Interleukin-17 producing effector memory T cells and $CD4^+CD25^+Foxp3^+$ regulatory T cells correlated with phosphate and parathyroid hormone levels in chronic hemodialysis patients

Cheng-Lin Lang[1], Min-Hui Wang[2], Sung-Hao Hsu[3],
Kuan-Yu Hung[4], Chih-Kang Chiang[4], Kuo-Cheng Lu[2]

[1]Department of Internal Medicine, Cardinal Tien Hospital Yonghe Branch
[2]Department of Internal Medicine, Cardinal Tien Hospital , Fu Jen Catholic University
[3]Institute of Zoology, College of Life Science, National Taiwan University
[4]Department of Internal Medicine, National Taiwan University Hospital, National Taiwan University

INTRODUCTION

T helper (Th) lymphocytes play critical roles in the immune activation and inflammation in the chronic hemodialysis (HD) patients and mineral bone disorders including hyperparathyroidism and hyperphosphatemia contribute to the inflammatory effects. Interleukin-17 producing effector memory T (Th17) cells and $CD4^+CD25^+$ regulatory T (Treg) cells both come from naive Th cells, share reciprocal development pathways but exhibit opposite effects. Here we investigated the relationship between the Treg and Th17 cells and mineral bone disorder in the chronic HD patients.

MATERIALS AND METHODS

One hundred and five patients (age ≥ 35 years old) on chronic HD over 3 months were enrolled. Patients with systemic infection or malignancy, taking immunosuppressive medication were all excluded. The peripheral blood mononuclear cells were collected, cultured and stimulated by phytohemagglutinin-L (PHA-L), phorbolmyristate acetate (PMA) and ionomycin in different time point. The Treg cells and Th17 cells were then stained and analyzed by flow cytometry. Hematological and biological markers were detected. The relationship was analyzed by statistical analysis.

RESULTS

The T cell differentiation were as follows: $IL\text{-}17^+CD4^+$T (Th17) cells (mean ± standard deviation (SD): 25.61% ± 10.2%) and $CD4^+CD25^+Foxp3^+$T (Treg) cells (8.45% ± 4.3%). In the mineral aspect, the Th17 cell differentiation correlated with serum phosphate (P) ($r = 0.211$, $p < 0.05$) and intact parathyroid hormone (iPTH) levels ($r = 0.277$, $p < 0.05$, **Fig 1**). The Treg cell differentiation negatively correlated with P and iPTH levels ($r = -1.97$, $p < 0.05$ and $r = -1.76$, $p < 0.05$, **Fig 2**). Besides, the Th17/Treg cell ratio also correlated with the age and albumin levels ($r = -0.25$, $p < 0.01$ and $r = 0.26$, $p < 0.05$) but did not correlat with the calcium, alkaline-P or CRP levels as determined by statistical analysis. In the non-diabetes patient group (n= 53), the Th17 cell differentiation more predominant correlated with P and iPTH levels ($r = 0.443$, $p < 0.001$ and $r = 0.384$, $p < 0.005$, **Fig 3**).

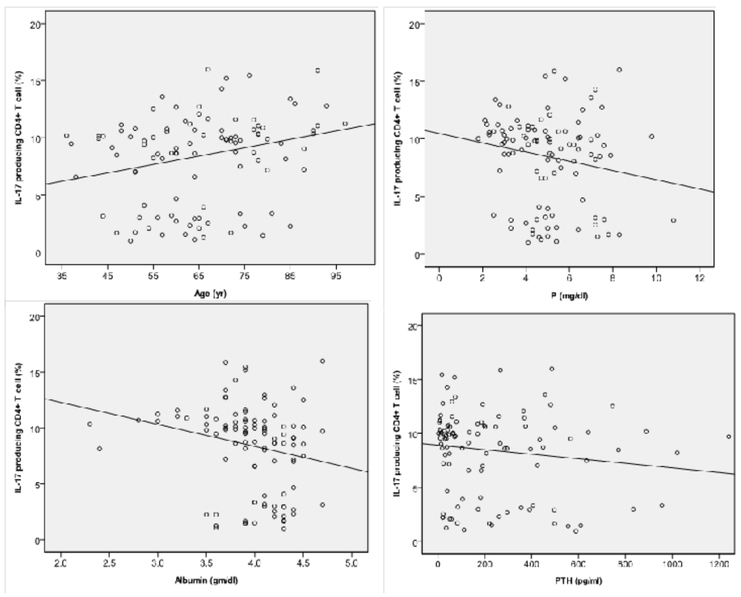

Fig 1
IL-17 producing CD_4^+ T cell differentiation correlated with age (left upper), albumin (left lower), phosphorus (right upper) and parathyroid hormone (right lower)

