ACTH RESISTANCE SYNDROME: A CASE REPORT AND REVIEW OF THE LITERATURE

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ABSTRACT
ACTH resistance syndrome is a very rare disease group with autosomal recessive inheritance. It is seen as familial glucocorticoid deficiency (FGD) and triple A syndrome. The disease is presented with adrenal insufficiency signs. In this paper, we report a 38-year-old female patient in whom ACTH resistance is detected. The disease is genetically inherited being seen in the young age. We suggested acquired ACTH syndrome due to our patient's being in advanced age and absence of family history. We aimed to remember this rare condition.

KEYWORDS: ACTH resistance, adrenal insufficiency, acquired

INTRODUCTION
ACTH resistance syndrome is a genetically heterogeneous disease group. It is rare and seen as familial glucocorticoid deficiency (FGD) and triple A syndrome. These diseases are characterized by ACTH resistance and inherited autosomal recessively.⁵ FGD is associated with the mutations in the gene which encodes ACTH receptor or melanocortin-2 receptor helper protein, triple A syndrome (AAAS, Allgrove syndrome) is associated with the mutation in AAAS gene.⁶

Patients are usually presented with hyper-pigmentation, hypoglycemia, nausea, hypotension, abdominal pain, diarrhea in the young age. In this paper, we presented a 38-year-old patient detected to have ACTH resistance syndrome. We aimed to remember this rare condition.

Case
A 38-year-old female patient was admitted to Endocrinology Outpatient Clinic with complaints of fatigue, dizziness, hypotension, fasting intolerance, hyper-pigmentation. In her medical history, she was learned not to recover from anesthesia for 3 hours after caesarean section operation. On her physical examination, blood pressure was 90/60 mmHg, heart rate was 80 bpm. She had widespread hyper-pigmentation, erythematous plaques measuring 3x5 cm in both axillae and elbows (Image 1,2). Laboratory findings were as follows: WBC 11x10⁹ (4.5-11x10⁹) /l, hemoglobin 14.7 (12-16) g/dl, ESR 50 (0-20) mm/ hour, glucose 84 (60-100) mg/dl, sodium 139 (135-145) mEq/l, potassium 4.4 (4-5.5) mEq/l, ACTH 91 (7.2 – 63.3) pg/ml, cortisol 5.4 (5-25) μg/dl, aldosterone 7.8 (1.0-21) ng/dl, plasma renin activity 6.7 (0.20-3.40) ng/ml/s, TSH 5.3 μIU/ml, fT4 1.01. Both surrenal glands were found normal on surrenal tomography. ACTH stimulation test was performed (Table 1). Not detecting an increase in cortisol, testosterone, DHEA-S, 1.4-delta andostenedion, aldosterone and 17-OH-progesterone in ACTH stimulation test indicates that the patient whose basal cortisol is 5- 8 μg/dl has ACTH resistance. Triple A syndrome was not considered. ACTH resistance has been detected, however, achalasia, alacrism was not detected. Family history of ACTH resistance syndrome was not detected. The patient was diagnosed with acquired mutation-related ACTH resistance syndrome under the light of these data. Prednisolone 5 mg daily was started. Clinical signs of the patient improved, hyper-pigmentation was seen to improve (Image 3).

DISCUSSION
Familial glucocorticoid deficiency, resistance is an autosomal recessive disorder. Laboratory findings include cortisol deficiency, elevated ACTH level. Clinical signs include hyper-pigmentation, nausea, vomiting, hypoglycemia.⁷ Our patient was presented...
with hyper-pigmentation, nausea, fatigue, hypoglycemia and hypotension. Family history was not detected. ACTH was high, cortisol was at lower limit. Cortisol response was not obtained after 250 mcg ACTH stimulation test. ACTH resistance syndrome should be considered in patients who are clinically suggested to have adrenal insufficiency although basal cortisol levels are within normal ranges. Cortisol replacement particularly at stress gains vital importance. We considered the case as a sporadic case due to the absence of family history.

The disease usually appears with failure to thrive, developmental retardation, and susceptibility to infections in newborn or early infancy period (4). The disease was detected when the patient was 38 years old in our patient. She was learned not to have failure to thrive, developmental retardation, and susceptibility to infections. Hyper-pigmentation was not seen in her earlier photos (Image 4). We suggested acquired ACTH resistance syndrome due to absence of family history, her childhood development's being normal.

This disorder may be confused with primary adrenal insufficiency and Allgrove syndrome. While mineralocorticoid synthesis is impaired in primary adrenal insufficiency, it is preserved in familial glucocorticoid insufficiency. All grove syndromes are defined as ACTH resistance syndrome. AAAS/ALADIN gene was defined to be responsible for this syndrome. The disorder is clinically presented with alacrima, achalasia and adrenal insufficiency. Two of three main findings are detected in 100% of the cases. Mineralo-corticoid production is preserved in 15% of the cases. Alacrima, achalasia was not detected in our case.

MC2R, TXNRD2, NNT, MRAP, MCM4, STAR were detected to be responsible for familial glucocorticoid insufficiency syndrome. Alacrima, achalasia was not detected in our case. Cortisol, aldosterone, total testosterone, DHEA-SO4, 17-OH-progesterone response was not obtained against 250 mcg ACTH stimulation test. Mineralo-corticoid production was found normal. Acquired causes of adrenal insufficiency was excluded through medical history and laboratory tests for adrenal hemorrhage, infection, infiltration and trauma. Congenital adrenal hyperplasia was excluded with the absence of an increase in 17-OH progesterone against ACTH stimulation test. Our patient was considered to have ACTH resistance under the light of these data.

**CONCLUSION**

In conclusion, this type of adrenal insufficiency is characterized by isolated glucocorticoid deficiency, normal aldosterone production, increased ACTH level. Early diagnosis, proper treatment are of vital importance particularly under stress conditions. ACTH resistance syndrome may be acquired without family history.

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**Table 1: Results of 250 mcg ACTH stimulation test**

Image 1. Hyper-pigmented erythematous plaques in both axillae
Image 2. Widespread hyperpigmentation on the body surface

Image 3. Hyper-pigmentation is seen to regress with treatment

Image 4. The patient was seen not to have hyperpigmentation when she was younger

REFERENCES


