Case Report

# Primary cutaneous gamma delta T-cell lymphoma with complete remission after CHOP therapy: The first case report from Thailand with literature review

Naree Warnnissorn*, Worapop Suthiwartnarueput*,
Panlop Chakkavittumrong**, Wasithep Limvorapitak**

**Abstract**

Primary cutaneous gamma delta T-cell lymphoma (PCGD-TCL) is a rare, clonal proliferation of mature activated gamma delta T-cells with cytotoxic phenotype. The skin lesion is epidermotropic with deep dermal or subcutaneous infiltrates. PCGD-TCL is usually resistant to chemotherapy and/or radiation with poor prognosis and median survival of 15 - 31 months. This first reported case of PCGD-TCL in Thailand was a 19-year-old male with multiple flesh color, velvety surface nodules at face and scalp, which had progressed in 3 months. Skin biopsy demonstrated epidermotropism with superficial dermal infiltration by small to medium size atypical lymphoid cells. The tumor cells were positive for CD3, TCR-gamma/delta, TIA-1 and CD4, and negative for betaF1, CD5, CD8, CD56, CD34, and Epstein-Barr encoding region (EBER) in situ hybridization. The disease stage was IA. After treatment with 8 cycles of CHOP chemotherapy, the patient achieved complete remission for 55 months. This PCGD-TCL case with unusual for 1) complete remission after CHOP chemotherapy and 2) tumor cell immunophenotype of CD4+ and CD56-.

**Key words:** Primary cutaneous gamma delta T-cell lymphoma, Thailand, diagnosis, CHOP, complete remission

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* Department of Pathology and Forensic Medicine, Faculty of Medicine, Thammasat University, Thailand
** Department of Internal Medicine, Faculty of Medicine, Thammasat University, Thailand
**Correspondence author:** Naree Warnnissorn MD, Department of Pathology and Forensic Medicine Faculty of Medicine, Thammasat University, Thailand Email: Medicine nareeaw@gmail.com

## Introduction

Primary Cutaneous Gamma-Delta T-Cell Lymphoproliferative (PCGD-TCL) was recognized by WHO classification of tumours of haematopoietic and lymphoid tissues (2017) under primary cutaneous peripheral T-cell lymphomas, rare subtypes by ICD-O code as 9726/3. The tumor cells are composed of a clonal proliferation of mature activated gamma delta T cells with cytotoxic phenotype. This is a rare entity representing less than 1% of all cutaneous T-cell lymphoma. Clinical presentations vary from patch/plaque to ulcer and commonly seen at extremities. The tumor cells have characteristic immunophenotype of CD3+, betaF1-, TCR-gamma+ or delta+, CD5-, cytotoxic protein+, CD56+ and mostly CD4-/CD8-.[1] The disease is usually resistant to multi-agent chemotherapy and has aggressive clinical course with median survival vary from 15 to 31 months.[1, 2]

Normal gamma delta (GD) T cells have T-cell receptor (TCR) composed of GD chains. They function in immune regulation, surveillance of homeostasis and also behave as cytotoxic cells. CD4/CD8 expression is CD4-/CD8- in 70%, CD4-/CD8+ in 30% and <1% CD4+/CD8-.[3] They comprise less than 5% of total T lymphocytes in the body, <5% in normal skin, and <10% in inflammatory skin diseases.[4]

One PCGD-TCL case had been documented in the series of mature T-cell and NK-cell lymphomas in Thailand: an analysis of 71 cases.[5] In which, the case was previously diagnosed as nodular mycosis fungoides but then changed to PCGD-TCL in the study due to absence of betaF1 on immunostaining and revision of WHO classification of year 2008 from 2001. The case was not described in details of clinical data and pathology.

