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Piddling and Moderate-Primary Cutaneous CD4+ Small/Medium T Cell Lymphoproliferative Disorder

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Abstract

Initially contemplated as a provisional subtype of cutaneous T cell lymphoma (CTCL), primary cutaneous CD4+ small / medium T cell lymphoproliferative disorder manifests as an indolent, solitary cutaneous lesion in the absence of accompanying cutaneous lymphoma as mycosis fungoides. Preponderantly, infiltration of upper dermis with miniature to intermediate, pleomorphic CD4+ T cells in the absence of preceding or concurrent patches and plaques with focal epidermotropism is encountered. Primary cutaneous CD4+ small/medium T cell lymphoproliferative disorder commonly appears in adults as a solitary plaque, tumour or nodule situated upon face, neck, upper trunk or thoracic region. Upon cytology, pleomorphic, miniature, intermediate or occasionally enlarged T lymphoid cells with irregular nuclear contours are variably intermixed with miniature, reactive CD8+ T cells, B cells, plasma cells, histiocytes and monotypic plasma cells. Morphologically, an intense dermal infiltrate of atypical lymphoid cells or small / medium pleomorphic CD4+ T cells extending into subcutaneous tissue appears to configure a diffuse or nodular configuration wherein the enlarged, pleomorphic cells articulate < 30% of neoplastic cellular infiltrate. Neoplastic lymphocytes appear immune reactive to T cell markers as CD3, CD4, CD5 along with T follicular helper markers as CD279 (PD-1), ICOS and CXCL13. Primary cutaneous CD4+ small/medium T cell lymphoproliferative disorder necessitates segregation from mycosis fungoides, cutaneous involvement with systemic T cell lymphoma of T follicular helper immuno-phenotype, benign inflammatory infiltrate, extra-nodal marginal zone (MALT) lymphoma or adult T cell leukaemia /lymphoma. The disorder can be therapeutically managed with intralesional steroids, radiotherapy or surgical extermination of lesion.

Keywords: T cell, lymphoproliferative, dermal infiltrate

1. Introduction

As per World Health Organization/European Organization of Research and Treatment of Cancer (WHO/EORTC) classification, primary cutaneous CD4+ small/medium T cell lymphoma was initially contemplated as a provisional subtype of cutaneous T cell lymphoma (CTCL).

Primary cutaneous CD4+ small / medium T cell lymphoproliferative disorder represents as an indolent, solitary cutaneous lesion in the absence of an accompanying cutaneous lymphoma as mycosis fungoides delineating patches or plaques of extensive duration. Characteristically, the disorder exhibits preponderant infiltration of upper dermis with small to intermediate pleomorphic CD4+ T cells in the absence of preceding or concurrent patches and plaques typically encountered in mycosis fungoides. Accompanying epidermotropism is focal.

Terminology of primary cutaneous CD4+ small / medium T cell lymphoma is contemplated to be obsolete as the clinical course is benign.

Staging of characteristic lesions of primary cutaneous CD4+ small/medium T cell lymphoproliferative disorder delineating an excellent prognosis is not recommended (Besch-Stokes JG, Costello CM et al., 2022; Plumptre IR,

Said JT et al., 2022).

The exceptionally encountered, primary cutaneous CD4+ small/medium T cell lymphoproliferative disorder configures an estimated 2% of cutaneous T cell lymphomas / lymphoproliferative disorders. Generally, adults or elderly population is incriminated. Paediatric subjects are rarely involved. An equivalent gender predisposition is observed.

Primary cutaneous CD4+ small/medium T cell lymphoproliferative disorder commonly appears as a solitary plaque, tumour or nodule situated upon face, neck, upper trunk or thoracic region. Multifocal lesions or tumefaction confined to lower extremities are exceptionally exemplified (Besch-Stokes JG, Costello CM et al., 2022; Plumptre IR, Said JT et al., 2022). Primary cutaneous CD4+ small/medium T cell lymphoproliferative disorder is engendered from cutaneous homing CD4+ T cells demonstrating follicular T helper phenotype.

