


# The enigmatic ear: Unveiling a rare case of a primary cutaneous CD8+ acral T-cell lymphoproliferative disorder with a literature review

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## Abstract

**Introduction:** Primary cutaneous CD8+ acral T-cell lymphoproliferative disorder (CD8+ ATCLPD) is a rare form of cutaneous T-cell lymphoma that commonly presents on the acral regions of the body. We report a case of a 61-year-old man diagnosed with primary cutaneous CD8+ ATCLPD of the ear. **Case presentation:** A 61-year-old man presented with a non-healing, erythematous painful macule on the ear that had been evolving for the past 3 months. The lesion was resected, and histopathological examination revealed a primary cutaneous CD8+ ATCLPD with acral localization. Further investigations including CT scan of the thorax, abdomen and pelvis were done to stage the disease. The results showed no extracutaneous involvement. **Conclusion:** Accurate identification of primary cutaneous CD8+ ATCLPD is crucial due to its distinct prognostic and therapeutic implications compared to other CD8+ cytotoxic lymphoid proliferations. Primary cutaneous CD8+ ATCLPD can be treated conservatively and typically follows a slow clinical course, regardless of the treatment method. Understanding the clinical context, as well as the morphological and immunophenotypic characteristics, can assist in making a precise diagnosis.

## Keywords

CD8-Positive, cutaneous T-cell, lymphoproliferative disorder, primary cutaneous acral

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## Introduction

Primary cutaneous CD8+ acral T-cell lymphoma is now classified as primary cutaneous CD8+ acral T-cell lymphoproliferative disorder (CD8+ ATCLPD), introduced in the 5th edition of WHO classification and the International Consensus classification in 2022.<sup>1,2</sup> It typically presents as solitary or, rarely, bilateral single nodular lesions at acral sites, namely the ears, face and feet.<sup>3</sup> It is characterized by skin infiltration of clonal atypical CD8+ cytotoxic T-lymphocytes. Due to its infrequency and resemblance to other CD8+ lymphoid proliferations in terms of morphology and immunophenotype, identifying this condition can be difficult. However, accurately categorizing this disease is

critical because of its slower clinical progression when compared to other CD8+ T-cell lymphomas. This case report focuses on a patient who presented with a painful lesion on palpation on his ear, which was initially thought to be an infection. Further examination and testing revealed a diagnosis of primary cutaneous CD8+ ATCLPD in the ear.

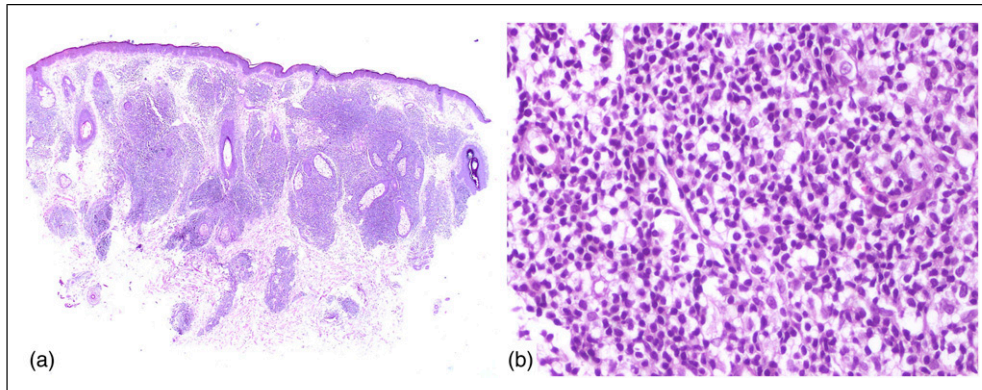
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**Figure 1.** (a)/Low power, H&E  $\times 20$ : Skin tissue showing a thinned-out epidermis and dense infiltration of dermis by lymphoid cells (b)/ High power, H&E  $\times 100$ : Dense infiltration with moderately atypical lymphoid cells.

The case highlights the importance of considering rare malignancies in the differential diagnosis of skin lesions and aim through a review of the literature to discuss the clinicopathological characteristics of this uncommon entity in this site.

### Case presentation

We present the case of a 61-year-old male who presented with a 3 cm macule on his right ear that had been evolving for 3 months. The patient did not report any significant medical history and had no symptoms other than mild pain on palpation. Initial physical examination revealed a solitary, pinkish-red, non-blanchable lesion with indistinct borders. No regional lymphadenopathy was noted. The patient was referred to a dermatologist for further evaluation. The dermatologist conducted a thorough clinical examination and considered various differential diagnoses, including an infectious or inflammatory process, as well as neoplastic conditions such as basal cell carcinoma and melanoma. The lesion was excised, and histopathological analysis revealed dense dermal infiltrates of medium-sized atypical lymphoid cells with small nucleoli. Mitotic figures were sparse (1-2 mitoses/10 HPF). There was no angiocentric and angiodestructive growth pattern. There was no epidermotropism. The epidermis was separated from the infiltrate by a grenz zone (Figure 1). Immunohistochemical staining showed a predominance of CD8+ T-cells, consistent with a diagnosis of primary cutaneous CD8+ ATCLPD of the ear. Tumor cells were negative for CD4, TdT, CD20, CD30, CD10, Bcl6, CD56, Granzyme B, and perforin. CD68 was focally positive with dot-like perinuclear staining. The Ki67 expression was low  $< 5\%$  (Figure 2). Chromogenic in situ hybridization was used to test for Epstein-Barr virus (EBV) using the EBER probe and revealed negative. Further evaluation with a computed tomography scan of the chest, abdomen, and pelvis was performed, and no evidence of systemic involvement was