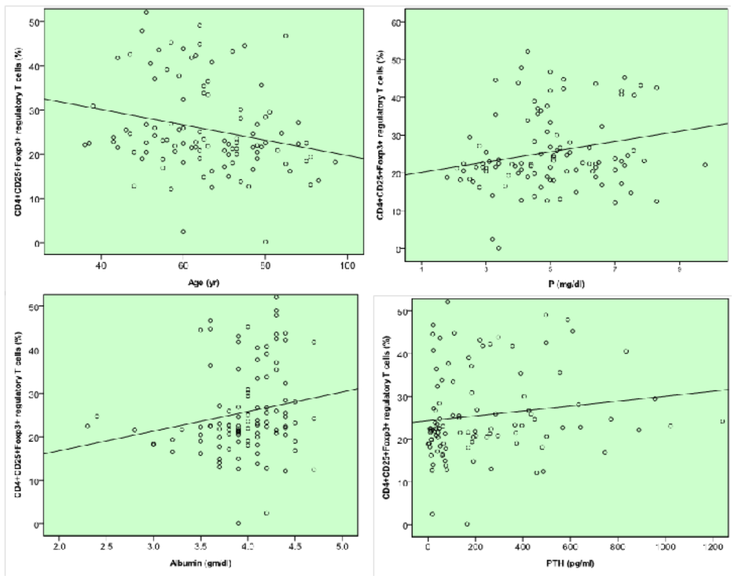

Fig 2
$CD4^+CD25^+Foxp3^+$T cell differentiation correlated with age (left upper), albumin (left lower), phosphorus (right upper) and parathyroid hormone (right lower)

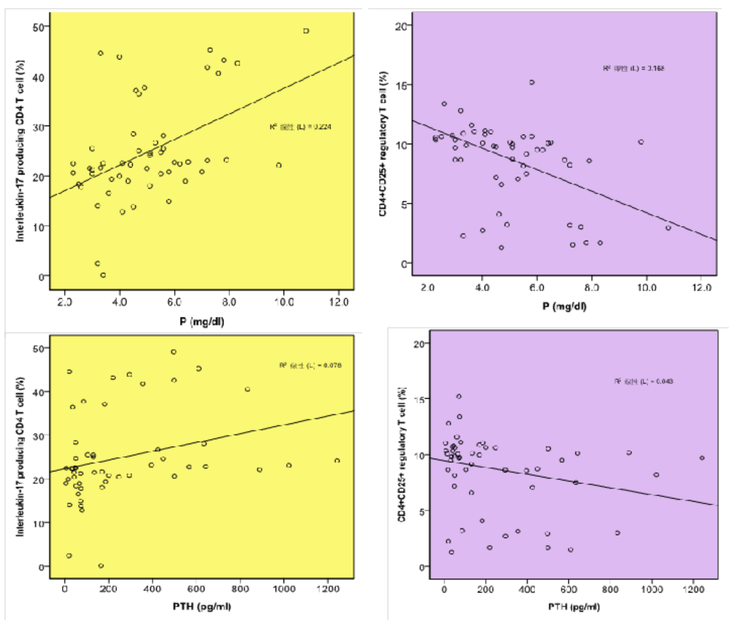

Fig 3
Phosphorus correlated with Th17 cell (left upper) and Treg cell (right upper) differentiation, and parathyroid hormone correlated with Th17 cell (left lower) and Treg cell (right lower) differentiation

CONCLUSIONS

The results indicate that the Th17/Treg imbalance in the chronic HD group. High serum phosphate and intact parathyroid hormone levels and low serum albumin levels presented with increasing Th17 cell differentiation, especially in the non-diabetes, chronic HD patients.

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