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Corresponding Author
Vaibhav V. Bisne,
Department of General Medicine, D. Y. Patil Medical College and Hospital, Kolhapur, India
dr.vbisne@gmail.com

Author Designation
[1]Assistant Professor
[2]Junior Resident

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Primary Cutaneous CD8+ Aggressive Epidermotropic Cytotoxic T-Cell Lymphoma: A Case Report

[1]Rais Ahemad A.Patvegar and [2]Vaibhav V. Bisne
[1,2]Department of General Medicine, D.Y. Patil Medical College and Hospital, Kolhapur, India

Abstract
Primary Cutaneous CD8+Aggressive Epidermotropic Cytotoxic T-Cell Lymphoma (PCAE-CTL) is a rare and aggressive variant of cutaneous T-cell lymphoma. We present a case of a 29-year-old male with an unusual presentation of PCAE-CTL, characterized by crusted, fungating skin lesions, significant weight loss and a mild fever. The patient exhibited striking clinical features, including extensive skin lesions over the body. Biopsy findings revealed an epidermotropic infiltration of large lymphocytes with papillary dermal edema. Immunohistochemistry confirmed a CD8+T-cell lineage. PET-CT demonstrated multiple hyper metabolic subcutaneous nodules and ultrasound revealed hepatomegaly, splenomegaly and enlarged mesenteric lymph nodes. Initial antibiotic therapy with piperacillin-tazobactam yielded no improvement, leading to a shift to meropenem and clarithromycin. Unfortunately, the patient's health deteriorated rapidly and he passed away before chemotherapy initiation.

INTRODUCTION

Primary cutaneous CD8-positive aggressive epidermotropic cytotoxic T-cell lymphoma (PCAE-CTL) is an uncommon histopathological variant of cutaneous T-cell lymphoma (CTCL). This particular subtype was originally documented by Berti[1]. It was provisionally classified by the WHO in 2008[2] and has more recently been recognized as a rare yet distinct subtype in the latest WHO classification[3]. This rare condition accounts for <1% of all cases of CTCL. It is more frequently observed in the elderly population, typically during the sixth and seventh decades of life and exhibits a higher prevalence in males[1,4-6].

Primary cutaneous lymphomas (PCLs) are non-Hodgkin's lymphomas that develop in the skin with no signs of any extracutaneous disease at the time of diagnosis[7].

Currently, there is no established effective therapy for PCAE-CTL. This subtype has been documented as unresponsive to standard chemotherapy and its prognosis is exceedingly poor[8].

This case report introduces a singular and compelling clinical instance of PC-CD8+AECTCL in a 29-year-old male patient, marked by an uncommon and perplexing presentation.

Case Presentation: A 29-year-old male was referred to our hospital with a concerning and distressing clinical presentation. He presented with fever and crusted erythematous-scaling patches, plaques and papulonodular hemorrhagic lesions distributed prominently across various areas of his body, including the face, abdomen, limbs, neck and back. These symptoms had been present for 15 days. (Fig. 1a and 1b). He reported a 2-week history of mild fever with gradually extending nodular lesions. The patient's history was marked by significant weight loss since two months. He also reported experiencing intermittent abdominal pain over the past six months. During the physical examination, the patient's vital signs were stable, with an elevated temperature. Localized tenderness was observed over the abdomen and palpable lymph nodes were detected.

Laboratory investigations revealed a decreased white blood cell count (3300/cumm) and a reduced platelet count (57000/ul). Abdominal and pelvis ultrasound uncovered hepatomegaly, splenomegaly and the presence of enlarged mesenteric lymph nodes that formed a palpable mass in the right iliac fossa.

A diagnostic biopsy of the skin lesions revealed a nodular dense infiltrate of lymphocytes in both superficial and deep skin layers, with a predominant presence of large lymphocytes accompanied by papillary dermal edema. Notably, most of the lymphocytes within the dermal infiltrate exhibited large cell size, abundant cytoplasm, moderate nuclear atypia, marked pyknosis and significant extravasation of red blood cells (Fig. 2a and 2b).

Subsequent immunohistochemistry revealed were these lymphoid cells immune positive for CD2, CD3, CD7, CD8 and TIA1, confirming subcutaneous nodules on the patient's body.

Medical Interventions: The initial therapeutic approach involved administering an injection of piperacillin-tazobactam (4.5mg, 8hourly). Unfortunately, no significant improvement in the patient's condition was observed, prompting a change in treatment to an injection of meropenem (1gm, 8 hourly) and an injection of clarithromycin (500mg bis in a day). Tragically, the patient's health deteriorated.

RESULTS AND DISCUSSIONS

PCAE-CTL constitutes a rare subset, representing less than 1% of all diagnosed cutaneous lymphoma cases[9]. This malignancy is distinguished by an expansion of cytotoxic CD8+T cells primarily confined to the epidermis, resulting in extensive epidermal necrosis and the formation of skin ulcers. CD8+PCAE-CTL predominantly afflicts adults and exhibits an aggressive clinical course characterized by rapid disease progression. Prognostically, it carries a bleak outlook, with median overall survival ranging from 12-32 months[1,6,10]. Notably, there are instances where the characteristic markers CD8 or TCR-ß/ßF1+ may be absent, prompting the consideration of the broader term "primary cutaneous aggressive epidermotropic cytotoxic T-cell lymphoma" to encompass such cases[6].

