Primary cutaneous peripheral T cell lymphoma: A rare case with review of literature

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Abstract
Primary cutaneous lymphomas are a heterogeneous group of malignancies, exhibiting clinical differences from the systemic lymphomas. Peripheral T-cell lymphomas not uncommonly involve the skin, either as primary or secondary manifestation of the disease. Within this group, three rare provisional entities are delineated in the WHO-EORTC classification for cutaneous lymphomas. We present an extremely rare case of primary cutaneous CD4 positive small/medium-sized T-cell lymphoma in a 45-year-old patient with multi-focal skin lesions. The clinicopathological features have not been clearly established due to limited awareness and rarity of this entity. Hence there is yet no consensus on the optimal treatment of the disease and future trials need to be performed for elucidating targeted and optimal treatment.

Keywords: D4 positive small/medium; Cutaneous; Lymphoma

Introduction
Primary cutaneous T-cell lymphomas (PCTCL) are a heterogeneous group of malignancies, exhibiting clinical differences from the systemic lymphomas (1-2). Based on the newer classification proposed by World Health Organization (WHO)-European Organization for Research and Treatment of Cancer (EORTC), PCTCL are subdivided into three provisional entities, including the primary cutaneous CD4 positive small/medium T-cell lymphoma (PCSM-TCL), primary cutaneous CD8 positive aggressive epidermotropic cytotoxic T cell lymphoma and the primary cutaneous gamma delta T cell lymphoma (Willemze et al., 2005; Choi et al., 2011). Due to the fact that (PCSM-TCL) have a very rare occurrence and represent a heterogeneous group of diseases, their clinicopathological features are not well-established. Delay in the diagnosis, lack of specific markers and no common consensus on treatment of these patients. This report describes very rare clinical features of PCSM-TCL and discusses its review of literature.

Case report
A 45-year-old male patient presented with multiple deep ulcerated lesions, occurring first in the right hand followed by similar lesions at the right femoral proximal medial and lateral sites since three months. There were no B symptoms. The physical examination revealed multiple significant lymphadenopathy in the inguinal region, and widespread swollen, purple to violet-colored papular lesions with an approximate diameter of 1-3 cm in the back, abdomen, suprapubic area, and both the extremities (Figure 1). There was no hepatosplenomegaly. The laboratory findings were as follows: creatinine: 1.0 mg/dl, liver function tests were near normal, Lactate Dehydrogenase: 1451 U/L, Erythrocyte Sedimentation rate: 52 mm/hour, coagulation tests were normal. Laboratory tests showed a normal complete blood cell count with haemoglobin at 13.7 g/dl, platelet at 241 × 10⁹/L, leucocyt at 6.7 × 10⁹/L (neutrophils: 65%, lymphocytes: 23%, monocytes: 11%). ECOG score was one. The biopsy from the newly emerging lesions detected a neoplastic infiltration, formed by small and middle-sized, rippled, lymphoid cells with dark-staining nuclei, in the papillary dermis and extending to the deep reticular dermis surrounding the hair follicles (Figure 2A). Overlying epidermis was unremarkable. Immunophenotyping revealed widespread positive reaction with the CD2, CD3, CD4 and CD5
and positive reaction in some cells with CD8 (Figure 2 B, 2 C, 2 D). A weak positive reaction with Bcl-2 and reaction in a few histiocytic cells with CD68 in dispersed pattern was observed. With Ki67, a positive reaction was detected in 60-70% of the lymphoid population. No reaction was seen with CD20, CD30, BCL-6, CD10 and CD65. Epstein Barr Virus (EBV) DNA was detected to be negative. Bone marrow was uninvolved. Positron emission tomography detected diffuse fluorodeoxyglucose (FDG) uptake in both arms, hands, the back, chest and the abdominal skin lesions, inguinal and neck adenopathies. The patient was started on CHOP (Cyclophosphamide, Adriamycin, Vincristine, Methylprednisolone) treatment. He received eight courses of CHOP in total. While there was an improvement in the lesions after the 3rd course, the lesions were observed to re-occur subsequently. Upon detection of progression in the skin lesions on follow-up, ESHAP (Etoposide, Citarabine, Methylprednisolone) treatment was started. The patient died due to sepsis despite the minimal regression in the lesions.

