

## Aggressive Epidermotropic CD8+ Cutaneous T cell lymphoma: Rare Variant of Cutaneous T cell lymphomas

Dhauna Karam\*, Hosam Hakim, Khalid Al-Khafaji, Pant Mukta Purohit, Bharat Agrawal

Capt James A lovell Federal health care center, 3001 Green bay Road, N.Chicago.

**Corresponding Author:** Dhauna P Karam, Capt James A lovell Federal health care center, 3001 Green bay Road, N.Chicago, **Tel:** 224-610-5554; **Email:** dhauna.karam@gmail.com

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### ABSTRACT

Primary cutaneous aggressive epidermotropic CD8+ cytotoxic T cell lymphomas (AECTCL) are extremely rare of all cutaneous primary T cell lymphomas (PTCL) with less than 1% incidence. A 77 year old male presented to emergency department for evaluation of head to toe rash. He was bit by a wolf spider 5-6 weeks earlier. Patient woke up with spider biting him on his face. Few days later, he developed a maculopapular rash in chest, which failed to respond to OTC ointments. On examination, patient was vitally stable, skin exam revealed multiple confluent erythematous lesions and bullae in the face, neck, back, chest, and extremities. The lesions had central ulceration with necrosis. Punch biopsy of lesion revealed cutaneous aggressive epidermotropic CD8+ cytotoxic T cell lymphoma (AECTCL). Whole body CT/PET scan revealed multiple cutaneous based mass lesions associated with subcutaneous edematous changes. Immunohistochemistry was positive for CD3/CD8/Granzyme B, beta-F1 and TIA-1 further confirming the diagnosis. Patient was treated with gemcitabine for this aggressive variant of T-cell lymphoma. This case highlights a rare and atypical, aggressive variant of cutaneous T cell lymphomas. A constellation of clinical, histopathological, immunophenotypic features aided in our diagnosis.

### KEYWORDS

Cutaneous Lymphoma; T Cell; CD8 + Cell; Systemic Chemotherapy; Gemcitabine; Punch Biopsy; Cytotoxicity; and Primary Cutaneous Aggressive Epidermotropic CD8+ Cytotoxic T Cell Lymphomas.

### ABBREVIATIONS

PTCL- cutaneous primary T cell lymphomas.

AECTCL - Primary cutaneous aggressive epidermotropic CD8+ cytotoxic T cell lymphomas.

### INTRODUCTION

Primary Cutaneous T cells Lymphomas (PTCL) are characterized by skin involvement without systemic involvement at the time of diagnosis and disease onset. PTCL accounts for more than 75% of cutaneous lymphomas [1]. 90% of PTCL in western world are classical clinical entities such as mycosis fungoides and its variants, sezary's syndrome on one hand and CD 30 + lymphoproliferative disorders such as anaplastic large cell lymphoma and lymphomatoid papulosis on the other hand. As per the 2016 update of WHO-EORTC classification of tumors of the hematopoietic and lymphatic tissue, there are few other uncommon variants of PTCLs such as subcutaneous panniculitis like T cell lymphoma, extranodal natural killer T cell lymphoma, nasal primary T cell lymphoma, pri-

mary cutaneous peripheral TCL, not otherwise classified and rare subtypes. Rare Subtypes of primary cutaneous TCL (PTCL) include: a) Primary cutaneous gamma delta T cell lymphoma, b) Primary cutaneous aggressive epidermotropic CD8+ cytotoxic T cell lymphomas (AECTCL), c) Primary cutaneous acral CD8+ lymphoma and d) Primary cutaneous CD4+ small/medium T cell lymphoproliferative disorder. AECTCL is considered a provisional diagnosis because of its rare incidence and varied presentation [1]. AECTCLs are aggressive variants and are characterized by proliferation of CD 8+ cytotoxic T cells which express CD3/CD8 [2, 3]. In 1991, Berti et al were the first to describe this variant in a 35 year old man [3]. The incidence is 1% of all PTCLs with a male predominance [4]. All proliferating CD 8+ lymphocytes also express a set of toxic proteins such as

perforins, granzymes A (GrA), B (GrB), and the T-cell intracellular antigen-1 (TIA-1) that are markers of cytotoxicity [5, 6]. Here we describe a case of primary cutaneous aggressive epidermotropic CD8+ cytotoxic T cell lymphoma (AECTCL), which presented aggressively with a poor outcome.

### CASE REPORT

A 77 year old caucasian male presented for evaluation of head to toe rash. He was bit by a wolf spider 5-6 weeks earlier. Few days later, he developed rash in chest, which slowly progressed to become generalized with itching. The patient denied fever or chills. He declined history of recent infections. He thought the rash to be an allergic reaction to spider bite and tried OTC ointments to no avail. Physical examination revealed a vitally stable patient. Multiple confluent erythematous skin lesions and bullae were noted, with central ulceration and necrosis in the face, neck, back, chest, and extremities, sparing palms and soles. There were also many superficial hyperkeratotic plaques and patches [Figure 1, 2, 3].



