ARMC5 Gene Mutation in a Patient with Bilateral Macronodular Adrenal Hyperplasia: A Case Report

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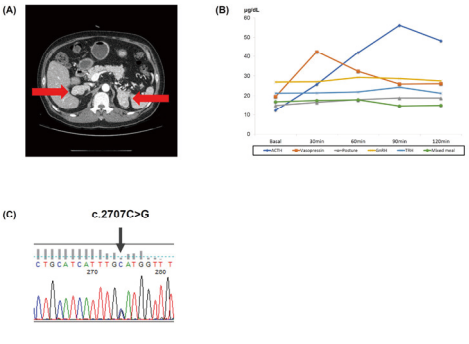
Background: Bilateral macronodular adrenal hyperplasia accounts for <1% of the causes of Cushing's syndrome. BMAH is a disease causing excessive secretion of cortisol independent of adrenocorticotropic hormone. BMAH is a heterogeneous disease whose expression varies from subclinical cortisol secretion to overt Cushing's syndrome. It is characterized by bilateral enlargement of the adrenal glands, with an adrenocortical nodule larger than 10mm. BMAH is more frequently genetically determined. About 50% of familial cases of BMAH are associated with mutations in ARMC5, a tumor suppressor gene. ARMC5 mutant patients present with more severity not only in the size of the adrenal gland but in the prevalence of clinical Cushing's syndrome and hypertension with higher secretion of cortisol than wild-type patients. Although there is a connection between BMAH and ARMC5 mutations, the resulting phenotypes vary as to the nature of the mutations. In the present work, we have studied a case of a patient with BMAH with an ARMC5 mutation, whose daughters do not yet have overt Cushing's syndrome but do have the ARMC5 mutation. **Case Presentation:** A 54-year-old man with an underlying disease of liver cirrhosis presented with generalized edema. Serum cortisol and urine free cortisol levels were significantly increased, while his plasma adrenocorticotropic hormone was normal. Aberrant cortisol response tests stimulated by ACTH, mixed meal, gonadotropin-releasing hormone, vasopressin and upright position was performed. Adrenal CT scan revealed bilateral adrenal masses. The patient underwent a right adrenalectomy and histopathology substantiated the BMAH diagnosis. In this case of BMAH, the sequencing results identified a novel heterozygous germline ARMC5 mutation.(c.2707C→G, p.H903D) in the patient and all his daughters. **Conclusion:** A novel germline ARMC5 mutation(c.2707C→G, p.H903D) was identified. The search for ARMC5 will allow familial screening through a blood test and select who should undergo further evaluations. Further family studies will be useful to clarify the clinical penetrance of ARMC5 mutations. It can lead to prevention of the occurrence of the disease.



Variable	Value
Basal	
ACTH (pg/mL)	1.0
Cortisol (μg/dL)	19.1
Urine free cortisol (μg/day)	537.1
Low dose dexamethasone suppression test	
ACTH (pg/mL)	1.0
Cortisol (μg/dL)	20.1
Urine free cortisol (μg/day)	302.9
High dose dexamethasone suppression test	
ACTH (pg/mL)	1.3
Cortisol (μg/dL)	12.1
Urine free cortisol (μg/day)	524.8