CASE REPORT

Primary Cutaneous T Cell Lymphoma (Gamma Delta subtype)

Yong Khee Guan, MRCP, Chye Chung Gan, MRCP

Department of Medicine, Hospital Melaka, Melaka, Malaysia

SUMMARY

Primary cutaneous T-cell lymphoma gamma-delta subtype is an extremely rare entity of all the cutaneous T-cell lymphomas. Our case provides an insight on clinical behavior and treatment response with feasible effective combination chemotherapy. We believe this will be of great interest to clinicians when facing this difficult clinical entity. We present a case of a 66-year-old Malay man with a three-week history of rapidly growing skin nodules and plaques which spread throughout his body. He was commenced on combination chemotherapy gemcitabine, etoposide, and carboplatin with near complete remission on completion of second cycle but he defaulted. He relapsed within a month and he progressed despite treatment with the same regime. He was salvaged with fludarabine, cytarabine, and vinblastine combination chemotherapy but progressed with brain metastasis and died. However, more investigations and studies need to be done in this relatively unknown rare entity. A rare lymphoma registry might be of help to better understand and treat similar conditions.

KEY WORDS:
Cutaneous lymphoma, Gamma delta subtype, T cell lymphoma

INTRODUCTION

Primary cutaneous gamma-delta (γδ) subtype is a lymphoma composed of a clonal proliferation of mature, activated γδ T-cells with a cytotoxic phenotype. It is extremely rare and represents approximately 1% of all cutaneous T-cell lymphomas.[1] In our own cohort, all cutaneous T-cell lymphoma comprises only 2% of our total Non Hodgkin Lymphoma population. We report a case of primary cutaneous T cell lymphoma (gamma delta subtype) which is probably the first reported case in Malaysia.

CASE REPORT

A 66-year-old Malay man with Type 2 Diabetes Mellitus presented with a three-week history of rapidly growing skin lesions in August 2014. They started as multiple non-tender, non-pruritic nodules and plaque over the trunk which spread to the scalp, face, neck, and limbs (Figure 1). He denied having fever, weight loss and loss of appetite. The lesions were erythematous and indurated with some necrotic lesions. There were no lymphadenopathies or hepatosplenomegaly.

Peripheral blood film revealed monocytosis (1.6 x 10^3/uL) and neutrophilia (10.7 x 10^3/uL) but with no cytopenia and no blasts or abnormal cells. An excision skin biopsy taken from a nodule at the trunk showed unremarkable epidermis but the dermis showed scattered atypical lymphoid cells infiltrate and aggregates involving panniculitic changes of deeper adipose tissue. These atypical lymphoid cells were admixture of medium to large sized cells, exhibiting vesicular nuclei, clumped chromatin to conspicuous 1-2 nucleoli and irregular nuclear membrane (Figure 2-A). Immunohistochemical staining showed that the atypical cells were showing strong and diffuse immunoreactivity to CD2, CD3, strong cytotoxic properties (Perforin +ve, TIA +ve) but CD56-, CD8-, and CD4- (Figure 2-B & 2-C). These T-cells were also TCR-Beta (BF-1) negative. Other markers were: Tdt-, MPO-, CD30-, CD34-, CD117-, CD20-, and PAX5-. These lesions showed high proliferative index (Ki67 >60%) especially those in perifollicular and subcutaneous adipose tissue area (Figure 2-D). Bone marrow examination showed no marrow infiltration.

He was then diagnosed to have stage III primary cutaneous T-cell lymphoma gamma delta subtype with TNM classification of T_4, N_0, M_0. He was commenced on combination chemotherapy gemcitabine 1000mg/m2 Day 1 & Day 8, etoposide 100mg/m^2 Day one to Day three, and carboplatin (AUC 4) on Day two. He went into partial remission post first cycle of chemotherapy. He completed his second cycle of the chemotherapy with near complete remission but he then defaulted. He relapsed within a month with increasing number and size of similar lesions with constitutional symptoms such as loss of weight and appetite. He was recommenced back with gemcitabine, etoposide, and carboplatin but he progressed. He was then salvaged with fludarabine, cytarabine, and vinblastine combination chemotherapy but progressed on treatment. He died four months from the time of diagnosis due to disease progression and brain metastasis.

Fludarabine-high dose, cytarabine, and vinblastine combination was chosen as salvage chemotherapy. Fludarabine-Cytarabine combinations have synergistic effect and were also of a different class of chemotherapy. This combination also provide some central nervous system protection. Unfortunately, we were unable to assess his tolerability to this combination chemotherapy as he progressed even with this treatment.

