THE ATXN2 GENE LOCUS IN TURKISH ALS PATIENTS AND CONTROLS

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Introduction

Amyotrophic Lateral Sclerosis (ALS) is a late-onset, rapidly progressive and devastating neurodegenerative disorder. ALS is generally associated with selective degeneration of both upper and lower motor neurons (MNs) in the brain, brainstem and spinal cord. 10% of all ALS cases are inherited and referred to as familial ALS (fALS); the remaining 90% are sporadic ALS (sALS). Although the mechanisms, causing ALS, are not well understood yet, several genes have been linked to the disease. Among these, SOD1 ,TARDBP and FUS, involved in oxidative stress and RNA-processing, respectively[1], are the most frequent causes of fALS,.

Recently, Elden et al.(2010) reported that ataxin 2 (ATXN2), which is the causative gene of Spinocerebellar Ataxia Type 2 (SCA2), influences the TDP-43-dependent toxicity seen in ALS[2]. The polyglutamin (polyQ) domain of the ATXN2 is variable in length, and the most common alleles consist of 22-23 repeats. Expansions of >34 are known to cause primarily SCA2, while intermediate variations of polyQ tract-lengths in ATXN2 are recently shown to be linked to Parkinsonism, ALS and FTLD (Figure 1)[3]. There are several new studies claiming that Intermediate-length polyQ (27-33 Q) expansions in the ATXN2 gene increase the risk of ALS in 3-4% of European, French-Canadian and Chinese patients [2,4,5].

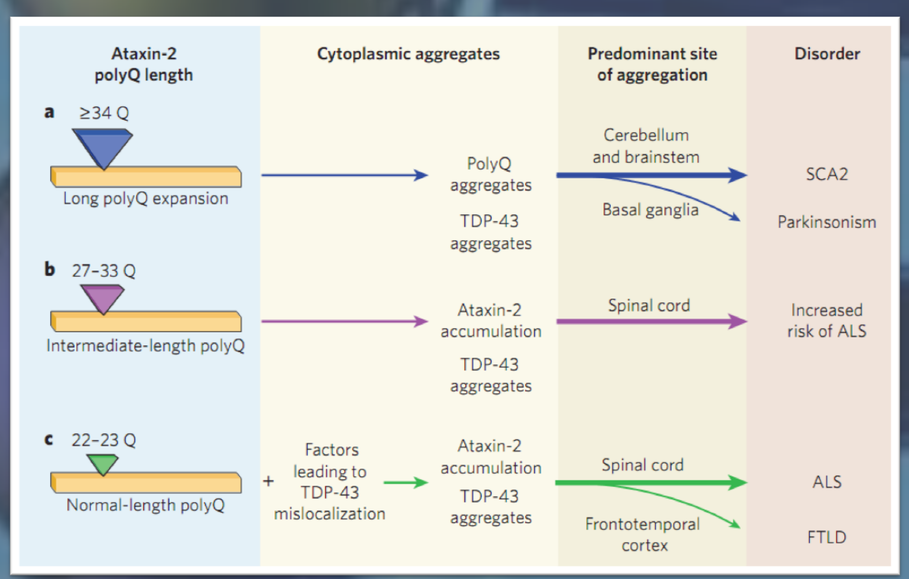

Figure 1. ATXN2 PolyQ expansion spectrum associated with different diseases.

Aim of the Study

This study aims to test the possible influence of the ATXN2 gene on the risk of developing ALS in Turkish ALS patients by comparing 115 sALS patients to 100 healthy controls.

Materials and Methods

The ATXN2 polyQ region was amplified by PCR using 5'-6-FAM labelled primers. Repeat numbers were determined by GeneScan analysis.

Results

PolyQ alleles observed in the individuals genotyped, varied between15 to 32 in Turkish sALS patients and 19 to 24 in controls. 22 repeats account for approximately 90% of cases and controls (Figure2). Among 115 cases, 3 (corresponding to 2.6%) showed intermediate-length polyQ expansions (27-32 Q), whereas none of the healthy controls had polyQ repeats ≥24 (Figure 3).