Basic laboratory investigation including complete blood count and basic metabolic profile were within normal limits. Further workup with HIV/HTLV 1 & 2 testing, hepatitis B and C panel, Epstein–Barr virus (EBV), toxoplasma, rubeola, syphilis, brucellosis, tuberculosis and rickettsiosis panel testing were negative. Autoimmune etiology was ruled out by testing for anti-nuclear antibody, antineutrophil cytoplasmic antibodies (ANCA) and cryoglobulin. Dermatology was consulted and they performed punch biopsy of one of the lesions. Histopathologic examination revealed dense lymphoid cells infiltrating dermis and subcutaneous tissue, which was CD3/CD8 +, Granzyme B + suggestive of AECTCL. Further immunohistochemical testing revealed that the neoplastic cells were positive for CD 7 and BCL- 2, weakly positive for CD 5. The neoplastic cells were negative for CD 20, Pax-5, Bcl- 6, CD 10, CD 30, CD 4, CD 56, CD 34, CD 117, MPO, CD 33 and ALK- 1. Ki-67 was positive in 80% of

neoplastic cells. Cyclin- D1 was positive on a small number of lymphocytes but FISH for t (11:14) translocation was negative in peripheral blood ruling out mantle cell lymphoma. Peripheral flow cytometry was negative for seza's cells ruling out seza's syndrome. Few other immunohistochemical markers of AECTCL such as TIA-1 and Beta F1 were also positive. TIA -1 revealed dot like staining pattern. Pan CT scan and whole body PET scan was performed with 14.5 mCi of F-18 Fluoro-deoxyglucose (FDG). Imaging revealed extensive FDG avid cutaneous lesions. The lesions in external ear and surrounding retro auricular tissues had maximum SUV of 11.7. Soft tissue mass arising from L shoulder and neck were seen, with a SUV of 12.3. Inguinal region lesions had SUV of 15.2. There were some small supraclavicular and axillary lymph nodes with SUV ranging from 6.4 to 10. Patient received gemcitabine chemotherapy for this aggressive variant of T-cell lymphoma.

### DISCUSSION

Cutaneous T cell lymphomas are rare malignancies and knowledge about their behavior is limited [7]. Most common of PTCLs are mycosis fungoides and seza's syndrome (CD 4 + PTCL). The rare PTCL subtypes include four varieties, of which Primary cutaneous aggressive epidermotropic CD8+ cytotoxic T cell lymphomas (AECTCL) are highly lethal malignancies and account for only 1% of all PTCL. Though there are few case reports published on CD 8+ PTCLs [2, 8-10], AECTCL is a clinically unexplored entity. Most CD8+ PTCLs including AECTCL do not respond to treatment and are fatal [2, 4, 9, 10].

Berti et al were the first to describe AECTCL and proposed an earlier classification which evolved over time to the current WHO classification [4, 11-13]. The morphologic features of AECTCL are highly variable. The presentation can involve localized, early patch like lichenoid pattern lesions with marked pagetoid epidermotrophism and subepidermal edema to diffuse dermal infiltrates with nodular tumor-like lesions as seen in our patient. The immunohistochemical findings are positive CD3/CD8, granzyme, perforins, beta- F1and TIA-1. CD 45RA/ CD 45RO, CD2, CD7 may be positive or negative. CD4 and CD5 are usually negative. Genetic testing revealing clonal T cell receptor gene rearrangements are characteristic of CD8+ AECTCL. The diagnosis of AECTCL is based on the constellation of clinical, histopathological and immunophenotypic findings as evident by our case report. Sometimes, the CD4 + lymphomas like Mycosis fungoides and Seza's syndrome also express CD 8 positivity [14, 15]. Since several PTCLs express CD8+, detailed clinical evaluation with other investigations are needed to diagnose AECTCL.

The treatment of AECTCL involves a multimodal approach. Vowels et al in 1994 examined skin biopsies of 12 patients with PTCL and reported presence of Th2 cytokine mRNA in almost all patients [16]. This translates to presence of Th2

helper cell phenotype in PTCL including AECTCLs, which led to development of treatment modalities targeting Th1 response augmentation such as interferons (IFN- alpha, IFN- gamma, IFN-2, IFN-12) and retinoids [17]. Over years, gemcitabine was approved as single agent therapy for patients with untreated AECTCL [18]. Despite its adverse effects, gemcitabine is considered very effective for advanced stages of AECTCL [19]. We used Gemcitabine chemotherapy for our patient and he tolerated it well initially. But over time, he was unable to tolerate therapy and chose hospice care. He died in 9 weeks after diagnosis of AECTCL.

## CONCLUSION

Our case highlights the importance of a step wise approach including history and physical exam, followed by investigations in clinical practice that led to diagnosis of a rare clinical presentation. The constellation of clinical, histopathologic and immunohistochemistry help clinch the diagnosis in our patient.

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