The combination chemotherapy of gemcitabine, etoposide and carboplatin was toxic. The main toxicities were haematological with grade 3-4 anaemia, neutropaenia and

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Corresponding Author: Chye Chung Gan, Clinical Specialist, Department of Medicine, Hospital Melaka, Jalan Mufti Haji Khalil, 75400 Melaka, Malaysia. Email: drgancc85@hotmail.com

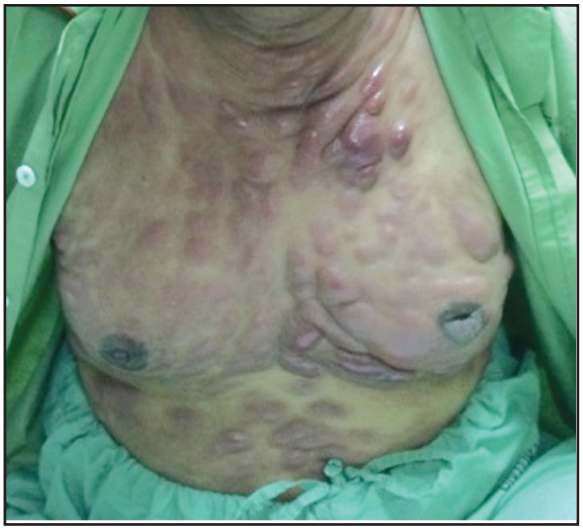

Fig. 1: Multiple nodules and plaque over the trunk.

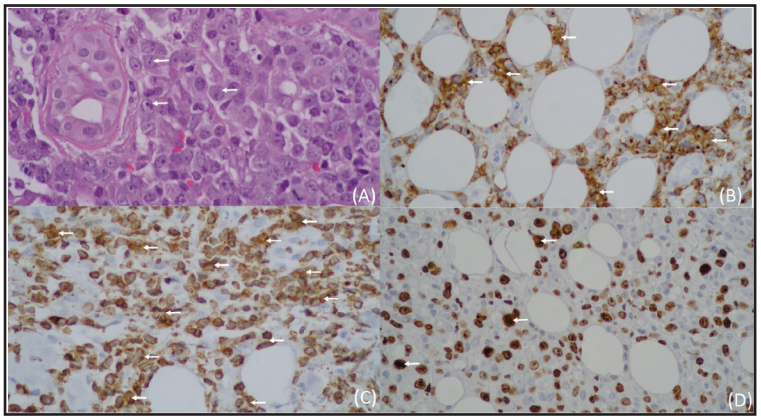

Fig. 1: Histopathology of the skin nodule.
(A) Lymphoma cells morphology (arrows) (H&E, x 60)
(B) Positive cells are the cells with cytoplasm stained brown in colour for CD2 (arrows) (CD2+ IHC, x 40)
(C) Positive cells are the cells with cytoplasm stained brown in colour for CD3 (arrows). Both CD2 and CD3 are T Cell Markers (CD3+ IHC, x 40)
(D) Ki67 is a proliferative index of the malignant cells. The positive cells are stained brown (arrows) (Ki 67 IHC, x 40)

thrombocytopaenia requiring transfusions and filgrastim support. The nadir of the cytopaenia was at a mean of day 10 and mean recovery was day 14. There was grade 1 rise in serum creatinine and alanine aminotransferase (ALT) level which resolved spontaneously.

DISCUSSION

Primary cutaneous T cell lymphoma (gamma delta subtype) is a provisional entity in the Revised European American Lymphoma (REAL) classification and the World Health Organization (WHO).[1] It is an aggressive lymphoma and overall prognosis is poor with median survival of approximately 15 months[1] and not much is known about the entity. Subcutaneous adipose tissue involvement seemed to have worse outcome. The conventional cyclophosphamide, vincristine, doxorubicin, and prednisolone combination (CHOP) chemotherapy is inadequate as treatment for this condition.[2,3] Carboplatin was chosen due to the known refractoriness of peripheral T cell lymphoma to anthracyclines.[3] Gemcitabine has previously been shown to have better efficacy in T cell Non Hodgkin Lymphoma and better tolerability in the elderly.[2] Etoposide is known to be effective in cutaneous lymphoma.[4,5] However, more investigation and studies need to be done in this relatively unknown rare entity.

CONCLUSION

Our case illustrated the extremely aggressive and rapid progression of this disease and the initial response to chemotherapy and the subsequent chemo-refractoriness of the disease. The gemcitabine, etoposide, and carboplatin combination chemotherapy appeared feasible and safe and warrants further investigation. We suggest setting up a rare lymphoma registry which might help to pool together clinical course and data to help to treat this uncommon condition later.

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