

CASE REPORT

A Case of Primary Cutaneous CD4 Positive Small/medium T Cell Lymphoma

Mira Choi, M.D., Se Young Park, M.D., Hyun Sun Park, M.D., Hee Jin Byun, M.D., Kwang Hyun Cho, M.D.

Department of Dermatology, Seoul National University College of Medicine, Seoul, Korea

Primary cutaneous CD4 positive small/medium T cell lymphoma (PCSM-TCL) is a provisional entity in the new WHO-EORTC classification for cutaneous lymphoma, and it is a rare disease with a favorable clinical course. PCSM-TCL may present with different clinical and pathologic features associated with the biologic behavior of the disease. Herein we report on a 63-year-old woman with multiple, multifocal, erythematous to violaceous papules and plaques that progressed despite local radiotherapy. (**Ann Dermatol 23(1) 76~80, 2011**)

-Keywords-

CD4, Cutaneous T cell lymphoma, Small/medium

INTRODUCTION

Primary cutaneous lymphoma represents a heterogeneous group of malignancies with clinical findings that are different from those of systemic lymphoma¹⁻³. The recent WHO-European Organization for Research and Treatment of Cancer (EORTC) classification proposed a consensus for a new classification to facilitate more uniformity when diagnosing these cancers¹⁻⁵. In the new classification, three rare subtypes of primary cutaneous peripheral T cell lymphoma with particular clinical features have been recognized: primary cutaneous CD4 positive small/medium T cell lymphoma (PCSM-TCL), primary cutaneous CD8 positive aggressive epidermotropic cytotoxic T cell

lymphoma and primary cutaneous $\gamma\delta$ T cell lymphoma^{2,3}. PCSM-TCL usually presents as a solitary plaque or tumor on the trunk of the body and it has a rather favorable prognosis. However, owing to the rarity and heterogeneity of the PCSM-TCL, the precise clinicopathologic characteristics of PCSM-TCL have not been well characterized, and only three such cases have been reported in Korea⁶⁻⁸. We present here an additional rare case of PCSM-TCL that occurred in a 63-year-old woman with multiple, multifocal skin lesions.

CASE REPORT

A 63-year-old Korean woman presented with a 5-month history of multiple, multifocal erythematous to violaceous nodules and plaques on the face, abdomen and leg. The skin lesions were intermittently itchy and they had gradually increased in size and number. She had undergone coronary artery bypass graft surgery due to angina in June 2008. Physical examination showed multiple bean-sized erythematous nodules and plaques on the face, leg and abdomen (Fig. 1). There were neither any other systemic symptoms nor lymphadenopathy. The skin biopsy from the thigh demonstrated a dense infiltration in the dermis. The dermal infiltrate showed a proliferation of histiocytes and small/medium-sized atypical lymphocytes with pleomorphism (Fig. 2). On the immunohistochemical studies, most of the infiltrated cells were positively stained with CD3, CD4 and Bcl6, but a few cells were also CD8 and CD20-positive. CD30, CD56 and cytotoxic granules such as granzyme were not seen (Fig. 3). The nuclei of 10% of the tumor cells were stained with Ki-67. Epstein-Barr virus was not detected by *in situ* hybridization. The staining for terminal deoxynucleotidyl transferase was negative. Monoclonality was demonstrated by means of T-cell receptor γ -chain consensus polymerase chain reac-

Received January 22, 2010, Revised March 15, 2010, Accepted for publication March 23, 2010

Corresponding author: Kwang Hyun Cho, M.D., Department of Dermatology, Seoul National University College of Medicine, 101 Daehangno, Chongno-gu, Seoul 110-744, Korea. Tel: 82-2-2072-2410, Fax: 82-2-742-7344, E-mail: khcho@snu.ac.kr

