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Prognostic significance of CEBPA mutations and BAALC expression in acute myeloid leukemia Egyptian patients with normal karyotype

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Cytogenetic aberrations are important prognostic factors in acute myeloid leukemia (AML). However, about 50% of newly diagnosed acute myeloid leukemia (AML) cases have normal karyotype. These patients are very heterogenous with respect to acquired gene mutations and gene expression changes. The identification of these genetic alterations may lead to improved prognostification and generation of novel risk-adapted therapies. The aim of this work was to study the prognostic impact of mutations in the myeloid transcription factor gene CEBPA (for CCAAT/enhancer binding protein-alpha) and expression of the BAALC gene (for brain and acute leukemia, cytoplasmic), a novel gene involved in leukemia, in 38 adults with AML and normal cytogenetics. Screening for mutations of CEBPA gene was assessed using PCR-single-strand conformation polymorphism (PCR-SSCP), and BAALC expression was determined by real-time reverse transcriptase polymerase chain reaction in blood or bone marrow samples. CEBPA mutations were found in 7 (18.4%) of 38 patients, 36.8 % (14 of 38) had low BAALC expression and 63.2 % (24 of 38) had high BAALC expression. Patients with CEBPA mutations had favorable course of their disease. They had higher rate of complete remission (CR) (85.7 % vs 51.6 %; P = 0.108), lower incidence of relapse (0% vs. 41.9%; P = 0.038). Disease free survival (DFS) and overall survival (OS) were significantly longer for patients with CEBPA mutations compared with patients without mutations (mean 13.65 +/- 5.41 vs. 7.32 +/- 4.33 months, P = 0.047; mean 15.32 +/- 6.5 vs 8.5 +/- 3.21 months, P = 0.039; respectively). Compared to low BAALC expressers, high BAALC expressers had lower incidence of CR (50% vs 71.4%; P = 0.171), higher incidence of relapse (50% vs. 14.3%; P = 0.029), and showed significantly shorter DFS (mean 7.5 +/- 2.12 vs. 11.67 +/- 4.6 months, P = 0.038) and inferior overall survival (mean 9.1 +/- 3.52 vs. 13.22 +/- 4.21 months, P = 0.024). On multivariable analysis, wild-type CEBPA as well as high BAALC expression were confirmed as independent risk factors predicting inferior DFS (CEBPA, hazard ratio 0.066, P = 0.001; BAALC, hazard ratio 3.98, P = 0.003) and inferior OS (CEBPA, hazard ratio 0.125, P = 0.002; BAALC, hazard ratio 4.215, P = 0.001). Data obtained in this study suggest that CEBPA mutation status and BAALC expression are important prognostic factors in AML patients with normal cytogenetics and their incorporation into novel risk-adapted therapeutic strategies may improve the currently disappointing cure rate of this group of patients.