

# Two Siblings and Three Cousins with Allgrove (4A Syndrome) Syndrome in a Turkish Family: A Novel Mutation in the 'Aladin' Gene



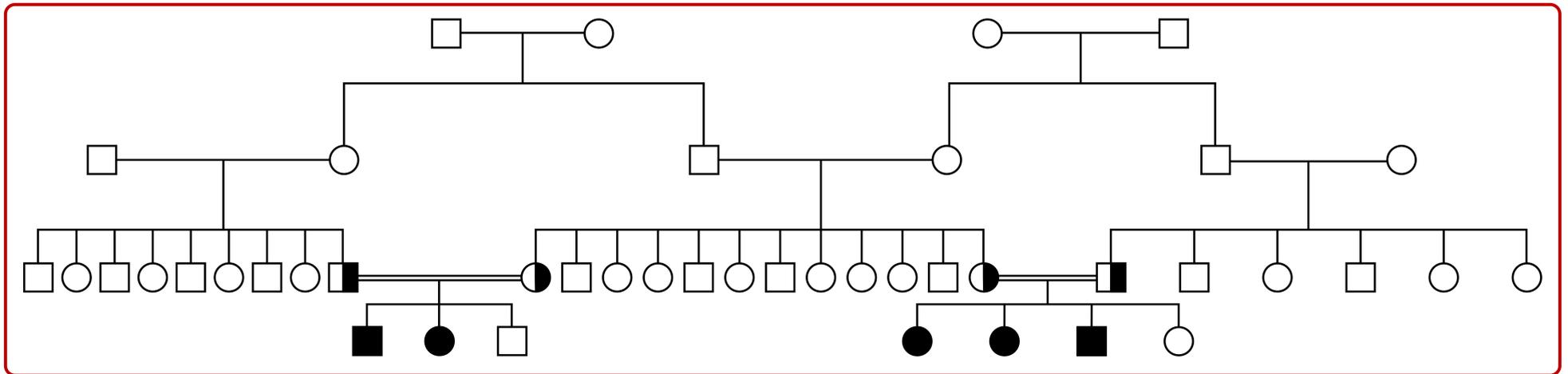
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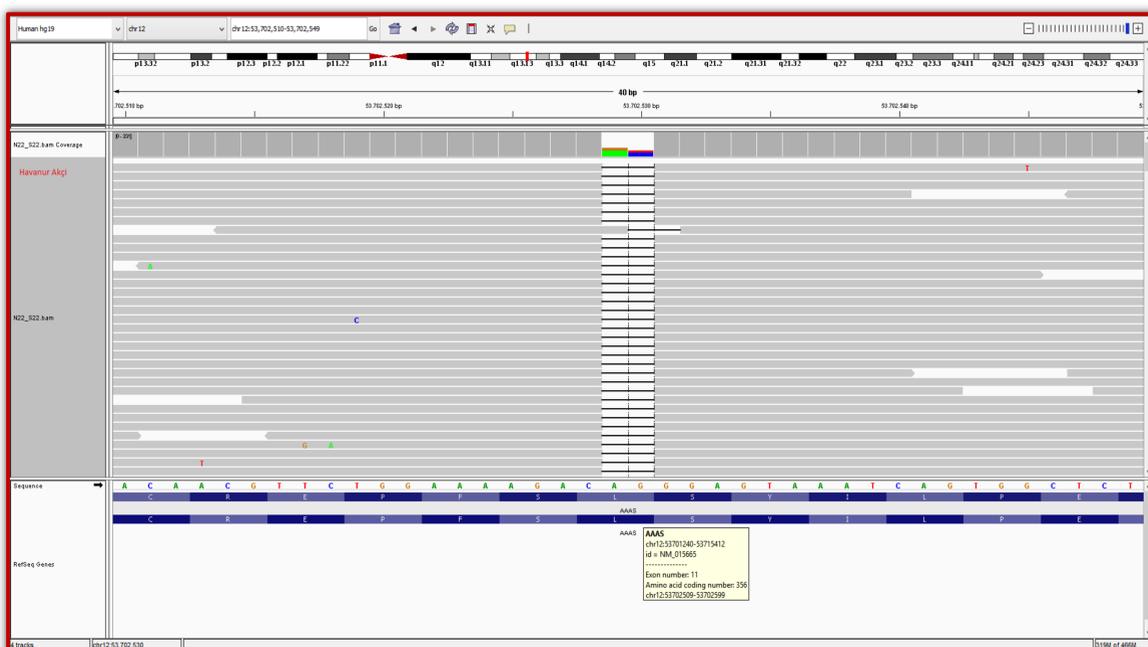
Allgrove's or '4A syndrome' is a rare autosomal recessive multisystem disorder characterised by adrenocorticotropin hormone resistant adrenal insufficiency, alacrima, achalasia and neurological abnormalities. The disease - causing gene (AAAS) encodes a protein of 546 amino acids called 'aladin' (for alacrima-achalasia-adrenal insufficiency-neurologic disorder). We report two siblings and three cousins suffering from Allgrove syndrome in a Turkish family. In this family, a novel homozygous mutation (p.L356Vfs\*8, c.1066\_1067delCT) in exon 11 in the AAAS gene was identified in all affected family members.

## Case Report

A 13-year-old female was admitted to our department with the complaint of fatigue and hyperpigmentation. According to the family history, she has been followed with adrenal insufficiency from 8 months old, then after 3 years of the first diagnosis she was presented with achalasia, alacrima and psychomotor developmental delay. Laboratory examinations were as follows: Serum ACTH >1200 pg/ml, basal cortisol <1 µg/dl, and she has been followed with the diagnosis of triple A syndrome since three years of age. The family history has revealed that her brother (7 years 4 months old age) has been followed with adrenal insufficiency, alacrima, achalasia and developmental delay for 3 years. Their cousins, 7 and 12 years old female and 15 years old male, they have also been followed with the same physical and laboratory findings since 5 years of age (Figure 1). Genetic analysis showed a novel homozygous mutation (p.L356Vfs\*8 (c.1066\_1067delCT) in exon 11 in the AAAS gene in both siblings and their cousins (Figure 2). This mutation was not reported before. Both parents were heterozygous for this mutation.



**Figure 1.** Family pedigree



**Figure 2.** AAAS gene: Next-generation sequencing

## References

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