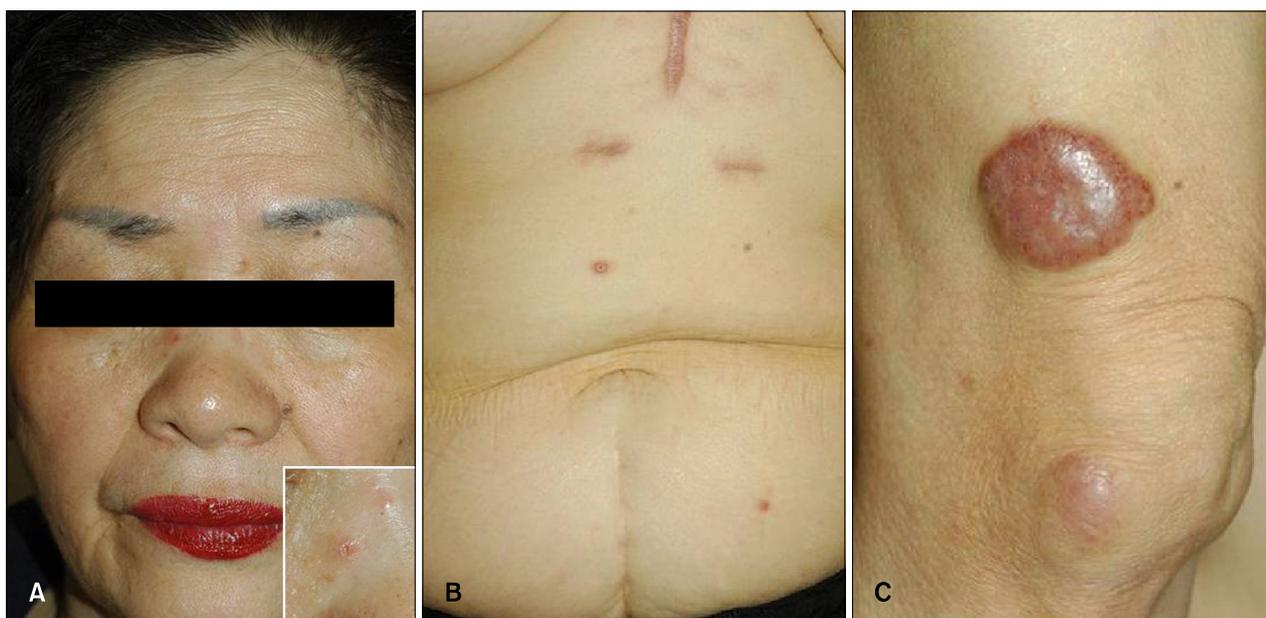


Fig. 1. Multiple erythematous to violaceous papules and plaque on the face (A), abdomen (B) and thigh (C).

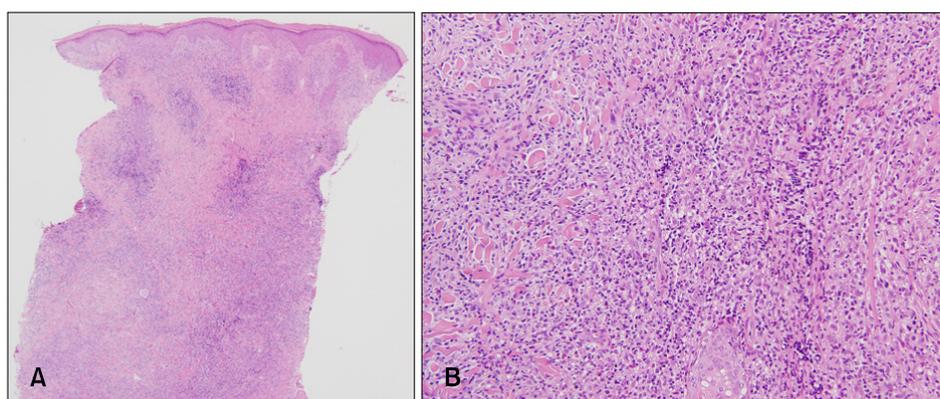


Fig. 2. (A) The skin biopsy obtained from the right thigh reveals a dense lymphoid infiltrate in the dermis (H&E, $\times 40$). (B) The infiltrate is mainly small/medium sized pleomorphic lymphocytes (H&E, $\times 200$).

tion. No human T-lymphotropic virus type I DNA was detected in the skin biopsy by polymerase chain reaction. The laboratory examinations at the time of the diagnosis, including a complete blood cell with the differential count, liver function tests, renal function tests, an antinuclear antibody test, serum protein electrophoresis and urinalysis were all within the normal limits. The chest X ray, computed tomography of the neck and abdomen and whole body F-18 fluorodeoxyglucose fusion positron emission tomography revealed no abnormalities. The bone marrow aspiration revealed no evidence of malignancy.