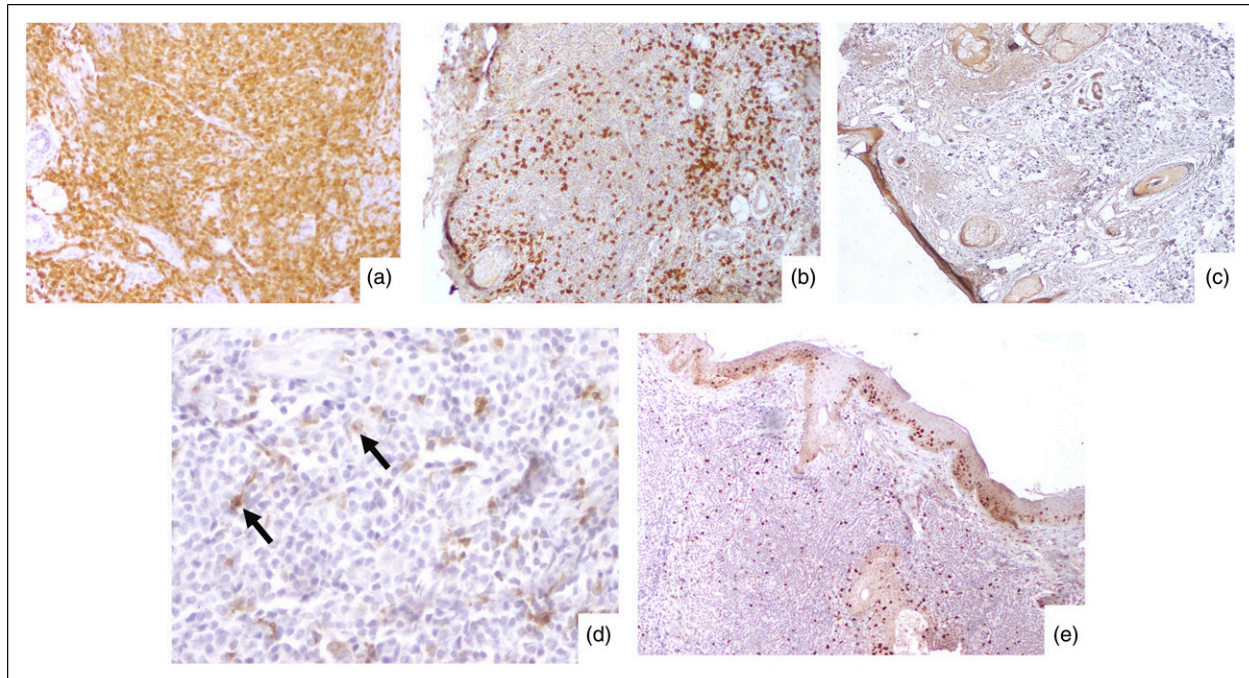
found. The patient is doing well after 2 years of follow-up, with no signs of disease recurrence or progression on extracutaneous sites.

### Discussion

Our patient had a slowly increasing erythematous lesion localized to the external ear with no systemic involvement, and a benign clinical course.

Primary cutaneous CD8+ ATCLPD most commonly affects adults over the age of 50, with a slight male predominance.<sup>4</sup> The majority of cases are characterized by a single, slowly developing nodule.<sup>5,6</sup> There have been reports of bilateral, symmetrical, and recurrent disease,<sup>4,7</sup> but without prior patches or plaques or recurrences.<sup>8,9</sup> Although most of instances involve the ear,<sup>10</sup> other peripheral areas, including the nose, hands, and feet, have also been reported.<sup>4,7,8</sup> One recent case reported a novel entity hitherto-undescribed of primary cutaneous CD8+ cutaneous lymphomas of T-cell lineage which is characterized by multifocal cutaneous localization that presented on the legs, later involving the ears bilaterally, with multiple lesions on each ear.<sup>3</sup> These results indicate that a local, antigenic stimulation localized to the ear is improbable.<sup>9</sup> There has also been suggestion that primary cutaneous CD8+ ATCLPD might be a reactive process due to the consistently indolent clinical course; nonetheless, the frequent monoclonality and aberrant loss of T-cell antigens support these lesions being a real lymphoproliferative condition.<sup>9</sup>

