中文題目：超高白血球增多症之急性骨髓性白血病獨特的基因突變與臨床預後

英文題目：**Acute myeloid leukemia patients with Hyperleukocytosis have distinct genetic alterations and poor prognosis**

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**Background**

Acute myeloid leukemia (AML) with hyperleukocytosis (HL), commonly defined as white blood cell (WBC) counts >100,000/uL, are intuitively thought as a unique group with dismal prognosis. However, comprehensive studies regarding the genetic alterations and clinical outcome in this group of patients are limited, and the role of hematopoietic stem cell transplantation (HSCT) is controversial.

**Method**

A cohort of 757 *de novo* AML patients diagnosed from 1994 to 2011 who had cryopreserved cells for analysis were enrolled. The mutation status of 20 genes was determined by Sanger sequencing and/or next generation sequencing (NGS). We compared cytogenetics and relevant mutations in these genes between AML patients with and without HL, and exposed their prognostic implications.

**Results**

The median age was 54 (range 15-94). 102 (13.5%) patients had HL. HL was associated with younger age, higher peripheral blast percentage. HL was correlated with French-American-British (FAB) M1, M4 or M5 subtypes, but

inversely with M2 or M3 subtypes. The HL patients had more frequently AML with intermediate-risk cytogenetics, but less commonly good-risk or poor-risk cytogenetic AML. The most common genetic alteration in the patients with HL was *FLT3*/ITD (35.0%), followed by *NPM1* (28.4%), *CEBPA* (26%), *NRAS* (21.6%), and *TET2* (19.8%) mutations. The HL patients had significantly higher incidences of *FLT3*/ITD (35.0% *vs*. 17.3%, P<0.0001), *NPM1* (28.4% *vs*. 17.9%, P=0.013), *CEBPA* (26% *vs.* 11.1%, P<0.0001), *NRAS* (21.6% *vs*. 13.8%, P=0.04), and *TET2* (19.4% *vs*. 9.9%, P=0.006) mutations.

Survival analysis was performed on the 525 patients who received standard intensive chemotherapy. The HL patients had lower complete remission (CR) rates compared to those without (62.9% *vs.* 78%, P=0.006). Further, the HL patients had significantly poorer overall survival (OS) and disease-free survival (DFS) than those without (median 24 months *vs.* not reached (NR), P=0.042; 6.5 *vs.* 11.8 months, P=0.005, respectively). In the multivariate Cox proportional hazards regression analysis, HL was still an independent poor prognosis factor for OS and DFS (RR, 1.72; 95% CI, 1.22-2.44, P=0.002 and RR, 2.07; 95% CI, 1.29-3.33, P=0.003, respectively). Intriguingly, among the HL patients, those with HSCT had longer OS than those without (58.2 vs 10.7 months, P=0.004). Among the 172 patients receiving HSCT, the poor prognostic impact of HL on survival was ameliorated.

**Conclusion**

The HL patients represented 13.5% of our AML cohort and showed distinct genetic alterations compared to those without HL. HL was an independent poor prognosis factor irrespective of other prognostic factors, and the HL patients may potentially benefit from HSCT.