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Upregulation of microRNA-375 is associated with poor prognosis in pediatric acute myeloid leukemia

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Abstract A genome-wide serum miRNA expression analysis previously showed the upregulation of microRNA-375 (miR-375) in acute myeloid leukemia (AML) patients compared with healthy controls. The aim of this study was to investigate the expression patterns and the prognostic relevance of miR-375 in pediatric AML. Expression levels of miR-375 in bone marrow mononuclear cells were detected by real-time quantitative PCR in a cohort of 106 patients with newly diagnosed pediatric AML. Expression levels of miR-375 in the bone marrow of pediatric AML patients were significantly higher than those in normal controls ($P < 0.001$). Then, miR-375 upregulation occurred more frequently in French–American–British classification subtype M7 than in other subtypes ($P < 0.001$). Regarding to cytogenetic risk, the expression levels of miR-375 in pediatric AML patients with unfavorable karyotypes were dramatically higher than those in intermediate and favorable groups ($P = 0.002$). Moreover, high miR-375 expression was significantly associated with shorter relapse-free survival ($P < 0.001$) and overall survival ($P < 0.001$) in pediatric AML patients. Multivariate analysis further identified miR-375 expression and cytogenetics risk as independent prognostic factors for both relapse-free survival and overall survival. In particular, the prognostic relevance of miR-375 expression was more obvious in the subgroup of patients with intermediate-risk cytogenetics. Our findings suggest for the first time that the upregulation of miR-375 may be one of the molecular mechanisms involved in the development and progression of pediatric AML. Since its correlation with poor relapse-free survival and overall survival, miR-375 may be a novel biomarker to improve the management of pediatric AML patients.

Keywords Pediatric acute myeloid leukemia · microRNA-375 · Real-time quantitative PCR · Prognosis

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Introduction

Acute myeloid leukemia (AML), characterized by the uncontrolled proliferation of granulocytic, monocytic, megakaryocytic, or rarely, erythroid blast cells, still leads to a very poor prognosis [1]. As a heterogeneous disease, AML is implicated in many different cytogenetic and molecular abnormalities, which are detected at the time of diagnosis and are important prognostic factors that help to determine the clinical outcome of patients [2]. In AML, the distinct feature of leukemogenesis is differentiation arrest and proliferative advantage of myeloid progenitors. AML makes up only 15–20 % of pediatric leukemia, however, it accounts for >30 % of the deaths from pediatric leukemia [3]. The relapse remains a major cause of failure and the clinical outcome of pediatric AML is still poor. The 5-year disease-free survival in pediatric AML patients is about 50 % in the most successful studies [4]. Although dose-intensive treatment by induction chemotherapy and allogeneic stem cell transplantation with a matched related donor has been considered as effective treatment for