## Case report

A 19-year-old male presented with multiple skin lesions which progressively enlarged within three months. He denied fever, weight loss or night sweating (B-symptoms). His personal history was negative for HIV risk behaviors. Physical examination showed multiple flesh color, velvety surface nodules, distributed at following areas: 1) left cheek, size 10 cm (representing 1% of total body surface area) with ulceration and serum oozing (figure 1); 2) right forehead, size 2 cm; and 3) chin, size 2 cm. The rests of physical examination were within normal limit. Laboratory investigations showed unremarkable CBC, BUN, creatinine and liver function tests. Serum lactate dehydrogenase was 331 U/dL [normal range <500 U/dL]. Serum HBsAg, anti-HCV and anti-HIV were negative. Contrast enhanced computed tomography (CT) of brain, paranasal sinuses, neck, chest and abdomen were all unremarkable except for multiple skin nodules and skin thickening at left temporal

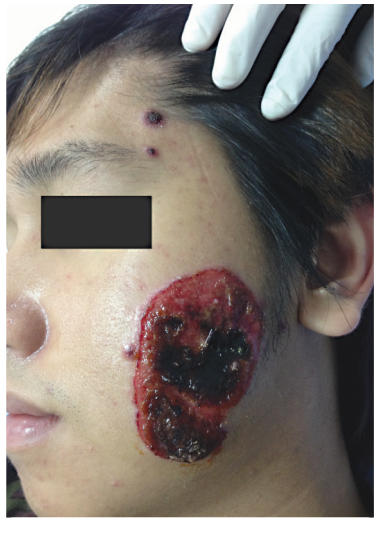

**Figure 1** Largest ulcerated lesion at left cheek

region, bilateral cheeks and chin.

Skin biopsy demonstrated epidermotropism with superficial dermal involvement (figure 2a) by small to medium size lymphoid cells with irregular hyperchromatic nuclei and small nucleoli (figure 2b). No subcutaneous fat tissue was seen. There was no Pautrier microabscess, angioinvasion or hemophagocytic activity. On the immunohistochemical staining, the tumor cells were CD3+ (figure 3a), betaF1-, TCR-gamma delta+ (figure 3b), CD5-, TIA-1+, CD2+, CD4+ (figure 3c), CD8-, CD56-, CD30-, CD34-, and TdT-, with proliferation index of 70-80% by Ki-67. EBER in situ

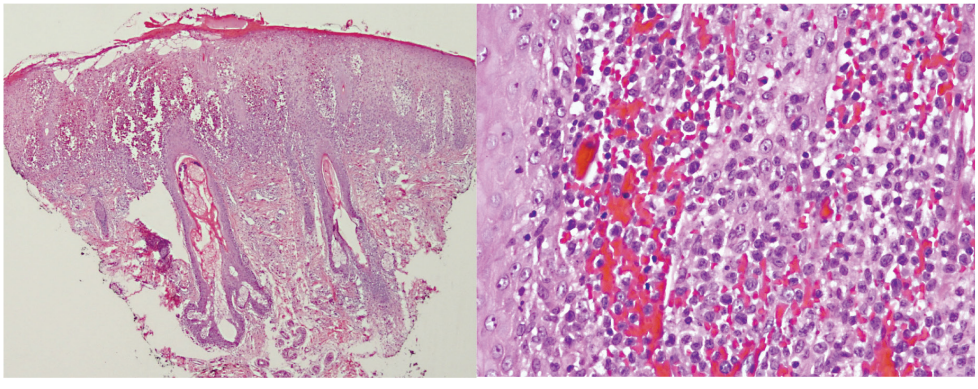

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**Figure 2** Skin biopsy from face. a) Epidermotropism with superficial dermal lymphoid infiltration (H&E x 2). b) Tumor cells are small to medium size lymphoid cells showing irregular hyperchromatic nuclei with small nucleoli (H&E x 40).