Generally asymptomatic, primary cutaneous CD4+ small/medium T cell lymphoproliferative disorder represents with a solitary, reddish purple, indolent cutaneous lesion. Tumefaction is predominantly situated upon the face, neck or upper trunk. Exceptionally, multiple lesions may be enunciated. However, discernible patches or plaques may indicate mycosis fungoides which requires exclusion.

Frozen section examination is not recommended.

Cytological examination delineates a pleomorphic population of miniature, intermediate or occasionally enlarged T lymphoid cells with irregular nuclear contours. Enlarged neoplastic T cells configure < 30% of atypical lymphoid infiltrate. Tumour cells appear variably intermixed with miniature, reactive CD8+ T cells, B cells, plasma cells and histiocytes. Monotypic plasma cells can be enunciated. Occasionally, multinucleated giant cells are observed (Besch-Stokes JG, Costello CM et al., 2022; Plumptre IR, Said JT et al., 2022).

Upon gross examination, the lymphoproliferative disorder manifests as a solitary, flesh coloured or reddish purple plaque or nodule.

Upon microscopy, neoplasm is configured of small / medium pleomorphic CD4+ T cells displaying T follicular helper (TFH) immuno-phenotype. An intense infiltrate of atypical lymphoid cells confined to the dermis with extension into subcutaneous tissue is observed. Tumour cell aggregates may manifest a diffuse or nodular configuration. Epidermotropism is focal. Frequently, small / medium pleomorphic CD4+ T cells configure the neoplastic infiltrate. Enlarged pleomorphic cells articulate < 30% of neoplastic cellular infiltrate (Besch-Stokes JG, Costello CM et al., 2022; Plumptre IR, Said JT et al., 2022). Tumour cells are variably intermixed with polymorphic cellular component such as miniature CD8+ T cells, B cells, plasma cells and histiocytes. The heterogeneous cellular background exemplifies hemato-lymphoid cells admixed with hyperplastic B cells. Multinucleated giant cells may be discerned. Ki67 proliferation index is minimal and varies from 5% to 20% (Besch-Stokes JG, Costello CM et al., 2022; Plumptre IR, Said JT et al., 2022).

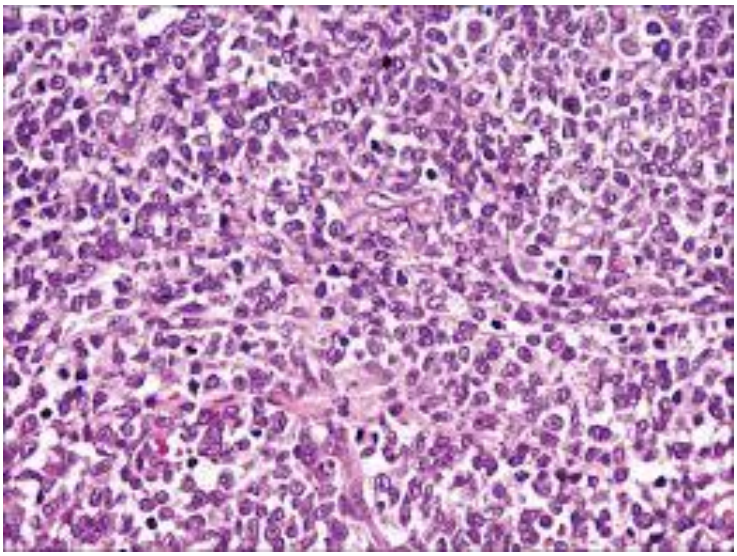

Figure 1. Cutaneous CD4+ small/ medium T cell lymphoproliferative disorder demonstrating a dermal infiltrate of small to intermediate atypical lymphocytes with irregular nuclear contours intermingled with a reactive population of lymphocytes and plasma cells

