



The 65th ASH Annual Meeting Abstracts

POSTER ABSTRACTS

508.BONE MARROW FAILURE: ACQUIRED

Clinical Features and Outcomes in Large Granular Lymphocyte Leukemia-Associated Pure Red Cell Aplasia with STAT3 MutationXiaoqing Liu¹, Xiaoyu Chen², Yuemin Gong, MD, PhD², Qiqiang Long³, Guangsheng He⁴, Jianyong Li, MD²¹Hematology, The Second Hospital of Nanjing, Nanjing University of Chinese Medicine, Nanjing, China²Department of Hematology, The First Affiliated Hospital of Nanjing Medical University, Jiangsu Province Hospital, Nanjing, China³The Second Hospital of Nanjing, Nanjing University of Chinese Medicine, Nanjing, China⁴Department of Hematology, The First Affiliated Hospital of Nanjing Medical University, Jiangsu Province Hospital, NANJING, China**Background**

Large granular lymphocyte leukemia (LGLL) is a rare disease frequently complicated with pure red cell aplasia (PRCA) [1, 2]. STAT3 mutations have been described in 30-40% of LGLL patients [3]. The aim of this work was to evaluate whether STAT3 mutations might be associated with specific clinical features and outcomes in LGLL-associated PRCA.

Methods and results

From January 2016 to July 2023, 81 patients with LGLL-associated PRCA were enrolled in the China Eastern Cooperation Group for Anemia (CECGA) database (ChiCTR2100043485). As an initial step in the STAT3 mutational analysis, we screened all patients with Sanger sequencing or Next-generation sequencing (NGS). The initial dose of CsA was 3-5mg/kg/day, and the serum concentration was adjusted to be 150-200ng/mL based on adverse reactions. After 12 months of maintenance, the dosage was slowly reduced. Cyclophosphamide combined with prednisone (CP) regimen was used as a salvage therapy for patients who failed to CsA. The initial dose of cyclophosphamide and prednisone were 100mg/day and 0.5-1mg/kg/day, respectively.

Among the 81 cases, 26% of them were positive for STAT3 mutations. The clinical characteristics of patients with or without STAT3 mutation were summarized in Table 1. Patients with STAT3 mutations had a higher reticulocyte percentage (0.88% vs 0.28%, $P=0.039$) and red cell distribution width-coefficient of variation (18.8% vs 15.8%, $P=0.008$) than patients without STAT3 mutations.

Y640F mutation were found in 9 of 21 cases. Subgroup analysis showed that patients with Y640F mutation were associated with younger age (44 vs 65 years old, $P=0.007$) and higher lymphocyte percentage in peripheral blood (63.7% vs 34.4%, $P=0.033$). Deep sequencing of rearranged T-cell receptor V β complementarity-determining region 3 by NGS was conducted in 61 patients. The predominant V-gene of LGLL clonotypes belonged to the TRBV06 family gene was detected in 12 (25%) patients. The expression of TRBV06 family gene was a little lower in patients with STAT3 mutation than non-mutant groups (8% vs 31%, $P=0.189$).

The complete response rate (CRR) [31% (5/16) vs 33% (19/58), $P=0.909$] and overall response rate (ORR) [56% (9/16) vs 50% (29/58), $P=0.658$] of cyclosporine (CsA) treatment were similar in patients with STAT3 mutations or not. In STAT3 mutant group, the CRR [54% (7/13) vs 31% (5/16), $P=0.274$] and ORR [85% (11/13) vs 56% (9/16), $P=0.130$] of CP regimen tended to be better than CsA.

6 patients (67%) relapsed among the 9 patients who responded to CsA in STAT3 mutant group. In patients without STAT3 mutation, 19 of 29 (66%) CsA-responders relapsed. There was no significant difference in the relapse-free survival between the two group (Figure 1).

Discussion/Conclusions

In summary, STAT3 mutation was frequently recognized in LGLL-associated PRCA, and the hotspot site was Y640F. Patients with STAT3 mutations responded to CsA as well as those without the mutation. CP regimen could be used as a salvage therapy for patients who failed to CsA.