Mycosis fungoides and primary cutaneous CD30 positive T-cell lymphomas represent more than 90% of all cases (Grogg et al., 2008). While PCSM-TCL is considered as a provisional entity in the new classification of WHO-EORTC, it represents approximately 2-3% of all cutaneous lymphomas (Garcia et al., 2008).

A majority of patients present with the manifestations of head, neck and trunk solitary plaques or tumors. The mean age of disease onset is reported to be 60 years (Willemze et al., 1994; Bekkenk et al., 2003). Due to the fact that skin involvement is at the forefront, most of the patients without B symptoms particularly, are diagnosed inaccurately and thus the treatment is started late (Xue et al., 2010).

Histologically, in case of PCMS-TCL, an extensive infiltration of small/medium pleomorphic T cells occurs in the dermis sparing the epidermis (Choi et al., 2011, Bekkenk et al., 2003). Immunohistochemically, most of the patients were reported to be CD3 and CD4 positive, CD8 and CD30 negative; or CD8 positive and CD4 negative, or all the T cell markers were lost (Willemze et al., 2005, Garcia et al., 2008). In addition, patients with PCMS-TCL were demonstrated to have an associated reactive B cell infiltration (Rodríguez et al., 2009). The rare occurrence, the biological heterogeneity, and the geographic variations limit the identification of the disease (Xue et al., 2010). Thus, the clinicopathological properties of PCSM-TCL have not been clearly established and future trials need to

![Figure 1](image1.png) Figure 1 Deep ulcerated wounds in the right femoral proximal medial and lateral regions and the right hand, widespread swollen, purple to violet-colored papular lesions with an approximate diameter of 1-3 cm in the back and abdomen regions, suprapubic area and the bilateral arms and legs

![Figure 2](image2.png) Figure 2 Medium and large atypical lymphoid cells (hematoxylin-eosin, original magnification x400) (A), Most of the lymphocytes express CD3 (B) and CD4 (C) and A few CD8 positive cells (D) are also present (x100)

Discussion

While peripheral T/natural killer lymphomas represent 12% of the non-Hodgkin lymphomas, 65% of cutaneous lymphomas are the T-cell lymphomas (Xue et al., 2010; Brown et al., 2008). Primary cutaneous T cell lymphomas are a heterogeneous group of diseases.
be performed for elucidating differential diagnosis and optimal treatment.

Previous trials reported a better prognosis in patients with localized involvement relative to those with multifocal skin lesions (Choi et al., 2011; Willemze et al., 2005). In addition, the presence of stable small lesions (< 3 cm) and the low proliferative activity exhibit an indolent clinical behavior while the presence of rapidly transforming large skin lesion (> 5 cm), high level of proliferation, infection with the Human T cell lymphoma/leukemia virus-1, and EBV exhibit an aggressive pattern (Xue et al., 2010, Bekkenk et al., 2003). PCSM-TCL has a better prognosis than the primary cutaneous CD30 negative large T-cell lymphoma and extra-cutaneous involvement was reported to be an indicator of poor prognosis (Bekkenk et al., 2003). In addition, expression of CD4, negative CD8 and localized skin involvement are associated with a good prognosis (Bekkenk et al., 2003).

There is as yet no consensus on the optimal treatment of the disease. In those with localized involvement, topical therapies such as surgical excision, localized psoralene and ultraviolet a treatment or local radiotherapy are administered (Choi et al., 2011). However, in patients with generalized skin involvement, multi-agent chemotherapies, particularly CHOP and CHOP-like systemic chemotherapy regimens are tried since they don’t respond to topical treatment (Xue et al., 2010; Choi et al., 2011). However, systemic chemotherapies, more intense than the CHOP treatment, failed to provide a marked improvement in cutaneous T cell lymphomas (Xue et al., 2010). Our patient had a recurrence of lesions and progression while on treatment with multi-agent systemic chemotherapy (CHOP).

Conclusion

We report a very rare case of PCMS-TCL; with unusual multifocal skin lesions in a young male. It was refractory to treatment. Patient exhibited systemic involvement with an extranodal involvement at more than one site, was at an advanced stage, had high serum LDH levels and a high Ki-67 expression. Studies that investigate a large number of cases are needed to provide the establishment of an exact diagnosis and optimal treatment.

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