Source: Courtesy: *India Journal of Cancer*

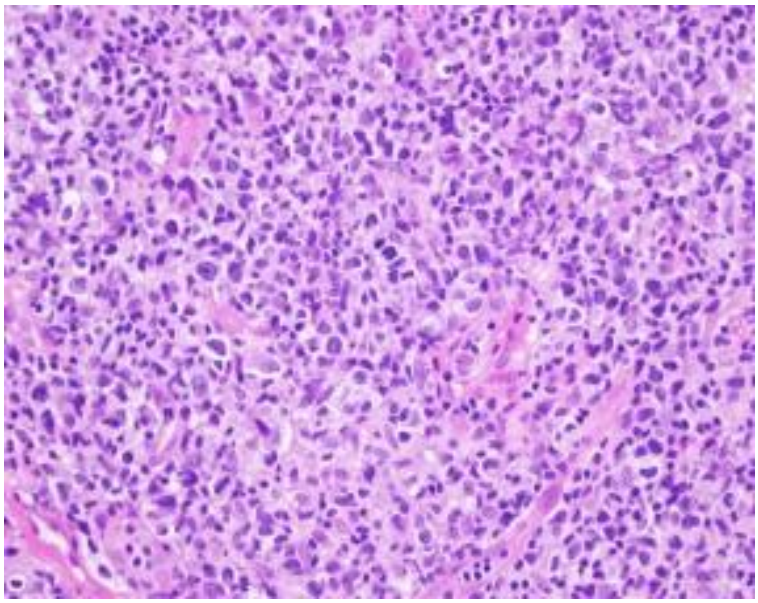

Figure 2. Cutaneous CD4+ small/medium T cell lymphoproliferative disorder demonstrating an intense inflammatory infiltrate of small and intermediate atypical lymphocytes with irregular nuclear contour interspersed with small reactive lymphocytes and plasma cells

Source: Courtesy: Pathology Outlines.

Neoplastic lymphocytes appear immune reactive to T cell markers as CD3, CD4, CD5 along with T follicular helper markers such as CD279 (PD-1), ICOS and CXCL13 and are variably reactive to BCL6. Uncommonly, decimation of pan T cell markers is observed. Nevertheless, loss of CD7 may occur. Primary cutaneous CD4+ small/medium T cell lymphoproliferative disorder is immune non reactive to CD8, CD10, CD30 and Epstein Barr encoded small RNAs (EBER) (Kim J, Jeong M et al., 2021; Surmanowicz P, Doherty S et al., 2021).

Upon flow cytometry, ≥ 1 pan T cell markers appear as dim or absent as manifested by a population of anomalous CD4+ T cells. Neoplastic cells may be devoid of CD10. Besides, CD4: CD8 ratio appears normal on account of abundant reactive CD8+T cells. Additionally, B cells may represent with polytypic expression of kappa and lambda light chains.

Primary cutaneous CD4+ small/medium T cell lymphoproliferative disorder preponderantly exhibits clonal rearrangement of T cell receptor (TCR) genes. Additionally, specific genetic anomalies remain undefined.

Primary cutaneous CD4+ small/medium T cell lymphoproliferative disorder necessitates segregation from neoplasms such as mycosis fungoides, cutaneous involvement with systemic T cell lymphoma of T follicular helper immuno-phenotype, benign inflammatory infiltrate, extra-nodal marginal zone (MALT) lymphoma or adult T cell leukaemia /lymphoma (Kim J, Jeong M et al., 2021; Surmanowicz P, Doherty S et al., 2021).

Cogent sampling of surgical tissue complemented with pertinent immunohistochemistry, clonal assessment of T cell receptor genes and clinical concordance is optimal for appropriate disease discernment.

Although spontaneous regression of the lesion is documented, non resolving lesions of primary cutaneous CD4+ small/medium T cell lymphoproliferative disorder can be therapeutically managed with intralesional steroids or radiotherapy. Alternatively, surgical extermination of lesion may be adopted. Primary cutaneous CD4+ small/medium T cell lymphoproliferative disorder demonstrates excellent prognostic outcomes. Spontaneous disease remission following surgical tissue sampling is documented. Localized tumour reoccurrence is exceptional (Kim J, Jeong M et al., 2021; Surmanowicz P, Doherty S et al., 2021).

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