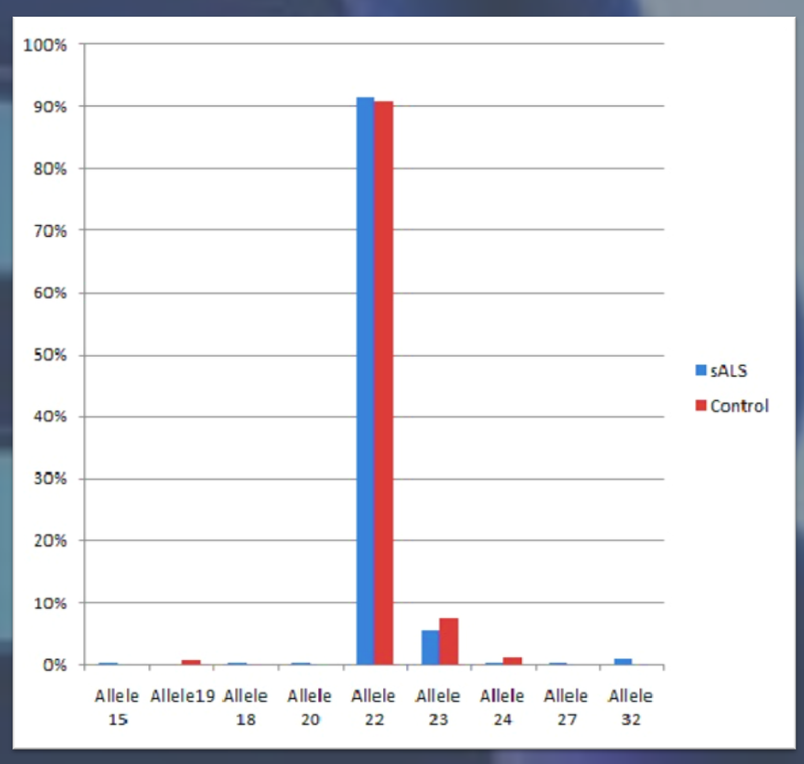

Figure 2. Distribution of ATXN2 polyQ repeat-lengths.

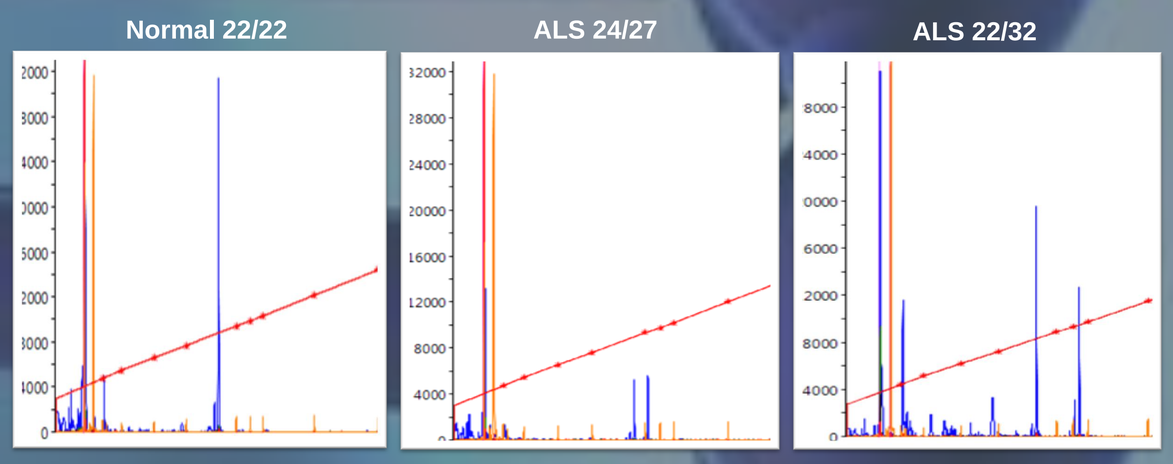

Figure 3. Representative examples of GeneScan analysis.

Discussion

This study reveals that 2.6% of Turkish sALS patients have an intermediate-length polyQ tract, correlating well with the literature (3-4%). However, the significance of the results should be further questioned by increasing the sample size. In the next step, the effect of ATXN2 expansion in fALS patients will be investigated.

References
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