Petrella et al.,<sup>11</sup> described a diffuse proliferation of monomorphic, intermediate-sized CD8+ T-cells in the dermis and subcutis. Each example showed a clear grenz zone free of epidermotropism. The neoplastic cells exhibited lymphoblast-like nuclei that were irregular. CD3, CD8, T-cell receptor-F1, and T-cell intracytoplasmic antigen-1 were expressed in immunoperoxidase studies with a low proliferation index (10%). There was a varied loss of several T-cell antigens but no CD4, CD30, CD56, granzyme B, or Epstein-Barr virus-encoded



**Figure 2.** Immunohistochemical staining: (a)/CD8 highlighting the neoplastic cells (original magnifications  $\times 400$ ); (b)/Neoplastic cells negative for CD20 (original magnification  $\times 40$ ); (c)/Neoplastic cells negative for TdT (original magnification  $\times 20$ ); (d)/Tumor cells focally positive for CD68 with a dot-like staining (original magnification  $\times 40$ ); (e)/Low Ki-67 proliferation index (original magnification  $\times 40$ ).

small RNA. A monoclonal T-cell  $\gamma$ -gene rearrangement was seen in all three of the cases in the three cases that underwent molecular investigation.<sup>11</sup> Similarly, in our case, immunohistochemical staining showed a predominance of CD8+ T-cells, consistent with a diagnosis of primary cutaneous CD8+ ATCLPD of the ear. Tumor cells were negative for CD4, TdT, CD20, CD30, EBER, CD10, Bcl6, CD56, Granzyme B, and perforin.

Current research suggests that CD68 may serve as a selective marker to separate aggressive T-cell lymphomas with a cytotoxic CD8+ phenotype from primary cutaneous primary cutaneous CD8+ ATCLPD.<sup>12,13</sup> Wobser et al.<sup>12</sup> looked into 44 cases of CD8+ cutaneous T-cell lymphomas and found 5 cases of primary cutaneous acral CD8+ T-cell lymphoproliferative disorder. All 5 primary cutaneous CD8+ ATCLPD patients showed unique, dot-like perinuclear positivity for CD68 in the Golgi zone of malignant cells during immunohistochemistry study. They concluded that CD68 with a dotlike pattern may be useful in detecting primary cutaneous CD8+ ATCLPD because none of the other CD8+ cutaneous lymphomas expressed CD68. In the present case, CD68 was focally positive with dot-like perinuclear expression.

Biopsy and histological examination are typically required to confirm the diagnosis and distinguish it from other skin diseases. Immunohistochemical and molecular studies may also be necessary to differentiate primary cutaneous CD8+ ATCLPD from other cutaneous T-cell lymphomas.

Among CD8+ variations of mycosis fungoides, primary cutaneous CD8+ ATCLPD, and type D lymphomatoid papulosis, epidermotropism is the principal morphologic marker used to identify primary cutaneous CD8+ ATCLPD from these other conditions.<sup>6</sup> Although epidermotropism and a single intraepidermal Pautrier collection have been seen in a few uncommon cases of primary cutaneous CD8+ ATCLPD, the majority of cases show epidermal sparing with a distinct grenz zone.<sup>7</sup>

Despite having high-grade morphologic characteristics and a cytotoxic immunophenotype, primary cutaneous CD8+ ATCLPD always has an indolent clinical course.<sup>10</sup> Although there have been cases of cutaneous relapse, there are no reports of extracutaneous disease at diagnosis, and no staging investigations have revealed progression to systemic disease during follow-up durations of 3 to 168 months, regardless of the treatment technique (topical steroids, radiotherapy, surgical excision, or simple observation).<sup>4</sup> Patients with multifocal cutaneous disease have been treated with methotrexate, interferon, and psoralen-ultraviolet A phototherapy to reduce the chance of relapse, with varied degrees of success.<sup>4</sup> Our patient has just done a resection of the lesion.

## Conclusion

In conclusion, our case emphasizes the critical importance of accurate diagnosis and proper management of primary

cutaneous CD8+ ATCLPD. Misdiagnosis can lead to inappropriate treatment and delay in appropriate therapy. Accurate diagnosis of this rare condition requires a high index of suspicion, thorough clinical evaluation, and histopathological analysis of the tissue. Dermatologists, oncologists, and pathologists need to be aware of this rare entity and its clinical and histopathological features to avoid misdiagnosis.

### Credit authorship contribution statement

All the authors read and approved the final version of the manuscript. Ghada Sahraoui (MD): conception, acquisition of clinical data, and revising the manuscript. Farah Sassi (MD): conception, acquisition of data, literature research and preparing the manuscript. Lamia Charfi (MD): revising the manuscript. Raoudha Doghri (MD): manuscript editing and revising the manuscript critically. Karima Mrad (MD): revising and accepting the final version of the manuscript critically.

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### Ethical statement

#### Ethical approval

Salah Azaiez Institute does not require ethical approval for reporting individual cases or case series.

#### Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

### Guarantor

Sassi Farah.

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