Clinically, PCAE-CTL manifests as the sudden appearance of rapidly advancing, often widespread, ulcerative and haemorrhagic lesions in the form of plaques, papulo nodules, or tumors. Additionally, it may involve extracutaneous sites, including the oral mucosa, lungs, adrenal glands, testes and even the central nervous system[1,6]. In contrast, lymph node or bone marrow involvement is relatively infrequent[6,10]. Notably, some patients may exhibit a preceding, poorly defined eczematous or papulosquamous rash[6,11].

Histopathologically, PCAE-CTL is characterized by a marked epidermotropic proliferation of atypical lymphocytes arranged in a pagetoid pattern. This is frequently accompanied by localized confluent keratinocyte necrosis and the development of open ulcers. Infiltration of the skin's adnexal structures is common and upper dermal red cell extravasation is often observed. Tumoral lesions can display dermal and subcutaneous infiltration and the presence of such lesions at the time of diagnosis is associated with an unfavorable prognosis[10,12].

Immunopheno typing typically reveals that the lymphoid cells are positive for CD3, CD8, ßF1 and

Fig. 1a. Primary cutaneous CD8+aggressive epidermotropic cytotoxic T-cell lymphoma over the face

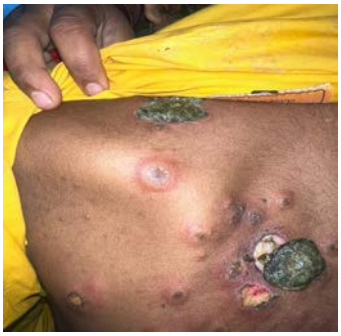

Fig. 1b. Primary cutaneous CD8+aggressive epidermotropic cytotoxic T-cell lymphoma over the back

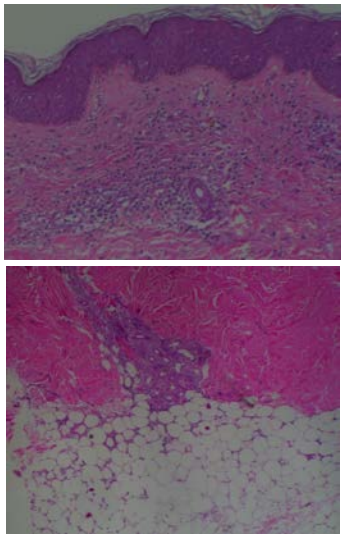

Fig. 2(a-b): Histopathology of skin lesions

CD45RA and they possess cytotoxic granules marked by the presence of TIA1, granzyme B and perforin. CD7 is frequently positive, while CD2, CD4, CD5 and CD45RO tend to be negative[1,10]. There have been reports of cases exhibiting CD4/CD8 double -negativity[12]. Furthermore, the neoplastic cells show monoclonal TCR gene rearrangements, indicating their clonal nature[4,9]. Notably, there is no association between PCAE-CTL and the Epstein-Barr virus (EBV).

Distinguishing CD8+ PCAETL from more indolent CTCLs and inflammatory conditions that mimic its presentation can be challenging. This diagnostic difficulty may lead to delays in diagnosis and subsequently, impact the overall outcome for affected individuals[13,14].

Numerous therapeutic approaches have been attempted in the management of PCAE-CTL, however, none have achieved the status of a standard therapy. The only potentially curative method recognized is allogeneic hematopoietic cell transplantation (alloHCT). Several reports have documented cases of PCAE-TCL in which alloHCT was employed as a treatment strategy, showing promise as a potential curative option[8,15-19]. In two instances where patients underwent alloHCT with only skin lesions present before transplantation and they received a myeloablative conditioning regimen, which included total body irradiation, both cases have been documented to have achieved long-term survival without any evidence of disease[15,16]. In all these cases, transplantation was carried out with matched unrelated donors. This suggests that the process of finding suitable donors may have allowed for adequate time to coordinate the transplant without disease progression. However, it's worth noting that the case that presented with lymph node lesions ultimately succumbed to the disease, highlighting the heterogeneity in outcomes and the challenges in managing PCAE-CTL, especially when extra-cutaneous involvement is present[17,18].

In our case the initial antibiotic therapy with piperacillin-tazobactam was followed by a more potent regimen involving meropenem and clarithromycin, indicating the challenge in managing this condition. Unfortunately, the patient's health deteriorated rapidly and he succumbed to the disease before chemotherapy could be initiated. The unique presentation of this case emphasizes the need for healthcare professionals to maintain a high level of clinical suspicion for PCAE-CTL, even in younger individuals and highlights the urgency of investigating new therapeutic approaches for this aggressive lymphoma.

CONCLUSIONS

This case underscores the challenging diagnostic and clinical landscape associated with PCAE-CTL. The rarity of this lymphoma subtype, its atypical presentation in a younger patient and the limited treatment options available all contribute to the complexity of managing this aggressive disease.

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