Prognostic impact of ID1 and ID4 genes expression on adult Egyptian patients with acute myeloid leukemia

Amira M. N. Abdelrahmana, Magda A. E.-A. M. Zidana, Mona S. Abdellateifb, Ola S. E. D. Awada, Naglaa M. Hassanc

Background Acute myeloid leukemia (AML) pathogenesis and treatment are currently being better understood at an accelerated rate. Determining genetic and epigenetic changes that can identify patients who are at risk of poor outcomes is therefore desired to optimize treatment options. Many solid tumors have been reported to overexpress Inhibitors of DNA binding proteins (ID1), but few research has looked at the clinical significance of ID1 expression in AML. Additionally, little research has been focused on the direct role of ID4 in myeloid malignancies, as well as its expression and methylation patterns. The aim of the current study was to assess ID1 and ID4 gene expression in bone marrow (BM) aspiration specimens of 91 AML patients, compared with 14 control donors of bone marrow transplantation (BMT), using real-time polymerase chain reaction (RT-PCR). Data were correlated with patients’ clinicopathological features, response to treatment, disease-free survival (DFS), and overall survival (OS) rates. Results ID1 transcript level was significantly increased in AML bone marrow samples compared with normal controls (P = 0.002), while ID4 gene expression showed a nonsignificant difference (P = 0.717). In addition, there was a significant increase in ID1 gene expression in fms-like tyrosine kinase 3 (FLT3) mutant group than fms-like tyrosine kinase 3 wild group (P = 0.010). The total leukocytic count (TLC) was significantly higher in patients with high ID1 expression (P = 0.038) and patients with undetected ID4 expression (P = 0.025). No significant associations were detected between ID1 and ID4 expression levels and patients’ clinicopathological characteristics and OS rates. Conclusion In contrast to ID4, overexpressed ID1 can be adopted as a genetic biomarker for diagnosing AML. ID1 and ID4 expressions did not affect the patients’ OS or DFS. Keywords: Acute myeloid leukemia, genes expression, Inhibitors of DNA binding proteins1, Inhibitors of DNA binding proteins4, leukemia, myeloid a Clinical and Chemical Pathology, Faculty of Medicine, Benha University, Benha, bMedical Biochemistry and Molecular Biology, Cancer Biology Department, National Cancer Institute, Cairo University, c Clinical and Chemical Pathology, Faculty of Medicine, Cairo University, Cairo, Egypt Correspondence to Received: 15 August 2023 Revised Accepted: 20 August 2023 Published: Introduction Acute myeloid leukemia (AML) is the most prevalent form of leukemia in adults. It is characterized by the clonal growth of immature ‘blast cells’ in the bone marrow (BM) and peripheral circulation, which causes BM failure and inefficient erythropoiesis [1]. The cure rates have increased by up to 15% for individuals over 60 and by roughly 40% for patients under 60. However, the prognosis for the older population is still very bad [2]. The inhibitors of differentiation proteins (ID), also known as DNA-binding proteins, were discovered for the first time at 1990. ID proteins are members of the helix-loop-helix (HLH) family. They are divided into four subtypes, namely ID1, ID2, ID3, and ID4 [3]. Cell differentiation and cell linkage commitment are coordinated by ID proteins, which also tightly control the expression of cell cycle regulators. In undifferentiated, highly proliferative, embryonic, or cancer cells, ID gene expression is typically positively regulated, particularly for ID1, ID2, and ID3 [4]. ID1 is considered a tumor promotor and is overexpressed in several tumors. Overexpression of ID1 is seen in acute myeloid leukemia patients. Previous studies demonstrated that the oncogenic
tyrosine kinases, such as BCR-ABL, TEL-ABL, TEL-PDGF beta R, and FLT3-ITD, play a major role in the development of hematopoietic malignancy. ID1 was identified as a common downstream target of constitutively activated oncogenic tyrosine kinases [3]. Furthermore, loss of ID1 inhibited t (8;21) leukemia initiation and progression by abrogating AKT1 activation. Additionally, ID1 could immortalize hematopoietic progenitors in vitro, and especially common myeloid progenitors, and promote a myeloproliferative disease in vivo [5]. On the other hand, ID4 is a tumor suppressor gene since it is found to be epigenetically silenced in several