

## Screening of *AIP* Gene Mutations in Young Sporadic Pituitary Adenoma Patients

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### Abstract

**Introduction:** "Aryl hydrocarbon receptor-interacting protein (*AIP*)" gene mutations have been associated with sporadic pituitary adenomas (PAs) in different populations with a prevalence range of 3.6-11.7%. Among mutation carriers, male patients were more frequent and young patients ( $\leq 30$  years) with treatment resistant have been shown to exhibit *AIP* mutations. *AIP* mutation prevalence was detected 1% in sporadic acromegaly patients from Anatolian part of Turkey, by another group. The aim of our study was to form a broader cohort composed of acromegaly, prolactinoma and Cushing patients from different parts of Turkey and screen *AIP* gene mutations in this group.

**Material and Methods:** A total of 97 patients (55 somatotrophinoma, 25 prolactinoma, 17 corticotrophinoma), who were followed-up at our pituitary out-patient clinic and were diagnosed before 40 years old have been recruited. Previously, 56 of these patients' *AIP* genetic screen have been reported. DNA was isolated from peripheral blood of the patients and Sanger sequencing of *AIP* gene's coding and flanking regions were performed for point mutation screening, where mutation negative patients were subjected to MLPA method to detect copy number variations.

**Results:** The previous screen on 56 of our patients did not carry point mutations and MLPA method did not reveal copy number variations in these patients, too. However two of the additional 41 patients revealed to carry *AIP* c.911G>A p.Arg304Gln (rs104894190) clinical variant. One of the patients was diagnosed with acromegaly (1/55; %1.8), where the other was with prolactinoma (1/25; %4). Differing treatment models (2 operations, radiotherapy, SSA, SSA+DA) was performed on the acromegaly patient. Prolactinoma patient underwent surgery due to DA intolerance (heavy symptomatic hypotension), post-operative hypopituitarism has been developed, but tumor did not relapse. None of the patients exhibited copy number variations.

**Conclusion:** We detected a lower *AIP* gene mutation prevalence (%2.1; 2/97) has been detected among the cohort of young sporadic pituitary adenoma with hyperfunction patients in a cosmopolitan city. However, it should be kept in mind that mutation carriers could be "apparently sporadic", thus family history should be questioned with care.

**Keywords:** Sporadic pituitary adenoma, *AIP* gene, Arg304Gln clinical variant