Reference

1. Balasubramanian SK, Sadaps M, Thota S, et al. Rational management approach to pure red cell aplasia. *Haematologica*. 2018, 103(2): 221-230.
2. Wu X, Cheng L, Liu X, et al. Clinical characteristics and outcomes of 100 adult patients with pure red cell aplasia. *Ann Hematol*. 2022, 101(7):1493-1498.
3. Barilà G, Teramo A, Calabretto G, et al. Stat3 mutations impact on overall survival in large granular lymphocyte leukemia: a single-center experience of 205 patients. *Leukemia*. 2020, 34: 1116-1124.

Disclosures No relevant conflicts of interest to declare.

Table 1 *STAT3* mutation and clinical features in LGLL-associated PRCA

	Mutated <i>STAT3</i> (<i>n</i> =21)	Non-mutated <i>STAT3</i> (<i>n</i> =60)	Statistical value	<i>P</i> -value
Age, years, median (range)	51 (22-86)	62 (16-89)	<i>t</i> =-1.44	0.154
Sex (male/female)	12/9	26/34	$\chi^2=1.19$	0.275
Hemoglobin level, g/L, median (range)	66(43-99)	58 (35-101)	<i>t</i> =1.88	0.063
Reticulocyte percentage, %, median (range)	0.88(0.12-4.12)	0.28 (0.03-4.25)	<i>Z</i> =-2.06	0.039
ANC, $\times 10^9/L$, median (range)	1.49(0.10-3.90)	1.85 (0.19-8.09)	<i>Z</i> =-1.79	0.073
RDW-CV, %, median (range)	18.8(12.7-28.3)	15.8 (11.9-26.4)	<i>Z</i> =-2.66	0.008
Lymphocyte ratio, %, median (range)	53.8(4.8-90.0)	34.2 (6.3-83.0)	<i>Z</i> =-1.58	0.113
CD3+CD4+, %, median (range)	62.8(3.0-88.8)	63.0 (15.5-91.0)	<i>Z</i> =-0.02	0.987
CD3+CD8+, %, median (range)	19.1(8.1-57.3)	21.8 (6.7-57.9)	<i>Z</i> =-0.77	0.444
CD3+CD57+, %, median (range)	12.6(7.3-41.0)	22.1 (1.8-55.3)	<i>t</i> =-1.23	0.189
Serum ferritin level, ng/mL, median (range)	486(25-3674)	516 (24-5659)	<i>Z</i> =-0.37	0.709
Serum LDH level, u/L, median (range)	232(125-311)	198 (103-640)	<i>Z</i> =-1.63	0.104
Serum $\beta 2$ -MG level, mg/L, median (range)	2.95(1.92-6.50)	2.74 (1.35-7.22)	<i>Z</i> =-1.08	0.282
Myelofibrosis, +/-	3/18	3/57	$\chi^2=0.84$	0.361

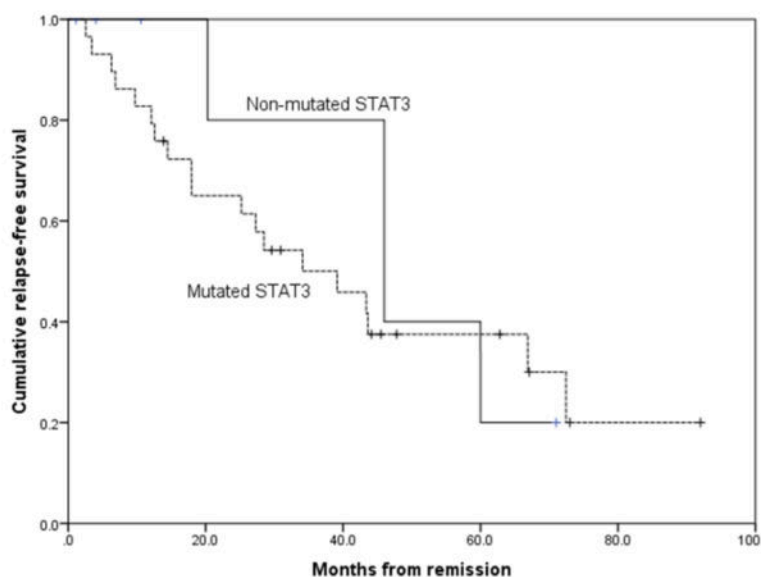


Figure 1 The relapse-free survival following CsA therapy. Based on the log-rank test, the median RFS of mutated group and non-mutated group were similar [46 (20.3-60.0) months vs 39.1 (2.6-72.4) months, (*P*=0.647)].

Figure 1

<https://doi.org/10.1182/blood-2023-186337>