

CEBPA gene mutations in Egyptian acute myeloid leukemia patients: Impact on prognosis

Mohamed Awad, Doaa A. Aladle, Nashwa K. Abousamra, Doaa M. Elghannam and Iman m fawzy
Mansoura University, Egypt

Aim: To assess the prognostic role of myeloid transcription factor gene CEBPA (CCAAT/enhancer binding protein- α), a novel gene involved in leukemia in Egyptian adults AML.

Materials and Methods: Screening for CEBPA mutations was assessed using PCR-single-strand conformation polymorphism (PCR-SSCP) in pretreatment bone marrow samples from 55 newly diagnosed adult AML.

Results: CEBPA mutations were found in 11 (20%) of 55 AML patients. They had significantly higher hemoglobin ($p=0.037$), and lower LDH ($p=0.003$) levels when compared to those without. CEBPA mutations were frequently detected in M4 (45.5%) and M2 (27.2%) subtypes, and significantly associated with normal karyotype (90.9%, $p=0.007$). We distinguished 6 cases with 2 different mutations or one homozygous mutation (CEBPA^{double-mut}) as well as 5 cases with only one single heterozygous mutation (CEBPA^{single-mut}). Patients with CEBPA mutations had significantly higher complete remission ($p=0.047$), lower mortality ($p=0.047$). Double CEBPA mutant cases showed longer disease free survival (DFS) and overall survival (OS) when compared to wild type CEBPA (for DFS; median=27 versus 24 months respectively; $p=0.009$ and for OS; median=28 versus 25 months respectively; $p=0.008$). No significant differences were found between CEBPA^{single-mut} cases and wild type cases regarding DFS and OS (for DFS; median=13 versus 24 months respectively; $p=0.615$ and for OS; median=14 versus 25 months respectively; $p=0.703$).

Conclusion: CEBPA mutation status is known to be a prognostic factor for favorable outcome in AML patients. CEBPA^{double-mut} is associated with favorable DFS and OS. In contrast, CEBPA^{single-mut} AMLs survival studies did not differ significantly with wild-type cases. These results demonstrate significant underlying heterogeneity within CEBPA mutation positive AML with prognostic relevance. Based on these findings, we propose that CEBPA^{double-mut} should be clearly defined from CEBPA^{single-mut} AML and considered as a separate entity in the classification of AML. Furthermore, incorporation of CEBPA mutation status into novel risk-adapted therapeutic strategies in Egypt will improve the currently disappointing cure rate of this group of patients.

abosamrana@yahoo.com