

HYPERANDROGENEMIA INDUCES RENAL T CELL TRAFFICKING AND IMMUNE IMBALANCE IN A PCOS RAT MODEL

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ABSTRACT

Background: Polycystic ovary syndrome (PCOS) is one of the most common hormonal disorders in women of reproductive age. It is associated with elevated androgens, increased inflammation, immune dysfunction, high blood pressure, and a higher risk for cardiovascular diseases (CVD). However, the T lymphocyte trafficking in the kidney as a potential mechanism for higher blood pressure has not been elucidated. **Aim:** To test the hypothesis that T lymphocyte intracellular trafficking is increased in the kidneys of hyperandrogenemic female (HAF) rats, which could potentially play a role in kidney injury and higher blood pressure. **Methods:** Female Sprague Dawley rats at 4 weeks of age were implanted subcutaneously with dihydrotestosterone or placebo pellets. Kidneys were collected after allowing the rats to age 15 weeks. Renal immune cells were isolated, and the number of renal infiltrated lymphocytes was measured using flow cytometry. **Results:** It was found that HAF rats had a significantly higher percentage of renal infiltrated CD4⁺, Th17, and CD4⁺CD28^{null} T lymphocytes; and a novel prevalence of CD4⁺CD8⁺ double-positive (DP) T lymphocytes; a 5-fold increase compared to placebo control. Notably, the study revealed a significant reduction in the renal infiltrated Regulatory T (Treg) cells in HAF rats compared to their placebo counterpart. **Conclusion:** These findings suggest that hyperandrogenemia may trigger T lymphocytes migration, disrupt the immune homeostasis of the kidney, induce tissue injury, and contribute to higher blood pressure, which will eventually allow the navigation of new therapeutic targets that may improve outcomes in hypertension and CVD in hyperandrogenemia and/or PCOS patients.

Keywords: PCOS, Inflammation, Cardiovascular, Th17, Treg cells, CD4⁺CD8⁺ double-positive (DP)

INTRODUCTION

Polycystic ovary syndrome (PCOS) is a prevalent endocrine disorder, affecting up to 10–15% of women of reproductive age globally [1]. Characterized by hyperandrogenism, polycystic ovarian morphology, and chronic low-grade inflammation. PCOS has traditionally been viewed through the lens of reproductive health. However, emerging evidence reveals that PCOS extends far beyond gynecological implications, acting as a systemic disorder that predisposes women to metabolic, cardiovascular, and immunological dysfunction [2-6]. Notably, women with PCOS often exhibit elevated blood pressure; an increased risk of cardiovascular disease (CVD), and abnormalities in immune regulation [2, 3, 7]. Understanding these associations is essential for early intervention and comprehensive patient care. One of the most frequently reported cardiovascular comorbidities in PCOS is high blood pressure. Studies have consistently demonstrated that women with PCOS are more likely to develop elevated blood pressure compared to age-matched controls. The mechanism behind this phenomenon appears to be multifactorial, involving insulin resistance, sympathetic nervous system overactivity, and endothelial dysfunction [2-4, 8].