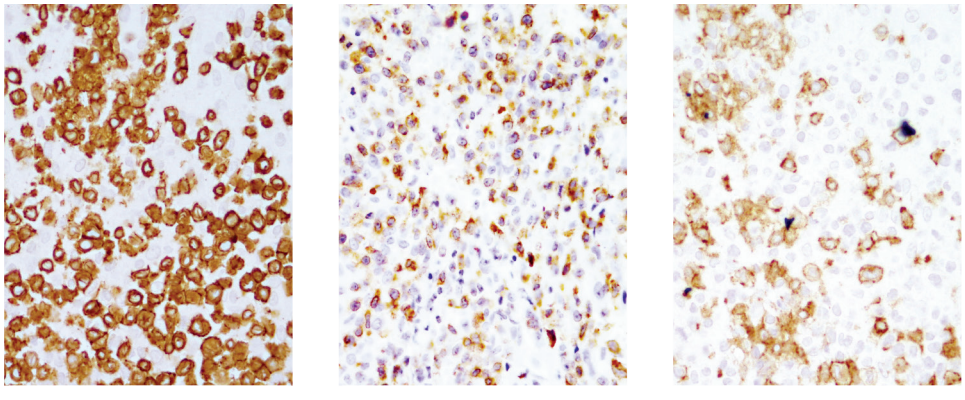

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**Figure 3** The tumor cells are positive for a) CD3, b) TCR-gamma delta and c) CD4 (focally).

hybridization was negative.

Investigations (nasal endoscopy, bone marrow biopsy) were negative for systemic involvement, indicating stage IA (disease limited to facial skin and scalp).

He was treated with CHOP chemotherapy regimen (cyclophosphamide 750 mg/sq.m., doxorubicin 50 mg/sq.m., vincristine 1.4 mg/sq.m., prednisolone 60 mg/sq.m.) every 3 weeks for 8 cycles, starting from June 2013. After 2 cycles of chemotherapy, all lesions were much improved, with only residual abrasion and serum oozing size 4 cm at left cheek. Complete remission (CR) was documented with CT follow-up after 4$^{th}$ cycle of chemotherapy. A CT follow-up showed CR after complete chemotherapy. He had been doing well without relapse at 55 months after CR.

The authors report this PCGD-TCL case for the unusual features of 1) complete remission after CHOP chemotherapy and 2) tumor cell immunophenotype of CD4+ and CD56-.

## Discussion

PCGD-TCL is a rare entity. In the largest series of PCGD-TCL (53 cases) the median age of patient was 61 years (ranging from 25 to 91 years) with median duration of skin lesions 1.25 years (ranging from 1 month to 20 years).[2] The common sites are legs, torso and arms. Head and neck region was affected less frequently (26%). Constitutional symptoms were reported in 54%. Skin presentation was commonly described as deep plaques resembling panniculitis, less as patches mimicking mycosis fungoides and ulcerated overtime. This patient had atypical clinical presentation of being 19 years old, short duration of skin lesion for 3 months, involving sites at face and scalp and absence of B-symptoms.

Establishing diagnosis is challenging due to wide range of morphologic pattern mimicking other cutaneous T-cell lymphomas such as epidermotropism as in mycosis fungoides; dermal lesion as in lymphomatoid papulosis; and subcutaneous infiltration as in subcutaneous panniculitis-like T-cell lymphoma. The epidermotropic or dermal pattern was noted in 36% of the cases.[6] Epidermotropic PCGD-TCL has better prognosis and longer median survival than more common type dermal PCGD-TCL.[7]

Demonstration of TCR gamma or delta chain by immunophenotype is crucial for diagnosis, because the lack of betaF1 expression does not always predict gamma delta T-cell derivation in TCR silent cases.[8] TCR-gamma expression was reported in 8.2% of primary cutaneous T-cell lymphomas.[9] CD4+/CD8- has been reported in 7%[2] and believed to contribute to the more indolent course.[10] CD56- was noted in 62%. There is no significant difference in survival between cases with CD56+ and CD56-.[11] CD4+/CD56- has been reported in a patient partially responded to CHOP but died of infectious complication.[12]

PCGD-TCL is resistant to multi-agent chemotherapy and/or radiation. In only 3 of 14 PCGD-TCL with subcutaneous panniculitis-like T-cell lymphoma pattern treated with CHOP had achieved complete remission.[11]

PCGD-TCL is a relatively new and rare disease. Clinical presentation and morphologic findings are overlapping with other more common T-cell lymphomas (mycosis fungoides, lymphomatoid papulosis, subcutaneous panniculitis-like T-cell lymphoma, and extranodal NK-/T-cell lymphoma). Establishing diagnosis requires extensive ancillary tests including at least immunohistochemical stains for CD3, CD4, CD5, CD7, CD8, CD20, CD30, CD34, CD56, TIA1, betaF1, TCR gamma delta and in situ hybridization for EBER. Certain features are associated with better outcome such as early disease stage, epidermotropic pattern of infiltration and CD4 expression. Aggressive chemotherapy may induce complete remission.

