The spectrum of ATM gene mutations in Iranian patients with ataxia-telangiectasia

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Abstract

Abstract Background: Ataxia-telangiectasia (A-T) is a rare genetic disorder characterized by a distinct range of clinical manifestations, including progressive ataxia, immunodeficiency, and radiosensitivity. Methods: Clinical data, laboratory results, and genetic data were collected from forty-three A-T patients. Whole exome sequencing and Sanger sequencing were done for the patients clinically diagnosed as suffering from A-T. Based on the phenotype severity of the disease, patients were divided into severe and mild sub-groups. Results: The median (IQR) age of diagnosis in this cohort was 5 (3-7) years and various types of clinical manifestations, including fever (p= 0.005), lower respiratory tract infection (p= 0.033), diarrhea (p= 0.014), and hepatosplenomegaly (p= 0.032) were significantly higher amongst patients diagnosed with the severe phenotype. Our results showed a strong correlation between phenotype severity and mutation type. The chance of having severe phenotype in patients who have severe mutations, including frameshift and nonsense, was 7.3 times higher compared to patients who were categorized in the mild genotype group (odds ratio= 7.3, p= 0.006). Thirty-four types of mutations including 9 novel mutations, were observed in our study. Conclusion: Molecular analysis provides the opportunity for accurate diagnosis and timely management in A-T patients with chronic progressive disease, especially infections and the risk of malignancies. This study characterizes for the first time, the broad spectrum of mutations and phenotypes in Iranian A-T patients which are required for carrier detection and reducing the burden of disease in future using the patients' families and for the public health care system. Keywords: Ataxia-telangiectasia (A-T), ATM, Whole-exome sequencing, Class switching recombination (CSR), phenotype severity.

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