACHE)⁶. However, the histological findings of prominent blood vessels within the dense dermal lymphocytic infiltrate without vascular dilatation in the upper dermis are inconsistent with angiokeratoma. In our case, the dermoscopic appearance of the lesion (Fig. 1B) did not support the diagnosis of angiokeratoma, lacking the classical and sensitive features of red lacunae, further sustaining the concept that this is not a true angiokeratoma. Acral pseudolymphomatous angiokeratoma of children was reported to present with dermoscopic rainbow pattern⁷ as was seen in our case.

Various studies have investigated the dermal lymphocytic infiltrate of T-cells predominance (CD4+ cells³, CD8+ cells⁶ or both^{5,8}), B-cells predominance⁸ or admixture of the two^{4,8-10} concluding this entity as a unique type of pseudolymphoma^{5,9,10}. Clonal analyses of the lymphocytic infiltrate showed no evidence of clonality, suggesting that these infiltrates were polyclonal both for B and T cells.^{8,10,11} A recent study of the vascular component within the dermal infiltrate in this condition demonstrated the expression of Wilms tumor-1 (WT-1) by the prominent blood vessels, favoring a proliferative vascular process rather than vascular malformation¹². This finding supports the concept that the prominent vasculature is probably secondary to the dense lymphocytic infiltration as a result of local hypoxia or cytokine influence.

A review of 26 previously published APACHE cases reported that this uncommon condition is more frequent in females (77%) on acral regions (52%), mostly involving the foot, and 30% of the cases were reported in adult patients¹³. Unlike other previous cases, the skin biopsy in our patient was positive for monoclonal T-cell population, a finding which is more consistent with lymphoma, but which may be found infrequently in pseudolymphoma¹⁴. A low grade lymphoproliferative disorder such as CD4+ SMPTC-LPD is included in the histopathological differential diagnosis of a dense dermal T-follicular helper (Tfh) phenotype lymphocytic infiltrate² as was seen in the current case. The distinction of SMPTC-LPD from pseudolymphoma is challenging and it is debated whether it should be considered a lymphoma at all. Recently, the 2016 revision of the WHO classification of lymphoid neoplasms modified the terminology of primary cutaneous CD4+ small/medium-sized pleomorphic T-cell lymphoma into primary cutaneous CD4+ small/medium T-cell lymphoproliferative disorder to reflect the limited clinical risk and uncertain significance of a malignant diagnosis in this localized disease¹⁵. CD4+ SMPTC-LPD presents as a solitary nodule or plaque in most of the cases, located mostly on the head and neck or upper trunk, and has an indolent clinical course^{1,16}. Clinically, the morphology and distribution of two adjacent scaly vascular papules localized to the toe are very unusual for SMPTC-LPD. Cutaneous involvement by a peripheral T-cell lymphoma, such as angioimmunoblastic T-cell lymphoma (AITL) that can present histologically with dense lymphocytic infiltrate rich in

Tfh cells and vascular hyperplasia¹⁷, was ruled out as the patient presented with a chronic indolent course, localized papular disease and no constitutional symptoms.

The presented patient is a 59-year-old-woman with a 2-year history of indolent, scaly violaceous vascular-appearing papules on the greater toe. A clonal T-cell lymphocytic dermal infiltrate predominated by CD4+/PD-1+ cells is in keeping with SMPTC-LPD, however the patient's age and gender, as well as the morphology of the lesions their distribution and dermoscopic appearance are more consistent with acral angiokeratoma-like pseudolymphoma. Clinicopathologic correlation is important in such cases in order to avoid over-diagnosis of low grade cutaneous lymphoma, and mis-diagnosis of high grade lymphoma.

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Fig. 1.

Clinical images of the acral lesions. (A) Scaly erythematous-violaceous papules on the lateral aspect of the left first toe. (B) Dermoscopic appearance of the distal papule show structureless violaceous areas displaying a rainbow pattern, scaling and a focal hemorrhagic crust are seen as well.

Fig. 2.

Histopathology of an acral papule. (A) Hematoxylin & eosin, 400x. Dense dermal lymphoid infiltrate with plasma cells showing mild nuclear pleomorphism. Associated blood vessels are rounded in some foci and ectatic in others with variable thickness of the vessel wall..(B) Hematoxylin and eosin, 200x, shows the overlying attenuated epidermis, adjacent hyperkeratosis, small epithelial collarette, and superficial capillary proliferation as well as slight thickening of the intralesional blood vessels.

Fig 3.

Immunohistochemistry A. CD4 labels the vast majority of lymphocytes B. PD-1 co-labels the CD4+ population C. CD20 shows single and aggregated B-cells and D) CD163 positive histiocytes typically seen within T- follicle helper cell proliferations such as CD4+ small/medium T-cell lymphoproliferative disorders.