## Acknowledgements

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**Potential conflicts of interest**

The authors have no conflict of interest to declare.

**What is already known on this topic**

- Establishing diagnosis of cutaneous T-cell lymphoma requires knowledge of new lymphoma entities and extensive immunohistochemical study.

- Features associated with better outcome are epidermotropic infiltration, CD4 expression and early stage.

**What this study adds**

- PCGD-TCL in young patient with early stage, no B-symptoms, prompt diagnosis and aggressive therapy could result in favorable outcome.

- PCGD-TCL treated with CHOP can achieve complete remission for 55 months.

**Note**

This case report was presented at XXXI International Congress of the IAP and 28th Congress of the ESP (Cologne, Germany, 25 - 29 September 2016) and abstract was presented at the conference published at the society's journal https://rd.springer.com/journal/428/471/1/suppl/page/1 page s290[13]

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## บทคัดย่อ

**Primary cutaneous gamma delta T-cell lymphoma ตอบสนองต่อการรักษาด้วยเคมีบำบัด CHOP: รายงานผู้ป่วยรายแรกจากประเทศไทยและทบทวนบทความ**

**นารี วรรณิสสร*, วรภพ สุทธิวาทนฤพุฒิ*, พัลลภ จักรวิทย์ธำรง**, วศิเทพ ลิ้มวรพิทักษ์****

* ภาควิชาพยาธิวิทยาและนิติเวชศาสตร์ คณะแพทยศาสตร์ มหาวิทยาลัยธรรมศาสตร์
** ภาควิชาอายุรศาสตร์ คณะแพทยศาสตร์ มหาวิทยาลัยธรรมศาสตร์

Primary cutaneous gamma delta T-cell lymphoma (PCGD-TCL) เป็นโรคที่พบไม่บ่อย โดยเซลล์มะเร็งเป็น mature activated gamma delta T-cells ซึ่งมี cytotoxic phenotype ที่ก่อให้เกิดรอยโรคได้ตั้งแต่ในชั้นผิวหนังกำพร้า หนังแท้ ถึงไขมันใต้ผิวหนัง มะเร็งชนิดนี้มักไม่ตอบสนองต่อการรักษา และพยากรณ์โรคไม่ดี มีอัตราการรอดชีวิตเฉลี่ย 15 - 31 เดือน รายงานผู้ป่วยชายอายุ 19 ปี ได้รับการวินิจฉัยโรค PCGD-TCL เป็นรายงานแรกในประเทศไทย โดยผู้ป่วยมีก้อนสีแดงหลายก้อนบนใบหน้าและหนังศีรษะ รอยโรครุนแรงภายในเวลา 3 เดือน การตรวจชิ้นเนื้อที่เป็นแผลบนใบหน้า พบเซลล์มะเร็งเป็นลิมโฟไซท์ขนาดเล็กถึงกลางที่ชั้นหนังแท้และหนังกำพร้า และเซลล์ให้ผลบวกต่อ CD3, TCR-gamma/delta, TIA-1, CD4 และให้ผลลบต่อ betaF1, CD5, CD56, CD34 และ EBER และระยะของโรค IA ผู้ป่วยได้รับการรักษาด้วยยาเคมีบำบัด CHOP 8 ครั้ง โรคสงบเป็นเวลา 55 เดือน ผู้ป่วย PCGD-TCL รายนี้มีความแตกต่างจากผู้ป่วยส่วนใหญ่ 1) โรคสงบหลังได้รับการรักษาด้วยเคมีบำบัด CHOP และ 2) เซลล์มะเร็งมีลักษณะ CD4+ และ CD56-

**คำสำคัญ:** ทีเซลล์ลิมโฟมาที่ผิวหนังชนิดแกมมาเดลตา, ประเทศไทย, วินิจฉัย, เคมีบำบัด, โรคสงบ