She was diagnosed as having primary cutaneous CD4 positive small/medium T cell lymphoma and so electron beam therapy was initiated. The patient received a total dose of 45 Gy for the nasal dorsum in 25 fractions, and 54.2 Gy for the thigh and knee area in 30 fractions twice

weekly for 42 days. Approximately 4 weeks after the initiation of treatment, the patient noted flattening of the skin lesion. However, 1 month after completing electron beam therapy, she reported the development of new skin lesions on her back. The skin biopsy specimen from her new skin lesions on the back was consistent with PCSM-TCL. Therefore, she was treated with cyclophosphamide, doxorubicin, vincristine and prednisolone (CHOP) for cutaneous relapse. After the first cycle of chemotherapy, she showed a complete remission of the skin lesions. She is currently being treated with a sixth cycle of CHOP chemotherapy and there is no evidence of local spread or metastasis.

DISCUSSION

PCSM-TCL was included as a provisional entity in the new

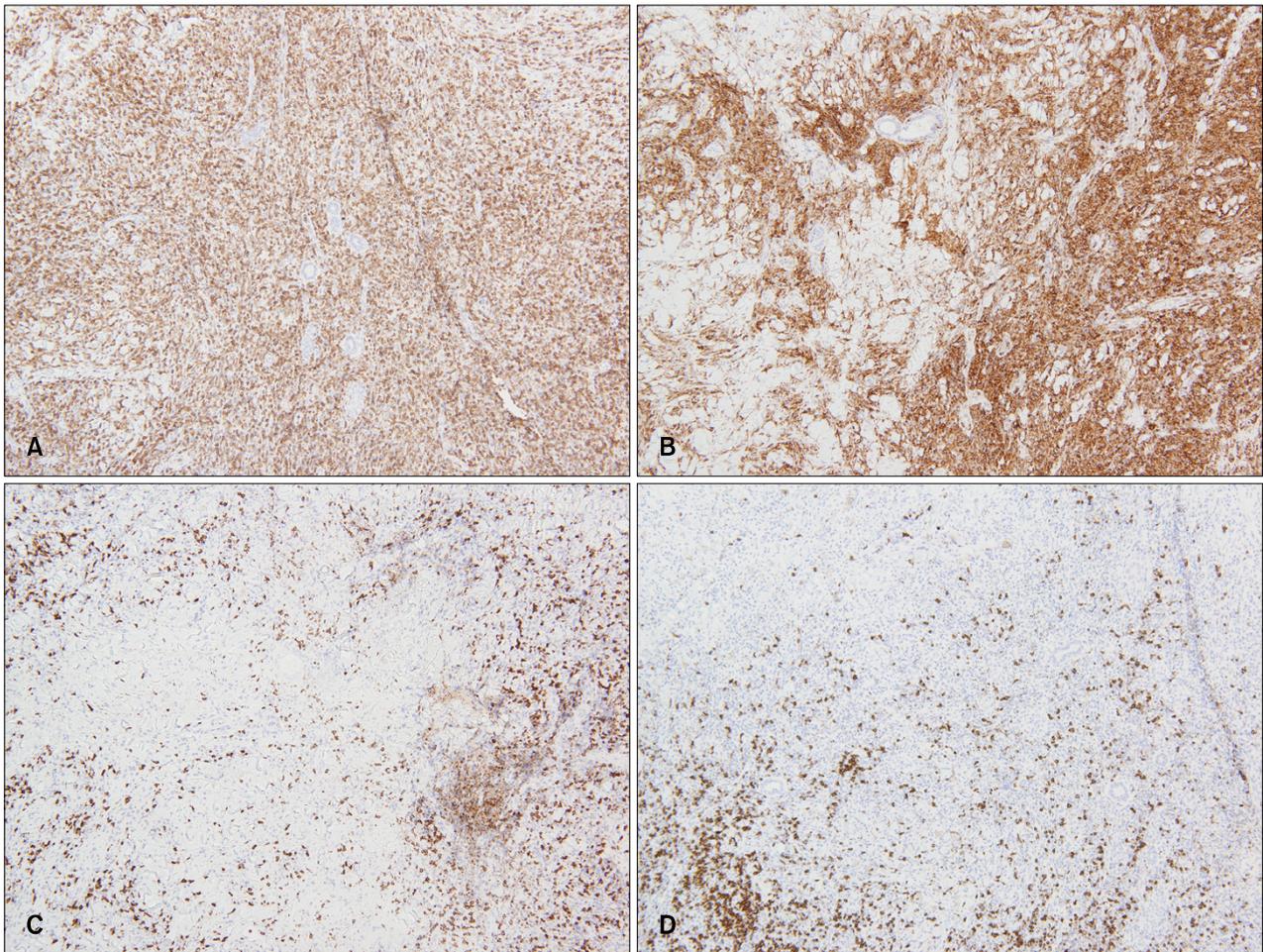


Fig. 3. Most of the lymphocytes express CD3 (A) and CD4 (B). A few CD8 positive cells (C) and reactive CD20 cells (D) are also present ($\times 100$).

