BAK, BAX and NBK/BIK Pro-apoptotic gene alterations in Iranian patients with Ataxia Telangiectasia

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Ataxia Telangiectasia (AT) is an autosomal recessive multi-system disorder, characterized by variable immunodeficiency, progressive neurodegeneration, oculocutaneous telangiectasia, and increased susceptibility to malignancies. This study was designed to study the role of pro-apoptotic BAK, BAX, NBK/BIK genes in a group of patients with AT to elucidate the possible role of these genes in progression of malignancies in this disease. Fifty Iranian patients with AT were investigated in this study. The entire coding regions of the BAK gene (exons 2-6), NBK/BIK gene (exons 2-5), and BAX gene (exons 1-7) were amplified by Polymerase Chain Reaction (PCR), and all positive samples were verified by direct sequencing of PCR products using the same primers used for PCR amplification, (BigDye chemistry and Avent 3100 Genetic Analyzer) following the manufacturer’s instructions (Applied Biosystems). Eight out of fifty Iranian AT patients (16%) exhibited a C>T transition in exon 2 (c342C>T) of the BAK gene, while none of the healthy controls had such an alteration (P=0.0001). Higher frequency of another nucleotide substitution in the BAX exon 7 (6855G>A) in non coding region was also identified in 68% of the patient group vs. 24% in the controls (P<0.0001). Sequence alteration in intronic region of the NBK/BIK gene IVS4-12delTC was observed in 52% of AT patients, which was significantly higher than 20% in the control group (P=0.0023). Frequency of IVS1146C>T alteration in the intronic regions of the BAX gene was 78% in the patients, which was significantly higher than 10% in the controls (P<0.0001). Frequency of alteration in intronic region of exon 3 of the BAX gene (IVS3+14A>G) was also significantly higher in AT patients (P<0.0001). Several alterations in the pro-apoptotic genes BAK, NBK/BIK, and BAX were found which could elucidate the involvement of the mitochondrial pathway mediated apoptosis in accelerating and developing cancers and help to understand the immunopathogenesis of AT.

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