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ORIGINAL ARTICLE

T cell clonal expansion and *STAT3* mutations: a characteristic feature of acquired chronic T cell-mediated pure red cell aplasia

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Abstract

Acquired chronic pure red cell aplasia (PRCA) develops idiopathically or in association with other medical conditions, including T cell large granular lymphocytic leukemia (T-LGLL) and thymoma. T cell dysregulation is considered a cardinal pathogenesis of PRCA, but genetic–phenotypic associations in T cell abnormalities are largely unclear. We evaluated an extended cohort of 90 patients with acquired PRCA, including 26 with idiopathic, 36 with T-LGLL-associated and 15 with thymoma-associated PRCA, for their T cell immuno-phenotypes, clonalities and *STAT3* mutations. TCR repertoire skewing of $CD8^+$ T cells was detected in 37.5% of idiopathic, 66.7% of T-LGLL-associated and 25% of thymoma-associated PRCA patients, and restriction to Vβ1 was most prominent (41%). Clonalities of TCRβ or γ chain and *STAT3* mutational status were statistically associated ($P = 0.0398$), and they were detected in all three subtypes. The overall response rate to cyclosporin A was 73.9%, without significant difference by subtypes nor *STAT3* mutational status. The T cell dysregulations, such as TCR repertoire skewing with predominant Vβ1 usage, clonality and *STAT3* mutations, were frequently found across the subtypes, and the close associations between them suggest that these T cell derangements reflect a common pathophysiological mechanism among these PRCA subtypes.

Keywords Pure red cell aplasia · *STAT3* · T cell receptor · Thymoma · Large granular lymphocytic leukemia

Introduction

Acquired chronic pure red cell aplasia (PRCA) is a syndrome defined by anemia with the marked reduction or absence of erythroid production and normal hematopoiesis of other lineages, developing predominantly via T cell-mediated or

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