WHO-EORTC classification for cutaneous lymphomas, and PCSM-TCL makes up 2~3% of all cutaneous lymphomas¹⁻⁵. This classification of PCSM-TCL is restricted to the cases with predominance of the small/medium-sized pleomorphic CD4 positive T cell phenotype without features of mycosis fungoides¹⁻⁵.

The majority of patients present with solitary plaques or tumors on the head and neck area or on the trunk. The median age at the onset of the PCSM-TCL was reported to be 60 years^{9,10}. In our case, the age at the onset of the skin lesion was 63 years and she presented with multiple, multifocal lesions. Multifocal lesions similar to our case have been less commonly described¹¹⁻¹⁴.

Histologically, PCSM-TCL is characterized by a dense infiltration of small/medium sized pleomorphic T cells^{9,11-14}. Clonal T cell receptor gene rearrangement has been detected in most cases. Immunohistochemically, CD3 and CD4 are positive, but CD8 and CD30 are negative in the majority of the case, and sometimes this is combined with

the loss of the pan T cell markers^{1,5,11-14}. However, many studies have also reported tumors that are CD8 positive or CD4 negative^{1,5,9,11,12}. In addition, many PCSM-TCL cases have shown a rich infiltrate of reactive B cells¹⁴. Therefore, the precise clinicopathologic features of PCSM-TCL are not well established and further studies will be needed to define the precise diagnosis and optimal treatment.

The important differential diagnoses are localized mycosis fungoides and T cell pseudolymphoma^{4,6-8,14}. Localized mycosis fungoides is characterized by prominent epidermotropism, which is not present in PCSM-TCL. The other important differential diagnosis is T cell pseudolymphoma, which is characterized by reactive T cell infiltration. It may be difficult to differentiate PCSM-TCL from pseudolymphoma because they demonstrate similar findings such as small lesions with a dense infiltrate of CD8 positive cells and B cells. In this current case, it was helpful to confirm the monoclonality of the T cell receptor gene, which represents true cutaneous lymphomas.

Table 1. Summary of the previously reported PCSM-TCL cases in Korea

Case	Gender	Age	Clinical presentation	Location	Initial therapy	Relapse	Follow-up (months)
Kim et al. ⁶	M	16	Solitary plaque	Face	Local radiation therapy	None	14
Oh et al. ⁷	M	55	Multifocal nodules	Elbow, thigh, hand	Local radiation therapy	None	3
Chung et al. ⁸	F	42	Multiple localized papules	Neck	Chemotherapy	Development of new lesion → Cleared after local radiotherapy	6
Our case	F	63	Multifocal nodules, plaque	Face, abdomen, leg	Local radiation therapy	Progression of multifocal cutaneous disease after local radiotherapy → Chemotherapy	Ongoing CHOP chemotherapy

PCSM-TCL: primary cutaneous CD4 positive small/medium T cell lymphoma, CHOP: cyclophosphamide, doxorubicin, vincristine and prednisolone.

PCSM-TCL has a favorable prognosis with the 5-year survival rate being approximately 60~80%¹⁻⁴. In previous studies, the overall median survival was significantly better for the patients with localized disease than for the patients with multifocal skin lesions^{5,15}. Furthermore, indolent clinical behavior was associated with stable small lesions (<3 cm), low proliferative activity and an intense CD8 positive lymphocyte infiltration, whereas an aggressive course was associated with rapidly evolving large skin lesions (>5 cm), high levels of proliferation markers and rare CD8 lymphocytes⁹.

The optimal treatment for this malady has still not been defined⁴. Localized cases may be treated with topical therapy such as surgical excision, localized psoralen plus UVA (PUVA) treatment bath therapy and local radiotherapy^{4,6-8,15}. In patients with more generalized skin lesions or those who are unresponsive to topical therapy, multi-agent chemotherapy that includes cyclophosphamide may be effective^{4,5}.

