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POSTER ABSTRACTS

508.BONE MARROW FAILURE: ACQUIRED

Clinical Features and Outcomes in Large Granular Lymphocyte Leukemia-Associated Pure Red Cell Aplasia with *STAT3* Mutation

Xiaoqing Liu[1], *Xiaoyu Chen*[2], *Yuemin Gong, MD, PhD*[2], *Qiqiang Long*[3], *Guangsheng He*[4], *Jianyong Li, MD*[2]

[1] Hematology, The Second Hospital of Nanjing, Nanjing University of Chinese Medicine, Nanjing, China
[2] Department of Hematology, The First Affiliated Hospital of Nanjing Medical University, Jiangsu Province Hospital, Nanjing, China
[3] The Second Hospital of Nanjing, Nanjing University of Chinese Medicine, Nanjing, China
[4] Department 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 higer lymphocyte percentage in peripheral blood (63.7% vs 34.4%, *P*=0.033).

Deep sequencing of rearranged T-cell receptor Vβ 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 litter 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 siginificant 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

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Disclosures No relevant conflicts of interest to declare.

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

	Mutated *STAT3* (*n*=21)	Non-mutated *STAT3* (*n*=60)	Statistical value	*P*-value
Age, years, median (range)	51（22-86）	62（16-89）	*t*=-1.44	0.154
Sex (male/female)	12/9	26/34	χ^2=1.19	0.275
Hemoglobin level, g/L, median (range)	66(43-99)	58（35-101）	*t*=1.88	0.063
Reticulocyte percentage, %, median (range)	0.88(0.12-4.12)	0.28（0.03-4.25）	*Z*=-2.06	**0.039**
ANC, $\times10^9$/L, median (range)	1.49(0.10-3.90)	1.85（0.19-8.09）	*Z*=-1.79	0.073
RDW-CV, %, median (range)	18.8(12.7-28.3)	15.8（11.9-26.4）	*Z*=-2.66	**0.008**
Lymphocyte ratio, %, median (range)	53.8(4.8-90.0)	34.2（6.3-83.0）	*Z*=-1.58	0.113
CD3+CD4+, %, median (range)	62.8(3.0-88.8)	63.0（15.5-91.0）	*Z*=-0.02	0.987
CD3+CD8+, %, median (range)	19.1(8.1-57.3)	21.8（6.7-57.9）	*Z*=-0.77	0.444
CD3+CD57+, %, median (range)	12.6(7.3-41.0)	22.1（1.8-55.3）	*t*=-1.23	0.189
Serum ferritin level, ng/mL, median (range)	486(25-3674)	516（24-5659）	*Z*=-0.37	0.709
Serum LDH level, u/L, median (range)	232(125-311)	198（103-640）	*Z*=-1.63	0.104
Serum β2-MG level, mg/L, median (range)	2.95(1.92-6.50)	2.74（1.35-7.22）	*Z*=-1.08	0.282
Myelofibrosis, +/-	3/18	3/57	χ^2=0.84	0.361

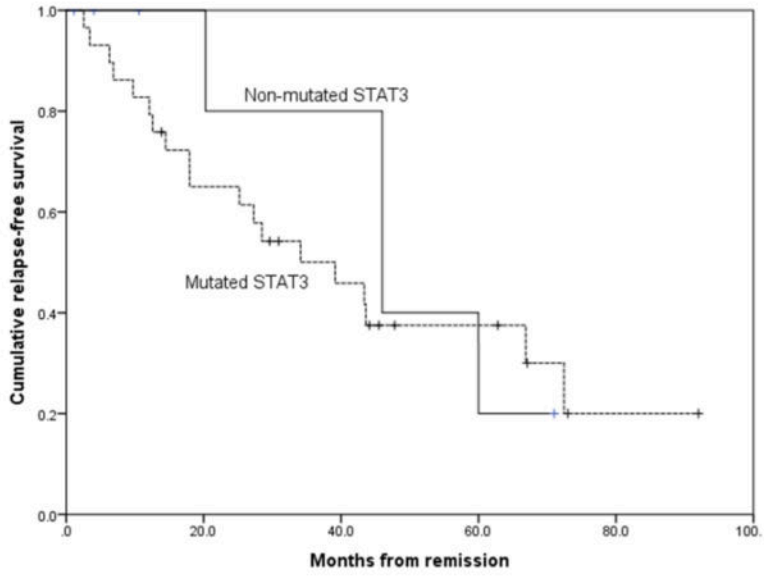

Figure 1 The relapse-free survival following CsA therapy. Based on the log-rank test, the median RFS of mutated group and non-mutated group were similar [46 (20.3-60.0) months vs 39.1 (2.6-72.4) months, (*P*=0.647)].

Figure 1

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