**Introduction**

Cutaneous T-cell lymphomas (CTCLs) are a heterogenous group of lymphomas that make up approximately 80% of primary cutaneous lymphomas. CTCLs include mycosis fungoides (MF), Sézary syndrome, and cutaneous CD30+ T-cell lymphoproliferative disorders among others.

Based on the 2005 World Health Organization–European Organisation for Research and Treatment of Cancer (WHO-EORTC) classification, CD4+ primary cutaneous small/medium-sized pleomorphic T-cell lymphoma (PCSM-TCL) was listed as a provisional entity of CTCLs. Currently the 2016 WHO classification, a revision to the 2008 WHO classification also keeps PCSM-TCL as a provisional entity but will rename the entity primary cutaneous CD4+ small/medium T-cell lymphoproliferative disorder (SMT-LPD) as it is considered a limited clonal response to an unknown stimulus as opposed to an overt lymphoma.

PCSM-TCL is a rare type of lymphoproliferative disorder that clinically presents as a solitary plaque, nodule, or tumor most commonly on the face or the neck. It generally runs an indolent course with an excellent prognosis. Histologically, it has dense, diffuse or nodular infiltrates in the dermis, with a predominance of CD4 + small/medium-sized pleomorphic T-cells. A small proportion (<30%) of large pleomorphic cells may be present. Immunophenotyping demonstrates CD3+, CD4+, CD8- and CD30- neoplastic cells.

It was recently found that the atypical T cells in CD4+ PCSM-TCL express PD-1, BCL6 and CXCL13, suggesting that these cells originate from T follicular helper cells (TFHs). CD8+ T-cells, B-cells, histiocytes, plasma cells and eosinophils can also be found in differing proportions in the infiltrate. It is imperative to distinguish CD4+ PCSM-TCL, which is generally indolent in nature, from other lymphoid disorders in order to offer the most appropriate treatment and management.

**Case**

46-year-old male with no significant past medical history presented with a reddish-brown plaque on his left inferior postauricular neck that had been present for about five months. The patient complained that it was increasing in size along with burning and itching. The lesion was at the site of a previous biopsy that was diagnosed as a inflamed lenticule.

The histologic sections demonstrated an atypical lymphoid infiltrate extending from the papillary dermis into the reticular dermis with contiguous extension along follicular epithelium. Numerous atypical mitoses, hyperchromatic and pleomorphic lymphocytes were noted within the atypical infiltrate, Immunohistochemical staining demonstrated a highly proliferative atypical T-cell infiltrate with a predominant 10:1 CD4 to CD8 ratio with diffuse expression of PD-1. With the combined clinical and histological findings, the patient was diagnosed with CD4+ primary cutaneous small/medium-sized pleomorphic T-cell lymphoma. The lesion was excised and a PET scan and hematology/oncology consultation did not reveal any systemic involvement.

**Discussion**

As PCSM-TCL has similar histological features with cutaneous lymphomas such as mycosis fungoides (MF), angioimmunoblastic T-cell lymphoma (AITL), lymphomatoid papulosis (LP), subcutaneous panniculitis-like T-cell lymphoma (SPTCL), and marginal zone B cell lymphoma, it imperative to differentiate between these entities due to the therapeutic and prognostic implications. PCSM-TCL demonstrates a CD3+, CD4+, CD8-, CD30- immunophenotype. In addition, it has also been shown to originate from follicular T helper cells by demonstrating a positive staining pattern for PD-1, BCL-6, and CXCL13. PD-1 is found in a subset of T-cells within the germinal center and helps promote B-cell survival and differentiation. Although PD-1 is not specific for THFs, it can be helpful when differentiating PCSM-TCL from other lymphomas. The follicular helper T-cell origin may also explain the admixture of B-cells. Of note, a new marker, calcineurin/nuclear factor of activated T-cells c1 (NFKB1), has shown a nuclear staining pattern that is very sensitive and specific for PCSM-TCL allowing differentiation from some histologically similar lymphomas such as MF which demonstrates a cytoplasmic staining pattern.

Histologically, PCSM-TCL may have worrisome features. It may mimic tumor stage MF even demonstrating foci of epidermotropism. MF may also stain positive for PD-1, but clinically there is no history of plaques and plaques. PCSM-TCL may also mimicAITL, which is a lymphoma derived from TFHs. Like MF, AITL differs from PCSM-TCL clinically with systemic findings such as generalized lymphadenopathy. A positive PD-1 also helps differentiate PCSM-TCL from LP and anaplastic large cell lymphoma. PCSM-TCL has been shown to involve the subcutis, therefore the generalized lesions of SPTCL help distinguish the two along with the CD3+, CD4+, CD8+ phenotype of SPTCL.

Lastly, it is debatable whether PCSM-TCL and T-cell pseudolymphoma represent two separate entities. Both present with a solitary plaque or nodule and both may stain for PD-1. In addition, not all cases of PCSM-TCLs are monoclonal. But T-cell pseudolymphoma is different in that it lacks an aberrant immunophenotype and is usually polyclonal. However, T-cell pseudolymphoma has at times demonstrated a monoclonal phenotype. The lines between PCSM-TCL and T-cell pseudolymphoma may be blurred and of little use prognostically.

Due to the indolent nature of PCSM-TCL, surgical excision is the treatment of choice. For cases with recurrence or with multiple lesions, radiation or chemotherapy has been used with success. In most cases, toxic treatment should be avoided and staging evaluation is not necessary.

**References**