Three Korean cases of PCSM-TCL cases have been reported and only one of the cases presented with multifocal lesions (Table 1). In contrast to the previous reports, our case exhibited an unfavorable course. The patient was treated with multiagent systemic chemotherapy due to the disease progression and cutaneous relapse despite radiotherapy. We think that this may be due to the large, multifocal skin lesions, the scarce CD8 lymphocyte infiltration in the lesion and her relatively old age at the time of the diagnosis.

In summary, we report here on a case of PCSM-TCL in 63-year-old woman with an unfavorable clinical course. PCSM-TCL is a rare heterogeneous disease with various clinicopathologic features that can affect the prognosis. We need to accumulate more cases to facilitate making the diagnosis of this rare entity.

REFERENCES

1. Willemze R, Jaffe ES, Burg G, Cerroni L, Berti E, Swerdlow SH, et al. WHO-EORTC classification for cutaneous lymphomas. *Blood* 2005;105:3768-3785.
2. Macon WR. Peripheral T-cell lymphomas. *Hematol Oncol Clin North Am* 2009;23:829-842.
3. Lim MS, de Leval L, Quintanilla-Martinez L. Commentary on the 2008 WHO classification of mature T- and NK-cell neoplasms. *J Hematop* 2009;2:65-73.
4. Slater DN. The new World Health Organization-European Organization for Research and Treatment of Cancer classification for cutaneous lymphomas: a practical marriage of two giants. *Br J Dermatol* 2005;153:874-880.
5. Garcia-Herrera A, Colomo L, Camós M, Carreras J, Balague O, Martinez A, et al. Primary cutaneous small/medium CD4+ T-cell lymphomas: a heterogeneous group of tumors with different clinicopathologic features and outcome. *J Clin Oncol* 2008;26:3364-3371.
6. Kim YC, Vandersteen DP. Primary cutaneous pleomorphic small/medium-sized T-cell lymphoma in a young man. *Br J Dermatol* 2001;144:903-905.
7. Oh SH, Kim HS, Kee JH, Chang SN, Kim D. Cutaneous T cell lymphoma, pleomorphic, small/medium-sized with tissue and blood eosinophilia. *Korean J Dermatol* 2002;40:410-414.
8. Chung WK, Kim MS, Kang SM, Chang SE, Lee MW, Choi JH, et al. A case of primary cutaneous CD4+ small/medium-sized pleomorphic T-cell lymphoma. *Korean J Dermatol* 2009;47:338-342.
9. Bekkenk MW, Vermeer MH, Jansen PM, van Marion AM, Canninga-van Dijk MR, Kluin PM, et al. Peripheral T-cell lymphomas unspecified presenting in the skin: analysis of prognostic factors in a group of 82 patients. *Blood* 2003;102:2213-2219.
10. Willemze R, Beljaards RC, Meijer CJ. Classification of primary cutaneous T-cell lymphomas. *Histopathology* 1994;24:405-415.
11. Beltraminelli H, Leinweber B, Kerl H, Cerroni L. Primary

- cutaneous CD4+ small-/medium-sized pleomorphic T-cell lymphoma: a cutaneous nodular proliferation of pleomorphic T lymphocytes of undetermined significance? A study of 136 cases. *Am J Dermatopathol* 2009;31:317-322.
12. Leinweber B, Beltraminelli H, Kerl H, Cerroni L. Solitary small- to medium-sized pleomorphic T-cell nodules of undetermined significance: clinical, histopathological, immunohistochemical and molecular analysis of 26 cases. *Dermatology* 2009;219:42-47.
 13. Grogg KL, Jung S, Erickson LA, McClure RF, Dogan A. Primary cutaneous CD4-positive small/medium-sized pleomorphic T-cell lymphoma: a clonal T-cell lymphoproliferative disorder with indolent behavior. *Mod Pathol* 2008;21:708-715.
 14. Rodríguez Pinilla SM, Roncador G, Rodríguez-Peralto JL, Mollejo M, García JF, Montes-Moreno S, et al. Primary cutaneous CD4+ small/medium-sized pleomorphic T-cell lymphoma expresses follicular T-cell markers. *Am J Surg Pathol* 2009;33:81-90.
 15. von den Driesch P, Coors EA. Localized cutaneous small to medium-sized pleomorphic T-cell lymphoma: a report of 3 cases stable for years. *J Am Acad Dermatol* 2002;46:531-535.
-